

NEW RESEARCH

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ABSTRACTS

AMERICAN PSYCHIATRIC ASSOCIATION
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PSYCHOSOMATIC MEDICINE
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158TH ANNUAL MEETING
ATLANTA, GEORGIA, MAY 21-26, 2005
AMERICAN PSYCHIATRIC
ASSOCIATION

ABSTRACTS

ATLANTA, GA ♦ MAY 21-26, 2005

NR1 Monday, May 23, 9:00 a.m.-10:30 a.m.

Anemia in Opioid Abusers: Prevalence and Ethnic Differences

Supported by National Institute on Drug Abuse

Shaun E. Smith, B.S., *Department of Psychiatry, Jefferson Medical, 261 South 9th Street, Philadelphia, PA 19107*; Allen Zeiger, Ph.D., Phillip Matthews, M.S., Ashwin A. Patkar, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize rates of anemia among opioid abusers and understand the role of ethnicity.

Summary:

Objective: The objectives were to determine the prevalence of anemia among opiate abusers and to examine the relationship of anemia with ethnic differences.

Method: Complete blood counts of 300 patients attending a university-affiliated methadone program were recorded by chart review. Those with incomplete records, or infected with HIV were excluded. Red blood cell count, hemoglobin, hematocrit, white blood cell values, bilirubin levels, and platelet counts, as well as demographic information on remaining 241 subjects were analyzed.

Results: All lab values for opiate abusers were near the low end of reported ranges. Using the stringent WHO criteria for anemia (<13.0 g Hgb/dl for males and <12.0 g Hgb/dl for females), we found that 26.1% of all opioid abusers were anemic. The prevalence of anemia was significantly higher among African Americans (43.7%) than Caucasians (16.2%) ($p < .001$). There were no gender differences. The pattern of anemia did not appear to be due to hemorrhage, hemolysis, folate, or iron deficiency.

Conclusions: Whether the higher rates of anemia among African-American compared with Caucasian opioid abusers reflect similar ethnic differences in the healthy population merit further investigation. The high prevalence of anemia observed among opioid users may pose a major public health problem, especially in view of the association of drug use with exposure to HIV.

Supported by NIDA grant # R21 DA15504-01

References:

1. Zeiger AR, Patkar AA, Fitzgerald R, Lundy AC, Ballas SK, Weinstein SP: Changes in mu opioid receptors and rheological properties of erythrocytes among opioid abusers. *Addiction Biol* 2002; 7:207-217.
2. Van der Werf MJ, Van Benthem BHB, Van Ameijden EJC: Prevalence, incidence, and risk factors of anaemia in HIV-positive and HIV-negative drug users. *Addiction* 2000; 95:383-392.

NR2 Monday, May 23, 9:00 a.m.-10:30 a.m.

Prevalence of Violence by and Against Puerto Rican Women With Mood Disorders

Sana Loue, Ph.D., *Department of Epidemiology/Biostatistics, Case Western Reserve University, School of Medicine, 10900 Euclid Avenue, Cleveland, OH 44106-4945*; Susan J. Hatters-Friedman, M.D., Martha Sajatovic, M.D., Nancy Mendez

Educational Objectives:

At the conclusion of this session, the participant should be able to identify factors related to the commission of violent acts by and against Puerto Rican women diagnosed with major depression or bipolar disorder, and identify implications of differential rates of violence among women with bipolar disorder and major depression.

Summary:

Background: Few studies have compared the prevalence of victimization across diagnostic categories. We report preliminary findings relating to victimization of and by a sample of Puerto Rican women diagnosed with major depression (MD) and bipolar disorder (BD).

Methods: We recruited 14 BD women and 19 MD women from community programs and clinics. Diagnosis was confirmed using the SCID. Participants were interviewed and also shadowed by interviewers for periods of time ranging from three to 18 months in order to verify reported behavior.

Results: Women with both mood disorders had histories of abuse by children, sexual partners, and other family members. Compared with BD women, MD women were more frequently the victims of sexual abuse ($p < .05$). Compared with BD women, a lesser proportion of MD women reported having inflicted violence on children, partners, and other individuals both in the past (MD, 52.6% vs. BD, 85.7%) and currently (MD, 26.3% vs. BD, 71.4%).

Conclusions: Women with both types of severe mood disorder had high levels of abuse histories. However, violence by these women toward others was also frequent. This has implications for the prevention of family violence and for psychiatrists addressing issues related to future probability of violence.

References:

1. Darves-Bornoz JM, Lempérière T, Degiovanni A, Gaillard P: Sexual victimization in women with schizophrenia and bipolar disorder. *Social Psychiatry and Psychiatric Epidemiology* 1995; 30, 78-84.
2. Hien D, Buzsapan C: Interpersonal violence in a 'normal' low-income control group. *Women and Health* 1999; 29(4):1-16.

NR3 Monday, May 23, 9:00 a.m.-10:30 a.m.

Predictors of Mental Health and Health-Related Quality of Life in Tortured Refugees

Jessica M. Carlsson, M.D., *Department of Research, RCT, Borgergade 13 Postboks 2107, Copenhagen 1014, Denmark*; Erik L. Mortensen, Ph.D., Marianne C. Kastrup, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize frequent mental health problems in tortured refugees and pre- and post-migratory factors associated with mental health problems.

Summary:

Objective: Frequently-reported mental health problems in traumatized refugees are depression, anxiety, and post traumatic stress disorder (PTSD). The aim of this study is to investigate the importance of past trauma and post-migratory factors for mental health, and for health-related quality of life in two samples of tortured refugees.

Methods: The two samples studied included 63 male tortured refugees admitted to a pre-treatment assessment at the Rehabilitation and Research Centre for Torture Victims in 2001-2002, and 139 tortured refugees admitted to a pre-treatment assessment in 1991-1994, and re-interviewed in 2002-2003. Data on personal background, trauma, present social situation, symptoms of depression, anxiety (the Hopkins Symptom Checklist-25, HSCL-25), and PTSD (the Harvard Trauma Questionnaire), and on health-related quality of life (the WHO Quality of life-Bref) were collected.

Results: Similar predictors were identified in the two samples. Previous trauma, weak social relations, no present occupation, and pain were identified as predictors of emotional distress. Social relations was a significant predictor of health-related quality of life.

Discussion/conclusion: As found in other studies on severely traumatized refugees, long-lasting high levels of emotional dis-

tress were observed. Post-migratory factors such as social relations and occupation are of special interest when planning health-related and social interventions.

This study was supported by Aase og Ejnar Danielsens Fond, Elly Valborg og Niels Mikkelsens Fond, FLS Industries Gavefond, Henrik Henriksens Fond, Illum Fondet, Læge Sofus Emil Friis.

References:

1. Gurr R, Quiroga J: Desk study on approaches to torture rehabilitation: a desk study covering effects, cost effectiveness, participation and sustainability. *Torture Quarterly Journal on Rehabilitation of Torture Victims and Prevention of Torture* 2001; Suppl. 1.
2. Hermansson A-C, Timpka T, Thyberg M: The mental health of war-wounded refugees: an 8-year follow-up. *The Journal of Nervous and Mental Disease* 2002; 190(6):374-380.

NR4 Monday, May 23, 9:00 a.m.-10:30 a.m.

Association of Alzheimer's Disease Risk and UBQLN1

Michael Slifer, M.D., *Department of Genetics, Duke University, 2502 Francis Street, Durham, NC 27707*; Margaret Pericek-Vance, Ph.D.

Educational Objectives:

At the conclusion of this session, participant should be able to recognize some of the genetic diatheses underlying Alzheimer's dementia.

Summary:

Hypothesis: The purpose of this study is to examine the relationship of risk of late-onset Alzheimer's dementia and the gene UBQLN1 on Chromosome 9q.

Method: Our analysis set includes a family data sample (n=1119) and an independent case-control sample (n=1775) from the Collaborative Alzheimer's Disease Project. Seven single nucleotide polymorphisms (SNPs) within the UBQLN1 gene were studied for association with AD risk. Statistical analyses included tests of linkage disequilibrium, family-based analyses of association and age of onset, case-control analyses of association and age of onset. All tests were conducted in the overall sample and conditional on APOE genotype.

Discussion: In this study, we examine the effect of polymorphisms within the UBQLN1 gene on development of late-onset AD. We present corroborative evidence of an effect of the UBQLN1 gene on late-onset AD risk in a data set independent from the one previously reported (Tanzi et al. unpublished data). Additionally, we present the first evidence of an association of the UBQLN1 gene with age of onset within the late-onset AD subtype. These results contribute to the growing body of knowledge identifying genetic risks for the development of Alzheimer's dementia.

References:

1. McKhann G, Drachman G, Folstein M: Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of the department of health and human services task force on Alzheimer's disease. *Neurology* 1984; 34:939-944.
2. Pericak-Vance MA, Yee IML, Haynes CS, et al: Genetic linkage studies in Alzheimer's disease families. *Experimental Neurology* 1988; 102:271-279.

NR5 Monday, May 23, 9:00 a.m.-10:30 a.m.

Education and Regional Glucose Metabolism During a Continuous Performance Task

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NY 10003; John A. Matochik, Ph.D., Lisa J. Cohen, Ph.D., Edythe London, Ph.D., Igor I. Galynker, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize an association between education and regional brain metabolism and to appreciate the importance of research exploring mechanisms of possible education-associated cognitive protective effects in brain disease.

Summary:

Background: Despite research suggesting that education may protect cognition in the face of neural injury, little is known about the influence of higher education on regional brain processing. This study compared cerebral metabolic activity in subjects with varying levels of undergraduate and graduate education.

Methods: Fourteen healthy adults with educational backgrounds ranging from 12 to 18 years of school underwent positron emission tomography scanning with 18F-fluorodeoxyglucose while performing an auditory continuous discrimination task.

Results: Years of education correlated positively with glucose metabolism at the left lingual gyrus (p=0.024, 84 voxels, z-score=2.97), right lingual gyrus (p=0.002, 213 voxels, z-score=3.49), left posterior cingulate (p=0.025, 69 voxels, z-score=3.29), and left precuneus (p=0.015, 112 voxels, z-score=3.53). A positive correlation that approached statistical significance existed at the right precuneus (p=0.056, 57 voxels, z-score=3.59).

Conclusions: Individuals with more educational experience are able to enact greater metabolic activity in medial posterior cortical regions previously shown to be areas of early impairment in dementia. Further investigation is required to explore whether modulation of processing pathways in the precuneus, lingual gyrus and posterior cingulate may contribute to the possible protective effect of higher education on cognition.

References:

1. Dufouil C, Alperovitch A, Tzourio C: Influence of education on the relationship between white matter lesions and cognition. *Neurology* 2003; 60:831-6.
2. Kesler SR, Adams HF, Blasey CM, Bigler ED: Premorbid intellectual functioning, education, and brain size in traumatic brain injury: an investigation of the cognitive reserve hypothesis. *Appl Neuropsychol* 2003; 10:153-62.

NR6 Monday, May 23, 9:00 a.m.-10:30 a.m.

Mental Health Service Use Among Adolescents Aged 15-18 With Depression

Amy H. Cheung, M.D., *Department of Psychiatry, University of Toronto, 33 Russel Street, 3rd Floor Tower, Toronto, ON M5S 2S1, Canada*; Carolyn S. Dewa, Ph.D., Anthony J. Levitt, M.D.

Educational Objectives:

At the conclusion of this session, the participant should learn about the gender differences in service use of adolescents with depression.

Summary:

Objective: This study examined the 12-month service use rates in youth aged 15-18 who met diagnostic criteria for major depression as part of a Canada wide community survey.

Method: Data from the Canadian Community Health Survey Cycle 1.2 (CCHS) were used to examine the 12-month service use rate of youth who met criteria for major depression in the 12 months preceding the interview. The sample size for subjects aged 15-18 was 2,886 and service use rates were calculated over the 12 months prior to interview. Odds ratios were calculated to examine possible gender differences.

Results: Fifty-five percent of adolescents with depression (95%CI 40.7-71.1) reported mental health service use in the previous 12 months. Females with depression were significantly more likely to see social workers as compared with males (male = 10.8%, female = 39.9%, OR = 0.18, 95% CI 0.18-0.19). As compared with females, males were significantly more likely to see psychiatrists (male = 45.5%, female = 21.4%, OR = 4.39, 95% CI 4.26-4.52) and psychologists (male = 25.2%, female = 16.7%, OR = 1.67, 95% CI 1.62-1.73).

Conclusions: A significant portion of adolescents who met diagnosis for depression in the past 12 months was not receiving mental health services. There were also gender differences in the type of providers that were seen. Issues that impact this pattern of utilization include identification of those at risk, and access to, and availability of, services.

Funding: Ministry of Health, Ontario and the Ontario Mental Health Research Foundation.

References:

1. Wu P, Hoven CW, Cohen P, et al: Factors associated with use of mental health services for depression by children and adolescents. *Psychiatr Serv* 2001; 52:189-95.
2. Rushton JL, Forcier M, Schectman RM: Epidemiology of depressive symptoms in the National Longitudinal Study of Adolescent Health. *J Am Acad Child Adolesc Psychiatry* 2002; 41:199-205.

NR7 Monday, May 23, 9:00 a.m.-10:30 a.m. **Guidelines for Adolescent Depression in Primary Care**

Amy H. Cheung, M.D., *Department of Psychiatry, University of Toronto, 33 Russel Street, 3rd Floor Tower, Toronto, ON M5S 2S1, Canada*; Rachel A. Zuckerbrot, M.D., Peter S. Jensen, M.D.

Educational Objectives:

At the conclusion of this session, the participant should learn about the management of adolescent depression in the primary care setting.

Summary:

Objectives: With the shortage of mental health providers and frequent misinformation in the media about treatments for depression, there is an increasing need for the development of guidelines to assist primary care providers in the management of adolescent depression. This clinical practice guideline provides evidence- and consensus-based recommendations for the management of adolescent depression in primary care.

Method: Using a combination of evidence- and consensus-based methodologies, guidelines were developed in six phases as informed by three information sources: current scientific evidence (published and unpublished); focus groups with professionals, adolescents with depression, and their parents; and consensus of 80 clinical and research experts derived from a formal survey and a consensus workshop.

Results: Recommendations were developed corresponding to phases of management. Specific recommendations include surveillance of high risk youth; systematic assessment procedures (i.e., reliable depression scales), patient/family psychoeducation, active monitoring of mild depression, application of evidence-based medication and psychotherapeutic approaches in moderate/severe depression, monitoring of side effects, consultation/coordination of care with mental health specialists, tracking of outcomes, and steps taken in instances of partial or no improvement after initial treatment.

Conclusions: This guideline offers substantial new opportunities to assist primary care clinicians in managing depressed youth.

Further research must address the many current gaps in scientific information for managing youth depression in primary care.

Funding: Center for Substance Abuse Treatment, SAMHSA; Josiah Macy, Jr. Foundation; New York State Office of Mental Health; Lowenstein Foundation; Centre for the Advancement of Children's Mental Health, Columbia University; Sunnybrook and Women's College Health Sciences Centre, University of Toronto; American Academy of Pediatrics New York Chapter 3, District II; New York Council on Child and Adolescent Psychiatry; Children's Health Forum, NY Academy of Medicine; Kellogg Foundation; Civic Research Institute, Inc.

References:

1. Rushton JL, Forcier M, Schectman RM: Epidemiology of depressive symptoms in the National Longitudinal Study of Adolescent Health. *J Am Acad Child Adolesc Psychiatry* 2002; 41:199-205.
2. Pappadopulos E, Macintyre II JC, Crismon ML, et al: Treatment recommendations for the use of antipsychotics for aggressive youth (TRAAAY) Part II. *J Am Acad Child Adolesc Psychiatry* 2003; 42:145-61.

NR8 Monday, May 23, 9:00 a.m.-10:30 a.m. **Comparison of Outpatients With Depression Who Do or Do Not Report a Suicide Attempt**

Ghazala Fayyaz, M.D., *Department of Psychiatry, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160*; Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.A., Ekkehard Othmer, M.D., Barbara J. Powell, Ph.D., Marsha R. Read, Ph.D., William F. Gabrielli, Jr., M.D.

Educational Objectives:

At the conclusion of this session, the participant should learn how psychiatric outpatients who report a previous suicide attempt differ clinically from those who do not.

Summary:

Objective: To contrast the sociodemographic and clinical characteristics of depressed psychiatric outpatients who do or do not report a previous suicide attempt when they first present for treatment.

Method: Most new admissions to a large psychiatric outpatient clinic over a five-year period (N=1458) received a clinical examination, the structured Psychiatric Diagnostic Interview, a psychosocial interview and the Symptom Checklist 90-R. Approximately two-thirds satisfied DSM-III criteria for major depression at some point in their lives (N=1002). Of these new admissions with Major Depression, 723 (72%) denied making a previous suicide attempt, while 279 (28%) reported a previous suicide attempt.

Results: These two groups did not differ according to gender or race. Patients reporting a previous suicide attempt were significantly younger when first seen, less likely to have married, and more likely to be unemployed. Patients who reported a previous suicide attempt, compared with those who did not, indicated higher rates of psychiatric comorbidity among themselves, more lifetime depressive symptoms, greater childhood unhappiness, and more treatment received at an earlier age. Significantly more patients who attempted suicide reported a family history of alcoholism, drug abuse, and antisocial personality disorder, but not a family history of attempted or completed suicide.

Conclusions: Depressed patients who come into outpatient treatment with a prior history of attempted suicide are likely to require more pharmacological and psychosocial assistance, for longer periods of time, than patients with no prior suicide attempt.

References:

1. Moller HJ: Suicide, suicidality and suicide prevention in affective disorders. *Acta Psychiatr Scand* 2003; 418:73-80.

2. Oquendo MA, Galfalvy H, Russo S, Ellis SP, Grunebaum MF, Burke A, Mann JJ: Prospective study of clinical predictors of suicidal acts after a major depressive episode in patients with major depressive or bipolar disorder. *Am J Psychiatry*, 2004; 161:1433-1441.

NR9 Monday, May 23, 9:00 a.m.-10:30 a.m.

The Swedish Study of Metabolic Risks in Psychosis Supported by LAKSAK (Stockholm County Council Medication Authority)

Anna Lothman, M.D., *Department of Clinical Neuroscience, Karolinska Institutet, Psykiatri Centrum Vast Byggnad, Bromma 161 04, Sweden*; Helena Ring, M.D., Signy Reynisdottir, M.D., Soren Akselson, M.D., Claes-Goran Ostensson, M.D., Martin Schalling, M.D., Urban P. Osby, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the importance of preventing increased metabolic risks to improve outcome for patients with long-term psychosis.

Summary:

Objective: This is a prospective study of metabolic risks for patients with long-term psychosis, including schizophrenia, related to antipsychotic medication, lifestyle factors, and risk genes for psychosis and metabolic disorders.

Method: Information on diagnosis, level of functioning (GAF and CGI), duration of illness, duration of treatment, and present and previous antipsychotic medication will be recorded for 1,000 patients from specialized outpatient psychosis units. CHD, diabetes, and hypertension among patients and first-degree relatives will be assessed, as well as smoking habits and alcohol intake. Blood pressure, weight, height, and waist circumference will be measured, as well as Hb, ASAT, GT, creatinin, blood glucose, TSH, Chol, TG, LDL-cholesterol, and HDL-cholesterol. Blood samples for DNA preparation will be taken. Patients will be assessed prospectively for four years. Drug-naïve patients will be assessed before and after the start of medication. Recruitment of patients has started.

Results: Large population-based studies of metabolic risk factors in psychosis are necessary to determine the degree of metabolic risks and to what extent drug treatment, lifestyle factors or shared genetic risks contribute.

Conclusion: The prospective design will enable prevention of metabolic risks. The findings of the study will form the basis for intervention and preventive programs.

References:

1. Ösby U, Correia N, Brandt L, Ekblom A, Sparén P: Excess mortality in schizophrenia in Stockholm County, Sweden. *Schizophrenia Research* 2000; 45:21-28.
2. Cohn T, Prud'homme D, Streiner D, Kameh H, Remington G: Characterizing coronary heart disease risk in chronic schizophrenia: high prevalence of the metabolic syndrome. *Canadian Journal of Psychiatry* 2004; 49:753-760.

NR10 Monday, May 23, 9:00 a.m.-10:30 a.m.

EEG Guidance of Psychopharmacologic Treatment: Multi-Site Experience

Mark J. Schiller, M.D., *Department of Psychiatry, San Francisco General Hospital, 7M-6, San Francisco, CA 94110*; Stephen Suffin, M.D., W. Hamlin Emory, M.D., James T. Hamilton, M.D., Daniel A. Hoffman, M.D., Jay H. Shaffer, M.D., Albert Davis, M.D.

Educational Objectives:

At the end of this session, the participant should be able to: (1) understand the background and methodology of referenced EEG; (2) understand the clinical use of Referenced EEG in guiding psycho-pharmacologic treatment; and (3) assess the potential benefits of use of Referenced EEG in the treatment of non-psychotic treatment-refractory patients.

Summary:

Introduction: Referenced EEG (rEEG) provides a neurophysiological basis for the selection of effective psychiatric medications for patients with non-psychotic psychiatric disorders. rEEG utilizes commonly-used digital electroencephalography (EEG) in conjunction with normative and clinical treatment (symptomatic) databases to identify abnormal patient physiology. Appropriate medications are then statistically selected specifically to normalize identified electrophysiological abnormalities. This process has been correlated to treatment outcome in a database of over 1,600 patients and their cumulative 10,000 medication trials.

Methods: This is a multi-site case series to assess clinical outcomes to date and the value of further research. Psychiatrists in five clinical sites chose to use rEEG to guide psycho-pharmacologic treatment of non-psychotic, treatment-refractory psychiatric patients. They assessed clinical improvement using the CGI-Improvement Scale and rated the helpfulness of rEEG in achieving clinical outcome using a seven-point scale.

Results: A total of 258 patients were treated following rEEG guidance. In all, 199 (77%) of these treatment-refractory patients were rated as much improved or very much improved.

Conclusions: Referenced EEG led to significant clinical improvement in a greater number of treatment-refractory patients than would normally be expected with standard treatment. These initial results warrant a randomized, double-blind study of this innovative, neurophysiologic-based technology.

References:

1. Suffin SC, Emory WH: Neurometric subgroups in attentional and affective disorders and their association with pharmacotherapeutic outcome. *Clin EEG Neurosci* 1995; 26:76-83.
2. Emory WH, Schiller M, Suffin SC: Referenced-EEG in the treatment of eating disorders in New Clinical Drug Evaluation Unit 2004 Program Abstracts. Washington, DC, NCDEU, 2004, poster 221.

NR11 Monday, May 23, 9:00 a.m.-10:30 a.m.

Childhood Abuse and Neglect in BDD

Elizabeth R. Didie, Ph.D., *Butler Hospital/Brown University, 345 Blackstone Boulevard, Providence, RI 02906*; Katherine A. Phillips, M.D., Courtney Pope, Christina Tortolani, M.A., William Menard, B.A., Christina Fay, B.A.

Educational Objectives:

At the conclusion of this presentation, the participant will be familiar with results from the first study of the prevalence and correlates of childhood abuse and neglect in patients with body dysmorphic disorder.

Summary:

Background: To our knowledge, no published studies have examined childhood abuse and neglect in body dysmorphic disorder (BDD). This study examined the rates and clinical correlates of abuse and neglect in individuals with this disorder.

Methods: 75 subjects with DSM-IV BDD (69.3% female, age = 35.4 ± 12.0) participating in a study of the course of BDD completed the Childhood Trauma Questionnaire and were interviewed with other reliable and valid measures.

Results: 78.7% of subjects reported a history of childhood maltreatment: emotional neglect (68.0%), emotional abuse (56.0%), physical abuse (34.7%), physical neglect (33.3%), and sexual abuse (28.0%). One-third (33.3%) of subjects reported severe maltreatment in these areas. Among women (n = 52), severity of emotional abuse and neglect were .44 and .41 standard deviation units higher than the normative mean. Severity of sexual abuse was the only type of maltreatment related to current BDD severity (r = .23, p=.047) and female gender (p=.02) was also significantly associated with severity of sexual abuse. However, sexual abuse severity did not predict current BDD severity (p=.15) when entered into a simultaneous multiple regression equation with age, gender, and current treatment status. A history of attempted suicide was significantly related to childhood emotional (p=.004), physical (p=.014), and sexual abuse (p=.038) for the entire sample. Nonwhite racial/ethnic status was associated with severity of physical abuse (p=.043), sexual abuse (p=.002), and physical neglect (p=.002) for the entire sample. Childhood emotional abuse was associated with a lifetime substance-use disorder (r=.265, p=.02) and physical abuse was negatively associated with lifetime mood disorder (r=-.37, p=.001).

Conclusion: Individuals with BDD have high rates of abuse and neglect, but abuse and neglect appear to be only modestly associated with BDD symptom severity and comorbidity.

References:

1. Bernstein D, Fink L: Manual for the Childhood Trauma Questionnaire. New York, The Psychological Corporation.
2. Phillips KA: Body dysmorphic disorder, Somatoform and Factitious Disorders. Review of Psychiatry Series, Volume 20, Number 3; Oldham JM and Riba MB, series editors. Washington DC, American Psychiatric Publishing, 2001.

NR12 Monday, May 23, 9:00 a.m.-10:30 a.m.

A Clinical Comparison of Major and Minor Depression

Jean Fils, M.D., *Department of Psychiatry, University of Kansas Medical Center, 3901 Rainbow Blvd, Kansas City, KS 66160*; Elizabeth J. Nickel, M.A., Elizabeth C. Penick, Ph.D., Ekkehard Othmer, M.D., Cherilyn M. De Souza, M.D., Edward N. Hunter, Ph.D., William F. Gabrielli, Jr., M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize similarities and differences between patients with major and minor depression derived from a large outpatient psychiatric clinic.

Summary:

Objective: To clinically contrast outpatients suffering from major and minor depression.

Method: During a five-year period, 1,458 largely consecutive, new outpatient admissions were seen in a psychiatric outpatient clinic at a teaching hospital. Comparative data were drawn from a personal data form, the structured Psychiatric Diagnostic Interview, the Symptom Checklist-90R, and the clinician's initial screening note. Of the 1,458 outpatients, 1,002 (69%) satisfied inclusive DSM-III lifetime criteria for a major depressive episode. Of the 456 outpatients who did not satisfy criteria for a major depressive episode, 79 (17%) acknowledged significant depressive symptoms that caused some kind of interference in their lives, but failed to meet DSM-III criteria for a major depressive episode. These 79 outpatients were classified as suffering from minor depression. They represented 5% of the total clinic sample.

Results: No gender or other sociodemographic differences were found between the two outpatient groups except that the minor depression group had achieved a higher educational level when

first seen. No differences were found for a family history of psychiatric illness among first-degree relatives, including a family history of depression. Ratings of childhood unhappiness/problems did not distinguish the two groups. As expected, outpatients with major depression endorsed significantly more lifetime depressive symptoms. Psychiatric comorbidity was slightly higher in the major depressive group, especially for mania and the anxiety disorders. The major depression group reported poorer psychosocial functioning when first seen and greater amounts of treatment. Recommendation of an antidepressant did not distinguish the two groups.

Conclusion: Minor depression seems to represent the same illness as major depression but in a less severe form.

References:

1. Shelbourne CD, Wells KB, Hays RD, Rogers W, Burnam A, Judd LL: Subthreshold depression and depressive disorder: clinical characteristics of general medical and mental health specialty outpatients. *Am J Psychiat* 1994; 151:1777-1784.
2. Merikangas KR, Ernst C, Maier W, Hoyer EB, Angst J: Minor depression in Widiger TA, Francis, AJ, Pincus HA, Ross R, First MB, Davis WW (Eds). *DSM-IV Source Book (Vol. 2)*. Washington, D.C., American Psychiatric Association Press, 1996, pp 97-109.

NR13 Monday, May 23, 9:00 a.m.-10:30 a.m.

Do Childhood ADHD and Antisocial Personality Disorder Predict Alcoholism at Age 40?

National Institute on Alcohol Abuse and Alcoholism

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Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the predictive relationship between childhood ADHD and ASPD and alcoholism that develops years later.

Summary:

Objective: To determine whether childhood symptoms of attention deficit/hyperactivity disorder (ADHD) and antisocial personality disorder (ASPD) predict male alcoholic drinking at age 40.

Method: This subsample (N=96) from the Danish Longitudinal Study of Alcoholism contained all of the subjects followed from birth who participated in the 40-year follow up and for whom an 85-item school teacher questionnaire was available. Approximately two-thirds (N=65) were high-risk sons of alcoholic fathers. This sample was comprehensively studied at birth, one year, 19-20 years, 30 years, and at 40 years. At age 40, a Danish psychiatrist assigned up to eight DSM-III-R diagnoses to each subject after individually examining subjects with structured interviews and rating scales. ADHD symptoms were derived from items of a teacher questionnaire completed before any had developed a drinking problem. At age 40, the *Connors Adult ADHD Rating Scale* was also administered. ASPD was derived from the 30-year follow up Antisocial Personality Disorder module in the *Psychiatric Diagnostic Interview* that operationalizes DSM-III-R criteria and requires significant antisocial activity prior to age 15.

Results: By age 40, 36 of the subjects (37%) had developed alcohol abuse/dependence. Significantly more (p<.04) of the high-risk sons of alcoholics drank alcoholically (45%vs.23%). Alcohol abuse/dependence occurred more often among subjects who scored above the median on the school-teacher derived ADHD scale (75%vs.43% p<.003). Childhood ADHD scores were correlated with Conner's ADHD scores two decades later (r=0.31; p<.0002). Subjects with ASPD were three times more likely (RR

to develop alcohol abuse/dependence than those without (90%vs.10%, $p<.0003$). Both a multiple and logistic regression showed that ADHD and ASPD independently predicted alcoholism at age 40.

Conclusion: Among men, ASPD and ADHD appear to be strong premorbid predictors of alcoholic drinking.

References:

1. Knop J, Teasdale T W, Schulsinger F: A prospective study of young men at high risk for alcoholism: school behavior and achievement. *Journal of Studies on Alcohol* 1985; 46:273-278.
2. Tapert SF, Baratta MV, Abrantes AM, Brown SA: Attention dysfunction predicts substance involvement in community youth. *Journal of the American Academy of Child and Adolescent Psychiatry* 2002; 41:680-686.

NR14 Monday, May 23, 9:00 a.m.-10:30 a.m.

Alcoholism in the Clinical Setting: Does Gender Matter?

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Educational Objectives:

At the conclusion of this session, the participant should be able to appreciate the effect of gender on the clinical needs of patients who present to an outpatient psychiatric clinic.

Summary:

Objective: To investigate differences between men and women alcohol-dependent patients treated in a general outpatient psychiatry clinic.

Method: During a five-year period, consecutive patients received an initial workup that contained two structured interviews, rating scales, and an initial evaluation by a physician. This clinic did not operate an independent substance abuse program. The interviews were administered independently of the clinical examination.

Results: Of the 1,458 new outpatients, 271 (19%) satisfied DSM-III criteria for lifetime alcohol dependence on a structured interview. They were evenly divided between men (56%) and women (44%). Sixty-eight percent of the men and women patients reported problems with alcohol within the last two years; 40% reported problems with alcohol in the previous month. The average age was 36 years. Alcohol dependent women reported a later onset and a shorter duration of problem drinking than men. A lifetime measure of alcoholism severity was the same for both, and rates of a family history of alcoholism did not differ. Women reported other kinds of psychiatric disorders more often among their first-degree relatives than men. Women were more likely to suffer from a comorbid mood, anxiety, or eating disorder, while men alcoholic patients were more likely to suffer from antisocial personality disorder. Problem drinking was recorded as a presenting problem for only 12% of the 271 patients; in only 50% was alcohol abuse/dependence included in the final clinic diagnoses.

Conclusion: Male and female alcohol-dependent patients who seek treatment in a general psychiatric outpatient clinic differ in clinically relevant ways. The majority of these patients did not indicate that drinking was a problem and alcohol dependence was recognized by the examining clinician in only one-half of them.

References:

1. Walter H, Gutierrez K, Ramskogler K, Hertling I, Divorak A, Lesch OM: Gender-specific differences in alcoholism: implications for treatment. *Arch Women Ment Health* 2003; 4:253-258.

2. Mann K, Hintz T, Jung M: Does psychiatric comorbidity in alcohol-dependent patients affect treatment outcome? *Eur Arch Psychiatry Clin Neurosci* 2004; 3:172-181.

NR15 Monday, May 23, 9:00 a.m.-10:30 a.m.

Does Depression Affect Sleep in Patients With Obstructive Sleep Apnea?

Aliuddin M. Khaja, M.D., *Department of Psychiatry, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160*; Barry I. Liskow, M.D., John A. Hunter, Psy.D., Elizabeth C. Penick, Ph.D., Vernon D. Rowe, M.D., Kodidhi Sankar, M.D., Raymond C. Lake, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to appreciate the effect of depression on the sleep of patients with obstructive sleep apnea (OSA).

Summary:

Objective: To compare the sleep architecture of obstructive sleep apnea patients with and without depression.

Method: This is a retrospective chart review from a sleep clinic where patients were referred for a sleep evaluation during 2000-2004 in the same demographic region. Patients were divided into two groups, one having only obstructive sleep apnea (OSA) and the other with OSA and depression (depression was self-reported and they were on medication). Pt were matched for age and BMI, and RDI (number of apnea and hypopneas per hour). A total of 136 patients were included in the study, men (N=45) and women (N=91), were between the ages of 30-50 yrs, combined mean age was 41.2 yrs (SD±1.6) and. All these patients had overnight polysomnography.

Results: Pts with OSA and depression were found to have significantly increased percentage of stage-1, ($P<0.003$), stage-3 ($P<0.04$) sleep and REM latency ($P<0.004$). There was no significant difference in stage-2, % REM, sleep efficiency, arousal index sleep efficiency, oxygen desaturation, and Epworth scale (scale of sleepiness).

Conclusion: Our findings are consistent with findings by Bardwell, et. al. High prevalence of depression has been reported in obstructive sleep apnea. Depression combined with OSA seems to result in more fragmented sleep.

References:

1. Bardwell WA, Moore P, Ancoli-Israel S, Dimsdale JE: Fatigue in obstructive sleep apnea: driven by depressive symptoms instead of apnea severity? *Am J Psychiatry* 2003; 160(2):350-5.
2. Baran AS, Richert AC: Obstructive sleep apnea depression. *CNS Spectrums* 2003; 8(2):120-134.

NR16 Monday, May 23, 09:00 a.m.-10:30 a.m.

A Retrospective Review of Assaults at a State Hospital

Joseph F. Motacki, M.D., *Department of Psychiatry, Hershey Medical Center, PO Box 850, Hershey, PA 17033*; Paul A. Kettl, M.D.

Educational Objectives:

At the conclusion of the session, the participant should be able to appreciate the problem of repetitively assaultive patients in a chronic care setting, and understand characteristics that may be associated with violent behavior.

Summary:

Introduction: Patient assaults are a serious problem in psychiatric facilities.

Method: In a 270-bed chronic psychiatric hospital, 23 patients accounted for 68% of all assaults over a six-month period. They were compared using t tests and chi square statistics with a control group of 23 non-assaultive patients matched for age, sex, and ward. The 23 assaultive patients were then compared with other assaultive patients for psychiatric and legal history.

Results: Assaultive patients were more likely to have a shorter length of stay ($p=0.036$) and have a diagnosis of mental retardation ($p=0.022$). There was a tendency for assaultive patients to have a history of violent crime ($p=0.063$).

Of the 23 frequently assaultive patients, 13 had a diagnosis of schizophrenia. They were less likely to have a personality disorder diagnosis ($p=0.022$) or be a victim of abuse ($p=0.074$). Patients with a personality disorder (six of the 23 patients) were more likely to have a history of violent crime ($p=0.025$). Seven of the 23 patients who had a history of violent crime had a tendency to have a history of substance abuse ($p=0.066$). Patients with mental retardation (10 of the 23 patients) were more likely to have a legal history ($p=0.024$), and more likely to have been abused in the past ($p=0.007$).

Conclusion: Assaults are often concentrated in a small group of patients. They may be severely ill, or have a cluster of an abuse history, legal problems, and substance abuse.

References:

1. Flannery R: Repetitively assaultive psychiatric patients: review of published findings 1978-2001. *Psychiatric Quarterly* 2002; 73(3):229-237.
2. Chou, Kuoi-Ru, Lu, Ru-Band; Mao, Wei-Chung: Factors relevant to patient assaultive behavior and assault in acute inpatient psychiatric units in Taiwan. *Archives of Psychiatric Nursing* 2002; 16(4):187-195.

NR17 Monday, May 23, 09:00 a.m.-10:30 a.m. A Comparison of Anxiety Sensitivity in Panic Disorder and OCD

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Educational Objectives:

At the conclusion of this session, the participant should be able to recognize differences on anxiety sensitivity between patients with panic disorder without agoraphobia, patients with panic disorder with agoraphobia, and patients with obsessive-compulsive disorder.

Summary:

Objective: Anxiety sensitivity is a measure of the extent to which anxiety symptoms are feared. Taylor et al. (1992) found that patients with obsessive-compulsive disorder (OCD) were characterized by lower anxiety sensitivity than those with panic disorder. Research has demonstrated that individuals with low anxiety sensitivity are more likely to choose denial and self-deceptive responses over task-oriented responses when confronted with a hypothetical threat (Werhun and Cox, 1999). The present study attempts to further delineate these differences by comparing individuals with OCD with those with panic disorder with agoraphobia (PDA) and panic disorder without agoraphobia (PD).

Methods: Eighty-three outpatients meeting the DSM-IV criteria for OCD, PDA, or PD were administered the Anxiety Sensitivity Index (ASI; Peterson and Reiss, 1987; Peterson and Reiss, 1992) and total scores were compared.

Results: Patients with PDA ($p<0.01$) and patients with PD ($p<0.05$) scored higher on the ASI than patients with OCD.

Conclusions: These findings suggest that the physiological arousal that is part of panic disorder and/or the interpretation of these symptoms leads to distress and may be related to greater compliance with treatment for individuals with panic disorder. Further implications for treatment will be discussed.

References:

1. Taylor S, Koch WJ, McNally RJ: How does anxiety sensitivity vary across the anxiety disorders? *Journal of Anxiety Disorders* 1992; 6:249-259.
2. Werhun CD, Cox BJ: Levels of anxiety sensitivity in relation to repressive and self-deceptive coping styles. *Journal of Anxiety Disorders* 1999; 13:601-609.

NR18 Monday, May 23, 09:00 a.m.-10:30 a.m. Relationship Between Glycated Hemoglobin and Emotional States in Patients With Diabetes

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Educational Objectives:

At the conclusion of this session, the participant should be able to recognize psychiatric problems according to diabetes control in diabetic patients.

Summary:

Objectives: This study was designed to investigate depression, anxiety, alexithymia, and stress responses between well-controlled and poorly-controlled diabetic patients by glycated hemoglobin levels.

Methods: The subjects were 55 diabetic patients (mean age: 49.9 ± 9.9 , 27 men and 28 women) who were confirmed to have diabetes depending on the laboratory findings as well as clinical symptoms at the St. Vincent Hospital Diabetes Clinic, from March 2004 to August 2004. Korean version of Beck Depression Inventory (BDI), State and Trait Anxiety Inventory (STAI), Toronto Alexithymia Scale (TAS), and Stress Response Inventory (SRI) were used for assessment.

Based on glycated hemoglobin levels, the patients were divided into ten well-controlled group (below 7%) and 45 poorly-controlled group (below 7%). We compared BDI, STAI, TAS, and SRI scores between the two groups by independent t-test.

Results: (1) In well-controlled diabetics, compared with poorly controlled group, manifested decreased illness duration (12.2 ± 55.4 months vs. 55.4 ± 66.6 months) ($p=0.000$), but other demographic data showed no difference between two groups. (2) The STAI scores of poorly-controlled group were significantly higher in both state anxiety sores (38.7 ± 3.8 vs. 43.7 ± 6.7) ($p=0.29$) and trait anxiety scores (36.9 ± 5.7 vs. 41.5 ± 6.4) ($p=0.43$) than well-controlled groups. (3) No significant differences were found in the score of BDI, TAS, SRI between well and poorly-controlled diabetic groups.

Conclusion: The above results suggest that poorly-controlled diabetic patients are more likely to have higher anxiety levels than well-controlled diabetic patients. However, there were no differences in depression, alexithymia, or stress responses between the two groups. We suggest that physicians should consider integrated approaches for psychiatric problems in the management of diabetes.

References:

1. Musselman DL, Betan E, Larsen H, Phillips LS: Relationship of depression to diabetes type 1 and type 2: epidemiology, biology and treatment. *Biol Psychiatry* 2003; 54(3):317-29.
2. Thomas J, Jones G, Scarinci I, Brantley P: A descriptive and comparative study of the prevalence of depressive and anxiety disorders in low-income adults with type 2 diabetes and other chronic illness. *Diabetes Care* 2003; 26(8):2311-7.

NR19 Monday, May 23, 9:00 a.m.-10:30 a.m.

Association Between 5HT 2A and 1B Receptor Gene Polymorphism and Suicide Attempt With Drug Intoxication in Korean Populations

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Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that Korean suicide attempters with drug intoxication have no association with serotonin 2A(T102C) and 1B(G861C) receptor gene polymorphism.

Summary:

Objectives: Recently, polymorphism of several serotonin genes have been suggested to be associated with suicide, but the results are still unclear. We examined whether the T102C polymorphism of the serotonin 2A receptor gene and the 816C polymorphism of the serotonin 1B receptor gene were associated with suicidal behavior using drug intoxication.

Method: The suicidal attempters consisted of 52 patients who visited the emergency room. Fifty controls were selected from healthy volunteers matched for sex and age to the suicide subjects. The polymorphism were analyzed with TagMan assay using primers based on previous studies.

Results: The T102C polymorphism of the serotonin 2A receptor gene showed no significant difference between the suicidal attempters and controls in both genotype and allele frequency analyses ($p=0.179$, $p=0.422$, respectively). There was no statistically significant difference between the two groups in the G861C polymorphism of the serotonin 1B receptor gene ($p=0.092$) and any significant effect of the genotype distributions or the allele frequencies was not observed ($p=0.987$).

Conclusion: These findings suggest that the T102C polymorphism in serotonin 2A receptor gene and the G861C polymorphism in serotonin 1B receptor gene are not related to the susceptibility of suicidal attempters with drug intoxication in Korean populations.

References:

1. Du L, et al: Frequency of long allele in serotonin transporter gene is increased in depressed suicide victims. *Biol Psychiatry* 1999; 46:196-201.
2. Statham DJ, et al: Suicidal behavior: an epidemiological and genetic study. *Psycho Med* 1998; 28:839-855.

NR20 Monday, May 23, 9:00 a.m.-10:30 a.m.

Psychiatric Diagnosis in Clinical Practice: Accuracy and Stability

Dante M. Durand, M.D., *Department of Psychiatry, Maimonides, 920 48th Street, Brooklyn, NY 11219-2948*; Gabriel Ghitan, M.D.

Educational Objectives:

At the conclusion of this session, the participant will recognize that in hospital clinical practice diagnoses do not meet DSM-IV diagnostic criteria 40% of the time. There is rarely a change in diagnosis from admission to discharge for residents or staff psychiatrists. These findings have clear implications for resident education.

Summary:

Introduction: There are very few studies of the accuracy and short-term stability of psychiatric diagnoses in clinical practice.

Methods: Seventy-two consecutive charts of patients admitted to an acute psychiatric unit with the diagnoses of major depressive disorder (MDD), bipolar I disorder (BD), or schizophrenia were examined. Admission history and discharge summaries were reviewed to evaluate if either or both met DSM-IV diagnostic criteria and if they remained the same or changed.

Results: Almost half (47.2%) of patients' diagnoses did not meet DSM-IV criteria at admission and a third (33.3%) at discharge. The accuracy of diagnosing schizophrenia was greater than diagnosing MDD or BD at admission ($p=.01$) and MDD at discharge ($p=.02$). Residents and staff psychiatrists, each of whom had about half the cases, missed DSM-IV criteria at admission and discharge in about 40% of the cases. Diagnostic stability was very high (90%) across all diagnoses.

Discussion: DSM-IV criteria were not met in about 40% of cases because they may not be needed for clinical work, documentation is time consuming, and the clinical focus is more on treatment than detailed diagnosis. Diagnostic accuracy and stability in schizophrenia are higher than in MDD or BD. This has been found in other reports and may relate to the less remitting nature of schizophrenic illness.

Conclusions: Diagnostic accuracy only occurred about 60% of the time, which may be all that is necessary in clinical practice. Residents as well as staff psychiatrists show similar performance in diagnostic accuracy and stability. These findings raise questions about the use of DSM-IV in clinical work and teaching.

References:

1. Dalman C, Broms J, Cullberg J, Allebeck P: Young cases of schizophrenia identified in a national inpatient register. Are the diagnoses valid? *Social Psychiatry and Psychiatric Epidemiology* 2002; 37(11):527-531.
2. Ashley RV, Gladsjo A, Olson R, Judd LL, Sewell DD, Rockwell E, Jeste DV: Changes in psychiatric diagnoses from admission to discharge: review of the charts of 159 patients consecutively admitted to a geriatric psychiatry inpatient unit General Hospital Psychiatry 2001; 23:3-7.

NR21 Monday, May 23, 9:00 a.m.-10:30 a.m.

Suicidal Intent Among Patients With Traumatic Brain Injury

Christopher Tam, M.D., *Department of Psychiatry, University of Toronto, 7 Carlton Street, #606, Toronto, ON M5B 2M3, Canada*; Anthony Feinstein, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to (1) appreciate the extent of suicidal intent in patients with traumatic brain injury; and (2) recognize that suicidal intent is difficult to predict in this particular population.

Summary:

Objective: To determine clinical correlates of suicidal intent in patients with traumatic brain injury (TBI) of varying severities.

Methods: A consecutive sample of 970 patients who presented to a TBI clinic three months post-injury were enrolled. Data collec-

tion included demographic information, indices of TBI severity, and self-report measures of postconcussion disorder, psychological distress, and psychosocial outcome. Suicidal intent was ascertained from questions included in the General Health Questionnaire. Patients with (n=193) and without suicidal (n=744) intent three months post-injury were compared across all relevant variables.

Results: Overall, 20.6% of patients (51.6% mild; 13.0% moderate; 35.3% severe) endorsed suicidal intent. Suicidal patients were more likely to have a past psychiatric history ($p=0.014$), anosmia ($p=0.008$), prominent pain complaints ($p=0.000$), and be involved in litigation ($p=0.026$). However, a logistic regression analysis revealed that these variables could account for only 9.3% of the variance when it came to predicting suicidal intent.

Conclusions: Suicidal intent is common in the subacute period of recovery following TBI, particularly in cases of mild and severe injuries. Known demographic and psychiatric predictors derived from non-TBI populations cannot be used reliably to predict suicidal intent in TBI patients. Hence, clinicians need to exercise added vigilance in assessing risk in this population.

References:

1. Fann JR, Burington B, Leonetti A, Jaffe K, Katon WJ, Thompson RS: Psychiatric illness following traumatic brain injury in an adult health maintenance organization population. *Arch Gen Psychiatry* 2004; 61:53-61.
2. Simpson G, Tate R: Suicidality after traumatic brain injury: demographic, injury, and clinical correlates. *Psychological Medicine* 2002; 32:687-697.

NR22 Monday, May 23, 9:00 a.m.-10:30 a.m.

Does Moderate Alcohol Use in Bipolar Disorder Impact Course and Symptom Burden?

Benjamin I. Goldstein, M.D., *Department of Psychiatry, University of Toronto, 2075 Bayview Avenue, Room 646, Toronto, ON M4N 3M5, Canada*; Vytas P. Velyvis, M.A., Sagar V. Parikh, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to appreciate the impact of alcohol use on the course and symptom burden of bipolar disorder among non-alcoholic patients, and recognize the varying associations of beer, wine, and spirits consumption with course and symptom burden in bipolar disorder.

Summary:

Objective: Comorbid alcohol use disorders (AUDs) are known to increase the severity of bipolar disorders (BD). No previous study has examined the association of alcohol consumption with course and symptom burden among non-alcoholics with BD.

Method: 84 adult outpatients with BD I or II enrolled in a longitudinal study of CBT versus psychoeducation participated. Subjects were included if they were taking mood stabilizers, in at least partial remission, and without active substance abuse/dependence. Study measures included SCID-IV, Hamilton Depression Rating Scale, Clinician-Administered Rating Scale for Mania, Social Adjustment Scale, and Khavari Alcohol Test.

Results: Mean number of alcoholic beverages consumed was 2.2/week. 16% of men and 15% of women reported binges of at least five alcoholic beverages. The primary hypothesis, that overall alcohol consumption would be associated with overall mood symptoms, was not confirmed. Beer consumption was negatively associated with depressive symptoms ($r=-0.31$, $p<0.01$). Overall alcohol consumption and spirits consumption were associated with lifetime number of manic episodes ($r=0.35$ and 0.38 , respectively; $p<0.01$).

Conclusions: Even moderate alcohol consumption may worsen the life course of BD. Spirits consumption may be particularly hazardous. Abstinence from alcohol may be indicated for individuals with BD, especially those who have experienced a manic episode.

References:

1. Brady KT, Sonne SC: The relationship between substance abuse and bipolar disorder. *J Clin Psychiatry* 1995; 56(suppl 3):19-24.
2. Salloum IM, Thase ME: Impact of substance abuse on the course and treatment of bipolar disorder. *Bipolar Disord* 2000; 2:269-280.

NR23 Monday, May 23, 9:00 a.m.-10:30 a.m.

Increased Risk of MDD and Suicidality Among Women Who Drink in Moderation

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Educational Objectives:

At the conclusion of this session, the participant should be able to (1) understand that the association between alcohol consumption and depression differs by gender, (2) recognize that moderate alcohol consumption may be associated with adverse psychiatric outcomes, particularly among women.

Summary:

Objective: Alcohol-use disorders (AUD) are associated with increased illness severity and suicidality in major depressive disorder (MDD). We examined whether moderate alcohol consumption, in the absence of AUD, impacts the nature and severity of depression in a community sample.

Method: 496 adult subjects (201 males, 295 females) were recruited by random-digit dialing of residences in Toronto, Canada. Participation rate was 60%. The CAGE questionnaire, Khavari Alcohol Test, and a validated structured diagnostic interview for depression were utilized. Subjects were divided into three alcohol consumption groups: minimal (min), moderate (mod), and heavy (hvy) alcohol consumption.

Results: Among both male and female subjects with MDD, drinking group was not associated with measures of disability, health service utilization, or satisfaction. Among males, there was no association between drinking group and depression prevalence or suicidality. Among women, however, the prevalence of depression was significantly different across drinking groups: min=24.6%, mod=30.3%, hvy=44.0% ($\chi^2 = 4.1$, $df 1$, $p<0.05$). Similarly, among women with MDD, the prevalence of suicidality was significantly different across drinking groups: min=16.3%, mod=29.6%, hvy=45.5% ($\chi^2=4.5$, $df 1$, $p<0.05$).

Conclusion: Moderate alcohol consumption is associated with increased rates of depression among women, and with increased rates of suicidality among depressed women.

References:

1. Castaneda R, Sussman N, Westreich L, Levy R, O'Malley M: A review of the effects of moderate alcohol intake on the treatment of anxiety and mood disorders. *J Clin Psychiatry* 1995; 57:207-212.
2. Tondo L, Baldessarini RJ, Hennen J, Minnai PG, Salis P, Scamionatti L, Masia M, Ghiani C, Mannu P: Suicide attempts in major affective disorders patients with comorbid substance use disorders. *J Clin Psychiatry* 1999; 60(suppl 2):63-69.

NR24 Monday, May 23, 9:00 a.m.-10:30 a.m.

Brain MRI Study of Corpus Callosum in Patients With Major Depressive Disorder

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Educational Objectives:

The present findings point out the possible role of frontal lobe, especially subgenual prefrontal cortex, abnormality in pathophysiology of major depressive disorder.

Summary:

Objective: The purpose of this study was to investigate differences in regional areas of the corpus callosum in subjects with major depressive disorder and healthy comparison subjects. Based on previous reports that have suggested reduced frontal lobe volume and reduced subgenual prefrontal cortex in depression, we hypothesized that the area of the corpus callosum that interconnects the frontal regions of the brain will be smaller compared with that of healthy comparison subjects.

Method: Twenty-one subjects with major depressive disorder, as defined by the DSM-IV, and 21 healthy comparison subjects were collected. Single best view for the corpus callosum, midsagittal slice images were selected for analysis. MR images were analyzed with BRAIN IMAGE version 1.5.1 software.

Results: In the subjects with major depressive disorder, there were significant reductions of corpus callosum regional areas. Depression subjects had a smaller genu ($t=2.216$, $p=0.010$) and rostrum ($t=2.719$, $p=0.032$) of the corpus callosum compared with the healthy comparison subjects. In male depression subjects, there was significant reduction of rostrum ($t=2.588$, $p=0.025$) of corpus callosum compared with the healthy comparison subjects. And in female depression subjects, there was significant reduction of genu ($t=2.587$, $p=0.015$).

Conclusion: These findings suggest structural and functional abnormalities of the frontal lobe in patients with depressive disorder. Moreover, the present findings point out the possible role of frontal lobe, especially subgenual prefrontal cortex, abnormality in pathophysiology of major depressive disorder.

References:

1. Wu JC, Buchsbaum MS, Johnson JC, Hershey TG, et al: Magnetic resonance and positron emission tomography imaging of the corpus callosum: Size, shape and metabolic rate in unipolar depression. *J Affect Disorder* 1993; 28:15-25.
2. Lyoo IK, Kwon JS, Lee SJ et al: Decrease in genu of the corpus callosum in medication-naïve, early-onset dysthymia and depressive personality disorder. *Biol Psychiatry* 2002; 52:1134-1143.

NR25 Monday, May 23, 9:00 a.m.-10:30 a.m.

Elevated Levels of HERV-W Transcripts in PBMCs of Recent-Onset Schizophrenia

Supported by Stanley Medical Research Institute

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Educational Objectives:

At the conclusion of this session, the participants should be able to recognize that the over-activation of human-endogenous retroviral transcripts may contribute to the onset and initial progression of schizophrenia.

Summary:

Objective: To quantitatively and qualitatively investigate the transcripts from the human endogenous retrovirus (HERV)-W *gag* and *env* genes in peripheral blood mononuclear cells (PBMCs) from patients with recent-onset schizophrenia or schizoaffective disorder and healthy controls.

Method: Total RNA was isolated from PBMCs from 30 cases and 26 controls. By real-time quantitative PCR, we investigated the expression of *Wgag* and *Wenv* mRNAs.

Results: An approximately 2-fold ($P = 0.0039$) elevation in the expression of *Wgag* mRNAs in the PBMCs of recent-onset schizophrenia patients was detected as compared with controls. This increase in relative abundance resulted from an elevated transcriptional activity of certain *gag*-containing loci on chromosomes 5 and 11. No difference in the levels of the expression of *env* mRNAs was seen between the two groups. The levels of the transcription of the *Wgag* and *Wenv* correlated well with that of GCM1 in the PBMCs from recent-onset schizophrenia patients, but not from controls.

Conclusions: These data suggest that certain HERV-W loci are transcribed at higher levels in the PBMCs from recent-onset schizophrenia cases as compared with controls.

References:

1. Karlsson H, Bachmann S, Schroder J, McArthur J, Torrey EF, Yolken RH: Retroviral RNA identified in the cerebrospinal fluids and brains of individuals with schizophrenia. *Proc Natl Acad Sci U S A* 2001; 98(8):4634-9.
2. Karlsson H, Schroder J, Bachmann S, Bottmer C, Yolken RH: HERV-W-related RNA detected in plasma from individuals with recent-onset schizophrenia or schizoaffective disorder. *Mol Psychiatry* 2004; 9(1):12-3.

NR26 Monday, May 23, 9:00 a.m.-10:30 a.m.

Death Rates Among Antipsychotics Users Within a Managed Care Organization

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Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the value of using multiple baseline comparison groups when evaluating the association between antipsychotic drug exposure and mortality-related outcomes in a patient population whose lifestyle factors are inherently different from that of the general population.

Summary:

Objective: Quantify the rate of all-cause and cardiovascular-related mortality among current antipsychotic users and compare this rate with that of nonusers.

Methods: We conducted a retrospective database study within a large midwestern health maintenance organization and identified all new users of antipsychotics (1/1/95-6/1/02). For each antipsychotic-exposed patient, we randomly sampled one unexposed comparison patient matched on age, sex, and index date. We calculated mortality rates (MR) for "current" and "non-use" exposure categories; and person-time experience for both the general population cohort (GPC) and the unexposed comparison group to fit Poisson regression models (adjusting for race, cardiovascular disease, and diabetes).

Results: Compared with the unexposed GPC, a higher MR among antipsychotic-exposed patients [adjusted RR=1.83, 95% confidence interval (CI) 1.52, 2.21] was observed. However, when the referent group was restricted to unexposed person-time among antipsychotic users, a protective effect was observed [RR=

0.74 (CI=0.62, 0.88)]. Among schizophrenic-diagnosed patients, the RR for all-cause death was 0.33 (CI=0.15, 0.72) with unexposed schizophrenics as the referent.

Conclusion: Unlike previous studies, we did not observe an association between antipsychotic therapy and all-cause mortality. Exposure to antipsychotic therapy appears to confer an overall mortality benefit among all patients under treatment, including schizophrenia patients.

References:

1. Enger C, Weatherby L, Reynolds RF, Glasser DB, Walker AM: Serious cardiovascular events and mortality among patients with schizophrenia. *J Nerv Ment Dis* 2004; 192:19-27.
2. Ray WA, Meredith S, Thapa PB, Meador KG, Hall K, Murray KT: Antipsychotics and the risk of sudden cardiac death. *Arch Gen Psych* 2001; 58:1161-1167.

NR27 Monday, May 23, 9:00 a.m.-10:30 a.m. **History of Depression Increases Risk of Type 2 Diabetes in Younger Adults**

Lauren C. Brown, M.S.C., *Department of Public Health, University of Alberta, 1200 10405 Jasper Avenue, Edmonton, AB T5J 3N4, Canada*; Sumit R. Majumdar, M.D., Stephen C. Newman, M.D., Jeffrey Johnson, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that younger people with a history of depression have an increased risk of developing diabetes.

Summary:

Objective: To assess the history of previous depression in people with incident diabetes compared with people without diabetes.

Methods: We conducted a population-based nested case-control study using the administrative databases of Saskatchewan Health. We identified cases of type 2 diabetes based on diagnostic codes or prescription records for individuals over the age of 20 years. For each case, two controls were randomly selected from the non-diabetes population. History of depression, based on diagnostic codes and antidepressant prescription, was ascertained prior to index date. Simple and multivariate logistic regression analysis was used to estimate the odds ratio (OR) and 95% confidence intervals (CI), after adjusting for age, sex, and frequency of physician visits.

Results: People with diabetes were 30% more likely to have had a previous history of depression (1,622/33,257-4.9%) compared with people without diabetes (2,297/59,420-3.8%). This increased risk remained after controlling for sex and number of physician visits, but was limited to subjects 20 to 50 years of age (adjusted OR 1.23, 95% CI: 1.10-1.37), and not in those 51 years of age and older (adjusted OR: 0.92; 0.84-1.00).

Conclusions: Depression appears to increase the risk of developing diabetes by approximately 23% in younger adults. This suggests that younger people with depression should be screened for diabetes.

Funding: Canadian Institutes of Health Research (CIHR), and New Emerging Team Grant for Alliance for Canadian Health Outcomes Research in Diabetes (ACHORD).

References:

1. Anderson RJ, Clouse RE, Freedland KE, Lustman PJ: The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care* 2001; 24(6):1069-1078.
2. Ciechanowski PS, Katon WJ, Russo JE: Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. *Arch Int Med* 2000; 160:3278-3285.

NR28 Monday, May 23, 9:00 a.m.-10:30 a.m.

Type 2 Diabetes Does Not Increase the Risk of Depression

Lauren C. Brown, M.S.C., *Department of Public Health, University of Alberta, 1200 10405 Jasper Avenue, Edmonton, AB T5J 3N4, Canada*; Sumit R. Majumdar, M.D., Stephen C. Newman, M.D., Jeffrey Johnson, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize patients with type 2 diabetes do not have an increased risk of developing depression compared with people without diabetes.

Summary:

Objective: To assess the risk of developing new-onset depression in people with incident diabetes.

Methods: We conducted a population-based, retrospective cohort study using the administrative databases of Saskatchewan Health. A cohort of individuals with type 2 diabetes over the age of 20 was identified based on diagnostic codes or prescription records, and were compared with a non-diabetes cohort. Development of new-onset depression, based on diagnostic codes and antidepressant prescriptions, was ascertained. Cox regression analysis was used to estimate the hazards ratio (HR) and 95% confidence intervals (CI), after adjusting for age, sex, and frequency of physician visits.

Results: The incidence of new-onset depression was similar in people with diabetes (6.5 per 1000 person-years) compared with people without diabetes (6.6 per 1000 person-years). The lack of risk persisted after controlling for age, sex, and number of physician visits (adjusted HR: 0.97, 95% CI: 0.88-1.07).

Conclusion: Type 2 diabetes is not associated with an increased incidence of subsequent new-onset depression compared with those without diabetes. Screening for depression in people with type 2 diabetes is no more important than in other chronic medical conditions.

Funding: Canadian Institutes of Health Research (CIHR), and New Emerging Team Grant for Alliance for Canadian Health Outcomes Research in Diabetes (ACHORD).

References:

1. Anderson RJ, Clouse RE, Freedland KE, Lustman PJ: The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care* 2001; 24(6):1069-1078.
2. Carnethon MR, Kinder LS, Fair JM, Stafford RS, Fortmann SP: Symptoms of depression as a risk factor for incident diabetes: findings from the National Health and Nutrition Examination Epidemiologic Follow-Up Study, 1971-1992. *American Journal of Epidemiology* 2003; 158:416-423.

NR29 Monday, May 23, 9:00 a.m.-10:30 a.m.

Psychopathology of Children at Risk for Bipolar Disorder

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Educational Objectives:

At the conclusion of this session, the participant should be able to (1) learn about psychopathology for which children of bipolar parents are at risk, (2) consider appropriate screening for analysis of psychopathology in children, (3) consider psychopathology, which is not increased in children of bipolar parents.

Summary:

Objective: To compare the rates of psychopathology between children with at least one parent with bipolar disorder, type I, and demographically matched children of healthy control parents.

Methods: The Structured Clinical Interview for DSM-IV (SCID) was used to evaluate parental psychopathology (or lack thereof). Children were evaluated for any presence of DSM-IV pathology using the Washington University Kiddie Schedule for Affective Disorders and Schizophrenia (WASH-U KSADS).

Results: 38 children of 29 study families (mean age 10.37 +/- 2.6 years) and 29 children from 29 families without any previous psychiatric pathology in their parents or siblings (mean age 10.07 +/- 1.46 years) were recruited. No significant demographic differences were found between these two groups. 18.4% of the study group met DSM-IV criteria for bipolar disorder, type I (p=0.02) and 13.2% for bipolar disorder type II, (p=0.04). None of the control group met criteria for bipolar disorder I or II. Statistically significant differences in rates of ADHD, ODD/CD, and depression were also present.

Conclusion: Children of parents with bipolar disorder type I were at increased risk for many forms of Axis I pathology, including bipolar disorder types I and II, as well as depressive disorders, ADHD, and ODD/CD. Future studies are needed to determine risk factors associated with specific diagnoses.

References:

1. Delbello MP, Geller B: Review of studies of child and adolescent offspring of bipolar patients. *Bipolar Disorders* 2001; 3:325-334. Munksgaard, 2001.
2. Lapalme M, Hodgins S, LaRoche C: Children of parents with bipolar disorder: a metaanalysis of risk for mental disorders. *Canadian Journal of Psychiatry* 1997; 42:623-631.

NR30 Monday, May 23, 9:00 a.m.-10:30 a.m.

Hepatitis C, Bipolar Disorder, and Alcohol: Implications for Diagnosis and Treatment

Annette M. Matthews, M.D., *Department of Psychiatry, Oregon Health Science, 3591 S.E. Francis, #E, Portland, OR 97202*; Peter Hauser, M.D.

Educational Objectives:

Participants should know that hepatitis C has been targeted as the most important emerging blood-borne pathogen in the Veteran's Administration health care system, bipolar disorder is associated with increased risk of both hepatitis C and alcoholism, and this comorbidity results in unique screening, harm reduction, and prescribing implications for those with bipolar disorder.

Summary:

Objective: To determine the rates of hepatitis C testing and diagnosis and comorbid alcohol abuse or dependence in bipolar veterans.

Method: Subjects included all 112 Veterans enrolled in the Systematic Treatment Enhancement Program for Bipolar Disorder at the Portland Veteran's Administration Medical Center as of August 6, 2004. Charts were reviewed for demographic data, testing and diagnosis of hepatitis C, and current or former substance-use disorder.

Results: 81 (72.3%) were tested for hepatitis C and 10 of these (13.9%) were positive for Hepatitis C. Of the 10 positive for hepatitis C, six had a current or past substance use disorder and in all of them involved alcohol. Of the 31 (28.7%) patients not tested for hepatitis C, 14 (45.2%) had a current or past substance use disorder and in 11 of them involved alcohol. Overall, substance-use disorders were found in 55 (49.1%) with the majority involving alcohol abuse or dependence 50 (91%).

Conclusions: Bipolar disorder is associated with increased risk of alcohol dependence and hepatitis C. This suggests that bipolar patients would benefit from screening and education about alcohol dependence and hepatitis C and mental health professionals should be cautious around their use of potentially hepatotoxic drugs like valproic acid in this population.

References:

1. Mishra G, Sninsky C, Roswell R, Fitzwilliam S, Hyams KC: Risk factors for hepatitis C virus infection among patients receiving health care in a Department of Veterans Affairs hospital. *Digestive Diseases & Sciences* 2003; 48:815-20.
2. el-Serag HB, Kunik M, Richardson P, Rabeneck L: Psychiatric disorders among veterans with hepatitis C infection. *Gastroenterology* 2002; 123:476-82.

NR31 Monday, May 23, 9:00 a.m.-10:30 a.m.

Sleeping Pills and Decreased Longevity

Zujezdan Nuhic, M.D., *Department of Psychiatry, Maimonides Hospital, 232 91st Street, Brooklyn, NY 11209*; Milton Kramer, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be alerted to the controversy over a possible relationship between hypnotic use and decreased longevity.

Summary:

Introduction: Kripke (2002) reported an increased risk of death in sleeping pill users and expressed a concern for those over 65 because they are the heaviest users of sleeping pills.

Method: A review was done of the English language literature on sleeping pill use and mortality between 1979 and 2004.

Results: Kripke (2002) in a study of 1.1 million participants aged 30-102 found in sleeping pill users a 1.25 increase in mortality risk in six years. Kojima (1999) in a study of 5,322 participants aged 20 to 67 at 12-year follow-up found an increased mortality risk of 1.81 but only in female sleeping pill users.

No relationship between sleeping pill use and longevity was found in five studies (Pollak, 1990; Rumble, 1992; Brabbins, 1993; Hays, 1996; and Mallon 2002) with 10,000 participants ranging in age from 45 to 98 with 80% over 65 and a median follow-up period of four years. One study found an increased mortality risk of 2.5 in the elderly associated with analgesic use.

Discussion: A relationship between hypnotic use in the elderly and decreased longevity was not supported. The smaller number of subjects in the five studies and the shorter follow-up period may account for the failure to replicate Kripke (2002).

Conclusion: A prospective study or the examination of other large data bases, e.g. V.A. or H.M.O, with an adequate number of subjects, medication specification, and follow-up time in the elderly would be desirable.

References:

1. Kripke DF, Garfinkel L, Wingard DL, et al: Mortality associated with sleep duration and insomnia. *Arch Gen Psychiatry* 2002; 59:131-136.
2. Hays JC, Blazer DG, Foley DJ: Risk of napping. Excessive daytime sleepiness and mortality in an older community population. *J Am Geriatr Soc* 1996; 44:693-698.

NR32 Monday, May 23, 9:00 a.m.-10:30 a.m.

Antidepressant Treatment and Suicidality in Dysthymic Disorder

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T. Batchelder, Ph.D., Surendra Johri, M.D., David J. Hellerstein, M.D., Steven E. Hyler, M.D.

Educational Objectives:

At the conclusion of this session, the participant should better understand the relationship between antidepressant treatment and suicidality in adult dysthymic patients.

Summary:

Introduction: Recently, the FDA issued a warning that SSRI treatment may increase the risk of suicide in children and adolescents. Given the lack of studies regarding this risk in the treatment of dysthymic disorder (DD), this study examines suicidality in adult patients with DD, newly started on various antidepressants.

Method: Combining data from 144 dysthymic disorder (DD) patients from five completed clinical trials (fluoxetine, bupropion SR, venlafaxine, citalopram, trazodone), we tracked changes in suicidal ideation using the HDRS (Hamilton Depression Rating Scale), CDRS (Cornell Dysthymia Rating Scale), BDI, and SCL items at weeks 0, 2, 4, 6, 8, and 12.

Results: No suicide attempts were reported. Of 78 patients categorized as non-suicidal at baseline (score of 0 on HDRS question 3), 4.5% (n=3) reported suicidal ideation at week 2 (≥ 1 on HDRS q3) and all were non-suicidal at week 8. Suicidal ideation at week 2 was mild, increasing only one point (e.g. feeling "life is not worth living"). Of 66 patients with suicidal thoughts at baseline, 53.1% reported no suicidal thoughts at week 2, and 75.0% became non-suicidal by week 8. Other scales (BDI, CDRS, SCL) showed similar patterns of change.

Conclusion: A mild transient increase in suicidal ideation was seen during initial antidepressant treatment in a small percentage of adult dysthymics who were not suicidal at baseline. This effect disappeared by week 8. Moreover, our analysis shows that antidepressant treatment decreases suicidality in dysthymics who initially have suicidal thoughts.

References:

1. FDA Public Health Advisory 10/15/2004: Suicidality in children and adolescents being treated with antidepressant medications www.fda.gov.
2. Healy D, Whitaker C: Antidepressants and suicide: risk benefit conundrums. *J Psychiatry Neurosci* 2003; 28(5):331-7.

NR33 Monday, May 23, 9:00 a.m.-10:30 a.m.

Do Predictors of Alcohol Abuse/Dependence Also Predict Remission?

Maritza Buenaver, M.D., *Department of Psychiatry, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66163*; Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.A., Joachim Knop, M.D., Per Jensen, M.D., Fini Schulsinger, M.D., William F. Gabrielli, Jr., M.D.

Educational Objectives:

Most variables that predicted the development of alcoholism did not predict its remission in a 40-year followup study.

Summary:

Objective: To determine if premorbid factors that predicted the development of alcohol abuse/dependence also predicted remission from alcoholic drinking.

Method: A group of 360 males have been studied from birth to age 40 in the Danish Longitudinal Study of Alcoholism. Two thirds are high-risk sons of alcoholic fathers. A previous study identified 29 separate variables (out of 450) as putative premorbid markers for alcoholism collected during the prenatal phase, in early and late adolescence and at the 30-year followup. The 29 putative alcoholism markers were tested as predictors of remission. At age 40, 52, of the 202 men studied received a lifetime diagnosis of

alcohol abuse/dependence. Of these, 56% reported no problems with alcohol in the past six months.

Results: Only two of the 29 putative markers for alcoholism were significantly associated with remission at age 40: childhood deviance and childhood antisocial behavior. Two more tended to be associated with remission at $p < .06$, childhood CNS and low number of medical conditions. Surprisingly, *genetic risk did not predict remission from alcoholism*. Variables significantly correlated with remission at age 40 were largely measures of adult coping ability and mental health functioning, which are confounded with alcoholic drinking.

Conclusion: Measures that predicted who would drink alcoholically by age 40 failed to predict those who would stop. George Vallant summarized this finding, saying: "The skills it takes to fall into a hole are not the same skills it takes to crawl out".

References:

1. Moos RH: Why do some people recover from alcohol dependence whereas others continue to drink and become worse over time. *Addiction* 1994; 89:31-34.
2. Vallant GE: A 60-year followup of alcoholic men. *Addiction* 2003; 98:1043-1951.

NR34 Monday, May 23, 9:00 a.m.-10:30 a.m.

Benzodiazepine Use During Psychiatric Inpatient Hospitalization

James L. Megna, M.D., *Department of Psychiatry, State University of New York, UMU, 750 East Adams Street, Syracuse, NY 13210*; Biraj B. Bista, M.B., Arun R. Kunwar, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the pattern of use of benzodiazepine during psychiatric inpatient hospitalization.

Summary:

Objective: To study the prescribing patterns of benzodiazepines during psychiatric inpatient hospitalization.

Method: A retrospective chart review was conducted of all admissions to a university hospital psychiatric unit for a period of six months from March to September, 2001. The following data were obtained via chart review: age, sex, race, marital status, education level, employment status, living arrangement, and diagnosis.

Results: Out of 255 patients admitted during the period, 42 (16%) were prescribed benzodiazepines. Of these 42, 21 were males and 21 were females. Ninety-three percent were Caucasian, while 7% were African Americans. Fifty-four percent of the subjects were unmarried, and 69% had more than a high school education. The vast majority (83%) were unemployed and also living independently. Most (83%) of the subjects had more than one psychiatric diagnosis. The most common diagnoses were mood disorder (61%), followed by substance abuse/dependence disorder (53%). Twenty-one percent had psychotic disorders and 19% had an anxiety disorder diagnosis.

Conclusion: Only a small proportion of the patients is prescribed benzodiazepines during psychiatric hospitalization. The most common diagnoses in this group are mood disorder and substance abuse/dependence disorder.

References:

1. Clark RE, Xie H, Brunette MF: Benzodiazepine prescription practices and substance abuse in persons with severe mental illness. *J Clin Psychiatry* 2004; 65(2):151-5.

2. Stahl SM: Don't ask, don't tell, but benzodiazepines are still the leading treatments for anxiety disorder. *J Clin Psychiatry* 2002; 63(9):756-7.

NR35 **Monday, May 23, 9:00 a.m.-10:30 a.m.**
The Awareness of Complementary and Alternative Medicine (CAM) Amongst Physicians in Upstate New York

James L. Megna, M.D., *Department of Psychiatry, State University of New York, UMU, 750 E. Adams Street, Syracuse, NY 13210*; Nikhil Nihalani, M.D.

Educational Objectives:

At the end of the presentation, the participant should be able to understand the extent and quality of awareness of complementary and alternative medication use by consumers amongst physicians in Upstate New York.

Summary:

Introduction: In 1990, one in four Americans used alternative therapies for treatment; this number has increased to 69% as per recent statistics in 1998. 67% of the health maintenance organizations offer at least one modality of CAM. The current marketplace for CAM is close to 24 billion dollars and is expected to increase at 15% per year.

Aim: A survey was conducted to understand the extent of awareness of the use of complementary and alternative medications amongst physicians in Upstate New York.

Method: A voluntary/anonymous institutional review board-approved survey consisting of nine questions was offered to 354 allopathic physicians in the period of January to March 2004.

Results: 141 surveys were completed and returned to the study team. All were included in the final analysis. The results are discussed in detail in the paper.

Conclusion: The awareness of physicians regarding the use of CAM amongst their patients is increasing. The attitude of physicians toward CAM is becoming more critical. Reassuringly almost all the physicians who were surveyed were aware of the potential of CAM therapies to cause side effects and pharmacokinetic interactions with prescribed medications.

References:

1. Himmel W, Schulte M, Kochen MM: Complementary medicine: are patients' expectations being met by their general practitioners? *Br J Gen Pract* 1993; 43:232-235.
2. Marshall RJ, Gee R, Israel M, Neave D: The use of alternative therapies by Auckland general practitioners. *N Z Med J* 1990; 103:213-215.

NR36 **Monday, May 23, 9:00 a.m.-10:30 a.m.**
How Should a Psychiatrist Dress? A Psychiatrist's Perspective

James L. Megna, M.D., *Department of Psychiatry, State University of New York, UMU, 750 E. Adams Street, Syracuse, NY 13210*; Nikhil Nihalani, M.D., Arun Kunwar, M.D., Jud Staller, M.D., Steven Lamberti, M.D.

Educational Objectives:

At the end of the presentation, the participant should be able to understand what psychiatrists think they should wear to work and how it affects the doctor-patient relationship.

Summary:

Introduction: The importance of a person's attire cannot be stressed enough in the profession of medicine. Traditionally, the

white coat not only helps in defining a physician's personality but also has an impact on the doctor-patient relationship.

Aim: The aim of our study is to throw better light on the effect of dress on the doctor-patient relationship.

Method: A voluntary/anonymous IRB approved survey consisting of nine questions was offered to all psychiatrists, including psychiatrists in training at the State University of New York, Syracuse and at Strong Memorial Hospital, University of Rochester, Rochester, New York.

Results: Out of 78 psychiatrists who responded, all were included in the final analysis. Majority (60%) of responders were male and majority (52.5%) were between the age of 40-60 years. 93% of the respondents thought that dress is an important part of a Psychiatrist's appearance. Most preferred dress for a male psychiatrist was "Shirt tie and dress pants" (32%) and for a female "dress blouse/shirt with pants/skirts" (by 77%). 63% of the psychiatrists surveyed thought that they should not wear a white coat. Majority (30.7%) thought that it has a bad influence on doctor-patient relationship.

Discussion: Most preferred dress for a male psychiatrist was "Shirt, tie and dress pants" and for a female was "dress blouse/shirt with pants/skirts." Majority agreed that they should not wear a white coat. Details of the results are discussed further.

References:

1. Nair BR, Attia JR, Mears SR, Hitchcock KI: Evidence-based physicians dressing: a crossover trial. *Medical Journal of Australia* 2002; 177(11-12):681-2.
2. Gjerdingen DK, Simpson DE, Titus SL: Patients' and physicians' attitudes regarding the physician's professional appearance. *Archives of Internal Medicine*. 1987; 147(7):1209-12.

NR37 **Monday, May 23, 9:00 a.m.-10:30 a.m.**
Cross-Cultural Study of Depression in College Students

Supported by Eli Lilly and Company and Forest Pharmaceuticals

Shamsah B. Sonawalla, M.D., *Department of Psychiatry, Massachusetts General Hospital, WAC 812, 15 Parkman Street, Boston, MA 02114*; Rajesh M. Parikh, M.D., Santvana Sharma, M.D., Nabonita Chakraborty, M.D., Steven A. Safren, Ph.D., Albert Yeung, M.D., Maurizio Fava, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that depression is prevalent among college students across cultures and that it is important to screen for depression and plan effective intervention strategies in this population.

Summary:

Objective: Previous studies have reported significant depressive symptoms among college students. The purpose of this study was to compare the prevalence and symptom patterns of depression among college students in Bombay and Boston.

Methods: We screened 2,058 college students over the age of 18 years across Boston (N=701) and Bombay (N=1357) (Mean age: Boston: 21 years \pm 3.0 years; Bombay: 19.3 \pm 1.5 years; $t=-16.9$; $p<0.0001$; gender: Boston: 54.3% women, Bombay: 56% women; Chi Square=0.3; $p=0.6$, NS). After obtaining written, informed consent, the Beck Depression Inventory (BDI) and Symptom Questionnaire were distributed to all students. Chi-square tests, unpaired t-tests, and logistic regression were used for data analysis.

Results: The prevalence of significant depressive symptoms (total score of ≥ 16 on BDI) was 14.2% among college students in Boston and 24.0% among college students in Bombay; this

difference was statistically significant after adjusting for age ($p < 0.0001$). The prevalence of suicidal ideation (defined as a score of ≥ 1 on item #9 on the BDI) was 16.4% among college students in Boston and 25.0% among college students in Bombay; this difference was also statistically significant after adjusting for age ($p < 0.0001$). There were no significant differences across SQ subscales of anxiety, somatic symptoms, and anger-hostility across the two groups. However, college students in Bombay scored significantly higher on SQ-depression subscale compared with college students in Boston.

Conclusions: Significant differences in depressive symptoms and suicidal ideation among college students were noted cross-culturally across two countries. Our study emphasizes the importance of screening for depression among college students and the need to plan effective intervention strategies in this population.

References:

1. Peden AR, Hall LA, Rayens MK, Beebe L: Negative thinking mediates the effect of self-esteem on depressive symptoms in college women. *Nursing Res* 2000; 49(4):201-207.
2. Sonawalla SB, Kelly K, Neault N, Farabaugh A, Almeida D, Yeung A, Mischoulon D, Pava J, Otto M, Fava M: Predictors of suicidal ideation in a college population. 154th Annual Meeting of the American Psychiatric Association. New Orleans, 2001.

NR38 Monday, May 23, 9:00 a.m.-10:30 a.m.

Effects of Atypical Antipsychotics on Cognition and Outcome in Adolescents

Supported by AstraZeneca Pharmaceuticals

Liza A. Maldari, M.A., *Department of Research/Psychiatric Testing, Four Winds Hospital, 800 Cross River Road, Katonah, NY 10536*; David L. Pogge, Ph.D., Laura Coraci, M.A., Nicholas de Spaelberch, B.A., John Stokes, Ph.D., Philip D. Harvey, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the effects that atypical antipsychotics have on the cognition and functional outcome of a sample of adolescent psychiatric inpatients.

Summary:

Objective: Atypical antipsychotics medications have been found to lead to moderate improvements in aspects of cognitive functions in adult patients with schizophrenia. While they are commonly used in conditions other than schizophrenia, it is not clear whether these medication have similar cognitive benefits in non-schizophrenic adolescents or children.

Method: Non-schizophrenic adolescent psychiatric inpatients ($n=75$) were examined with a cognitive assessment prior to treatment with atypical antipsychotics. Measures of working memory, executive functioning, verbal fluency, attention, episodic memory, and functional outcome were administered at this time. They were reassessed at discharge and 120 days after discharge to assess their cognitive and functional status.

Results: Statistically significant improvements in episodic memory, attention, working memory, executive functioning, and verbal fluency were detected. Improvements in cognitive functions were associated with social functioning at follow-up, but not with residual symptom status.

Conclusions: Treatment-related changes in cognitive functioning were similar to those reported for patients with schizophrenia and the longer follow-up allowed for examination of functional status.

This study is funded by an investigator-initiated grant to David Pogge, Ph.D. from Astra-Zeneca Pharmaceuticals, L.P.

References:

1. Keefe RSE, Silva SG, Perkins DO, Lieberman JA: The effects of atypical antipsychotic drugs on neurocognitive impairment in schizophrenia: a review and meta-analysis. *Schizophrenia Bulletin* 1999; 25(2):201-222.
2. Meltzer HY, Sumiyoshi T: Atypical antipsychotic drugs improve cognition in schizophrenia. *Biological Psychiatry* 2003; 53(3):265-267.

NR39 Monday, May 23, 9:00 a.m.-10:30 a.m.

Personality Factors Affecting Patients' Preferences Among Medications

Isaac L. Meek, B.S., *Center for Attention, 2129 Belcourt Avenue, Nashville, TN 37212*; Robert D. Hunt, M.D., Brandon S. Vestal, B.A.

Educational Objectives:

At the conclusion of this session, participants will understand the role of personality factors as potential modulators of ADHD patients' preferences among psychostimulant medications.

Summary:

Objective: Our prior research has demonstrated a preference for short-acting amphetamine salts vs. MPH in about 60% of ADHD adults. This study determined the relationship of personality characteristics in addition to clinical diagnosis on patient preference among long-acting psychostimulant medications.

Method: DSM-IV diagnosis utilized the SCIDS; personality characteristics were measured using the Millon Personality Inventory in 30 adults with ADHD and no other significant DSM-IV comorbidities. Patients were then treated with two weeks each of Adderall XR (ADRL), and methylphenidate (MPH) (Oros) in a random, blinded sequence using functionally equivalent doses. The Conner's Adult ADHD RS and an ADD Side Effects Scale were used to determine overall clinical benefit. Patients then rated their preference of medication and reasons for selection.

Results: Although overall clinical response was about equivalent, patients' baseline personality characteristics impacted their medication preference. Patients who at baseline had lower energy and arousal tended to prefer ADRL; those who were more impulsive and dysinhibited, tended to prefer MPH.

Conclusions: These findings suggest a relationship between pretreatment personality characteristics and patients' subsequent preference among long-acting psychostimulant medications, that may help clinicians better match the treatment to the personalities of their patients.

References:

1. Depue R, Collins PF: Neurobiology of the Structure of Personality: Dopamine, Facilitation of Incentive Motivation, and Extraversion.
2. Rogers PJ, Martin J, Smith C, Heatherley SV, Smit HJ: Psychopharmacology (Berl) 2003; 167(1):54-62.

NR40 Monday, May 23, 9:00 a.m.-10:30 a.m.

Monitoring Response to Psychostimulant Medication Using a PDA (PATS)

Brandon S. Vestal, B.A., *Center for Attention, 2129 Belcourt Avenue, Nashville, TN 37212*; Robert D. Hunt, M.D., Isaac L. Meek, B.S.

Educational Objectives:

At the conclusion of this session, participants will recognize the usefulness and reliability of using PDAs to track medication

response in adults and adolescents. PATS is a helpful tool in establishing the preferred medication and its optimal dose.

Summary:

Purpose: Since an analogue classroom is inappropriate for monitoring medication response in adults, we developed a palm-pilot based paradigm for tracking medication response throughout the day.

Method: A Palm Pilot Attention Tracking System (PATS) prompts patients every two hours (8 am-10 pm) to record their task, attention, organization, mood, and discomfort. This was utilized in 30 ADD adults during a comparison of MPH and ADDERALL. Tasks are rated for complexity, familiarity, learning required, subjective interest, degree of sensory stimulation and interaction, and the demand on attention. For patients with internet connectivity, results could be forwarded to our office on a daily or weekly basis as needed. Patients' satisfaction and compliance was assessed after use in a one-month crossover therapeutic trial.

Results: The (PATS) was well accepted by patients, evident by a 85% compliance with 91% reporting that the system was easy to use. The PATS was clinically useful in helping clinicians regulate the dose and duration of effect of medication.

Discussion: The PATS appears useful for establishing the preferred medication and determining the optimal dose and duration in adults.

NR41 Monday, May 23, 9:00 a.m.-10:30 a.m.
Patients' Satisfaction With Hospitalization in a Mixed Psychiatric and Somatic Care Unit

Ariel Eytan, M.D., *Department of Psychiatry, Hug-Belle-Idee, 2 CH Petit-Bel-Air, Geneva 1225, Switzerland*; Laurence Bovet, M.D., Christel Alberque, M.D., Marianne Gex-Fabry, M.S.C.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the determinants of patients' satisfaction in a mixed psychiatric and somatic care unit. The results of a survey conducted in such a program in Geneva, Switzerland, are presented.

Summary:

Objective: To assess patients' satisfaction with hospitalization in a mixed psychiatric and somatic care unit.

Method: We designed an ad hoc self-administered satisfaction questionnaire to capture patients' satisfaction with both psychiatric and somatic dimensions of care. The survey was proposed anonymously to all hospitalized patients over a 12-week period.

Results: The questionnaire was completed by 60 patients. Median age was 42 (range 20-64), and the majority were female (63%). Main ICD-10 diagnostic categories were depressive disorders (52%), substance-related disorders (33%), and personality disorders (25%). Somatic comorbidity was present in 60% of patients. Overall satisfaction with care and setting was high. Higher satisfaction was significantly associated with a history of previous hospitalizations in a psychiatric hospital and with being referred to the program by a psychiatrist.

Conclusions: These findings emphasize the perceived advantages of mixed units, such as decreased stigmatization of psychiatric inpatients and opportunity to receive adequate treatment for both physical and mental problems during a single hospital stay.

References:

1. Gertler RE, Kopec-Schrader EM, Blackwell CJ: Evolution and evaluation of a medical psychiatric unit. *Gen Hosp Psychiatry* 1995; 17(1):26-31.
2. Harsch HH, Koran LM, Young L: A profile of academic medical-psychiatric units. *Gen Hosp Psychiatry* 1991; 13(5):291-5.

NR42 Monday, May 23, 9:00 a.m.-10:30 a.m.

Social Phobia Symptoms and Comorbidity With Specific Phobia: A Study of 850 Young Israeli Soldiers

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Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize issues regarding the epidemiology of social phobia across various countries and cultures, as well as about the comorbidity with specific phobia.

Summary:

Background: Social phobia (SP) and specific phobia are highly prevalent disorders and there is a high comorbidity rate. The aims of this study were to assess the prevalence of SP and specific phobia symptomatology in a non-clinical sample of Israeli young adults.

Methods: 850 young soldiers from the Israel Defense Forces participated in our study. Measures included the Liebowitz Social Anxiety Scale (LSAS; self-report version), a self-report questionnaire on specific phobias, and a socio-demographic questionnaire. Data on specific fears representing DSM-IV-TR specific phobias were analyzed to evaluate prevalence, comorbidity rate with SP symptomatology, and potential socio-demographic correlates.

Results: SP symptomatology was reported by a high percentage of the subjects, as displayed by the rather high mean LSAS scores in this non-clinical sample (mean LSAS=29). According to our cutoff point (LSAS score>79), 4.5% of the sample scored positive for SP. The prevalence of fears and phobias in our sample was 49.1% and 8.7%, respectively. The most frequent fears and phobias were from animals, heights, injury, and closed places. We found a significant positive correlation between the number of phobias and the LSAS score. Those with positive SP (LSAS > 79) had a 50% chance of also having a specific phobia. The following variables were accompanied by a greater number of phobias: male gender, role of soldier (mechanic), no matriculation exams, not being presently involved in a romantic relationship, not having at least two good friends, mental treatment before enlistment, mental treatment during the military service, and receiving psychotropic medications in the past.

Conclusions: Our findings corroborate findings from other studies in the Western world, regarding both the high prevalence of SP symptoms and specific phobias, as well as the high comorbidity rate between the two disorders.

References:

1. Kessler RC, Stein MB, Berglund P: Social phobia subtypes in the National Comorbidity Survey. *Am J Psychiat* 1998; 155:613-9.
2. Hwu HG, Yeh EK, Chang LY: Prevalence of psychiatric disorders in Taiwan defined by the Chinese Diagnostic Schedule. *Acta Psychiat Scandinavica* 1989; 79:136-147.

NR43 Monday, May 23, 9:00 a.m.-10:30 a.m.

The DRD4 48-bp-Repeat Polymorphism and Mood Disorders: A Meta-Analysis

Sandra Lopez Leon, M.D., *Genetic Epidemiology, Erasmus Medical Centre, Weimarstraat 122, Den Haag 2562 HC, Netherlands*; Esther Croes, M.D., Fakhredin Sayed-Tabatabae, M.D., Stephen Claes, M.D., Christine Van Broeckhoven, Ph.D., Cornelia van Duijn, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that meta-analyses are a valuable objective tool

for a quantitative summary of evidence for association studies in psychiatric genetics.

Summary:

Introduction: The role of the DRD4 48-bp-repeat polymorphism in mood disorders has been studied in a large number of studies, but the findings were not consistent. The possibility remains that these studies were underpowered due to their small sample size. The current study re-examines all published papers on association between this polymorphism and mood disorders available up to February 2004. 1616.

Methods: Frequencies of the three most prevalent alleles (2-repeat, 4-repeat, and 7-repeat) of the DRD4 48 bp-repeat polymorphism were compared between 917 patients with unipolar (UP) or bipolar affective disorder (BP), and 1,164 controls from 12 samples, using the Cochrane Review Manager.

Results: After correcting for multiple testing, a significant association was found for the DRD4 two-repeat allele in two groups: UP (OR 1.73, 95% CI 1.29-2.32, $P < 0.01$), and UP and BP combined (OR 1.41, 95% CI 1.18-1.68, $P < 0.01$). There was no evidence for heterogeneity or publication bias.

Conclusion: This meta-analysis showed evidence for a positive association of the DRD4 two-repeat allele with mood disorders. Meta-analysis may be a valuable objective tool for a quantitative summary of evidence for association studies in psychiatric genetics.

References:

1. Lohmueller KE, Pearce CL, Pike M, Lander ES, Hirschhorn JN: Meta-analysis of genetic association studies supports a contribution of common variants to susceptibility to common disease. *Nat Genet* 2003; 33:177-82.1616.
2. van Duijn CM, Porta M: Good prospects for genetic and molecular epidemiologic studies in the European Journal of Epidemiology. *Eur J Epidemiol* 2003; 18:285-6.

NR44 Monday, May 23, 9:00 a.m.-10:30 a.m.

Can Self-Reported Health Independently Predict Mortality?

Xingjia Cui, M.D., *Department of Psychiatry, University of Rochester Medical Center, 610 Elmwood Ave, Rochester, NY 14642*; George Vaillant, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should have knowledge of whether self-reported health can independently predict mortality.

Summary:

Method: Self-reported health indicated by 273 college men at age 50 and 306 core city men at age 60 were used to predict the 27-year and six-year all-cause and cause-specific mortality of college and core city samples, respectively. The prediction was examined while controlling for variables of objective physical health, DSM-alcohol abuse, maturity of defense, mood altering drug use, and smoking.

Results: It was illustrated that self-reported health status could not adequately and independently predict all-cause, cause-specific mortality, and its indicative of predicting effect is actually confounded by objective physical health and alcohol abuse in College sample and objective physical health and maturity of defense in core city sample. After controlling for the confounding variables, the hazard ratio of poor and fair VS. good and excellent health was reduced from 2.6 (95%CI: 1.49-4.9) to 1.2 (95%CI: 0.5-2.9) for College sample and from 2.2 (95%CI: 1.1-4.5) to 1.4 (95%CI: 0.6-3.3) for Core City sample.

Conclusion: This study failed to identify independent predicting effect of self-reported health on mortality. Objective physical health and other population-specific variables confound its seemingly predicting power.

References:

1. Kaplan GA, Camacho T: Perceived health and mortality: a nine-year follow-up of human population laboratory cohort. *American Journal of Psychiatry* 1983; 117(3):292-304.
2. Weinberger M. et al: The effects of positive and negative life changes on the self-reported health status of elderly adults. *Journal of Gerontology* 1986; 41(1):114-119.

NR45 Monday, May 23, 9:00 a.m.-10:30 a.m.

Behavioral Effects of Caffeinated Cola Consumption in First Graders

Alan R. Hirsch, M.D., *Department of Psychiatry, Rush-Presbyterian, 845 North Michigan Avenue, Suite 990W, Chicago, IL 60611-2201*; Ying Ye

Educational Objectives:

At the conclusion of this presentation, participants should be able to recognize effects of caffeinated cola consumption on young children.

Summary:

Introduction: Use of caffeinated cola by children is ubiquitous in our society. The potential psychological effects of this include DSM-IV caffeine induced anxiety and sleeping disorders, and withdrawal symptoms. Manufactures continue to add caffeine to cola, and target young children for marketing, despite that the effects of caffeinated cola in this age group have not been explored.

Methods: In a double-blinded fashion, 20 first graders were presented with caffeine-free cola and caffeinated cola for ad lib consumption in three-hour epochs sequentially over two weeks. Average consumption of caffeine-free cola and of caffeinated cola was 7.55oz and 9.45oz, respectively. After completion of each session, teachers rated each student with a six question modified Connors test.

Results: The modified Connors score was an average of 5.45 points higher for caffeine than for caffeine-free cola. ($p = 0.0017$) In response to caffeine intake, the number of students whose scores increased compared with those whose scores decreased was also significant, (60% vs. 12%, $p = 0.0079$). There was still a significant increase in the Connor score comparing caffeine with caffeine-free soda after adjusting for number of ounces. ($t = 2.69$, $p = 0.0151$)

Conclusion: First graders manifested behavioral problems when presented with caffeinated cola, suggesting that consumption of this should be minimized.

References:

1. Hale KL, Hughes JP, Oliveto AH, Higgins St: Caffeine self-administration and subjective effects in adolescents. *Exp Clin Psychopharmacol*.
2. Goldstein A, Kaizer S, Warren R: Psychotropic effects of caffeine in man. II. Alertness, psychomotor coordination, and mood. *J Pharmacol Exp Ther* 1965; 150:146-151.

NR46 Monday, May 23, 9:00 a.m.-10:30 a.m.

P50 Sensory Gating Differences Related to the Receptor Affinity of Newer Antipsychotics

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Ph.D., Robert Thoma, Ph.D., Kimberly Martin, B.A., Mingxiang Huang, Ph.D., Gregory Miller, Ph.D., Jose Canive, M.D.

Educational Objectives:

At the conclusion of this poster presentation, the participant should be able to have basic understanding of the sensory gating deficit in schizophrenia and how the level of gating may be used as a neurophysiological indicator of medication-related differences.

Summary:

Introduction: EEG (electroencephalography)-derived P50 sensory gating is a measure of impaired stimulus filtering, shown as an increase in the ratio of the 2nd click amplitude (S2) over the first (S1) in an auditory paired-click paradigm. Recent reports suggest that atypical antipsychotics are associated with less gating impairment than typical antipsychotics. We examined whether this relationship is medication-specific and related to dopamine receptor binding affinity.

Methods: In decreasing D2 binding affinity, schizophrenia patients receiving haloperidol (n=10), risperidone (n=8), and quetiapine (n=6) for at least three months were selected for this analysis. Both schizophrenia patients and control subjects (n=48) were run on a standard auditory paired-click paradigm (ISI=500ms) during EEG collection.

Results: As a group, schizophrenia patients in general had worse sensory gating (higher gating ratios) than controls (patients=.56, controls=.41, p=.074). Schizophrenia patients were then divided into medication groups resulting in the following gating averages: haloperidol=.65, risperidone=.56, quetiapine=.48. Using ANOVA with contrasts, each medication group was then compared with the control group: haloperidol p=.035, risperidone p=.232, quetiapine p=.924. This pattern suggests better gating as a function of decreased D2 binding affinity. In particular, quetiapine is associated with gating ratios indistinguishable from controls. Larger studies are likely to provide additional insight into the neurotransmitters involved in the gating machinery as well as neurophysiological phenomena in schizophrenia.

References:

1. Adler LE, Cawthra EM, McRae KA, et al: Varied effects of atypical neuroleptics on P50 auditory gating in schizophrenia patients, *AM J Psychiatry* 2004; 161:10, 1822-1828.
2. Light GA, Geyer MA, Clementz BA et al: Normal P50 suppression in schizophrenia patients treated with atypical antipsychotic medications. *Am J Psychiatry* 2003; 157:5, 767-771.

NR47 Monday, May 23, 9:00 a.m.-10:30 a.m.

Sensory Gating, Prefrontal Cognition, and COMT Polymorphism in Schizophrenia

Brett Y. Lu, M.D., *Department of Psychiatry, University of New Mexico Health Sciences Center, MSC 09-5030, 1 University of New Mexico, Albuquerque, NM 87131-0001*; Kimberly Martin, B.A., Robert Thoma, Ph.D., Faith Hanlon, Ph.D., Gregory Miller, Ph.D., Jose Canive, M.D.

Educational Objectives:

At the conclusion of this poster presentation, the participant should be able to have basic understanding of the sensory gating deficit in schizophrenia and how such a trait can be used as an endophenotype to explore the cognitive deficits and the genetic basis of schizophrenia.

Summary:

Introduction: As a measure of information filtering in schizophrenia, EEG (electroencephalography)-derived P50 sensory gating deficit is shown as an increase in the ratio of the 2nd click amplitude (S2) over the first (S1) in an auditory paired-click paradigm. Given the correlation between prefrontal impairment and COMT poly-

morphism (catechol O-methyltransferase), we investigated whether this interaction invokes a physiological defect in sensory gating. The Val allele of COMT increases dopamine metabolism and leads to prefrontal cognitive deficits.

Methods: Control and schizophrenia subjects underwent EEG/MEG (magnetoencephalography) testing to generate P50 and LM50/RM50 (left and right hemisphere MEG variants of P50). To assess prefrontal function, working memory impairment was measured as perseverative errors on the Wisconsin Card Sort Test (WCST).

Results/Significance: Schizophrenia subjects had worse gating, or higher S2/S1 ratio, for P50 (p<.019) and LM50 (p<.002) but not RM50. Only LM50 gating correlated significantly with WCST perseverative errors, for controls (p<.032) and patients (p=.000). COMT analysis showed higher P50 gating ratios associated with Val allele load in schizophrenia patients: (gating ratio average for 0 copy = .499, one copy = .588, two copies = .747). In addition, the few patients with the worst P50, LM50, or WCST performance were consistently found among Val homozygotes. These results support that (1) increased prefrontal dopamine metabolism can lead to impaired stimulus filtering and (2) such filtering defect, when localized to the left temporal lobe, results in prefrontal cognitive deficits, substantiating a disrupted temporal-prefrontal connectivity as a cardinal feature of schizophrenia.

References:

1. Egan M, Goldberg T, Kolachana B et al: Effect of COMT Val 108/158 Met genotype on frontal lobe function and risk for schizophrenia. *PNAS* 2001; 98(12):6917-6922.
2. Thoma R, Hanlon F, Moses S et al: Lateralization of auditory sensory gating and neuropsychological dysfunction in schizophrenia. *Am J Psychiatry* 2003; 160:1595-1605.

NR48 Monday, May 23, 9:00 a.m.-10:30 a.m.

Characterization of 424 Admissions and Readmissions in an Acute Geriatric Psychiatric Inpatient Unit

Benjamin K.P. Woo, B.S., *GeroPsy Department, UCSD School of Medicine, 5162 Hermosa Avenue, Los Angeles, CA 90041*; Daniel D. Sewell, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to: (1) understand how an acute inpatient geriatric psychiatry inpatient unit may be optimally utilized; (2) characterize the group of patients with multiple admissions; (3) identify particular admission variables associated with readmission.

Summary:

Objective: The purpose of this analysis was to determine if, upon hospital admission, particular patient characteristics could be linked to readmission to an acute geriatric psychiatry inpatient unit.

Methods: We collected demographic data on 424 voluntary admissions to a senior behavioral health inpatient unit at a university hospital during a period of 20 consecutive months. Pertinent demographic data at first admission for 338 patients, 65 of whom were admitted more than once, were analyzed.

Results: Among the 424 consecutive admissions, 64.4% (N=273) were single admissions, and 35.6% (N=151) were multiple admissions. Among the 338 unique patients admitted, 19.2% (N=65) were admitted more than once. Demographic characteristics of all the patients were compared with the single admission group and the group with multiple admissions. The only variable that significantly differentiated patients who were readmitted was male gender (p<0.01). Psychiatric diagnoses were similar for both groups.

Conclusions: Findings suggest that male patients are more likely to be readmitted. Further understanding of the factors that increase the probability of rapid readmission to acute geriatric psychiatry inpatient units could increase the quality of life of these patients and their family members as well as decrease the costs of caring for these patients.

References:

1. Kunik ME, et al: Health care utilization in dementia patients with psychiatric comorbidity. *The Gerontologist* 43(1):86-91.
2. Bernardo AC, Forchuk C: Factors associated with readmission to a psychiatric facility. *Psychiatric Services* 2001; 52(8):1100-1102.

**NR49 Monday, May 23, 9:00 a.m.-10:30 a.m.
Dilated Cardiomyopathy Associated With Clozapine**

Sungwon Roh, M.D., *Department of Neuropsychiatry, Hanyang University Hospital, 17 Haengdang-dong, Seongdong-gu, Seoul 133-792, Korea*; Dong Hyun Ahn, M.D., Jung Hyun Nam, M.D., Yang Suk Kim, M.D., Sun Kyoung Choi, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize clozapine-related cardiac complications such as cardiomyopathy.

Summary:

Introduction: Clozapine is an atypical antipsychotic agent that is more effective than the standard neuroleptics in the treatment of a patients with refractory schizophrenia. However, clozapine is also a drug associated with certain potentially serious adverse effects, such as cardiac complications as well as agranulocytosis. Clozapine-related agranulocytosis has been reported in Korea, whereas clozapine-related cardiac complications have never been reported. Case: In this report, it is found that a 31-year-old male schizophrenia treated with clozapine has developed a dilated cardiomyopathy. Especially the second trial of clozapine for managing relapse of psychotic symptoms caused a recurrence of dilated cardiomyopathy.

Discussion: To conclude, this report has attempted to raise an awareness of clozapine-related cardiac complications such as cardiomyopathy.

References:

1. Kilian JG, Kerr K, Lawrence C, Celermajer DS: Myocarditis and cardiomyopathy associated with clozapine. *Lancet* 1999; 354:1841-1845.
2. Grenade LA, Graham D, Trontell A: Myocarditis and cardiomyopathy associated with clozapine use in the United States. *N Engl J Med* 2001; 345:224-225.

**NR50 Monday, May 23, 9:00 a.m.-10:30 a.m.
Visual Continuous Performance Test Event-Related Potential in Patients With Chronic Liver Disease**

Sungwon Roh, M.D., *Department of Neuropsychiatry, Hanyang University Hospital, 17 Haengdang-dong, Seongdong-gu, Seoul 133-792, Korea*; Jung Hyun Nam, M.D., Sun-Kyoung Choi, M.D., Chang Woo Han, M.D., Seon-Cheol Park, M.D., Joonho Choi, M.D.

Educational Objectives:

At the conclusion of the presentation, the participants should be able to recognize the effect of chronic liver disease on brain dysfunction.

Summary:

Objective: The purpose of this study is to determine the effect of chronic liver disease by visual continuous performance test event-related potential(ERP), EEG, and neurocognitive function test.

Methods: Subjects were composed of 17 patients with chronic hepatitis and 39 with liver cirrhosis. We used ERP for analyzing cognitive executive function of chronic liver disease patients. ERP amplitudes were evaluated for brain activity; ERP latencies were evaluated for brain reactivity. Visual continuous performance test was tested as neuropsychological test.

Results: In patients with liver cirrhosis, ERP latencies were longer than chronic hepatitis on the midline of brain(Fz, Cz, Pz). Among patients with liver cirrhosis, ERP latencies of patients with Child A liver cirrhosis were longer than those of Child B and C. ERP amplitudes got smaller according to severity of chronic liver disease.

Conclusion: It suggests that patients with chronic liver disease have brain dysfunction. And the more severe liver disease they have, the worse brain cognitive function they have.

References:

1. Moeller FG, Barratt ES, Dougherty DM, Schmitz JM, Swann AC: Psychiatric aspect of impulsivity. *Am J Psychiatry* 2001; 158:1783-1793.
2. Groeneweg M, Moerland W, Quero JC, Hop WCJ, Krabbe PF, Schalm S: Screening of subclinical hepatic encephalopathy. *J Hepatol* 2000; 32:748-753.

**NR51 Monday, May 23, 9:00 a.m.-10:30 a.m.
Persisting Psychiatric Morbidity Related to Delusional Misperception in Delirium**

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Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that delirious patients form memories of psychotic experiences, especially perceptual distortions leading to increased distress and greater risk for enduring psychiatric morbidity.

Summary:

Delirium affects up to 80% of medically ill hospitalized patients. Research has focused on predictive risk factors and on developing assessment tools and treatment strategies. Little effort has been focused on specific symptoms and there effect on delirium recall, the delirium experience and subsequent post delirium morbidity. We report a case series of delirious patients who experienced delusional misperception with significant distress and persisting post delirium psychiatric morbidity.

The first patient was hospitalized with respiratory failure and developed delirium with delusional misperception of his ventilation tube as being a lobster placed in his throat by his persecutors. He retained a clear memory of the psychotic symptoms with subsequent posttraumatic stress disorder.

The second patient was hospitalized for treatment of cervical cancer and developed delirium with delusional misperception of surrounding stimuli as she experienced faces as grotesque, monstrous and threatening. She formed memories of these delusions with resultant anxiety symptoms.

The third patient was hospitalized for treatment of prostate cancer and developed delirium with the misperception of being dead after a clock in his room was stopped. This caused extreme dis-

tress and he refused to communicate until the cause of his terror was identified and remedied.

This case series highlights the importance of detailed exploration of specific symptomatology in delirium as patients may form memories of psychotic symptoms resulting in increased risk of ongoing psychiatric morbidity and simple environmental intervention may reduce this risk.

References:

1. Cole MG: Delirium in elderly patients. *Am J Geriatric Psychiatry* 2004; 12(1):7-21.
2. Breitbart W, Gibson C, Tremblay A: The delirium experience: delirium recall and delirium-related distress in hospitalized patients with cancer, their spouses/caregivers and their nurses. *Psychosomatics* 2002; 43(3):183-94.

NR52 Monday, May 23, 9:00 a.m.-10:30 a.m.

Association Between the COMT Val158Met Polymorphism and Alexithymia

Byung-Joo Ham, Ph.D., *Department of Neuropsychiatry Hangang Sacred Heart, Hallym University, 94-200 Youngdungpo-Dong, Youngdungpo-Gu, Seoul 150-719, Korea;* Min-Soo Lee, Ph.D., *Ihn-Geun Choi, Ph.D.*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the association between the COMT Val158Met polymorphism and alexithymia.

Summary:

It has been suggested that characteristics of alexithymia may be the result of deficits in frontal lobe functioning. The prefrontal cortex is particularly dependent on the catechol O-methyltransferase (COMT) pathway. We investigated the relationship between (COMT), serotonin transporter coding sequence (5-HT transporter gene-linked polymorphic region, 5-HTTLPR) polymorphisms, and alexithymia. The study sample comprised 109 medical students at Korea University Medical School. All participants were tested using the 20-item Toronto Alexithymia Scales (TAS-20). They were genotyped for COMT Val158Met and 5-HTTLPR polymorphisms. Genotyping was analyzed using polymerase chain reaction. Our results suggest that TAS-20 scores are associated with the COMT Val158Met genotype. However, there was no significant relationship between the 5-HTTLPR genotype and TAS-20 scores. We found a possible association between the COMT Val158Met gene polymorphism and alexithymia.

References:

1. Egan MF, Goldberg TE, Kolachana BS, et al: Effect of COMT Val108/158 Met genotype on frontal lobe function and risk for schizophrenia. *Proc Natl Acad Sci U S A* 2001; 98:6917-22.
2. Taylor GJ, Bagby RM, Parker JDA: *Disorders of Affect Regulation: Alexithymia in Medical and Psychiatric Illness.* New York: Cambridge University Press, 1997.

NR53 Monday, May 23, 9:00 a.m.-10:30 a.m.

Rates of Substance Use, Dependence, and Comorbid Psychiatric Disorders in Cocaine-Dependent Individuals Compared With Community-Based Controls: Results From the Family Study of Cocaine Dependence

Jeremy R. Thompson, M.D., *5433 Lindenwood Avenue, St. Louis, MO 63109;* Laura Bierut, M.D., *Jaime Kleinheider, M.A., Stephanie Afful, B.A.*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the rates of comorbid substance use, dependence, and psychiatric disorders among a population of cocaine dependent individuals compared with community based controls.

Summary:

Introduction: Polysubstance use, dependence, and psychiatric comorbidity are commonly observed among cocaine dependent individuals. This study compared substance use, dependence, and psychiatric disorders between cocaine dependents and community based controls as part of the Family Study of Cocaine Dependence.

Methods: 460 individuals aged 18-62 who met DSM-IV criteria for cocaine dependence were recruited from area treatment centers. 348 community based controls were recruited for comparison. Subjects and controls were evaluated using the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) with an expanded cocaine section.

Results: Overall, cocaine dependents were significantly more likely to use and be dependent on substances and to have psychiatric disorders than controls. Significant differences were found for dependence among several classes of substances and psychiatric disorders including tobacco (70% vs. 35%), alcohol (64% vs. 27%), marijuana (44% vs. 18%), opiates (23% vs. 5%), depression (43% vs. 25%), psychosis (27% vs. 17%), mania (28% vs. 9%), and post-traumatic stress disorder (36% vs. 22%). While rates of substance use, dependence, and psychiatric disorders among controls were significantly less than cocaine dependents, they were higher than established rates for the general population.

Conclusion: Cocaine dependent individuals represent a population with increased vulnerability for substance use, dependence and psychopathology.

References:

1. Bucholz K, Cadoret R, et al: A new, semi-structured psychiatric interview for use in genetic linkage studies: a report on the reliability of the SSAGA. *J Stud Alcohol* 1994; 55(2):149-158.
2. Warner LA, Kessler RC, et al: Prevalence and correlates of drug use and dependence in the United States. Results from the National Comorbidity Survey. *Arch Gen Psychiatry* 1995; 52(3):219-229.

NR54 Monday, May 23, 9:00 a.m.-10:30 a.m.

Eating Behaviors and Associated Psychopathology in Patients With Schizophrenia

Sun Young Yum, M.D., *Department of Mental Health & Behavioral Sciences, East Orange VAMC, 385 Tremont Ave, East Orange, NJ 07018;* Michael Y. Hwang, M.D.

Educational Objectives:

At the conclusions of the presentation, the participants should be able to recognize characteristic eating behaviors and associated psychopathological features that may predict metabolic outcome in patients with schizophrenia.

Summary:

Objective: To determine whether eating patterns and associated psychological characteristics can predict metabolic morbidity in schizophrenia.

Method: As a longitudinal observation study of eating behaviors and metabolic profiles in schizophrenia, we have thus far recruited 53 clinically stable, well-established male patients with schizophrenia from an urban VA outpatient clinic. Metabolic profiles were obtained from chart review. Psychological profiles were compiled from TFEQ, PAS, BASIS-32, and food preference survey. Spearman correlation tests were performed using SPSS Win11.5.

Results: Disinhibited eating behaviors correlated positively with hunger sensations ($p=0.000$) and distress from relationships ($p=0.006$), daily role function ($p=0.001$), depression/anxiety ($p=0.000$), impulsivity ($p=0.002$), psychosis ($p=0.010$). Disinhibited eating also had positive correlations with BMI ($p=0.001$), triglycerides ($p=0.010$) and negative correlations with HDL-cholesterol ($p=0.005$). Triglyceride levels were associated with distress associated with relationships ($p=0.020$), daily role function ($p=0.011$), depression/anxiety ($p=0.002$) and preferences for carbohydrate-fat dominant foods ($p=0.003$). Anhedonia negatively correlated with carbohydrate preferences ($p=0.008$) and had a negative correlation trend with preferences for carbohydrate-fat rich foods ($p=0.054$).

Conclusions: Our observations suggest that characteristic eating behaviors may be associated with increased metabolic morbidity in patients with schizophrenia and that such eating disturbances are associated with distinct psychopathological profiles.

References:

1. Yum SY: The starved brain: eating behaviors in patients with schizophrenia. *Psychiatric Annals*, in press.
2. Yum SY, Hwang MY: Demographic, metabolic, and psychopathologic profiles in normal weight and overweight/obese patients with schizophrenia. American Medical Association-Residents & Fellows Section 1st annual research poster symposium, pr 58. Atlanta, GA; Dec 3, 2004.

NR55 Monday, May 23, 9:00 a.m.-10:30 a.m.

Comorbidity of PTSD in the Elderly: A Controlled Study

Fulya Maner, M.D., *Department of Psychiatry, Bakirkoy Psy. Neu. St. Edu. Rsc. Hospital, Firildak sok. No: 20-22/2 Moda, Istanbul 81300, Turkey*; Erhan Ozguler, M.D., Sacide Cobanoglu, M.D., Tamer Aker, M.D., Oguz Karamustafaoglu, M.D.

Educational Objectives:

At the conclusion of the presentation, major depression and dysthymia should be as recognized the most common comorbid disorders in posttraumatic stress disorder in elderly and the rate of comorbid disorders significantly lower in elder patients than adults.

Summary:

Method: The sample was elderly people who experienced the August 17, 1999 Marmara Earthquake with the diagnosis of PTSD according to DSM-IV criteria. Sociodemographical form developed by the authors, Standardized Mini Mental Test (SMMT) both for educated and noneducated, SCID-I, CAPS were applied to elder and younger adults as a control group. The statistical analysis were performed by SPSS 11.0 programme.

Results: The age range of elder group($n:39$) was 60 years or more; mean age was 49.9(SS:14.943). The age range of the adult group($n:51$) was 18-55 years; mean age was 39.1 (SS:10.279)61.5% of elder group and 47.1% of the adult group had received no comorbide diagnosis in SCID-I. 23.1% of the elder group and 31.4% of the adult group diagnosed as affective disorders (major depression, dysthymia). 12.8% of the elderly group and 15.7% of the adult group had anxiety and somatization disorders. 22.6% of the elder group and 5.9% of the adult group had alcohol and other psychoactive substance use disorders. There was significantly difference among the two groups about the distribution of comorbidity ($p<0.001$).

Conclusions: Major depression appears to be the most common comorbide diagnosis in elder (17.9%) and adult (23.9%) PTSD group. The comorbid disorders are significantly more in adult than elderly PTSD patients.

References:

1. Chung MC, Werrett J, Easthope Y, Farmer S: Coping with post-traumatic stress: young, middle-aged and elderly comparisons. *Int J Geriatric Psychiatry* 2004; 19(4):333.
2. Zelst WH, Beurs E, Beekman ATF, Deeg DJH, Dyck R: Prevalence and risk factors of posttraumatic stress disorder in older adults. *Psychotherapy and Psychosomatics* 2003; 72:233-342.

NR56 Monday, May 23, 9:00 a.m.-10:30 a.m.

Factor Structure of the PHQ-9 and Depressive Symptom Presentation in Different Ethnic Groups

Frederick Y. Huang, M.D., *Institute for Health, Rutgers University, 30 College Ave., New Brunswick, NJ 08901*

Educational Objectives:

At the conclusion the presentation, the participant should be able to describe how the PHQ-9 functions in African-American, Chinese, Latino, and white populations.

Summary:

Objective: The present analysis was conducted (1) to compare the factor structure of the PHQ-9 between different ethnic groups and (2) to compare rates of endorsement of the nine items of the PHQ-9 that correspond with the DSM-IV criteria for major depressive disorder. 16

Method: Using data collected from the original PHQ-9 validation study and the Charles B. Wang Community Health Center, the factor structure of the PHQ-9 in African-American, Chinese American, Latino, and white patient populations were compared. Scoring of each of the nine items of the PHQ-9 was also compared between the different ethnic groups.

Results: One main factor that included all nine items of the PHQ-9 was found by principal components factor analysis in each ethnic group with alpha coefficients of 0.84, 0.79, 0.84, and 0.89 (for African-American, Chinese-American, Latino, and white populations, respectively). Amongst subjects scoring above threshold for moderate depression on the PHQ-9, Chinese-American subjects were half as likely to endorse difficulty with appetite and twice as likely to endorse psychomotor retardation.

Conclusions: The PHQ-9 consists of one single factor in African-American, Chinese-American, Latino, and white populations; but the different ethnic populations have significantly different responses on individual items of the scale.

References:

1. Kroenke K, Spitzer RL, Williams JB: The PHQ-9 validity of a brief depression severity measure. *J Gen Intern Med* 2001; 16(9):606-13.
2. Mackinnon A, McCallum J, Andrews G, Anderson I: The Center for Epidemiological Studies Depression Scale in older community samples in Indonesia, North Korea, Myanmar, Sri Lanka, and Thailand. *J Gerontol B Psychol Sci Soc Sci* 1998; 53(6):P343-52.

NR57 Monday, May 23, 9:00 a.m.-10:30 a.m.

Atomoxetine Decreases RADI (Reactive/Affective/Defensive/Impulsive) Aggression in ADHD

Manasi Rana, M.D., *Department of Psychiatry, Stanford, 401, Quarry Road, Stanford, CA 94305*; Hans Steiner, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand efficacy of atomoxetine in management of concomitant aggression in ADHD population.

Summary:

Objective: To demonstrate efficacy of a selective or epinephrine reuptake inhibitor (Atomoxetine) against reactive/affective/defensive/impulsive (RADI) aggression in the context of attention deficit/hyperactivity disorder (ADHD). Prior studies (Connor et al) have showed that stimulants reduced overt aggression, which is similar to RADI aggression. Atomoxetine has been shown to be efficacious in ADHD and thus also might be helpful against aggression, similar to stimulants.

Methods: A total of 11 patients (6 boys & 5 girls), mean age 13.2 years, SD= 3.5 with ADHD (DSM-TR) were eligible for this treatment. These were sequential admissions to our Disruptive Behavior Disorders Clinic. Comorbid diagnoses included oppositional defiant disorder, antisocial personality disorder, eating disorder — not otherwise specified and depression. A baseline Clinical Global Impression scores (Severity and Improvement) was obtained prior to starting atomoxetine. These patients were monitored weekly and atomoxetine was titrated to a mean dose of 60mg/day (range 120-25 mg). CGI-S and CGI-I was done at each visit over the mean duration of 10.6 months.

Results: There was a significant decrease in CGI-S scores from a mean of 4.5 at baseline to 1.2 at the last observation carried forward (p value = 0.00003).

Conclusion: Atomoxetine seems efficacious in reducing RADI aggression in ADHD.

References:

1. Connor DF, Glatt SJ, Lopez ID, Jackson D, Melloni RH Jr: Psychopharmacology and aggression. I: A meta-analysis of stimulant effects on overt/covert aggression-related behaviors in ADHD. *J Am Acad Child Adolesc Psychiatry* 2002; 41(3):253-61.
2. Connor DF, Barkley RA, Davis HT: A pilot study of methylphenidate, clonidine, or the combination in ADHD comorbid with aggressive oppositional defiant or conduct disorder. *Clin Pediatr* 2000; 39(1):15-25.

NR58 Monday, May 23, 9:00 a.m.-10:30 a.m. Complications Arising From Misattributed Physical Symptoms

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Robert Kores, Ph.D., Bhavesh Patel, M.D., Marie Tobin, M.D.,
Kristin Beizai, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be more cognizant of the need of a comprehensive patient assessment. The role of the consultation-liaison psychiatrist should be integral in the evaluation process to assume optimal care.

Summary:

Somatoform disorders are characterized by physical symptoms for which a physiological cause has not been identified. It is recognized that psychosocial distress is etiologically significant. These disorders can incur great interpersonal and economic cost. The prevalence of somatoform disorders in medically ill patients is 15% to 25%.

Consequently, a high index of suspicion is warranted. However, premature attribution of ambiguous physical symptoms to a purely psychological cause frequently results in incomplete medical evaluation.

This paper presents several cases where inconclusive laboratory findings and ambiguous physical symptoms resulted in an inaccurate attribution of symptoms to an exclusive psychiatric cause. The patients presented with vague physical symptoms and significant psychiatric history where eventual comprehensive

medical work-up indicated medical disorders. The cases presented highlight the need for a multidisciplinary approach to patients presenting with unexplained physical symptoms and comorbid psychiatric symptomatology. This is warranted to prevent inaccurate characterization of etiology and suboptimal management. A bias against patients with psychiatric comorbidity results in premature discontinuation of medical workup. Increased knowledge and awareness leads to the identification of patients at risk and assures their optimal medical management. The cases presented underscore the role of psychiatric services in the promotion of a biopsychosocial model of diagnosis and treatment.

References:

1. Verhaak P: Somatic disease and psychological disorder. *Journal of Psychosomatic Research* 1997; 42(3):261-273.
2. Ladwig K, Martin-Mittag B, Evazo N, Gundel H: Identifying somatization disorder in a population-based health examination survey. *Psychosomatics* 2001; 42(6):511-518.

NR59 Monday, May 23, 9:00 a.m.-10:30 a.m. A Comparative Study of Suicide Notes in Patients Over Age 65: Preliminary Data

Daniel Matusevich, M.D., *Av Del Libertador 2306 #1B, Buenos Aires 1425, Argentina*; Martin Ruiz, M.D., Carolina Vairo, M.D., Carlos Finkelsztejn, M.D., Jose Faccioli, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the importance of suicide notes in older age.

Summary:

Objective: To determine, in older suicide attempt inpatients, differences between leaving a suicide note and not leaving it as regards age, gender, marital status, religion, living alone, level of education, present psychiatric treatment, severity of suicidal attempt, previous suicidal arousal, afterwards suicidal arousal, suicidal ideation, hopelessness, depression, dementia, narcissistic personality disorder, physical pain, previous suicide attempt, familiar history of suicide or suicide attempt.

Material and Methods: This is a comparative, prospective, observational, transversal, single blind study.

Results: We studied 31 patients. Statistical significant associations were found between leaving a suicide note and hopelessness (p=0.03;OR=8.57;IC=1.19-95.33) and severe suicide attempt (p=0.022;OR=78.40;IC=7.28-63.88).

Discussion: Although associations between writing suicide notes and hopelessness have not been reported, our results are not surprising because, on one side, the severity of the suicide attempt is more related to hopelessness than to any other depressive parameter and, on the other side, leaving a suicide note is associated to severe suicide attempts. Finally, to feel hopeless and to leave a suicide note are associated to severe suicide attempts.

References:

1. Beck AT, Morris J, Lester DS: Suicide notes and risk of future suicide. *JAMA* 1974; 228:495-496.
2. Linn M, Lester D: Content differences in suicide notes by gender and age: serendipitous findings. *Psychol Rep* 1996; 78:370.

NR60 Monday, May 23, 9:00 a.m.-10:30 a.m. Sexuality in Dementia Case Studies

Daniel Matusevich, M.D., *Av Del Libertador 2306 #1B, Buenos Aires 1425, Argentina*; Carolina Vairo, M.D., Martin Ruiz, M.D., Carlos Finkelsztejn, M.D.

Educational Objectives:

Although there is a growing literature on the subject of sexuality and an increased knowledge of sexuality in older people, there is a dearth of information about sexuality among people with dementia.

Summary:

Objective: to describe the type of sexual expression, feelings and behaviors in people with dementia, and the family's and residential care staff's responses to such expressions.

Material and methods: 12 patients aged 70 to 90 were included (7 male and 5 female). 10 were institutionalized and 2 lived with their families. All suffered from Dementia (either Alzheimer or vascular). Three clinical interviews by three different psychiatrists were performed to each patient, residential caregiver and family member.

Results: Although most patients showed desinhibition, sexual incidents were infrequent. Men expressed higher sexual desires than women. Sexual activity was uncommon in institutions. Residential caregivers showed more positive attitudes towards patients sexuality than their families.

Discussion: Analyzing sexuality in dementia becomes a difficult and controversial issue because of cognitive impairment and ethic concern. Public versus private sexual expression constitutes a crucial aspect in this subject.

References:

1. Ehrenfeld M, Bronner G, Tabak N, Alpert R, Bergman R: Sexuality among institutionalized elderly patients with dementia. *Nurs Ethics* 1999; 6(2):144-149.
2. Holmes D, Reingold J, Teresi J: Sexual expression and dementia view of caregivers: a pilot study. *Int J Geriatr Psychiatry* 1997; 12(7):695-701.

NR61 Monday, May 23, 9:00 a.m.-10:30 a.m.

Relief of Metoprolol-Induced Nightmares With Melatonin Supplementation

Joseph J. Rasimas, Ph.D., *Department of Psychiatry and Psychology, Mayo Clinic, 200 1st Street SW, Rochester, MN 55905; Lee Ann Kelley, M.D.*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to appreciate the phenomenon of beta-blocker induced nightmares, recognize basic relationships between sleep architecture, melatonin, and central noradrenergic neurotransmission, and understand the therapeutic rationale for melatonin supplementation in beta-blocker induced parasomnias.

Summary:

Sleep disturbances become more common with age. Along with normal changes in sleep architecture that accompany advancing years, medical illness, which is more common in the elderly, adversely affects both the quality and quantity of sleep. With disease comes treatment, often in the form of medications that can profoundly disturb sleep, as well. Beta blockers, particularly those with high lipophilicity, are associated with the recollection of vivid dreams and nightmares. We describe a case in which metoprolol was initiated for ventricular rate control in atrial fibrillation, and the resulting severe parasomnia led to suicidal ideation. As metoprolol has been associated with significant suppression of melatonin secretion, and melatonin promotes non-rapid eye movement sleep phases, we postulated that melatonin supplementation might alleviate the patient's parasomnic distress. After eight consecutive nights of persecutory dreams, the patient slept without disturbance following the first of regular nightly doses of three milligrams of melatonin. While the detailed mechanisms of beta blocker-induced

parasomnias are not well understood, the relief provided by melatonin supplementation in this case suggests an association between noradrenergic modulation of the pineal gland and vivid dreams that warrants systematic biochemical and therapeutic investigation.

References:

1. Thompson DF, Pierce DR: Drug-induced nightmares. *Ann Pharmacother* 1999; 33(1):93-98.
2. Westerlund A: Central nervous system side-effects with hydrophilic and lipophilic beta-blockers. *Eur J Clin Pharmacol* 1985; 28(S):73-76.

NR62 Monday, May 23, 9:00 a.m.-10:30 a.m.

Transitioning Patients From Assertive Community Treatment to Less Intensive Services

Keith R. Stowell, M.D., *Department of Psychiatry, Western Psychiatric Institute & Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213; Ann L. Hackman, M.D.*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to identify recent changes in thought on the duration of Assertive Community Treatment (ACT) and recognize factors that might play a role in the success of a transition from ACT to a lower level of care.

Summary:

Background: Until recently, it was generally accepted that persons in an Assertive Community Treatment (ACT) Program would remain within this intensive level of care for an indefinite period of time. Newer research suggests that patients who have improved in ACT might be candidates for transition to a lower level of care.

Methods: A retrospective medical record review was undertaken to assess whether certain patient characteristics were associated with the success of such a transition. The charts of patients transitioned from the University of Maryland's ACT Program to traditional community mental health services between 1995 and 2003 were reviewed.

Results: Sixty-seven patients were transitioned during the review period. Of these patients, forty-eight remained at a lower level of care. Nineteen patients required a return to ACT services or were lost to follow-up. Survival analysis showed no significant difference in survival based on diagnosis, comorbid substance use, sex, race, or housing.

Conclusions: Though the relatively small size of the study population limited the statistical significance of the results, it is noteworthy that the overwhelming majority of patients in the group remained at a lower level of care. Further research might focus additional attention on assessing factors that predict a successful transition.

References:

1. RA Rosenheck, Dennis D: Time-limited assertive community treatment for homeless persons with severe mental illness. *Archives of General Psychiatry* 2001; 58:1073-1080.
2. Salyers MP, Masterton TW, Fekete DM: Transferring clients from intensive case management: impact on client functioning. *American Journal of Orthopsychiatry* 1998; 68:233-245.

NR63 Monday, May 23, 9:00 a.m.-10:30 a.m.

The Effect of Gene Polymorphisms on Clozapine Response and Drug-Induced Weight Gain

Kim Mi-Kyoung, M.D., *Department of Psychiatry, Kang-Buk Samsung Hospital, Jong Ro-Gu Pyung-Dong, Seoul, South*

Korea; Bae Myung-Gee, M.D., Lee Won-Seok, M.D., Lee Hee Jae, Ph.D., Kim Jong-Woo, M.D., Chung Joo-Ho, M.D., Noh Kyung-Sun, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize psychopharmacologic approach in treatment of schizophrenia with clozapine.

Summary:

The identification of the molecular variants that associated with the drug response and side effect important to predict, maximize clinical response and minimize side effects. Recently, these studies have focused on the new atypical antipsychotic agents, particularly clozapine. Weight gain, a common adverse effect of clozapine, may impair health and affect patient compliance during treatment. The goal of this study was to investigate the relationship of the 6242C/T polymorphism of the cytochrome P450 CYP 1A2, 5' Ins/Del polymorphisms and Glu148Glu polymorphism of the dopamine beta hydroxylase (DBH), and Ins/Del polymorphism of angiotensin converting enzyme(ACE) with therapeutic response to clozapine. Associations between the Leu229Met polymorphism of uncoupling protein 1(UCP1), Val55Ala polymorphism of uncoupling protein 2(UCP2), and Gly482Ser and Thr528Thr polymorphisms of the peroxisome proliferator activated receptor gamma coactivator-1(PGC-1) with clozapine-induced body weight change(BWC) were investigated. Twenty-six Korean schizophrenic patients with a history of non-response to typical antipsychotics were included in the study. The associations for the genetic variants, and psychiatric symptoms and clozapine response were performed using the Brief Psychiatric Rating Scale and body-weight change before and after 12 weeks of clozapine treatment. The results of these investigations suggest that the CYP 1A2 gene 6242C/T, DBH I/D and Glu148Glu and ACE I/D variants do not play a major role in susceptibility to clozapine response in schizophrenia. No statistically significant relationships were also demonstrated for the investigated Leu229Met polymorphism of UCP1, Val55Ala polymorphism of UCP2, Gly482Ser and G528A polymorphism of the PGC-1 in terms of BWC post-treatment, suggesting these four polymorphisms do not play a significant role in clozapine-induced BWC. Further pharmacogenetic studies pertaining to clozapine response and clozapine-induced weight gain are warranted.

References:

1. Arranz MJ, Munro J, Birkett J, Bolonna A, Mancama D, Sodhi M, et al: Pharmacogenetic prediction of clozapine response. *Lancet* 2000; 355:1615-1616.
2. Basile VS, Masellis M, McIntyre RS, Meltzer HY, Lieberman JA, Kennedy JL: Genetic dissection of atypical antipsychotic-induced weight gain: novel preliminary data on the pharmacogenetic puzzle. *J Clin Psychiatry* 2001; 62(Suppl 23):45-66.

NR64 Monday, May 23, 9:00 a.m.-10:30 a.m.

Objective Registration of Motor Activity Pattern in Schizophrenia and Depression

Jan O. Berle, M.D., *Department of Psychiatry, University of Bergen, Haukeland University Hospital, Box 7800, N-5021 Bergen, Norway*, Erik Hauge, M.D., Ketil Oedegaard, M.D., Fred Holsten, M.D., Ole Bernt Fasmer, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize actigraph registrations as a useful tool in acquiring objective data regarding motor activity in psychiatric patients.

Summary:

Objective: To use actigraphy to study objectively motor activity in schizophrenia and major depression.

Methods: Patients with schizophrenia (n=23), major depression (n=16), and controls (n=28), were compared. Motor activity was recorded by wrist-worn actigraphs (Actiwatch, Cambridge Neurotechnology Ltd, England) for two-week periods. Average activity, one minute epochs, was calculated and in addition two nonparametric variables, interdaily stability (IS), intradaily variability (IV) were used.

Results: The motor activity was significantly lower both in patients with schizophrenia (153 ± 61 , mean \pm SD, $p < 0.001$) and major depression (204 ± 82 , $p = 0.03$), compared with controls (287 ± 85). The schizophrenic patients had higher IS (0.53 ± 0.15 vs. 0.44 ± 0.12 , $p = 0.025$) and lower IV (0.74 ± 0.19 vs. 0.88 ± 0.17 , $p = 0.007$) than the controls. The depressive patients had values (0.45 ± 0.12 and 0.78 ± 0.30), that were not significantly different from controls.

Conclusions: The main finding is that schizophrenic patients show a more stereotypical motor activity pattern than controls. An implication of this is that actigraph registrations may be a useful tool in acquiring objective data regarding motor activity in psychiatric patients.

References:

1. Haug H-J, Wirz-Justice A, Rössler W: Actigraphy to measure day structure as a therapeutic variable in the treatment of schizophrenic patients. *Acta Psychiatr Scand* 2000; 102 (suppl. 407):91-95.
2. Teichner MH: Actigraphy and motion analysis: New tools for psychiatry. *Harvard Rev Psychiatry* 1995; 3:18-35.

NR65 Monday, May 23, 9:00 a.m.-10:30 a.m.

Prevalence of Diabetic Ketoacidosis in Patients Treated With Clozapine: Prevalence and Associated Risk Factors

Nikhil D. Nihalani, M.D., *Department of Psychiatry, Strong Memorial Hospital, 300, Crittenden Blvd, Rochester, NY 14642*, Steven Lamberti, M.D., David Olson, R.Ph., Telva Olivares, M.D.

Educational Objectives:

At the end of the presentation, the participant should be able to understand the validity of DKA in the above case reports and also the association between the risk factors and DKA.

Summary:

Introduction: Diabetes has been associated with the use of atypical antipsychotics. This may be due to an unknown mechanism or due to the weight gain caused by these agents. Diabetic ketoacidosis (DKA) has also been associated with the use of these agents, especially clozapine. The relationship between the emergence of DKA and the various co-factors associated with DKA is unclear.

Aim: The main aim of the study is to review all case reports published to date and determine the validity of the diagnosis of diabetic ketoacidosis (DKA) for each case. The study will examine associated clinical and demographic risk factors including substance abuse, body weight change, time of onset, duration, poly psycho-pharmacology, new onset/new exacerbation of previous diabetes, and treatment compliance.

Methods: A literature search was conducted in Medline from 1966 to date for any case reports published on DKA and clozapine. The key words used were clozapine, diabetes, and diabetic ketoacidosis. In addition, a cohort of 26 patients with clozapine-associated diabetes will be examined to find additional cases of DKA.

Results: 23 case reports have been published in English and one in Danish, which associate DKA with the use of clozapine. There were four cases that we report from a cohort of 26 patients with clozapine-associated diabetes. Further results will be discussed in detail.

Discussion: A detailed discussion of the presence of risk factors and association with the diagnosis of diabetic ketoacidosis will follow.

References:

1. Koval MS, Ramy M, Christie S: Diabetic ketoacidosis associated with clozapine treatment. *American Journal of Psychiatry* 1994; 151:1520-211616.
2. Kostakoglu AE, Yazici KM, Erbas T et al: Ketoacidosis as a side effect of clozapine: a case report. *Acta Psychiatrica Scand* 1996; 93:217-2181616.

NR66 Monday, May 23, 9:00 a.m.-10:30 a.m.

Acute and Transient Psychotic Disorder: A Follow-Up Study of Chinese Inpatients

Jenny Suk Kwan Tsang, M.B., Team 2, *Department of Psychiatry, Kwai Chung Hospital, 3-15, Kwai Chung Hospital Road, Lai King, Hong Kong HKSAR, Hong Kong*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the diagnostic instability and outcome predictors of acute and transient psychotic disorder.

Summary:

Background: Acute and transient psychotic disorder (ATPD) was reported to be an unstable diagnosis in a few western studies. Some of them suggested that the outcome of ATPD was good. This study evaluates the diagnostic stability and outcome of ATPD. In addition, this study also aims at finding the predictors of diagnostic stability and outcome.

Method: Fifty-six subjects consecutively admitted for inpatient treatment of ATPD from 1-7-97 to 31-12-98 were recruited into this study by screening around 5,000 discharge summaries. Their demographic data, premorbid adjustment, and other clinical variables were obtained from case notes. Follow-up interviews were carried out for 53 subjects, and outcome was measured in different domains.

Results: ATPD was an unstable diagnosis in Chinese inpatients, with 37.7% having changes in diagnoses at a mean follow-up period of 27.7 months. Those subjects with a stable diagnosis of ATPD had a very good outcome in both psychosocial and clinical aspect. The good predictors were being married, high premorbid GAF score, and younger age of onset. The presence of full schizophrenic symptoms at initial presentation predicted higher level of negative symptoms at follow up.

Conclusion: The findings in this study support the need of further validation of the concept of ATPD, as a portion of subjects evolved into more serious mental disorder. The predictors of outcome found in this study provide a basis for further research.

References:

1. Jorgensen P, Bennedsen B, Christensen J, Hyllested A: Acute and transient psychotic disorder: A 1-year follow-up study. *Acta Psychiatrica Scandinavia* 1997; 96, 150-154.
2. Schwartz JE, Fennig S, Tanenberg-Karant M, Carison G, Craig T, Galambos N, Lavelle J, Bromet EJ: Congruence of diagnoses 2 years after a first-admission diagnosis of psychosis. *Archives of General Psychiatry* 2000; 57:593-600.

NR67 Monday, May 23, 9:00 a.m.-10:30 a.m.

Relationship Between Severity of Atopic Dermatitis and Subject's Characteristics Attending Summer Atopy Camp in Korea

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Educational Objectives:

Research suggest that atopic dermatitis (AD) patients often exhibit psychological, behavioral and familial problems. It is useful to use a biopsychosocial model in the management of AD. This study was to assess the relationship between severity of AD and subject's characteristics who were attending summer atopy camp in Korea.

Summary:

Participants were children aged 7 to 12 years who had been treated for an atopic dermatitis and attended summer camp for atopic dermatitis. Children were previously examined using the Severity Scoring of Ad Index (SCORAD) by dermatologist and completed the questionnaires including Spielberger State-Trait Anxiety Inventory for Children (STAI-C), coping strategies, and the self-report Strengths and Difficulties Questionnaire (SDQ). Mothers also attended summer camp and completed the demographic data, Dermatitis Family Impact questionnaire (DFI), and the Korean version of SDQ (SDQ-Kr). All participants completed the wrap-up questionnaires.

The severity of AD was associated with the number of friends, number of self-avoiding foods, and children's behavioral problem. The severity of AD was also associated with total scores of DFI, subscales of food preparing, economic problems, and carer's tiredness. SCORAD was positively correlated with DFI and self-avoiding foods. Trait anxiety was positively correlated with passive coping strategies, total scores of SDQ-SR and SDQ-Kr. All participants answered that the summer camp was helpful.

The results suggest that the psychological and familial dimensions of AD should be taken into account as part of routine management in Korea. Further research will be needed to establish the effectiveness of any comprehensive intervention like summer camp.

References:

1. Howlett S: Emotional dysfunction, child-family relationships and, childhood atopic dermatitis. *Br J Dermatol* 1999; 140:381-384.
2. Kiebert G, Sorensen SV, Rvicki D, Fagan SC, Doyle JJ, Cohen J et al: Atopic dermatitis is associated with a decrement in health-related quality of life. *Int J Dermatol* 2002; 41:151-158.

NR68 Monday, May 23, 9:00 a.m.-10:30 a.m.

A Short-Term Follow-Up Study of Juvenile Acute and Transient Psychotic Disorders

Amit Razdan, *Department of Psychiatry, Virginia Treatment Center for Children, 515 N. 10th Street, PO Box 980489, Richmond, VA 23228; Kavir Saxena, M.D.*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to better understand the course, outcome, and prognosis of acute and transient psychotic disorders.

Summary:

Objective: To understand the outcome of acute and transient psychotic disorders (ATPD) in child and adolescent population as outcome studies in this age group are almost nonexistent.

Method: Twenty-eight children (ages 9-17), M/F=17/11, with a prior diagnosis of ATPD by ICD10-DCR were evaluated at least six months after the index episode. The sample population included subjects with a diagnosis of ATPD per ICD10 DCR who were enrolled in the child psychiatry unit, King George's Medical College, Lucknow, India from December 1, 1996, to January 31, 1998. Most were subjects in an earlier acute psychosis study conducted in the department; hence strict diagnostic criteria were applied at index episode. Acute drug and alcohol intoxication was ruled out. IRB approval was obtained. Tools used were (1) A semi-structured proforma to update the sociodemographic data and history; (2) Diagnostic Interview using the K-SADS-P; (3) Children Global Assessment Scale (CGAS); (4) Clinical Global Impression Scale (CGIS); (5) Parent Interview Schedule.

Results: (1) Out of 28 children evaluated, 22 patients (78.5%) had fully recovered and had no symptoms of any psychiatric illness at the time of evaluation; (2) Two patients were suffering from a new episode of psychiatric illness which fulfilled the criteria of a manic episode per ICD 10-DCR; (3) A third patient had an episode of hypomania at the time of evaluation per ICD 10 DCR; (4) One patient developed a relapse episode of ATPD; (5) One patient developed conduct problems after the resolution of the index episode. He fulfilled the criteria for conduct disorder of socialized type per ICD 10 DCR; (6) A sixth patient fulfilled the criteria for tension headaches; (7) Most of the patients were doing well from a psychosocial perspective. 23 out of 28 patients (82%) had ratings of above 70 on CGAS indicating superior to good functioning in almost all areas. Of the remaining five patients, two patients also had an diagnosis of MR, probably explaining their low scores on CGAS.

Conclusion: (1) It seems that at least in the short term follow up (12.32+/- 3 months), ATPD is a brief psychotic illness with a good outcome; (2) No significant predictor could be identified between the two groups to indicate a poor outcome.

References:

1. Jorgenson, Bennedson, Hylsted: Acute and transient psychotic disorders: a one year followup study. *Acta Psychiatr* 1996; 150-54
2. Russell AT, Bott L, Sammons C: The phenomenology of schizophrenia occurring in childhood. *JAACAP* 1989; (28):399-407.

NR69 Monday, May 23, 9:00 a.m.-10:30 a.m. **Psychiatric Comorbidity in Adult Patients With Mitochondrial Diseases**

Omar Fattal, M.D., *Department of Psychiatry, Cleveland Clinic Foundation, 1300 West 9th Street #847, Cleveland, OH 44113*; Kathleen Quinn, M.D., Bruce Cohen, M.D., Brewster Deborah, M.A., Jessica Link, B.S., Kathleen Franco, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to better appreciate the nature and prevalence of psychiatric disorders co-occurring with mitochondrial disease. Psychiatrists should entertain the diagnosis of mitochondrial disease earlier in patients with various physical signs and symptoms to save them unnecessary treatments and deterioration in their quality of life.

Summary:

Mitochondrial disease results from a malfunction in the energy process. Any organ system can be affected producing various physical and psychiatric signs and symptoms. Little is known about the relationship of psychiatric symptoms to the mitochondrial disease. Thirty-six eligible adult outpatients from Mitochondrial Disease Neurology Clinic participated. Each interview provided demographic, medical, and psychiatric history, MMSE, M.I.N.I.

International Neuropsychiatric Interview, and the SF-36 Health Survey. Seventy percent of the patients met criteria for major mental illness. Fifty-four percent had lifetime major depressive disorder, 17% had lifetime bipolar disorder, 11% had lifetime panic disorder and 11% had current generalized anxiety disorder. On average, mitochondrial disease was diagnosed 4.5 years after the onset of psychiatric symptoms and after 14 physicians were seen. We found that patients with comorbid psychiatric problems were older ($p=0.05$), had significantly more hospital admissions ($p=0.02$), more medical conditions ($p=0.01$), positive family history of mitochondrial disease ($p=0.04$), and lower quality of life ($p=0.01$) than patients with mitochondrial disease alone. In conclusion, psychiatric problems are very common in this population. Mood disorders are more common than anxiety disorders. Psychiatrists should consider the possibility of mitochondrial disease earlier in patients presenting with various physical signs and symptoms.

References:

1. Massimo Zoviani M, Stefano Di Donato S: Mitochondrial disorders. *Brain* 2004; 127:2153-2172.
2. Chinnery PF, Schon EA: Mitochondria. *Journal of Neurology, Neurosurgery, and Psychiatry* 2003; 74(9):1188-1199.

NR70 Monday, May 23, 9:00 a.m.-10:30 a.m. **Interrelationships Between Pain, Disability, and Psychological Factors in Patients With Lumbar Disc Herniation**

Tae-Suk Kim, M.D., *Department of Psychiatry, The Catholic University of Korea, 505 Banpo-Dong Seocho-Gu, Seoul 137-701, South Korea*; Chi-Un Pae, M.D., Woo-Young Jang, M.D., Chang-Ki Hong, M.D., Chang-Uk Lee, M.D., Chul Lee, M.D.

Educational Objectives:

At the conclusion of the presentation, the participants should be able to recognize the interrelationships between pain, disability, and psychological factors in LDH patients without surgical treatments.

Summary:

In this study, we compare the psychological factors between lumbar disc herniation (LDH) patients and healthy controls and evaluate the interrelationships between pain, disability, and psychological factors in LDH patients without surgical treatments.

The subjects consisted of 56 patients with LDH and 76 healthy controls, who are consecutively recruited. All patients and controls completed Beck's Depression Inventory, Spielberger's State-Trait Anxiety Inventory. To evaluate pain intensity and functional disability, Visual Analogue Scale and Modified Oswestry Low Back Pain Disability Questionnaire were used.

LDH patients had more depression and anxiety than healthy controls. The functional disability of the LDH patients was significant related to four variables: pain intensity ($p < .0001$), depression ($p = .005$), state anxiety ($p = .002$), and trait anxiety ($p = .026$). Correlations between pain intensity and depression, state anxiety, and trait anxiety in the LDH patients were all non-significant. Pain intensity ($p = .001$) and state anxiety ($p = .007$) contributed significantly to functional disability in the LDH patients.

This study suggests that LDH patients have some psychological problems, such as depression and anxiety, in comparison with healthy controls. Furthermore, the pain intensity and state anxiety predict the functional disability in LDH patients.

References:

1. Epker J, Block AR: Presurgical psychological screening in back pain patients; a review. *Clin J Pain* 2001; 17:200-5.
2. Carragee EJ: Psychological screening in the surgical treatment of lumbar disc herniation. *Clin J Pain* 2001; 17:215-9.

NR71 Monday, May 23, 9:00 a.m.-10:30 a.m.

The Evaluation of Pet Therapy on Negative Symptoms in Inpatients With Chronic Schizophrenia

Shiu-Mei Kung, R.N., *Department of Nursing, Yu-Li Hospital, DOH, 448 Chung-Hwa Road, Yu-Li Town, Hualien 981, Taiwan*; Tsoo-Hung Lan, M.D., Wen-Ching Chen, M.D., Shu-Chun Lin, R.N., Mei-Lien Tseng, R.N., Hsien-Jane Chiu, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to replicate the improvement of negative symptoms from pet therapy on chronic schizophrenic patients.

Summary:

Objective: To evaluate the treatment effect of pet therapy on negative symptoms in chronic schizophrenic patients.

Method: We recruited 100 chronic schizophrenic inpatients (50 males and 50 females), who had completed consent forms before inclusion in this study. All participants were matched on their daily dosage of pharmacotherapy for the following three months. The pet therapy was defined to keep all participants living with a 40gm hamster for 10 hours per day. Each individual was randomly assigned to the experiment and control group. Negative symptoms were evaluated by SANS for each patient at baseline, first month, second month, and third month after pet therapy intervened.

Results: The difference of SANS score change over time between the experiment group and the control group was statistically significant ($p < 0.0001$ under GEE model), even after adjusted for sex, age, education years, and hospital stay period.

Conclusions: It is suggested that chronic schizophrenic inpatients gain benefit in their negative symptoms from taking pet therapy.

References:

1. McCulloch W: An overview of the human-animal bond: present and future. JnR. Anderson, B.L. Hart & L.A. Hart (Eds.), *The pet connection* (pp. 30-35). Minneapolis: University of Minnesota, 1984.
2. Black DW, Andreasen NC: Schizophrenia, schizaphreniform disorder, and delusional disorder in R.E. Hales, & S.C. Yudofsky (Eds.), *The American Psychiatric Press Synopsis of Psychiatry* (2nd), 1966.

NR72 Monday, May 23, 9:00 a.m.-10:30 a.m.

Reducing the Dose of Antipsychotics Improved Paroxysmal Perceptual Alteration

Hiroyuki Uchida, M.D., *Department Neuro-Psychiatr., Keio Univ., School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan*; Takefumi Suzuki, M.D., Koichiro Watanabe, Ph.D., Haruo Kashima, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize this potentially important side effect of antipsychotics, to understand the clinical characteristics, and to learn the ideal treatment strategy.

Summary:

Introduction: There are sporadic reports of antipsychotic-induced paroxysmal perceptual alteration (PPA), which is characterized mainly by visual hypersensitivity and sometimes accompanied by an oculogyric crisis. However, some researchers regard PPA as a schizophrenia symptom. To determine whether PPA is the adverse effect, we examined the effect of dose reduction on PPA.

Methods: This was an open-label, 36-week study. Forty-two patients with PPA were divided into a reduced-dose group (N=

21) and a fixed-dose group (N=21). Assessment included the frequency and duration of PPA, the Clinical Global Impressions (CGI), the Positive and Negative Syndrome Scale (PANSS) for schizophrenia, and the CGI for other diagnoses.

Results: All participants completed the study. PPA diminished in 20 patients (95.2%) in the reduced-dose group in the CGI score, the frequency (number of episodes per week) and the duration of the episodes (from 4.14 to 1.62, $p < 0.001$; from 1.83 to 0.73, $p = 0.003$; and from 2.69 to 0.68 hours, $p < 0.001$ respectively), but there were no changes in the fixed-dose group. The total PANSS scores also significantly improved in the reduced-dose group, from 57.0 to 52.2 ($p = 0.005$).

Conclusion: Our findings support the hypothesis that PPA is an adverse effect of antipsychotics, and dose-reduction represents an ideal treatment for PPA.

References:

1. Uchida H, Suzuki T, Watanabe K, Yagi G, Kashima H: Antipsychotic-induced paroxysmal perceptual alteration. *Am J Psychiatry* 2003; 160:2243-416.
2. Uchida H, Suzuki T, Tanaka KF, Watanabe K, Yagi G, Kashima H: Recurrent episodes of perceptual alteration in patients treated with antipsychotic agents. *J Clin Psychopharmacol* 2003; 23:496-9.

NR73 Monday, May 23, 9:00 a.m.-10:30 a.m.

A Survey of Beliefs and Practices Regarding the Use of Second-Generation Antipsychotics

Rajnish Mago, M.D., *Department of Psychiatry, Thomas Jefferson University, 833 S Chestnut St East, Suite 210 E, Philadelphia, PA 19107*; Ashwin Patkar, M.D., Farhan Fazal, Paolo Mannelli, M.D., Prakash Masand, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate an understanding of some key clinical issues regarding the use of second-generation antipsychotics and the prevalent beliefs and practices regarding these issues.

Summary:

Objective: Understand beliefs and practices regarding second-generation antipsychotics (SGAs).

Methods: A survey of clinicians attending a Psychiatry Update conference using vignettes about use of SGAs in a 30-year-old woman with acute schizophrenia.

Results: 71.1% respondents would not do a baseline prolactin level before starting risperidone, 64.3% did not think that elevated prolactin without adverse effects was clinically significant, and 59% did not think that elevated prolactin can cause osteoporosis. Those who would not do prolactin at baseline before starting risperidone were more likely not to do laboratory tests at baseline for olanzapine ($p = 0.04$), or an ECG at baseline for ziprasidone ($p = 0.02$). After failure of a trial of 4mg/day of risperidone, psychiatrists were significantly more likely to increase the dose while non-psychiatrists were more likely to switch to another SGA ($p = 0.03$). 73.3% respondents would discuss risk of diabetes/lipid abnormalities and 69.2% would do relevant laboratory tests before starting olanzapine. For patients who responded to olanzapine but gained weight, 39.7% would switch to another SGA but 32.5% would add topiramate instead. 60.0% respondents would do a baseline ECG before starting ziprasidone.

Conclusions: Lack of agreement regarding use of SGAs indicates the need for consensus guidelines. Individual characteristics of the prescriber significantly affect the strategies used.

References:

1. Lehman AF, Lieberman JA, Dixon LB, McGlashan TH, Miller AL, Perkins DO, Kreyenbuhl J: *American Psychiatric Association*

tion Steering Committee on Practice Guidelines. Practice guideline for the treatment of patients with schizophrenia, second edition. *Am J Psychiatry* 2004; 161(2 Suppl):1-56.

2. Wirshing DA, Pierre JM, Erhart SM, Boyd JA: Understanding the new and evolving profile of adverse drug effects in schizophrenia. *Psychiatr Clin N Am* 2003; 26:165-190.

NR74 **Monday, May 23, 9:00 a.m.-10:30 a.m.**
Information Level About OCD Among Argentinean Psychologists and Psychiatrists

Ricardo L. Perez Rivera, M.D., *Department of Psychiatry, Asociacion Argentina de Trastornos de Ansiedad, Av. Libertador 930, 4to piso, 2do cuerpo, Buenos Aires C1001ABW, Argentina*; Enzo Cascardo, M.D., Tania Borda, Ph.D., Alfredo Cia, M.D., Pablo Resnik, M.D.

Educational Objectives:

Because of ongoing advances in these fields, we find it necessary to show the importance of continuing education throughout OCD spectrum disorders, attending conferences, reading scientific journals, books, and other publications containing the latest news to ensure that patients and trainees continue to receive the finest care and information.

Summary:

Obsessive compulsive disorder (OCD) is now recognized as a major health care problem in psychiatry. In many cases, the degree of psychosocial and economic impairments for the patient and his/her family resemble those found in schizophrenia, rather than in other anxiety disorders. Consistent research findings have established effective treatments for OCD, including serotonin reuptake inhibitor (SRI) and behavioral techniques of exposure and response (ritual) prevention (EX/RP). Up to 40% of compliant OCD patients respond poorly to these treatments. The aim of this study was to elucidate the variables of predictors of treatment outcome, in a group of 150 psychiatrists and psychologists that attended the Argentine Anxiety Disorder Association annual meeting. Explanations to these treatments failures are the fact that OCD is misdiagnosed in our country, due to the lack of knowledge in OCD condition specificities, and because the professionals who often perform the treatment also encounter difficulties.

References:

1. Goodman WK, Rudorfer MV, Maser JD: Obsessive-Compulsive Disorder: Contemporary Issue Intreatment. Lawrence Erlbaum Associates, Publishers, New Jersey, 2000.
2. Yaryura-Tobias JA, Neziroglu FA: Obsessive-Compulsive Disorder Spectrum America Psychiatric Press, Washington, 1997.

NR75 **Monday, May 23, 9:00 a.m.-10:30 a.m.**
Lithium Intoxication: The Experience of a Mood Disorder Unit in Turkey

Sermin Kesebir, M.D., *Department of Psychiatry, Yuksek Ihtisas Hospital, Yuksek Ihtisas Hospital, Kirikkale 71100, Turkey*, Simavi Vahip, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate the experience of a Mood Disorder Unit in Turkey about lithium intoxication.

Summary:

The aim of this study was to investigate the prevalence, mode (acute, acute on chronic, or chronic) and severity of neurotoxicity (absent, mild, moderate, severe) of lithium intoxication and evalu-

ate the risk factors associated with lithium intoxication in a specialized mood disorders unit from 1986 to 2002.

The data of 33 cases were excluded from analysis, either because of sufficient data or did not treat as poisoning. One case had died because of acute lithium poisoning. The lithium intoxication were evident in 26 (66.7%) female and 13 (33.3%) male patients. The mean age of the patients during intoxication was 53.1 (SD:16.0) years. One (2.6%) case was acute toxicity, 6 (15.4%) were acute on chronic) and 32 (82.0%) were chronic toxicity. The severity of neurotoxicity according to Hansen and Amdisen scale was: absent in 3 (7.7%), mild in 10 (25.6%), moderate in 13 (33.3%), and severe in 13 (33.3%) cases and no sequel were observed during follow-up period. The possible risk factors were concurrent medical illness (dehydration, impaired renal function, hypothyroidism, nephrogenic diabetes insipidus) in 16 patients, concomitant medication (angiotensin-converting enzyme inhibitors, thiazide diuretics, amiloride, nonsteroidal anti-inflammatory drugs) in 15 patients, and overdose (for suicide, treatment, therapeutic reason) in 10 (25.6%) patients.

References:

1. Hansen HE, Amdisen A: Lithium intoxication. (Report of 23 cases and review of 100 cases from the literature). *Q J Med* 1978; 47(186):123-144.
2. Oakley PW, Whyte IM, Carter GL: Lithium toxicity: an iatrogenic problem in susceptible individuals. *Australian and New Zealand J Psychiatry* 2001; 35:833-840.

NR76 **Monday, May 23, 9:00 a.m.-10:30 a.m.**
5-HTTLPR, Antidepressant Response, and Alcohol Use Disorder

Katherine Ruiz-Mellott, M.D., *Department of Psychiatry, Cedars-Sinai Medical Center, 8730 Alden Drive, E-123, Los Angeles, CA 90048*; Russell Poland, Ph.D., Jeffrey Wilkins, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate knowledge of genetic variations in the serotonin transporter protein promoter region; recognize its potential as candidate gene.

Summary:

Objective: To investigate the influence of 5-HTTLPR on citalopram response in subjects with co-occurring major depression and alcohol-use disorder. To investigate the effect of SSRI treatment on drinking outcomes and depression.

Method: Genotyping and clinical assessment of outpatients who met inclusion criteria of MDD and alcohol-use disorder within the last six months. Open-label, flexible-dose citalopram (20-60mg) was given over eight weeks and subjects underwent weekly assessments of drinking by TLFB report and depressive ratings by HAM-D and BDI. We seek to enroll 20 total subjects, up to now, we have eight subjects completed and three randomized. We present data from our first eight subjects.

Outcome measure: Change in alcohol intake from baseline to study completion. Secondary outcome measures were change in depression ratings.

Results: We found treatment with citalopram decreased subject's alcohol consumption. Five of our 6 subjects actively drinking had a decrease in alcohol intake, there was no association to the s or l allele. HAM-D and BDI response was however positive in four of four individuals homozygous for the s or l allele.

Conclusion: Antidepressant treatment may be useful in decreasing drinking in individuals with alcohol problems, response rate may be influenced by 5-HTTLPR.

References:

1. Cornelius JR, Salloum IM, Haskett RF, Daley DC, Cornelius MD, Thase ME, Perel JM: Fluoxetine versus placebo in depressed alcoholics: a 1-year follow-up study. *Addict Behav* 2000; 25:307-1016.
2. Konishi T, Calvillo M, Leng AS, Lin KM, Wan YJ: Polymorphisms of the dopamine D2 receptor, serotonin transporter, and GABA(A) receptor beta(3) subunit genes and alcoholism in Mexican-Americans. *Alcohol* 2004; 32:45-52.

NR77 Monday, May 23, 9:00 a.m.-10:30 a.m.

Correlation of Plasma Reproductive Hormone Levels With the Severity of Negative Symptoms in Female Schizophrenia Patients

Ko Young-Hoon, M.D., *Department of Psychiatry, Korea University College of Medicine, #97 Guro-2-dong, Guro-gu, Seoul 152-703, Korea*; Joe Sook-Haeng, M.D., Cho Woong, M.D., Park Jeong-Hyun, M.D., Lee Jung-Jae, M.D., Jung In-Kwa, M.D., Kim Seung-Hyun, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that the measurement of plasma reproductive hormone levels, especially estrogen and progesterone level could be a useful biological marker for the severity of negative symptoms in female schizophrenia.

Summary:

The aim of this study was to evaluate the relationship between plasma levels of reproductive hormones and the severity of negative symptoms in female schizophrenia. Twenty-one female schizophrenia whose psychiatric symptoms were stable for at least four weeks prior to examination participated in this study. For the assessment of negative symptoms, the scale for the assessment of negative symptoms (SANS) was used. The authors divided the patients into two subgroups: patients with moderate to severe negative symptoms (SANS scores over 55) and those with mild negative symptoms (SANS scores below 55). Plasma level of LH, FSH, prolactin, estradiol, and progesterone were measured by radioimmunoassay in follicular phase. Significant correlations between SANS total scores and plasma levels of estradiol and progesterone were found. However, there were no significant correlations between SANS total scores and plasma levels of other hormones. The subcategories of SANS, estradiol, and progesterone showed different relationships. Estradiol showed affinity to affective flattening or blunting, alogia, and attention. Progesterone showed significant relationship with affective flattening or blunting, alogia, and anhedonia association. Plasma level of progesterone and estrogen in patients with moderate-to-severe negative symptoms were significantly milder than those in patients with mild negative symptoms. This result suggests that low levels of estrogen and progesterone during follicular phase of the menstrual cycle would be associated with more severe negative symptomatology in women with chronic schizophrenia.

References:

1. Akhondzadeh S, Nejatiasafa AA, Amini H, Mohammadi MR, Larijani B, Kashani L, Raisi F, Kamalipour A: Adjunctive estrogen treatment in women with chronic schizophrenia: a double-blind, randomized, and placebo-controlled trial. *Prog Neuropsychopharmacol Biol Psychiatry* 2003; 27:1007-1012.
2. Kulkarni J, Riedel A, de Castella AR, Fitzgerald PB, Rolfe TJ, Taffe J, Burger H: A clinical trial of adjunctive oestrogen treatment in women with schizophrenia. *Arch Women Ment Health* 2002; 5:99-104.

NR78 Monday, May 23, 9:00 a.m.-10:30 a.m.

Weight Gain, Glucose, and Lipid Abnormalities of Patients Prescribed Clozapine

Myeong Jee Lee, M.D., *Department of Psychiatry, Inha University Hospital, 7-206, 3rd St. Shinheung-dong, Incheon 400-103, Korea*; Chul-Eung Kim, M.D., Jae Nam Bae, M.D., Jin Soh Park, M.D.

Educational Objectives:

Long-term clozapine treatment was associated with changes on glucose, cholesterol level, and weight. Clinicians should be aware of the potential risks of diabetes, hyperlipidemia, and weight gain in patients taking clozapine.

Summary:

Objectives: Purpose of this study is to investigate the effects of long-term clozapine treatment on changes of weight, glucose, and cholesterol levels and correlations between them in outpatients with chronic schizophrenia.

Methods: 19 consenting outpatients diagnosed with schizophrenia according to the DSM criteria, who were on long-term clozapine treatment were selected for the study. The serum level of clozapine, metabolites as well as weight, BMI, glucose, cholesterol level, insulin, and c-peptide were gathered and analyzed before and after the use of clozapine.

Results: Glucose increase after clozapine treatment was statistically meaningful but it was due to two patients who were diagnosed with diabetes. Glucose levels of other patients are all below 120mg/dl. Cholesterol level showed significant increase after the treatment. Weight and BMI changes over the treatment are not statistically meaningful overall, but eight out of 17 showed more than 7% increase. The changes were positively correlated with weight and BMI of pre treatment. Mean serum level of clozapine, metabolites were not correlated with glucose, cholesterol level, insulin, C-peptide.

Conclusion: Long-term clozapine treatment was associated with changes of glucose, cholesterol level and weight. Clinicians should be aware of the potential risks of diabetes, hyperlipidemia, and weight gain in patients taking clozapine.

References:

1. Henderson AC: Clozapine, diabetes mellitus, weight gain, and lipid abnormalities: a five-year naturalistic study. *Am J Psychiatry* 2000; 157:975-981.
2. Lindenmayer JP: Changes in glucose and cholesterol levels in patients with schizophrenia treated with typical or atypical antipsychotics. *Am J Psychiatry* 2003; 160:290-296.

NR79 Monday, May 23, 9:00 a.m.-10:30 a.m.

Lithium Attenuates Stress-Induced Suppression of Long-Term Potentiation (LTP) in the Rat Hippocampus

Jea Jin Yang, M.D., *Department of Psychiatry, Ajou University Hospital, School of Medicine, Wonchun-dong, Youngtong-gu, Suwon 442-721, Korea*; Deok Su Lee, Ph.D., Min Whan Jung, Ph.D., Jai Sung Noh, M.D., Young Ki Chung, M.D.

Educational Objectives:

Several studies have shown that the deleterious effects of stress to hippocampus-dependent memory formation and LTP. Some studies have reported the neuroprotective actions of lithium, including prevention of stress-induced structural remodeling and enhancement of LTP. We investigated whether lithium prevented the stress-induced deleterious effects on memory.

Summary:

Method: Rats were subjected to a single one hour restraint stress and then were immediately sacrificed by decapitation. The brain was dissected and two transverse hippocampal slices were prepared for each case. We monitored baseline synaptic transmission for at least 10 minutes and then induced LTP by theta burst stimulation (TBS) in one slice. Afterward, we treated 0.6mM or 1.0mM of lithium for 20 minutes and monitored baseline synaptic transmission for at least 10 minutes and then, we induced LTP by TBS in the other one. We recorded synaptic responsiveness for every minute during a period of 40 minutes each slice.

Results: Between the stressed group (M=112.37%, SD=±11.51) and the 0.6mM lithium-treated group (M=141.06%, SD=±8.45), means of LTP magnitudes were significantly different (p<0.05). Means of LTP magnitudes were also significantly different between the stressed group and the 1.0mM lithium-treated group (M=146.96%, SD=±18.58) (p<0.05). But there were no significant differences between the means of LTP magnitudes in the 0.6mM lithium-treated group and the 1.0mM lithium-treated group.

References:

1. Wood GE, Young LT, Reagan LP, Hen B, McEwen BS: Stress-induced structural remodeling in hippocampus: prevention by lithium treatment. *PNAS* 2004; 101(11):3973-3978.
2. Kim JJ, Diamond DM: The stressed hippocampus, synaptic plasticity and lost memories. *Nat Rev Neurosci* 2002; 3:453-462.

NR80 Monday, May 23, 9:00 a.m.-10:30 a.m.

A Genetic Epidemiology Study of Personality Disorders

Hui Cheng, M.P.H., *Institute of Mental Health, Peking University, 51 Hua Yuan Bei Rd., Beijing 100083, China*

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize personality disorder is a heritable mental disorder.

Summary:

Objective: To study the heredity of personality disorders (PD) in senior high school students, and to explore interactions between environmental risk factors and genetic risk factors of PD.

Methods: Using genetic epidemiology method, cross-sectional study and case-control study were carried out. By stratified-cluster sampling, 9892 high school students in Beijing were sampled. The students and their parents were investigated by IPDE, PDQ-4, EMBU and GIQ. It was calculated that family clustering, heritability of PD and interactions between genetic factor and family environmental factors. Results PDQ-4 scores of the students were linearly correlated to those of their parents, but were not correlated to those of non-parents; parental PDQ-4 scores and PD prevalence of PD students were higher than those of the general population and the controls. The heritability of overall PD was higher than 0.7. Father had greater influence than mother in forming of PD. Family income, parental relationship and parental rearing behavior had interactions in the development of PD.

Conclusion: Genetic factor plays an important role in development of PD. Genetic factor accelerates occurrence of PD with interaction of family income, parent relationship and parental rearing behavior.

References:

1. Thaker G, Adami H, Moran M: Psychiatric illnesses in families of subjects with schizophrenia-spectrum personality disorders: high morbidity risks for unspecified functional psychoses and

schizophrenia. *American Journal of Psychiatry* 1993; 150(1):66-71.

2. Torgersen S, Lygren S, Oien PA et al: A twin study of personality disorders. *Comprehensive Psychiatry* 2000; 41(6):416-25.

NR81 Monday, May 23, 9:00 a.m.-10:30 a.m.

Aripiprazole Possibly Acts As Dopamine Agonist When Administered With Other Antipsychotics

Bun Hee Lee, Ph.D., *Department of Psychiatry, Korea University, 516 Kochan-Dong Ansan-si, Kyongki, AK 425-070, South Korea*; Han Chang-Su, Ph.D., Kim Young-Ku, Ph.D., Kim Sung-Jae, D.M.

Educational Objectives:

Clinicians should consider cross-titration early on, with reduction of the first antipsychotic or total switch while switching antipsychotics either from or to aripiprazole.

Summary:

Aripiprazole is a novel antipsychotic that functions as a partial agonist at the D2 receptor and then might theoretically worsen psychosis when administered with dopamine antagonists. We report a series of two clinical cases of aggravation of psychosis related to combination of aripiprazole and dopamine antagonists. Two cases demonstrated the worsening psychosis and lowering serum prolactin levels when administered aripiprazole with dopamine antagonists during switching (cross-titrating) antipsychotics. In case 1, aripiprazole was switched to haloperidol. In case 2, amisulpride was switched to aripiprazole due to amisulpride-associated amenorrhea. In case 2, psychosis was aggravated but amenorrhea was improved during switching. After stopping aripiprazole, psychotic symptoms were improved in two cases. We report on two cases whose psychosis worsened after combination with aripiprazole.

References:

1. Ramaswamy S, Vijay D, et al: Aripiprazole possible worsens psychosis. *Int Clin Psychopharmacol* 2004; 19(1):45-81.
2. DeLeon A, Patel NC, Crismon ML: Aripiprazole a comprehensive review of its pharmacology, clinical efficacy, and tolerability. *Clin Ther* 2004; 26(5):649-66.

NR82 Monday, May 23, 9:00 a.m.-10:30 a.m.

Association Study of PRODH Gene With Schizophrenia in a Chilean Sample

Aida Ruiz, M.D., *Psiquiatria y Salud Mental, Universidad de Chile, Avenida La Paz 1003, Santiago, Chile*; Pak Sham, M.D., John Powell, Ph.D., Eduardo Miranda, M.D., Robin Murray, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand genetic association analysis using a family based design.

Summary:

Objective: Evidence for association between genetic variants in the neurogulin 1 gene (NRG1) at chromosome 8p21-22, and schizophrenia has been recently described. The objective of this study was to conduct an association analysis of NRG1 gene in a Chilean schizophrenic sample, to attempt the replication of these findings.

Method: Forty-four affected families, according to DSM-IV criteria, were collected in Santiago, Chile. Three SNPs reported to be associated with schizophrenia were genotyped. Linkage disequilibrium (LD) between markers was estimated using UNPHASED

program. The pedigree disequilibrium test (PDT) was used to analyse single marker and haplotype association. The PDT was performed using the PDTPhase program.

Results: Significant LD was observed for all pair-wise calculations ($D' = 0.83-1.00$). One SNP (SNP8NRG243177) achieved a significant allelic association ($P < 0.05$). Tests for haplotype analysis showed no association ($P > 0.05$).

Conclusions: A significant association between one SNP in the Neuregulin-1 gene and schizophrenia was observed in this sample; supporting that NRG1 may play a role in susceptibility to schizophrenia.

References:

1. Stefansson H, Sarginson J, Kong A, Yates P, Steinthorsdottir, Gudfinnsson E, Gunnarsdottir, Walker N, Petursson H, Crombie C, Inganson A, Gulcher JR, Stefansson K, St Clair D: Association of neuregulin 1 with schizophrenia confirmed in a Scottish population. *Am J Hum Genet* 2003; 72:83-87.
2. Iwata N, Susuki T, Ikeda M, Kitajima T, Yamanouchi Y, Inada T, Ozaki N: No association with the neuregulin 1 haplotype to Japanese schizophrenia. *Mol Psychiatry* 2004; 9:126-127.

NR83 Monday, May 23, 9:00 a.m.-10:30 a.m. **Neuregulin1 Gene and Schizophrenia in a Chilean Sample**

Aida Ruiz, M.D., *Psiquiatria y Salud Mental, Universidad de Chile, Avenida La Paz 1003, Santiago, Chile*; Pak Sham, M.D., John Powell, Ph.D., Eduardo Miranda, M.D., Robin Murray, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand genetic association analysis using a family-based design.

Summary:

Objective: Evidence for association between genetic variants in the neuregulin1 gene (NRG1) at chromosome 8p21-22, and schizophrenia has been recently described. The objective of this study was to conduct an association analysis of NRG1 gene in a Chilean schizophrenic sample, to attempt the replication of these findings.

Method: Forty-four affected families, according to DSM-IV criteria, were studied in Santiago, Chile. Three SNPs reported to be associated with schizophrenia were genotyped. Linkage disequilibrium (LD) between markers was estimated using UNPHASED program. The pedigree disequilibrium test (PDT) was used to analyse single marker and haplotype association. The PDT was performed using the PDTPhase program.

Results: Significant LD was observed for all pair-wise calculations ($D = 0.83-1.00$). One SNP (SNP8NRG243177) achieved a significant allelic association ($P < 0.05$). Tests for haplotype analysis showed no association ($P > 0.05$).

Conclusions: A significant association between one SNP in the Neuregulin-1 gene and schizophrenia was observed in this sample; supporting that NRG1 may play a role in susceptibility to schizophrenia.

References:

1. Stefansson H, Sarginson J, Kong A, Yates P, Steinthorsdottir, Gudfinnsson E, Gunnarsdottir, Walker N, Petursson H, Crombie C, Inganson A, Gulcher JR, Stefansson K, St Clair D: Association of neuregulin 1 with schizophrenia confirmed in a Scottish population. *Am J Hum Genet* 2003; 72:83-87.
2. Iwata N, Susuki T, Ikeda M, Kitajima T, Yamanouchi Y, Inada T, Ozaki N: No association with the neuregulin 1 haplotype to Japanese schizophrenia. *Mol Psychiatry* 2004; 9:126-127.

NR84 Monday, May 23, 9:00 a.m.-10:30 a.m. **Development of Appropriate ADHD Screening Scales in Korea**

Son Hyo-Il, Psy.D., *Department of Psychiatry, Dongguk University hospital, 1090-1, Sjukjangdong, Gyung Ju-Si, Korea Rep., Gyung Ju-Si 780-350, South Korea*; Song Chang-Jin, Psy. D., Lee Gwang-Heon, Psy.D., Kwak Kyung-Phil, Psy.D., Sakong Jeong-Kyu, Psy.D.

Educational Objectives:

This research demonstrates a more useful and reliable screening tool for ADHD children in Korea.

Summary:

Objective: Assessment of ADHD comprises multimodal approaches such as interviews with ADHD children, behavior scales reported by parents and teachers, and objective and self-report measures. Recent interest in this condition has been focused increasingly on the validity and reliability of such measures.

This study investigated the validity and reliability of ADHD behavioral symptoms scales and disclosed more appropriate measures for ADHD children in Korea.

Method: Children between age 7 to 12 ($N=946$) were divided into ADHD group ($N=392$) and control group ($N=432$) based on parent and teacher ratings of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition ADHD symptoms. We examined the diagnostic and screening utility of four ADHD scales (Attention Deficit Disorders Evaluation Scale—Home version [ADDES-HV], ADDH Comprehensive Teacher Rating Scale [ACT-ERS], Children Attention Profile [CAP], Swanson, Nolan, and Pelham [SNAP] Checklist) in children presenting for ADHD evaluation.

Results: There are no significant gender differences on the statistical analysis, compared the SNAP scores obtained by children from the ADHD group, whereas it is likely to show more high scores in males from control group than in females from control group, ($p < .01 \sim .001$).

The value of criterion validity of ADDES-HV and CAP are between .342 to .713 from ADHD group ($p < .05$), and between .551 to .789 from control group ($p < .05$).

References:

1. McCarney SB: The manual of attention deficit disorder evaluation scale—school version. Hawthorne Educational Service, Columbia, 1989, pp 1-34.
2. Swanson JM: School-based assessment and inventories for ADD students. KC Publishing Inc, Miami, Florida, 1990.

NR85 Monday, May 23, 09:00 a.m.-10:30 a.m. **Dynamics of Insight in the Prodrome of Schizophrenia**

Robert Bota, M.D., *7638 Goddard Drive, Shawnee, KS 66214*; Stuart Munro, M.D., Kemal Sagduyu, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the implication of insight deterioration for the patients in the prodrome of schizophrenia.

Summary:

Background: Schizophrenia is characterized by diminished insight, which fluctuates with disease progression. Insight deterioration in the prodrome of schizophrenia is poorly understood.

Objective: To determine if insight deterioration occurs during the prodrome, and if insight preservation predicts a better prognosis.

Method: Data were collected retrospectively from the records of patients initially diagnosed with schizophrenia during a two-

year period. Their progress was then tracked over a three-year period.

Results: Ten patients out of 24 were evaluated before a (Fourth Diagnostic and Statistical Manual of Mental Disorders, Text Revision) DSM-IV-TR schizophrenia diagnosis was given, and 12 were evaluated at least once after the initial diagnosis. Insight preservation correlated with less need for emergency visits and fewer hospitalization days ($p < 0.005$). It also was associated with more depressive and anxious mood. Patients and family members described early, ego-dystonic perceptual disturbances, followed by diminished insight. Willingness to get treatment significantly correlated (T-test) with decreased need for hospitalization, less medication for agitation, and more participation in group therapy.

Conclusion: Most patients maintain insight during the perceptual disturbance phase. Insight diminishes as the early delusional phase sets in. Higher levels of preserved insight correlates with lesser need for acute treatment.

References:

1. Keshavan MS, Rabinowitz J, DeSmedt G, Harvey PD, Schooler N: Correlates of insight in first episode psychosis. *Schizophr Res* 2004; 70(2-3):187-94.
2. Mutsatsa SH, Joyce EM, Hutton SB, Webb E, Gibbins H, Paul S, Barnes TR: Clinical correlates of early medication adherence: West London first episode schizophrenia study. *Acta Psychiatr Scand* 2003; 108(6):439-46.

NR86 Monday, May 23, 9:00 a.m.-10:30 a.m. **Antipsychotic Treatment in the Prodromal Phase of Schizophrenia: Predictor of Better Prognosis**

Robert Bota, M.D., 7638 Goddard Drive, Shawnee, KS 66214;
John Stuart Munro, M.D., Kemal Sagduyu, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the importance of early diagnosis and treatment of schizophrenia.

Summary:

Objective: To determine if early assessment of patients and treatment of prodromal symptoms correlates with a better prognosis than patients evaluated initially at the time of schizophrenia diagnosis.

Method: Data were collected from the medical records of patients initially diagnosed with schizophrenia in a state hospital over a two-year period. Their progress was then tracked over a three year period.

Results: Of 24 patients diagnosed with schizophrenia, ten patients had already presented to the center with prodromal symptoms, referred by their families. Of those patients, 70% received treatment and 30% were discharged without medication. The patients treated during the prodromal period had significantly fewer hospitalization days (18 days) than patients evaluated for the first time at the time of schizophrenia diagnosis (27.14 days) than patients that presented with prodromal symptoms but were not started on medication (69 days). The average length of treatment was seven months before the schizophrenia diagnosis. The patients had reported a prodromal period spanning 39 months. Behavior changes were reported 16 months later and bizarre behaviors were reported five months before the initial diagnosis.

Conclusion: Antipsychotic medication prescribed during prodromal period appears to have a protective effect. Having early presentation did not predict prognosis.

References:

1. Woods SW, Breier A, Zipursky RB, Perkins DO, Addington J, Miller TJ, Hawkins KA, Marquez E, Lindborg SR, Tohen M,

McGlashan TH: Randomized trial of olanzapine versus placebo in the symptomatic acute treatment of the schizophrenic prodrome. *Biol Psychiatry* 2003; 15:54(4):453-64. Erratum in: *Biol Psychiatry* 2003; 15:54(4):497.

2. McGorry PD, Yung AR, Phillips LJ, Yuen HP, Francey S, Cosgrave EM, Germano D, Bravin J, McDonald T, Blair A, Adlard S, Jackson H: Randomized, controlled trial of interventions designed to reduce the risk of progression to first-episode psychosis in a clinical sample with subthreshold symptoms. *Arch Gen Psychiatry* 2002; 59(10):921-8.

NR87 Monday, May 23, 9:00 a.m.-10:30 a.m. **Medical Screening in a Mentally Ill Population**

Richard Sanders, M.D., Department of Psychiatry, Dayton VA, 4100 West Third Street, Dayton, OH 45428; Shrikant Vaish, M.B., Richard Sanders, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to identify problems in medical screening of psychiatric patients and describe the potential advantages of structured instruments for this purpose.

Summary:

Objective: Key physical ailments in public-sector psychiatric patients are frequently missed during routine clinical care. A structured approach to medical evaluation, the Medical Evaluation Field Manual (MEFM) was developed to improve disease detection. Although it is the most extensively studied algorithm, it has not been validated externally. In order to explore the feasibility of testing the MEFM in a VA setting, we determined the rate of collection of MEFM data in the routine care of mentally ill veterans.

Method: Data gathered and processed in the MEFM approach for 104 outpatients seen by any psychiatrist in a VA within a single week.

Results: 104 patients were surveyed, 96 male and 92 Caucasian. Average age was 56.6(SD 13.55). No records contained recorded answers for all data types included in the MEFM screening protocol. For individual data points, rates of completion ranged from 3.8 to 99%. History items were less often available than laboratory tests.

Discussion: In routine practice, important history is neglected, although labs and vital signs are more consistently recorded. Much data found valuable in medical screening of psychiatric patients is not collected routinely. Structured tools such as the MEFM may improve the detection of comorbid disease in this population.

References:

1. Koran LM, Sheline Y, Imai K, et al: Medical disorders among patients admitted to a public sector psychiatric inpatient unit. *Psychiatric Services* 2002; 53:1623-1625.
2. Koran LM, Sox HC, Marton KI, et al: Medical evaluation of psychiatric patients: I. results in a state mental health system. *Archives of General Psychiatry* 1989; 46:733-740.

NR88 Monday, May 23, 9:00 a.m.-10:30 a.m. **The Possible Role of IL-12 and TGF- β 1 Cytokines in Drug-Free Schizophrenia**

Sung-Jae Kim, M.D., Department of Psychiatry, Korea University Ansan Hospital, 516, Gojan 1(ii)-dong, Danwon-gu, Ansan-si, Gyeonggi-do 425-707, South Korea; Yong-Ku Kim, M.D., Bun-Hee Lee, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that immune responses and cytokine abnormalities play an important role in pathophysiology and etiology of schizophrenia, and that the Th1 and Th3 cytokines differ in the roles in schizophrenia.

Summary:

Background: Several reports have suggested that cytokine alterations could be related to the pathophysiology of schizophrenia. In this study, we measured plasma level of Interleukin-12 (IL-12), a pro-inflammatory Th1 cytokine and transforming growth factor- β 1 (TGF- β 1), an anti-inflammatory Th3 cytokine before and after antipsychotic treatment in schizophrenic patients and normal controls.

Methods: The plasma concentrations of IL-12 and TGF- β 1 were measured in 23, schizophrenic patients and 31 normal controls at admission and eight weeks later using quantitative ELISA. The psychopathology was measured by brief psychiatric rating scale (BPRS).

Results: IL-12 and TGF- β 1 levels were significantly higher in schizophrenic patients than in controls before treatment. Following the 8-week treatment, the TGF- β 1 level returned to control values, while IL-12 levels were not significantly changed. There were no significant correlations between the changes of BPRS scores and the changes of IL-12 or TGF- β 1 levels.

Conclusion: Cytokine abnormalities in schizophrenia might be involved in the pathophysiology of the illness. It is possible that TGF- β 1 plays an important role in the schizophrenia.

References:

1. Kim YK, Suh IB, Kim H, Han CS, Lim CS, Choi SH, Licinio J: The plasma level of interleukin-12 in schizophrenia, major depression, and bipolar mania: effects of psychotropic drugs. *Mol Psychiatry* 2002; 7:1107-1114.
2. Muller N, Riedel M, Ackenheil M, Schwarz MJ: The role of immune function in schizophrenia: an overview. *Eur Arch Psychiatry Clin Neurosci* 1999; 249:62-68.

NR89 Monday, May 23, 9:00 a.m.-10:30 a.m.

Case Report: Topiramate for Hyperphagia Associated to a Third Ventricle Mass

Alejandra Postlethwaite, M.D., *Department of Psychiatry, Harvard Medical School, 940 Belmont St #116 A 7, Brockton, MA 02301; Bernardo Ng, M.D.*

Educational Objectives:

A case report of an individual with a mass in the third ventricle is presented. Neuropsychiatric manifestations included hyperphagia, agitation, and cognitive impairment. Pharmacological intervention with topiramate helped the hyperphagia and agitation, better than other agents tried. Possible mechanisms of action of this agent are discussed.

Summary:

The eating centers consist of the satiety center at the ventromedial hypothalamic (VMH) area that inhibits two lateral hypothalamic (LH) areas known as the hunger centers. These areas work in a constant equilibrium responding to different forms of input, in order to give the individual the feeling of hunger or satiety. Classic animal models have demonstrated how the destruction of the VMH area can lead an animal to overeat and gain excessive body weight, whereas the destruction of the LH areas can lead an animal to starvation.

Topiramate (TPM) is a novel anticonvulsant of wide spectrum that was introduced to the US market in 1997 as an adjuvant for uncontrolled epilepsy. It facilitates GABA effects, and inhibits

glutamate and carbonic anhydrase. Weight loss associated to TPM has been identified in several clinical studies and reports.

We present a case of a male with dementia, agitation, and uncontrollable hyperphagia. No pharmacological intervention helped like TPM, in spite of later finding that patient actually had a mass in the floor of the third ventricle.

References:

1. Yen DJ, Yu HY et al: A double-blind, placebo-controlled study of topiramate in adult patients with refractory partial epilepsy. *Epilepsia* 2000; 41:9:1162-6.
2. Ben-Menachem E, Henriksen O, et al: Double-blind, placebo-controlled trial of topiramate as add-on therapy in patients with refractory partial seizures. *Epilepsia* 1996; 37;6:539-43.

NR90 Monday, May 23, 9:00 a.m.-10:30 a.m.

Lack of Association Between Polymorphic Variations in the Alpha-3 Subunit GABA Receptor Gene (GABRA3) and Impulsivity of Suicide Attempts

Luis Jimenez-Trevino, M.P.H., *Area de Psiquiatria-Facultad de Medicina, Universidad de Oviedo, Julian Claveria 6, Oviedo 33006, Spain; Enrique Baca-Garcia, Ph.D., Carmen Díaz-Sastre, Ph.D., Eloy Garcia-Resa, Ph.D., Hilario Blasco-Fontecilla, Ph.D., Jeronimo Saiz-Ruiz, Ph.D.*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the role of polymorphic variations in GABRA3 gene and impulsivity of suicide attempts.

Summary:

Background: Growing evidence indicates that genetic factors contribute to suicide risk. Current research supports the hypothesis that a dysfunction in GABA activity affects variables such as anxiety or aggressiveness, involved in the impulsivity of suicidal behaviours.

Methods: We have conducted a genetic association study between suicide attempts and the polymorphic variations of the GABRA3 gene, located in chromosome X. The sample consisted of 371 suicide attempts, defined according to NIMH, and 488 healthy controls. Impulsivity of the attempt was assessed with Barrat Impulsivity Scale (BIS-11). A standard informed consent was provided. 16 DNA for genotyping was extracted according to standard methods. GABRA3 dinucleotide repeat polymorphism was studied by PCR amplification using primers previously described.

Results: Though we did not find an association between the impulsivity of suicide attempts and GABRA3 genotypes ($X^2=7, 105; \text{diff}=3; p=0.069$ for women; $X^2=3,758, \text{diff}=3, p=0.289$ for men), we found an association between the impulsivity of suicide attempts and homozygosity for allele (a1) (169-169) (Fisher's test $p<0.05$) in women.

Conclusions: The present study suggests an association between homozygosity for allele (a1) (169-169) in women and impulsivity of suicide attempts, being more impulsive the suicide attempts of those women with homozygosity for the mentioned allele.

References:

1. Hicks AA, Johnson KJ, Barnard EA, Darlison MG: Dinucleotide repeat polymorphism in the human X-linked GABAA receptor alpha 3-subunit gene. *Nucleic Acids Res* 1991; 19: 4016.
2. Baca-Garcia E, Vaquero C, Diaz-Sastre C, Saiz-Ruiz J, Fernandez-Piqueras J, de Leon J: A gender-specific association between the serotonin transporter gene and suicide attempts. *Neuropsychopharmacol* 2002; 26:692-69.

NR91 Monday, May 23, 9:00 a.m.-10:30 a.m.

ECT: Lesson From a Challenging Case With Hypertrophic Cardiomyopathy (HCM)

Xavier A. Preud'Homme, M.D., *Quantitative EEG and Sleep Research Laboratory, Duke University Medical Center, Box 3309, Durham, NC 27710*; Eric Christopher, M.D., Andrew Krystal, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the intricacies of managing electroconvulsivetherapy (ECT) in patients with comorbid hypertrophic cardiomyopathy (HCM).

Summary:

Administration of ECT to an elderly catatonic patient with melancholic depression led to cardiac arrest because of unsuspected preexisting HCM. The patient survived this event and a full course of ECT was completed achieving significant remission after adjusting treatment to account for the flow dependence state associated with HCM. Extra-care was required to counter ECT's parasympathetic/sympathetic effect on the cardiovascular system. In addition to an anticholinergic agent to attenuate vagal effects (bradycardia, hypotension), pretreatment included 500 ml NS bolus intravenously followed by a short-acting beta-blocker (esmolol drip) titrated to attenuate seizure-induced sympathetic effects (increased cardiac output, hypertension). Myocardial oxygen demand and delivery mismatch was then minimized. HCM is a genetic cardiac disorder (prevalence: 1/500). Most patients with HCM do not present with outflow obstruction under resting conditions but become at risk to develop dynamic subaortic gradients of varying magnitude with provocative maneuvers of which ECT is a prime example. Noninvasive echocardiography confirms the diagnosis, especially with a gradient > 30 mm Hg (2.7 m/s by Doppler). Because HCM is inherited as a Mendelian autosomal dominant trait, systematic screening for familial history of HCM-related symptoms/signs (exertional dyspnea, dizziness, (pre)syncope, sudden and unexpected deaths) should be part of the pre-ECT evaluation.

References:

1. Weiner RD, Coffey CE, Krystal AD: Electroconvulsive therapy in the medical and neurological patient, in A Stoudemire, BS Fogel and D Greenberg (Eds.) *Psychiatric care of the medical patient*, 2nd Ed. New York, Oxford University Press, pp 419-28, 2000.
2. Maron BJ, et al: ACC/ESC clinical expert consensus document on hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2003; 42:1687-713.

NR92 Monday, May 23, 9:00 a.m.-10:30 a.m.

Patterns of Comorbid Substance Use Disorder in Bipolar Rapid Cyclers

Keming Gao, M.D., *Department of Psychiatry, Case Western Reserve University, 11400 Euclid Ave., Cleveland, OH 44106*; Omar Elhaj, M.D., Melvin Shelton, M.D., Eric Youngstrom, Ph.D., Robert Findling, M.D., Joseph R. Calabrese, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the patterns of substance-use disorder in bipolar patients with rapid cycling.

Summary:

Objective: To study patterns of substance use disorders in bipolar rapid cyclers in an outpatient research setting.

Method: The Mini International Neuropsychiatric Interview was used to ascertain DSM-IV diagnoses in 106 dual diagnosis bipolar I or 11 patients.

Results: 86 met criteria for substance dependence and 20 for substance abuse. Over 92% had been dependent on at least one substance, including alcohol (76%), cocaine (32%), marijuana (31%), opiate (14%), stimulant (10%), and sedative (5%). In addition, this cohort of dependent patients also had a complicated lifetime history of abuse, including alcohol (45%), cocaine (29%), marijuana (46%), opiate (7%), stimulants (13%), sedatives (11%), and hallucinogens (34%). For those specifically dependent on alcohol (n=71), other complicated histories of dependence were also present, including dependence on one substance in 16%, two in 23%, and at least 3 in 10%. This cohort of 71 patients also had histories of abuse on one substance in 16%, two in 16%, three in 4%, and at least four in 1%. In contrast, patients with cocaine (n = 30) or marijuana (n = 29) dependence had been dependent on more substances, including one substance (30%, 24.1%), two (40%, 44.8%), and at least 3 (27%, 20.7%), respectively.

Conclusions: Patterns of presentation of bipolar disorder comorbid with substance use disorders are extremely complex. The majority of patients are dependent on at least one substance, and the majority of those have abused other substances. This degree of heterogeneity poses challenges for the design of future dual diagnosis studies.

References:

1. Frye MA, Altshuler LL, et al: Gender difference in prevalence, risk, and clinical correlates of alcoholism comorbidity in bipolar disorder. *Am J Psychiatry* 2003; 160:883-889.
2. Havassy BE, Arns PG: Relationship of cocaine and other substance dependence to well-being of high-risk psychiatric patients. *Psychiatr Serv* 1998; 49:935-940.

NR93 Monday, May 23 9:00 a.m.-10:30 a.m.

Assaults Against Residents in Two General Hospitals in Baghdad

Muhmmad Lafta, M.D., *Director of Al-Rashad Mental Teaching Hospita, Al Kadmeia 413/6/63, Baghdad, Iraq*

Educational Objectives:

At the end of the presentation, the participants should know the risk of violence against the physicians in their workplaces.

Summary:

Objective: Violence in the workplace is an ill-defined and under-reported concern for physicians. The study attempts to assess the risk of assault by patients on physicians.

Method: Eighty resident doctors working in Al-Urmook & Al-Kindy general hospitals, received questionnaires for each about the assault. All the doctors (100%) responded and completed the questionnaire (66 males & 14 females).

Results: Seventy doctors (87%) had been assaulted by patients and their relatives, and the assault was greatly verbal. The rate of assault was higher among the junior residents. Only 59% of victims inform the administration about the assault and 34% of them were satisfied with the steps done by the administration. Most of the victims did not like to talk about the assault and considered it painful experience.

Conclusion: Majority of the residents had been assaulted by patients or their relatives. The victims still suffered from the sequele of the assault. The new physicians should be trained to deal with the patient's possible assault.

References:

1. Anglin D, Kyriaco D, Huston H: Resident perspectives on violence & personal safety in emergency. *Ann-Emerg Med* 1994; 23(5):1082-4.
2. Yassi A: Assault & abuse of health care workers in a large teaching hospital. *CMAJ* 1994; 151(9):1273-9.

NR94 Monday, May 23, 9:00 a.m.-10:30 a.m. **Correlates of Artificial Sweetener Use Among Women With Bulimia Nervosa**

Diane A. Klein, M.D., *Department of Psychiatry, Columbia University, 1051 Riverside Drive, Unit 98, New York, NY 10032*; Gillian Boudreau, B.A., Michael Devlin, M.D., B. Timothy Walsh, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the prevalence and nature of use of artificially sweetened foods in bulimia nervosa, and identify clinical correlates of use of these products.

Summary:

Background: Women with eating disorders often describe use of artificially sweetened, low-calorie (diet) products; however, little research documents this. Previous, our group reported increased use of diet products among women with bulimia nervosa (BN), compared with women without eating disorders. The current study was designed to examine clinical correlates of use of these products.

Method: Forty-six women with BN completed a survey assessing weekly use of gum, artificially sweetened, low-calorie beverages, and packets of artificial sweetener in the previous month. Pearson correlation coefficient was calculated to assess the relationship between quantity of weekly use and clinical variables.

Results: Forty-four subjects (96%) endorsed use of one or more product in the prior month. Numerous participants endorsed "excessive" use (e.g., ten 12-oz beverage servings per day). Beverage consumption was significantly related to binge frequency ($r = .434$, $p = .008$) and weight suppression (maximum — current body weight; $r = .338$, $p = .044$). Gum use was inversely correlated with body mass index (BMI; $r = -.339$, $p = .024$).

Conclusions: Use of low-calorie artificially sweetened products by women with BN appears to be common and may be excessive. Our data suggest that greater use of some of these products may be associated with eating pathology and underweight. Clinical and research implications are discussed.

References:

1. Klein DA, Boudreau GB, Devlin MJ, Walsh BT: Use of artificially sweetened products in eating disorders. *Appetite* 2004; 42[3], 374.
2. Franklin JC, Schiele BC, Brozek J, Keys A: Observations on human behavior in experimental semistarvation and rehabilitation. *J Clin Psychol* 1948; 4:28-45.

NR95 Monday, May 23, 9:00 a.m.-10:30 a.m. **Prevalence of Tobacco Use Among Brazilian Elderly Living in Community**

Valeska Marinho, M.D., *Department of Psychiatry, Federal University of São Paulo, R. Botucatu 740, São Paulo 04023-900, Brazil*; Sergio Blay, Ph.D., Sergio Andreoli, Ph.D., Fabio Gastal

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the prevalence and predictors of tobacco use in elderly people living in urban areas of Rio Grande do Sul, Brazil.

Summary:

Methods: Cross sectional design. A representative sample of 6,963 subjects, aged 60 years and over, living in community, in urban areas, Brazil, was examined to estimate the frequency of smoking tobacco. Smoke use was measured by means of a household questionnaire that inquired about current tobacco use, socio-demographic characteristics, among other instruments. Bivariate and multivariate analysis between smoking and social and demographic variables were explored.

Results: The prevalence of tobacco use was 28.9% among men and 13.5% among women. Factors associated with increased risk of tobacco smoking were: less educated men, non-Caucasians, non-evangelic, lower income, and marital status. Two social characteristics interact: religiosity and race. Nonwhites and non-evangelic were 2.1 fold more likely to be a smoker than the other subjects (95% C. 1. 1.2-3.7). Factors associated with a decreased risk of tobacco smoking were: aging and religiosity.

Conclusion: The use of tobacco is more frequent in men than in women in a proportion of 2:1. The findings presented here indicate the potential of some sociodemographic variables to increase the risk of tobacco use. Being men, less educated, non white, non-evangelic, with lower income, and not married, is strongly related with smoking in community elderly in Brazil.

References:

1. Jha P, Ranson MK, Nguyen SN, Yach D: Estimates of global and regional smoking prevalence in 1995, by age and sex. *Am J Public Health* 2002; 92(6):1002-6.
2. Am J Public Health 2002; 92(6):1002-6.
3. Moreira L: Fuchs F, Morales RS: Brederneir M, Cardos S: Prevalence of smoking and associated factors in a metropolitan area of southern Brazil.
4. *Rev. Saúde Pública* 1995; 29(1):46-51.

NR96 Monday, May 23, 9:00 a.m.-10:30 a.m. **Physical and Psychosocial Correlates for Body Mass Index Among Young Adults**

Susan Shur-Fen Gau, M.D., *Department of Psychiatry, National Taiwan University Hospital, No. 7, Chung-Shan South Rd, Taipei, Taiwan*; Chi-Shin Wu, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that individuals with extreme BMI should receive comprehensive assessment and treatment for psychosocial and physical problems related to BMI.

Summary:

Objective: This study aimed to explore the physical, psychosocial, and sleep correlates for the extreme BMI.

Methods: The sample consisted of 2,697 first-year college students (participation rate = 78.5%, mean age = 18.9), 1,404 males and 1,293 females, who completed questionnaires for psychosocial variables, were interviewed for physical factors by healthcare professionals, and received routine laboratory examinations. BMI was grouped into four categories according to the criteria defined by the Department of Health, Taiwan.

Results: There were 144,899, 224, and 137 males, and 314, 849, 91, and 39 females in the categories of underweight, normal, overweight, and obese, respectively. The self-reported body weight and height were highly correlated with those measured by scale (ICC = 0.99). High BMI was associated with depressive

mood, morning type of sleep pattern, lack of affection/care from father, several physical problems, no regular exercise, irregular meal, bulimia, regular smoking, hyperglycemia, hypercholesterolemia, and higher blood pressure. Underweight was correlated to anxiety, phobia, regular meal, evening type of sleep pattern, and regular exercise.

Discussion: Findings from this study indicate that BMI is related not only to physical factors but also to psychosocial factors. Prevention of extreme BMI need to integrate the preventive psychiatry and control of BMI may help offset the physical complications.

References:

1. Lobstein T, Baur L, Uauy R, Task-Force IIO: Obesity in children and young people: a crisis in public health. [see comment]. *Obesity Reviews* 2004; 1:4-104.
2. Stunkard AJ, Faith MS, Allison KC: Depression and obesity. *Biological Psychiatry* 2003; 54(3):330-7.

NR97 Monday, May 23, 9:00 a.m.-10:30 a.m. **Prevalence of Dysfunctional Eating and Depression in U.S. Army Entry-Level Personnel**

Christopher H. Warner, M.D., *Department of Psychiatry, Walter Reed Army Medical Center, 7821 Golden Pine Circle, Severn, MD 21144*; Carolyn Warner, M.D., Theresa Matuszak, M.D., Thomas Grieger, M.D., Julianne Flynn, M.D., Douglas Waldrep, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant will be able to define the risk factors for eating and affective disorders and their application to our population, define diagnostic and screening methods for eating and affective disorders, and review the results of the screening in an entry level population.

Summary:

Objective: To determine the prevalence of and risk factors for dysfunctional eating and depressive disorders in an entry-level U.S. Army population.

Design and Setting: Cross Sectional Survey of Advanced Individual Training (AIT) US Army soldiers at Aberdeen Proving Grounds, MD

Study Populations: All (1,184) current AIT soldiers approached, 1,090 voluntarily chose to participate.

Interventions: An anonymous self-report survey containing demographics, past history including abuse and psychiatric treatment, the Eating Attitudes Inventory-26, and the Patient Health Questionnaire-9.

Main Outcome Measures: Prevalence of Dysfunctional Eating Behaviors, Prevalence and Severity of Depression

Results: Response rate was 91.2% (955 males, 135 females). 40% were overweight (BMI=25); 11% reported prior psychiatric history; 26% reported prior history of abuse; 9.8% endorsed dysfunctional eating (Male 7.0%, Female 29.6%); and 34.3% endorsed symptoms consistent with depression. Female gender (OR=7.177; CI95 3.3-15.6; p<0.0005), depression (OR=4.038; CI95 1.9-8.5; p<0.0005), overweight (OR=3.39; CI95 1.6-7.0; p=0.001), and prior psychiatric treatment (OR=3.138; CI95 1.3-7.8; p=0.013) placed soldiers at higher risk for dysfunctional eating. Dysfunctional eating (OR=4.174; CI95 2.0-8.8; p<0.0005) and history of verbal abuse (OR=2.212; CI95 1.1-4.4; p=0.022) placed soldiers at higher risk for depression.

Conclusions: Our study shows a higher than expected rate of dysfunctional eating and depression in AIT soldiers with identifiable risk factors for each. This indicates an important need for further study, effective screening, preventive counseling, and early intervention for treatment.

References:

1. Koslowsky M: The factor structure and criterion validity of the short form of the Eating Attitudes Test. *J Pers Asses* 1992; 58(1):27-35.
2. Kroenke K, Spitzer RL, and Williams JB: The PHQ-9: Validity of a brief depression severity measure. *J Gen Int Medicine* 2001; 16: 606-613.

NR98 Monday, May 23, 9:00 a.m.-10:30 a.m. **Impact of Four Psychiatric and 25 Somatic Conditions on Quality of Life**

Samuli I. Saarni, M.D., *Department of Mental Health and Alcohol Research, National Public Health Institute, Mannerheimintie 166, Helsinki 00300, Finland*; Arpo Aromaa, M.D., Jouko Lönnqvist, M.D., Seppo Koskinen, M.D., Harri Sintonen, Ph.D., Jaana Suvisaari, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to estimate the relative impact of different chronic conditions on HRQoL, and understand why different HRQoL instruments give different results and what this implies.

Summary:

Objectives: To investigate the impact of psychiatric disorders on health-related quality of life (HRQoL) and compare this with common, chronic somatic conditions. To compare two HRQoL measures.

Methods: The study is based on a national, comprehensive survey representing the Finnish population aged 30 or over. HRQoL was estimated using two generic, utility based, self-report measures, the 15D and the EQ-5D. Diagnosis of somatic conditions was based on self-report. Non-psychotic psychiatric disorders were diagnosed by CIDI and grouped as depressive-, anxiety- and alcohol-use disorders. Psychotic disorders were preliminary identified from the Finnish Hospital Discharge Register, but will be verified by SCID. Impact of different conditions on HRQoL were adjusted for sociodemographic variables and other conditions, and in a separate analysis, for prevalence.

Results: People reported on average two conditions. On a list of 29 conditions ranked by their impact on HRQoL, anxiety ranked 2 on EQ-5D (3 on 15D), depression ranked 6(2), psychotic disorders 13(4) and alcohol use disorders 16(10). Adjusted for prevalence, psychiatric disorders resulted in second largest loss of HRQoL after musculoskeletal disorders.

Conclusion: Psychiatric disorders have larger effect on HRQoL than most somatic conditions. EQ-5D estimates the HRQoL impact of psychiatric disorders lower and musculoskeletal disorders higher than the 15D.

References:

1. The EuroQoL Group: EuroQol-a new facility for the measurement of health-related quality of life. *Health Policy* 1990; 16(3):199-208.
2. Sintonen H: The 15D instrument of health-related quality of life: properties and applications. *Ann Med* 2001; 33(5):328-36.

NR99 Monday, May 23, 9:00 a.m.-10:30 a.m. **Antipsychotics and the Abnormality of Fasting Glucose and Total Cholesterol in Schizophrenia**

Jin-Yong Kim, M.D., *Department of Psychiatry, Asan Medical Center, PungNap-dong SongPa-Gu, Seoul, Korea*; Joong Sun Lee, M.D., Jae Hyun Lee, M.D., Jeong Won Jeon, M.D., Dong Eun Lee, M.D., Oh Su Han, M.D., Chang Yoon Kim, M.D.

Educational Objectives:

The concerns about significant weight gain induced by antipsychotics have been recently increased. It raised an issue about the possible effect of antipsychotics on the glucose and lipid metabolism. To address this issue, we investigated the prevalence of abnormal glucose metabolism (impaired fasting glucose (110mg/dl=fasting glucose=125mg/dl) or diabetes (fasting glucose=126mg/dl)) in patients taking antipsychotics and also compared the prevalence of abnormal glucose metabolism between typical and atypical antipsychotics.

Summary:

Objective: The concerns about significant weight gain induced by antipsychotics have been recently increased. It raised an issue about the possible effect of antipsychotics on the glucose and lipid metabolism. To address this issue, we investigated the prevalence of abnormal glucose metabolism (impaired fasting glucose (110mg/dl=fasting glucose=125mg/dl) or diabetes (fasting glucose=126mg/dl)) in patients taking antipsychotics and also compared the prevalence of abnormal glucose metabolism between typical and atypical antipsychotics.

Methods: The subjects included 76 outpatients and 109 inpatients with schizophrenia by DSM-IV diagnostic criteria who had been taking antipsychotics regularly for at least one month. We measured fasting glucose, total cholesterol level after midnight NPO. Information about demographic and clinical characteristics of patients was gathered from interview with patients, family members, and the medical records.

Results: 24 of 185 schizophrenia patients (13.0%) showed abnormal glucose metabolism. Six of 47 patients taking olanzapine (12.8%) and two of 34 patients taking haloperidol (5.9%) showed abnormal glucose metabolism. The prevalence of abnormal glucose metabolism was higher with olanzapine than with haloperidol, although the difference did not reach statistical significance. However, patients with olanzapine showed higher fasting glucose level than those with haloperidol. There was no significant correlation between medication dose and fasting glucose, total cholesterol level.

Conclusion: The prevalence of abnormal glucose metabolism was higher in patients with antipsychotics. Olanzapine was more likely to raise fasting blood glucose to higher level than haloperidol.

References:

1. Lieberman JA, Tollefson G, Tohen M, Green AI, Gur RE, Kahn R, et al: Comparative efficacy and safety of atypical and conventional antipsychotic drugs in first-episode psychosis: a randomized, double-blind trial of olanzapine versus haloperidol. *Am J Psychiatry* 2003; 160:1396-1404.
2. Mojtabai R, Lavelle J, Gibson PJ, Bromet EJ: Atypical antipsychotics in first admission schizophrenia: medication continuation and outcomes. *Schizophr Bull* 2003; 29:519-530.

NR100 Monday, May 23, 9:00 a.m.-10:30 a.m. Panic Disorder Subtypes and the Prevalence of Agoraphobia and Depressive Episodes

Rafael C.R. Freire, M.D., *Laboratory of Panic and Respiration, Inst of Psychiatry - Fed Univ of Rio de Janeiro, Av Visconde de Albuquerque 694 302, Rio de Janeiro 22450-000, Brazil;*
Alexandre M. Valenca, M.D., Isabella Nascimento, M.D., Fabiana L. Lopes, M.D., Marco A. Mezzasalma, M.D., Walter A. Zin, M.D., Antonio E. Nardi, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the panic disorder subtypes, their features, and their influence in the diagnosis and therapeutics.

Summary:

Objective: To establish correlations among panic disorder subtypes and demographic and clinical features, such as the prevalence of agoraphobia and depressive episodes.

Method: 193 panic disorder patients (SCID-I, DSM-IV) were examined in the Laboratory of Panic and Respiration of the Federal University of Rio de Janeiro. The subtypes of interest were the respiratory, with three out of four prominent respiratory symptoms during the panic attacks vs. non-respiratory, likewise PD with diurnal PAs vs. PD with only nocturnal (during sleep) PAs.

Results: Respiratory subtype represented 56.5% (n=109), non-respiratory 43.5% (n=84), diurnal subtype account for 82.4% (n = 159), and non-diurnal for 17.6% (n = 34). There were no significant demographic (gender, age, educational level, marital status and occupation) differences. There was no correlation between the subtypes and duration of the disorder, familial history, previous treatment and benzodiazepine use. The diurnal subtype was significantly associated with previous major depressive episodes (chi-square = 4.333; p = 0.037) and agoraphobia (chi-square = 19.278; p < 0.001), respiratory subtype was not associated with this two variables.

Conclusion: The PD can be discriminated based on symptomatologic and clinical features, especially the presence of agoraphobia and previous major depressive episodes.

References:

1. Briggs AC, Stretch DD, Brandon S: Subtyping of panic disorder by symptom profile. *British Journal of Psychiatry* 1993; 163:201-209
2. Valenca AM, Nardi AE, Nascimento I, Zin WA, Versiani M: Respiratory panic disorder subtype and sensitivity to the carbon dioxide challenge test. *Braz J Med Biol Res* 2002; 35(7):783-8.

NR101 Monday, May 23, 9:00 a.m.-10:30 a.m. Mirtazapine Versus Alprazolam in the Early Phase of Treatment in Panic Disorder

Kyung-Kyu Lee, M.D., *Department of Psychiatry, Dankook University Hospital, 29 Anseodong, Cheonan 330-714, Korea;*
Geon-Ho Bahn, M.D., Jong-Heun Lee, M.D., Sung-Kyu Choi, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to treat patients with panic disorder with mirtazapine in the early phase of treatment.

Summary:

Objective: Mirtazapine is an antidepressant that has anxiolytic effect with early onset of action. Alprazolam is well known to have a fast onset of action and is well tolerated by panic patients. To investigate the effect of mirtazapine in the early phase of treatment in panic disorder, the present study compared the effect of mirtazapine and alprazolam.

Methods: We studied 20 consecutive patients with a DSM-IV diagnosis of panic disorder (male 7/female 13) who had been randomly assigned to 8-week treatment with either mirtazapine (15-30mg) or alprazolam (0.5-3mg). The patients were assessed with daily and weekly panic diaries (including overall number and intensity of panic attack), Clinical Global Impressions scale, Hamilton Anxiety Scale, Sheehan's Phobic Scale, Sheehan's Disability Scale.

Results: Both groups improved significantly in all measure. ANOVA showed no significant differences between the two treatment groups in all measures at the baseline. Repeated measure of ANOVA showed no significant difference between two groups in all measures.

Conclusion: The results of this study suggest that mirtazapine is as effective as alprazolam in the early phase of treatment in panic disorder.

References:

1. The effect of mirtazapine in panic disorder: an open label pilot study with a single-blind placebo run-in period. *Int Clin Psychopharmacol* 2001; 16:363-368.
2. Rosenberg NK, Andersch S, Kullingsjo H, et al: Efficacy and safety of alprazolam, imipramine and placebo in treating panic disorder. *Acta Psychiatr Scand* 1991; suppl. 365:18-27.

NR102 Monday, May 23, 9:00 a.m.-10:30 a.m.
Major Depression in Canadian Women With Urinary Incontinence

Simone N. Vigod, M.D., *Department of Psychiatry, University of Toronto, 17-097, 30 Bond St., Toronto, ON M5B 1W8, Canada;*
Donna E. Stewart, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be familiar with the epidemiology of depression in Canadian women with urinary incontinence and the impact of such comorbid illness on their quality of life.

Summary:

Objective: Evaluate the relationship between urinary incontinence (UI) and major depression, highlighting characteristics of women with both UI and depression and the impact of such comorbid illness.

Methods: The Canadian Community Health Survey (CCHS 1.1) is a cross-sectional survey representative of the Canadian population that allows assessment of UI, major depression, and quality of life. Logistic regression was used to determine the likelihood of having depression in the presence of UI. A bootstrapping resampling procedure was applied to improve precision of the estimates.

Results: The 12-month prevalence of depression was higher in women with UI (overall: 15.5%, ages 18-44: 30%) than without UI (9.2%). The odds ratio for major depression in UI was 5.73, controlling for confounding factors. Women with comorbid illness were more likely to be younger, heavier, have higher incomes, and were less likely to be married than women with UI only. They also reported increased physician use, subjective distress, and permanent absence from work.

Conclusions: Urinary incontinence and major depression frequently occur together in Canadian women and the combined impact of UI and major depression exceeds the impact of either condition alone. It is imperative that physicians be attentive to these findings in a multitude of clinical settings.

References:

1. Steers WD, Lee KS: Depression and incontinence. *World Journal of Urology* 2001; 19:351-357.
2. Nygaard L, Turvey C, Burns T, Crischilles E, Wallace R: Urinary incontinence and depression in middle-aged united states women. *Obstetrics and Gynecology* 2003; 101:149-156.

NR103 Monday, May 23, 9:00 a.m.-10:30 a.m.
Depressive Symptom Prevalence and Association With Subjective Functional Status Assessment in Patients With Coronary Artery Disease, Cerebral Vascular Disease, or Peripheral Vascular Disease

Edward R. Norris, M.D., *Department of Psychiatry, Lehigh Valley Hospital, 1251 South Cedar Crest Blvd, Suite 202A, Allentown, PA 18104;* Yufei Xiang, M.D., Michael Kaufmann,

M.D., Thomas Wasser, M.D., Jane Nester, Ph.D., John Castaldo, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the association of depressive symptoms with functional health status in patients with cardiovascular diseases.

Summary:

Objective: The purpose of this study was to evaluate the prevalence of depression and the association with functional status in patients with coronary artery disease (CAD), cerebral vascular disease (CVD), and peripheral vascular disease (PVD).

Methods: 508 patients between 39-79 years-old who suffered a vascular event within six months were recruited from the Lehigh Valley Hospital. Patients were screened with the Beck Depression Inventory (BDI) and the Short Form Health Survey (SF-36). Independent t-tests and ANOVA were performed with Bonferroni correction.

Results: 355 (70%) had CAD, 87 (17%) had CVD, and 66 (13%) had PVD. 60 (17%) of CAD patients, 24 (28%) of CVD patients, and 22 (33%) of PVD patients had BDI scores suggesting depression. PVD patients were the most likely to have depression ($p < 0.001$).

Depressed CAD or PVD patients scored significantly lower in all SF-36 subscales except bodily pain ($p < 0.001$). Depressed CVD patients also scored significantly lower in physical role, general health, vitality, social functioning, and mental health ($p < 0.006$).

Conclusions: These results are the first to compare depressive symptoms in a single cohort of patients with different vascular diseases. This increased rate of depressive symptoms may be related to a trend in worsened subjective health scores.

References:

1. Sturm JW, Osborne RH, et al: Brief comprehensive quality of life assessment after stroke: the assessment of quality of life instrument in the north East Melbourne stroke incidence study (NEMESIS). *Stroke* 2002; 33(12):2888-94.
2. Rao R, Jackson, S, Howard R: Depression in Older People with Stroke, Carotid Stenosis and Peripheral Vascular Disease: A Comparison with Healthy Controls. *International Journal of Geriatric Psychiatry* 2001; 16:175-183.

NR104 Monday, May 23, 9:00 a.m.-10:00 a.m.
Improving Quality and Correspondence of Care in Severely and Persistently Mentally Ill Patients With Viral Hepatitis

Saranga Shah, D.O., *Department of Psychiatry, 151 Gregory Lane, Franklin Park, NJ 08823;* Anthony Tobia, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the importance of assignment to a medication group as it impacts coordination of care for viral hepatitis.

Summary:

Introduction: Hepatitis C virus infection is a public health problem affecting more than 4 million people in the U.S. Its comorbidity in the severe and persistently mentally ill is problematic to a greater extent than the general population.

Methods: Ten schizophrenic patients attending a partial hospitalization program were asked to participate in this pilot study. All patients had a comorbid diagnosis of hepatitis C infection. Baseline data were taken for three parameters, including Health-Related Quality of Life Questionnaire, Client Satisfaction Survey, and "pre-test" assessing the individual's knowledge of his medical illness. Patients were asked to participate in a medication group focusing on their mental hygiene and comorbid hepatitis. During

the group, patients were educated on hepatitis C infection. At six months the patients completed the three surveys to evaluate the impact of this specialized medication group on their psychiatric and medical illness.

Results: Patients attending a specialized medication group were found to have improved knowledge of their medical illness and greater rates of follow up with their gastroenterologists.

Conclusions: Treating psychiatrically ill patients in a medical group setting, specifically focused on medical comorbidity, is a unique and efficient method leading to improved quality of care and patient satisfaction.

References:

1. Managing patients with hepatitis C in primary care. Resident & Staff Physician 2004; (6):50.
2. Practice Guidelines From the American Gastroenterology Association.

NR105 Monday, May 23, 9:00 a.m.-10:30 a.m.
The Role of Paratonia in Alzheimer's Disease in a Multi-Racial Sample

Ipsit Vahia, M.D., *Department of Psychiatry, SUNY Downstate Medical Center, 372 State Street #1, Brooklyn, NY 11217*; Alla Prehogan, M.D., Carl Cohen, M.D.

Educational Objectives:

To demonstrate how paratonia may serve as a neurological indicator of progression of AD that is independent of race and other demographic variables.

Summary:

Rationale: Paratonia is an external stimulus dependent increase in muscle tone that is not present at rest. It is distinguishable from parkinsonian rigidity. It is thought to occur commonly in Alzheimer's disease (AD), but it has not been well studied. It is especially understudied among African-American patients with AD. This study examines the prevalence and impact of paratonia on a multiracial sample of AD patients.

Methods: The sample consisted of 80 new admissions to the Brooklyn Alzheimer's Disease Assistance Center. They met criteria for AD according to DSM-IV. Their mean age was 75 years, 79% were females; 76% were black and 24% were white. They received a battery of cognitive tests, neurological and physical examinations, and neuropsychiatric assessment. A board-certified neurologist trained in the assessment of paratonia conducted the examination. The paratonia rating scale ranged from 1 to 7, with scores of 3 or more used to demarcate moderate severity or greater. We used zero-order correlations to determine the associations between paratonia and various demographic and clinical variables.

Results: There were significant correlations between the presence of paratonia and MMSE ($r = -.30$, $p = .008$) and illness stage ($r = .29$, $p = .009$); paratonia was present in 48%, 70%, and 83% of persons in GDS stages 4, 5, and 6, respectively. Paratonia correlated with the number of frontal release signs ($r = .35$) even after controlling for illness stage. There were no significant correlations with age, race, gender, depression, physical health, neuroimaging findings, or behavioral disturbances. Although paratonia correlated initially with functional abilities ($r = .24$, $p = .03$), after controlling for GDS level there was no significant correlation between paratonia and functional activities ($r = .05$, $p = .66$).

Conclusions: Our data indicated that paratonia did not have any independent impact on daily functioning and was not associated with any neuropsychiatric or demographic variables. The only predictors of paratonia were stage of illness and the number of frontal release signs. The latter provides confirmation of earlier work that suggested that paratonia is associated with frontal lobe

dysfunction. Paratonia may serve as a neurological indicator of the progression of AD. Further studies are needed to confirm these findings.

References:

1. Beversdorf D, Heilman K: Facilitatory paratonia and frontal lobe functioning. *Neurology* 1998; 51:968-9971.
2. Chatterjee A: Feeling frontal dysfunction: facilitatory paratonia and the regulation of motor behavior. *Neurology* 1998; 51:937-939.

NR106 Monday, May 23, 9:00 a.m.-10:30 a.m.
Aggressive and Delinquent Behaviors and Their Relationship to Defenses

Sanja Medic, B.A., *Department of Child Psychiatry, Stanford University, 401 Quarry Road, Stanford, CA 94305-5719*; Katy Araujo, Ph.D., Hans Steiner, M.D.

Educational Objectives:

To update the participants with the correlation between defenses and reactive and proactive aggression; to provide the practitioner with implications for treatment.

Summary:

Objective: To examine the correlation between defenses and empirically validated subtypes of aggression. Maladaptive aggression has often been shown to be defensive in character. We hypothesized (1) that reactive/affective/defensive/impulsive aggression (RADl) correlates stronger with classic defenses than delinquent (proactive) aggression); (2) RADl aggression correlates stronger with Factor 1 defenses (immature, leading to less adaptive functioning) and (3) within Factor 1, RADl aggression correlates more with interpersonal and less with intrapsychic defenses.

Methods: This study included existing data of 1,472 high school students, 53% females, age 10-18 years old. Assessments included the Response Evaluation Measure (REM-71) and the Youth Self Report (YSR). We equated RADl aggression with the aggression subscale of the YSR, proactive aggression with the delinquent subscale of the YSR, as has been suggested by Achenbach.

Results: All hypotheses were confirmed. YSR Aggression correlates stronger with Factor 1 defenses than delinquent behavior. Aggressive and delinquent behavior correlate negatively with Factor 2 defenses. Within Factor 1, aggressive and delinquent behavior correlated significantly with interpersonal defenses: acting out, displacement dissociation, passive aggression, projection, and splitting.

Conclusion: YSR aggressive behavior is closely correlated with immature defenses involving other people. This confirms the role of affectively charged aggression as part of the defensive repertoire in humans.

References:

1. Steiner H, Saxena K, Chang K: Psychopharmacological strategies for the treatment of aggression in Juveniles. *CNS Spectrums* 2003; 8 (4):298-308.
2. Steiner H, Araujo K, Koopman C: The Response Evaluation Measure: a new instrument for the treatment of defenses. *American Journal of Psychiatry* 2001; 158 (3):467-473.

NR107 Monday, May 23, 9:00 a.m.-10:30 a.m.
Industry Funding, Study Design, and Positive Outcome in Clinical Trials in Psychiatry

Yelena P. Wu, B.A., *Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street Suite 580, Boston, MA*

02114; Roy Perlis, M.D., Megan Joseph, B.A., Cindy Hwang, B.A., Andrew Nierenberg, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the relationship between conflict of interest, study design, and positive outcome in clinical trials. This presentation aims to increase the awareness of conflict of interest in current psychiatric research.

Summary:

Introduction: Clinical trials in psychiatry, as in other areas of medicine, may be more likely to report positive outcomes when author conflict of interest (COI) is present. We hypothesized that differences in study design may contribute to these effects.

Method: We conducted a Medline search using the term "clinical trial" limited to articles published in four widely-read psychiatric journals between January 2001 and December 2003 and supplemented this search with a manual review of the table of contents in these issues. Reviewers then used a standardized template to extract data on study funding sources and study design.

Results: Of 209 randomized, controlled trials identified, 102 included at least one author with a financial conflict of interest. Compared with studies without COI, these studies were larger (median 96 vs 21, $z=0.798$, $p<0.0001$), of longer duration (median 70 vs 56, $z=1.93$, $p=0.05$), and more likely to include an active comparator (48% vs 32%; Fisher's exact $p=0.02$).

Conclusion: The design of studies with author COI differ from those without, which may contribute to observed differences in likelihood of reporting a positive outcome.

References:

1. Bekelman JE, Li Y, Gross CP: Scope and impact of financial conflicts of interest in biomedical research: a systematic review. *JAMA* 2003; 289(4):454-65.
2. Perlis RH, Wu Y, Hwang C, Joseph M, Perlis CS, Nierenberg AA: Extent and implications of financial conflict of interest in published clinical trials in psychiatry, in press.

NR108 Monday, May 23, 9:00 a.m.-10:30 a.m.

Divalproex Sodium in Outpatients With Disruptive Behavior Disorders

Kirti Saxena, M.D., *Department of Psychiatry, Stanford University, 401 Quarry Road, Stanford, CA 94305*; Laura Delizonna, Ph.D., Abbey Durkin, B.A., Linda Mora, B.A., Kelly Caywood, B.A., Hans Steiner, M.D.

Educational Objectives:

At the conclusion of the presentation, participants should be able to demonstrate knowledge about the efficacy of divalproex sodium in oppositional defiant and conduct disordered youth.

Participants should recognize that DVPX will be efficacious against Reactive/Affective/Defensive/Impulsive Aggression (RADI), as opposed to Proactive/Instrumental/Planned (PIPP).

Summary:

Objective: A pilot study testing the efficacy of divalproex sodium (DVPX) in outpatients with disruptive behavior disorders extended previous findings that DVPX is efficacious in inpatients. This study tested the hypothesis that outpatients with DBD taking DVPX would show improvements in Reactive/Affective/Defensive/Impulsive Aggression.

Method: Twenty-two participants (8 girls, mean age 14) diagnosed with oppositional defiant disorder or conduct disorder by using the K-SADS were randomized into TAU or 12 weeks of openly titrated medication (DVPX). Measures included the Clinical Global Improvement-Change (CGI-C), CGI-S (Severity) scales, and the Overt Aggression Scale (OAS).

Results: Five patients were in TAU, 17 in the DVPX group. CGI-C ratings indicated that the DVPX group showed substantial improvement by the last observation ($m=1.88$; 1=much improved, 2=minimally improved). Baseline and last CGI-S score carried forward were significantly different, $t(11)=6.09$, $p<.001$. The DVPX group showed reduced RADI aggression, indicated by the OAS, $t(9)=2.39$, $p<.05$.

Conclusion: This study supports that DVPX is efficacious in decreasing RADI aggression in DBD patients. These results are particularly noteworthy because the sociotherapeutic structures supporting patients in previous trials were not present.

References:

1. Steiner H, Cauffman E, Duxbury E: Personality traits in juvenile delinquents: relation to criminal behavior and recidivism. *Journal of the American Academy of Child and Adolescent Psychiatry* 1999; 38, (3):256-262.
2. Steiner H, Saxena K, Chang K: Psychopharmacological strategies for the treatment of aggression in youth. *CNS Spectrums* 2003; 8 (4):298-308.

NR109 Monday, May 23, 9:00 a.m.-10:30 a.m.

Association Study Between Smoking and Alpha-7-Nicotinic Receptor Subunit Gene in Patients With Schizophrenia, Adult ADHD, and Bipolar Disorder

Vincenzo De Luca, M.D., *Department of Psychiatry, University of Toronto, 250 College Street, Toronto M5T1R8, Canada*; Umesh Jain, M.D., Alber H.C. Wong, M.D., Greg Wong, B.A., Rachel Tyndale, Ph.D., James L. Kennedy, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate the importance of the research on the genetics of CHRNA7 receptor in the nicotine dependence in schizophrenia, ADHD, and bipolar disorder.

Summary:

A number of studies have suggested that the alpha-7-nicotinic receptor subunit gene D15S1360 polymorphism is associated with schizophrenia, and a deficiency in the normal inhibition of the P50 auditory-evoked response. Schizophrenia patients and some of their unaffected relatives show a failure of inhibition in their 50 ms response to the second of a pair of tones. Furthermore, high-dose nicotine transiently normalizes the abnormality in P50 inhibition in schizophrenia patients and in their relatives. There is an unusually high rate of smokers among psychiatric patients. This rate is higher than the general population. In this study we hypothesized that the D15S1360 marker is associated with (the increased) smoking in patients with psychiatric disorders. Our sample consisted of 300 DSM-IV patients affected by schizophrenia, Adult ADHD and bipolar disorder from the Toronto area. Current smoking status was assessed by medical history questionnaire, and there were 56% of smokers and 44% non-smokers. There was no difference in age or ethnicity between the two groups. We found no association between the D15S1360 alleles and smoking risk ($\chi^2=4.45$, 3df, $p=0.21$). Although these findings are negative, further study into the relationship between smoking and nicotine system genes is warranted in psychiatric population.

References:

1. Stassen HH, et al: *Am J Med Genet* 2000; 96:173-177.
2. Freedman R, et al: *PNAS* 1997; 94:587-592.

NR110 Monday, May 23, 9:00 a.m.-10:30 a.m.

Increased Medical Costs Associated With Neuropsychiatric Diagnosis in HIV-Infected Individuals

Helen P. Yeung, M.D., *Department of Psychiatry, University of Calgary, #21, 2318-17 Street SE, Calgary, AB T2G 5R5, Canada*; Hartmut Krentz, Ph.D., John Gill, M.D., Christopher Power, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to: (1) discuss the major HIV-induced neuropsychiatric comorbidities, (2) determine the significant medical costs of HIV care, and (3) determine the impact of different neuropsychiatric comorbidities on these medical costs.

Summary:

Objective: To determine added direct costs of medical care for HIV/AIDS persons with a neuropsychiatric comorbidity.

Methods: We conducted a retrospective study of 256 HIV patients using mean per patient per month (PPPM) costs between 1997 and 2002, comparing antiretroviral (ARV) and non-ARV drugs, clinic and physician visits, laboratory tests, hospitalizations, and home care prior to and after a neuropsychiatric diagnosis (sensory neuropathy or cognitive impairment). Neuropsychiatric patients were matched with a control group of HIV-infected individuals by age, CD4 count at diagnosis, and CD4 nadir.

Results: Prior to diagnosis, patients with cognitive impairment (\$1154 PPPM) or sensory neuropathy (\$1180) did not differ significantly from the control group (\$1077) in direct medical costs. Following neuropsychiatric diagnosis, mean PPPM costs increased by 63% (\$1754, $p < 0.001$) for cognitively impaired patients and 33% (\$1423, $p < 0.01$) for patients with neuropathy. Increased numbers of clinic and physician visits, non-ARV drugs, and hospitalizations accounted for the higher PPPM costs ($p < 0.05$).

Conclusions: Cognitive impairment or sensory neuropathy among HIV/AIDS patients significantly increases medical care costs due primarily to increased monitoring and management of the comorbidities. Cost analyses offer a useful measure of changing patient needs, and provide a framework for appropriate allocation of health care resources.

References:

1. Krentz HB, et al: The changing direct costs of medical care for patients with HIV/AIDS. *CMAJ* 2003; 169(2):106-110.
2. Valcour V, et al: Higher frequency of dementia in older HIV-1 individuals: the Hawaii Aging with HIV-1 Cohort. *Neurology* 2004; 63(5):822-7.

NR111 Monday, May 23, 9:00 a.m.-10:30 a.m.

Alcoholism, Mortality, and Chronic Health Conditions in a Rural Community in Korea: A Longitudinal, Case-Controlled Study

Seongho Min, M.D., *Department of Psychiatry, Yonsei University, 162 Ilsan-dong, Wonju 220-701, Korea*; Jongho Shin, M.D., Samuel Noh, Ph.D., Taehee Kim, M.D., Hyungmin Jang, M.D., Byungsoon Shon, R.N.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate the importance of addiction psychiatry by establishing health consequences of unmanaged drinking problems in longitudinal analyses.

Summary:

Objective: To determine the effects of excessive drinking and alcohol dependency on mortality and chronic health problems in a rural community in South Korea.

Methods: From a population survey (N=1058) of a rural community, 145 adults were identified as having alcohol problems, based on the Severity of Alcohol Dependence Questionnaire and daily alcohol consumption. Fifty-nine cases were classified as alcohol dependent and 86 as excessive drinker without dependency. A control sample consisting of 145 non-drinkers, matched the alcoholic sample on age and sex. In 2004, six years after the baseline survey, we identified 218 cases; 184 persons completed the follow-up interviews, 72 cases were lost to follow up, and 34 were deceased.

Results: Multivariate logistic regressions revealed significant effects of alcohol dependence. Mortality rate was 2.78 times greater for alcohol dependents, compared with the rate for non-drinkers ($p = .023$). Morbidity of chronic health conditions was 3.01 times higher for alcohol dependents compared with non-drinkers ($p = .015$). Excessive drinking without dependency was not associated with mortality or morbidity.

Discussion: Concerning the health effects of drinking problems, results were consistent with those found in western societies.

References:

1. Rehm J, Gmel G, Sempos CT, Trevisan M: Alcohol related morbidity and mortality. *Alcohol Research & Health* 2002; 27:39-51.
2. Thun MJ, Peto R, Lopez AD, et al: Alcohol consumption and mortality among middle-aged and elderly U.S. adults. *The New England Journal of Medicine* 1997; 337:1705-14.

NR112 Monday, May 23, 9:00 a.m.-10:30 a.m.

Duration of Untreated Psychosis and Social Position in First-Episode Schizophrenia in Korea

Seon-Cheol Park, M.D., *Department of Neuropsychiatry, 17 Haengdang-dong Seongdong-gu, Seoul 133-792, Korea*; Jung Hyun Nam, M.D., Joonho Choi, M.D., Sungwon Roh, M.D., Sun-Kyoung Choi, M.D., Chang Woo Han, M.D., Daeho Kim, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that the lower social position is positively correlated with prolongation of duration of untreated psychosis in first-episode schizophrenia.

Summary:

Objectives: Studies often suggest that long duration of untreated psychosis (DUP) predicts poor outcome in schizophrenia. This study looked at the relationship between patients' social background and DUP in 35 consecutive first-episode inpatients with SCID-I confirmed schizophrenia.

Methods: Data from 35 patients were obtained from inpatient wards at two university-affiliated hospitals. These data included scores on Index of Social Position. Positive and Negative Syndrome Scale (PANSS), Symptom Checklist-90-Revised (SCL-90-R), and sociodemographic/clinical information. Variables not normally distributed were either transformed or dichotomized for further statistical analysis.

Results: The mean value of DUP was 11.9 (SD=14.3, median=6.0) months. DUP was not significantly correlated with any total or subscale scores of PANSS and SCL-90-R. Lower social position ($r=0.62$, $P<0.001$), female sex ($r=0.41$, $P=0.015$), and having grown up in rural area ($r=0.34$, $P=0.045$) were significantly correlated with DUP. However, when partial correlation was used for

controlling mutual effects of these variables, only lower social position remained significant ($r=0.55$, $P=0.001$ & $r=0.58$, $P<0.001$).

Conclusion: Lower social position defined by education and occupation of patients or caretakers may affect the identification and concept of mental illness. Social adversity or barriers to psychiatric services may be more often the problem in this population.

References:

1. Loebel AD, Lieberman JA, Alvir JM, Mayerhoff DI, Geisler SH, Szymanski SR: Duration of psychosis and outcome in first-episode schizophrenia. *Am J Psychiatry* 1992; 149:1183-1188.
2. Ho BC, Alicata D, Ward J, Moser DJ, O'Leary DS, Arndt S, Andreasen NC: Untreated initial psychosis: relation to cognitive deficits and brain morphology in first-episode schizophrenia. *Am J Psychiatry* 2003; 160:142-148.

NR113 Monday, May 23, 9:00 a.m.-10:30 a.m.

Clinical Features of Korean Geropsychiatric Consultation

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Educational Objectives:

At the conclusion of the presentation, the participant should have knowledge of the characteristics of geropsychiatric consultation compared with young population in Korea.

Summary:

Objective: Geriatric admissions and geropsychiatric consultations are steadily increasing, but a systematic study has not been established in Korea.

Design: We compared 111 elderly patients with 109 young patients. Patients in both groups were admitted into various departments except neuropsychiatry, and consulted to neuropsychiatry from January 2004 to June 2004 in our hospital.

Materials and Method: We interviewed subjects or their caregivers personally. We ascertained compliance by reviewing charts after discharge.

Results: There were significant differences in marital status, education, occupation, and past psychiatric history between elderly patients and young patients.

Elderly patients had much more diagnoses and medications before consultation than young ones.

For the reasons of consultation, sleep disturbance, disorientation, and cognitive decline were more prominent in the elderly group, and alcohol related problems in the control group.

We diagnosed significantly more delirium and dementia, and less alcohol-related disorders and psychotic disorders in the elderly group.

We recommended more constant observation in the elderly group, and more instruction in psychologic management and close observation in the control group.

Conclusion: Elderly patients have different characteristics in neuropsychiatric consultations. They need a specific approach on psychiatric consultation.

References:

1. Lipowski ZJ: The need to integrate liaison psychiatry and geropsychiatry. *Am J Psychiatry* 1983; 140:1003-1005.
2. Cooper B: Psychiatric disorders among elderly patients admitted to hospital medical wards. *J R Soc Med* 1987; 80:13-16.

NR114 Monday, May 23, 9:00 a.m.-10:30 a.m.

Alcohol and Substance Use Comorbidity in Schizophrenia

Nihat Alpaya, M.D., *1. Psikiyatri Klinigi, Bakirkoy Ruh-Sinir Hastalıkları Hastanesi, Istanbul 34747, Turkey*; Cagatay Karsidag, M.D., Nesrin Tomruk, M.D., Nesrin Karamustafalioglu, M.D., Resit Kukurt, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should recognize that comorbid alcohol and substance use commonly seen among patients with schizophrenia can contribute to the morbidity of disorder.

Summary:

Objective: Comorbid alcohol and substance use commonly seen among patients with schizophrenia can contribute to the morbidity of disorder, but the etiology is unclear. This condition has probably been linked to self medication of negative symptoms of schizophrenia or extrapyramidal side effects of antipsychotics. Prevalence of substance and alcohol use in patients with schizophrenia was found 4.6 times more than general population. Relapses and suicidal risks must be evaluated carefully in this population. The aim of this study was to examine alcohol and substance comorbidity in patients with schizophrenia in Turkey. Data were collected from retrospective analysis.

Method: In this study five hundred and two patient were evaluated. 31.9% of patients were women, 68.1% of patients were men. Among those patients, 8.2% presented with lifetime history of substance, and 24.9% presented with lifetime alcohol abuse or dependence. 20.5% of patients attempted suicide at least one time. 17.7% of patients had a forensic life event. 46.2% of patients has neuroleptics sensitivity in and level.

Conclusion: This findings demonstrated that there is a high prevalence of alcohol and substance use comorbidity in patients with schizophrenia.

References:

1. Buckley PF: Substance abuse in schizophrenia: a review: *J Clin Psychiatry* 1998; 59 (Suppl. 3):26-30.
2. Evren E C, Evren B: Sizofreni ve Alkol Madde Kulianim Bozukluklari Ek Tanisi: Bir Gozden Gecirme: *Turk Psikiyatri Dergisi* 2003; 4(3):213-224.

NR115 WITHDRAWN

NR116 Monday, May 23, 9:00 a.m.-10:30 a.m.

Assessment of the Impact of Noradrenergic, Dopaminergic, and Cholinergic Medications on Fatigue and Executive Dysfunction Associated With Major Depressive Disorder

Mohammad Z. Hussain, M.D., *Department of Psychiatry, Prince Albert Mental Health Center, 605 32nd Street W, Prince Albert, Saskatchewan, C S6V 7T5, Canada*; Waqar Waheed, M.D., Zubaida Choudhry, M.D., Seema Hussain, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to appreciate the relative efficacy of noradrenergic and cholinergic medications in decreasing fatigue and executive dysfunction in patients with major depressive disorder.

Summary:

Significance: Studies in normal controls and depressed subjects are strongly suggestive of a close integration between the DLPFC,

subgenual cingulate and frontostriatal limbic network in depression and executive dysfunction. Pharmacological alterations in the level of neurotransmitters associated with these brain regions may result in an improvement in cognitive dysfunction and low energy associated with depressive illness.

Methodology: This was a prospective, randomized, open-label experimental study that included sixty patients with Major Depressive Disorder (m=23, f=27, mean age 45.8, duration of illness = 11.7 years and stabilized on antidepressant/mood stabilized regimen but having difficulty with fatigue and executive dysfunction) who were randomized to four groups to whom bupropion, modafinil, galantamine, and supportive therapy were added to their previous therapeutic treatments, respectively. Assessment of executive function and fatigue was performed at baseline one, three, six, and 12 weeks using HAM-D, Trail A&B, WAIS-III working memory subscales. Fatigue was measured on a scale of 1-10.

Results: The clinically significant improvement in fatigue and executive dysfunction in the groups receiving medication was tenfold greater as compared to supportive therapy.

Conclusions: Formal cognitive testing could be a useful adjunct in the clinical evaluation of patients with depression, both at index episode, but more particularly upon recovery.

References:

1. Alexopoulos GS: The depression-executive dysfunction syndrome of late life: a specific target for D3 agonists? *Am J Geriatr Psychiatry* 2001; 9(1):22-9, Review.
2. Austin MP, Mitchell P, Goodwin GM: Cognitive deficits in depression: possible implications for functional neuropathology. *Br J Psychiatry* 2001; 178:200-6.

NR117 Monday, May 23, 9:00 a.m.-10:30 a.m.

Quetiapine Use in the Acute and Maintenance Phases of Bipolar Disorder Treatment

Mohammad Z. Hussain, M.D., *Department of Psychiatry, Prince Albert Mental Health Center, 605 32nd Street W, Prince Albert, Saskatchewan, C S6V 7T5, Canada*; Waqar Waheed, M.D., Zuaida Choudhry, M.D., Seema Hussain, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to appreciate the efficacy of quetiapine in acute and maintenance phases of bipolar disorder treatment when used in conjunction with another mood stabilizer (lithium, valproate, or lamotrigine).

Summary:

Significance: There are scarce data evaluating long-term quetiapine use in Bipolar Disorder. This study intends to augment the current literature describing the benefit of concomitant use of two mood stabilizing medications.

Methodology: This is a non-experimental, open-label, prospective study. Quetiapine was added to the treatment of 37 hospitalized patients (m=16, f=21) of average age 39.8 years, average duration of illness= 14.8 years, Manic=9, Mixed=8, Depressed=20 who were receiving mood stabilizers. Patients were followed for a period of five years. Rating scales utilized to assess response included the HAM-D, YMRS, BPRS, and Global Assessment. The assessments were made at baseline, 1, 2, 3, and 6 weeks, and 3 months and every 6 months after one year up to five years. Hospitalization days three years before and after addition of Quetiapine were tabulated.

Results: Significant improvement was seen in all scales at 3, 6, and 12 weeks, which were sustained for five years. Hospitalization days per patient per year were reduced from 12.3 to 3.4.

Conclusions: Quetiapine in combination with another mood stabilizer was found to be effective not only for the acute treatment

of manic and depressive episodes of bipolar disorder but also for the maintenance treatment of the disorder.

References:

1. Sachs GS, Printz DJ, Kahn DA, Carpenter D, Docherty JP: The Expert Consensus Guideline Series: Medication Treatment of Bipolar Disorder 2000. *Postgrad Med* 2000; Spec No:1-104. Review.
2. Practice Guidelines for the Treatment of Patients With Bipolar Disorder (Second Edition). American Psychiatric Association. *Am J Psychiatry* 2002; 159(4):Supp 1-50.

NR118 Monday, May 23, 9:00 a.m.-10:30 a.m.

A Six-Year Follow-Up Analysis of Alcohol-Related Deaths in an Isolated Community in Korea

Kim Tae Hui, M.D., *Department of Psychiatry, Wonju College of Medicine, Yonsei University, Wonju 200-701, Korea*; Shin Jongho, M.D., Min Seongho, M.D., Lee Yula, M.D.

Educational Objectives:

At the conclusion of the presentation, the participants should be able to consider information about alcohol-related death in one's community as one of the most powerful effects to decrease alcohol consumption.

Summary:

The authors followed up a group of heavy drinkers and non-heavy drinkers after six years of original epidemiologic study in an isolated mountainous community. They are a relatively old population of 1,058 people with the mean age of 55.0(±16.87). Within six years, 33 (15.1%) subjects had died among 114 samples and 105 age-matched controls: 28 men (15.8%) and 5 (11.9%) women with the mean age of 68(±64).

All the dead were analyzed by sociodemographic data, health habits alcohol drinking pattern, and DRS (drinking restraint scale) investigated during the original survey. The results are as follows: They are 16 (17.4%) men and four (18.2%) women with the mean age of 67.45(±13.19) among heavy drinkers, and 12 (14.1%) men and one (5.0%) woman with the mean age of 70.46(±9.45) among controls. For problem drinkers, hepatoma (7) was the leading cause of death, followed by acute pancreatitis, gastric ulcer bleeding, stroke, traffic accident, and suicide. For controls cancer other than hepatoma (4) was the leading cause of death, followed by some lung disease, and unknown reasons. Between the two groups, no significant difference was found except duration of smoking and DRS subscale of subjective worrying at his (her) drinking pattern.

References:

1. Jongho Shin: Original Article: An epidemiologic study on alcoholism and alcohol abuse in an isolated Mountainous Rural Community. *J Korean Academy of Addiction Psychiatry* 1999; 3(2):99-106.
2. Neumark YD: Alcohol Dependence and death: survival analysis of the Baltimore ECA sample from 1981-1995. *Subst Use Misuse* 2000; 35(4):533-49.

NR119 Monday, May 23, 9:00 a.m.-10:30 a.m.

Agitation in the Swiss Emergency Departments: Guidelines and Clinical Practice

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Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize differences between guidelines and clinical practice for psychomotor agitation in emergency departments, from an up-to date literature review and a research (multivariate analysis) based on a questionnaire about the management of psychomotor agitation in Switzerland.

Summary:

Objectives: This is the first study evaluating the concordance between guidelines and current psychiatric clinical practice in psychomotor agitation (PMA) in Swiss emergency departments (EDs).

Methods: We sent a questionnaire concerning the management of PMA to 130 EDs in Switzerland. The items concern: (1) security in the emergency room, (2) somatic examination, (3) medical and nurse management (existence of guidelines, protocols for pharmacotherapy, side effects), and (4) expectedness of agitation situation. After a comprehensive review of literature, we compared the difference between Swiss, European, and American guidelines for PMA.

Results: The 40% spontaneous responsiveness rate increased at 70% after phone inquiries. The Swiss guidelines were largely followed in clinical practice, even if only 10% of EDs had written guidelines available. The antipsychotics (especially haloperidol) are more widely prescribed in Switzerland, whereas we found a larger use of benzodiazepines in the U.S. guidelines. Parenteral atypical antipsychotics (olanzapine) are available in Switzerland since March 2004; six months later only 8% of EDs use them. The systematic use of guidelines and the avoidance of physical coercion appeared as a qualitative factor in management of PMA. The prevalence of the violence in EDs need further epidemiological studies, in order to improve the care quality.

References:

1. Burnand Y, Andreoli A, Kolatte E, Venturini A, Rosset N: Psychodynamic psychotherapy and clomipramine in the treatment of major depression. *Psychiatr Serv* 2002; 53(5): 585-90.
2. Damsa C, Di Clemente T, Massarczyk O, Haupt J, Pull C: The impact of crisis intervention on the management of patients with personality disorder. *Bull Soc Sci Med Grand Duche Luxemb* 2003: 87-96.

NR120 Monday, May 23, 9:00 a.m.-10:30 a.m.

Familial Backgrounds of Runaway Adolescents Staying in Shelters in Korea

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Educational Objectives:

The change of gender differences in runaway youth's familial backgrounds that emerged in this study offer little support for the cultural hypothesis. These findings suggest the change of situations that make runaway adolescents choose to leave home. So we need new understanding of such adolescents.

Summary:

Objectives: It has been proposed that runaway girls are more likely to be from dysfunctional families and exhibit psychological distress than homeless runaway boys, reflecting cultural factors that result in differential norms for male and female behavior. But, in a recent test of the cultural hypothesis, several studies revealed that runaway boys and girls did not differ in their family situation.

Method: Reports of 151 runaway adolescents staying in the shelter in Korea were compared on measures of demographic data, symptom checklist-90, family adaptability cohesion evaluation scale III, conflict tactics scales II, and children of alcoholics screening test to learn more about the gender differences in runaway adolescents.

Result: Inconsistent with the cultural hypothesis, boys described more negative familial backgrounds than girls (e.g., they are likely to come from single or no parent home (male:female=52(68.4%):41(55.4%)) and their parents are more likely to have alcohol problems(CAST male:female=15.23(±9.33): 9.54(±9.37)).

Conclusion: The findings suggest the change of precipitating factors or situations that make runaway adolescents choose to leave home. So we need new recognition and understanding of such adolescents and need to design services that better address their needs.

References:

1. Tomb DA: The runaway adolescent, in Child and Adolescent Psychiatry: A Comprehensive Textbook. Edited by Melvin Lewis. 2002, pp 1381-1386.
2. Raffaelli M, Koller SH, Reppold CT, et al.: Gender differences in Brazilian street youth's family circumstances and experiences on the street. *Child Abuse Negl* 2000; 24: 1431-1441.

NR121 Monday, May 23, 9:00 a.m.-10:30 a.m.

Quality of Reports of RCTs of New Antidepressants in Geriatric Depression

Fernando Rico-Villademoros, M.D., *Medical Department, Biométrica, Eloy Gonzalo 27, Madrid 28010, Spain*; David Rossell-Ribera, B.S., Jerónimo Saiz-Ruiz, M.D.

Educational Objectives:

At the end of this presentation, the participant should be able to recognize the quality of reports of randomized, controlled trials of new antidepressants in geriatric depression.

Summary:

Objective: To assess the quality of reporting of RCTs of new antidepressants in geriatric depression.

Method: Published RCTs were identified using MEDLINE/EMBASE/Manual-cross-referencing and were included if efficacy was among primary outcomes evaluated. Prevention trials were excluded. The quality was assessed using a modified checklist (Verhagen 1998), which included five components: randomization concealment, blinding, baseline homogeneity, variability measures, and intent-to-treat analysis. We also assessed some ethical and external validity issues.

Results: Only three out of 57 (5.3%) RCTs adequately reported/performed all components of the checklist; the most common shortcomings were inadequate randomization concealment (52, 91.2%), lack of measures variability (44, 77.2%), inadequate report of blinding (25/56, 44.6%), and failure to present intent-to-treat analysis (22, 38.6%). Reporting of written informed consent and EsC/IRB approval was not available in 22 (38.6%) and 24 (42.1%), respectively. Age of inclusion was below 65 in 31 (54.4%) and only one RCT was run in patients >80. One trial was run in physically-ill patients and 4 (7%) in patients with dementia. Remission rates were reported in 19 (33.3%).

Conclusion: There is a considerable room for improvement in the reporting of RCTs in geriatric depression. Sponsors, authors, and editors should adopt/demand standard reporting recommendations (i.e. CONSORT).

References:

1. Jüni P, Altman DG, Egger M: Assessing the quality of controlled clinical trials. *BMJ* 2001; 323:42-6.

- Verhagen AP, et al: The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. *J Clin Epidemiol* 1998; 51:1235-1241.

NR122 Monday, May 23, 9:00 a.m.-10:30 a.m.

The Characteristics of Adolescent Children of Alcoholics: Psychopathology, Attachment, and Parent/Child Communication in South Korea

Eun-Ee Lee, M.D., *Department of Psychiatry, Ajou-University Hospital School of Medicine, Won-Chon Dong, Paldalgu, Suwon, South Korea*; Hyun-Soo Kim, M.D., Yunmi Shin, M.D., Youngkee Chung, M.D., Youngmoon Lee, M.D.

Educational Objectives:

At the conclusion of this presentation, the participants should recognize that the adolescent children of alcoholics experience more depressive and anxiety symptoms, disruptive behavior, drinking and smoking, sexual experience, run away, and adverse parental communication in spite of no difference in attachment style, social and academic activities between the two groups.

Summary:

CoA (children of alcoholics) seem to experience a different family environment from CoNA (children of non-alcoholics). It is already known that the family environment of CoA modify the normal psychological development. The hypothesis of this study is to show the difference between the attachment style and psychopathology of CoA and CoNA during the adolescent period. We wanted to see the differences in psychological development of adolescent children of alcoholics such as attachment style, psychopathology, parent-adolescent communication, family violence, parental conflict, and other family stressors.

In this cross-sectional study, CoA(n=113) and CoNA (n=1342) of the 1,489 middle and high school students in Seoul, South Korea, no significant sociodemographic difference between the two groups were surveyed on self-report; K-YSR(Korean-Youth self report), CAST(children of alcoholics screening test), BDI(Beck's depression index), CTS(conflict tactic scale) 2 and revised self-report attachment style. By using t-test, we tried to find the differences between the two groups among the variables. Adolescent children of alcoholics had a tendency to report more depressive and anxiety symptoms, disruptive behavior, drinking and smoking, sexual experience, run away, and adverse parental communication than adolescent children of non-alcoholics. This result confirms that parental alcoholism does have detrimental effects on offspring and that CoA are a population of clinical concern.

References:

- Anda RF, et al: Adverse childhood experiences, alcoholic parents, and later risk of alcoholism and depression. *Psychiatr Serv* 2002; 53(8):1001-9.
- Christensen HB, et al: Behavioural and emotional problems in children of alcoholic mothers and fathers. *Eur Child Adolesc Psychiatry* 2000; 9(3):219-26.
- King KM: Mediating and moderated effects of adolescent behavioral undercontrol and parenting in the prediction of drug use disorders in emerging adulthood. *Psychol Addict Behav* 2004; 18(3):239-49.

NR123 Monday, May 23, 9:00 a.m.-10:30 a.m.

The Profiles of Temperament, Character, and the Depressive Tendency in Internet-Overusing Adolescents

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Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the interrelations between the severity of depression and the temperament, character profiles in internet-overusing adolescents.

Summary:

Purpose: This study was conducted to investigate the interrelation between the severity of depression and the degree of internet addiction tendency and the patterns of TCI among adolescents in Korea.

Method: Four hundred and twenty-five middle school students (male/female=215/210) completed the Beck's depression inventory (BDI), the Young's Internet addiction test (IAT) and Cloninger's junior version of temperament and character inventory. We divided three group by IAT scores (the range of score: 20-100): high risk (≥ 70), moderate risk ($70 >$ and $=40$), non-risk (<40) and compared means of BDI score and JTCI subscales.

Results: 11.1% of participants were perceived to be in the internet high-risk addiction group and only 30% was non-risk group. The high-risk group revealed the highest BDI's mean score (15.5 ± 1.1), the moderate risk did the next (11.5 ± 0.8) and the non risk showed the lowest (8.2 ± 1.2). These differences were statistically significant ($p < 0.01$). Multiple linear regression analysis showed that the degree of internet addiction tendency were associated with increasing BDI's score ($p < 0.00$) but not sex, age, the grade point average, history of using tobacco, the economic status of family. The TCI's dimensions of high novelty-seeking and harm avoidance, and the dimensions of low persistence, reward dependence, self-directedness, and cooperativeness were associated with a severity of the internet addictive tendency.

Discussion: The degree of internet addiction tendency correlated to the severity of depression. Interestingly, P, RD, SD, and CO dimensions, which are concerned with gaining and maintaining positive reward from society, were significantly decreased in the risk groups. However, the ST dimension representing the notions of existential and positive psychology, which has been neglected in the field of psychiatry but adopted as one of personality factors by Cloninger's TCI, was not related with the severity of the internet addiction. It is suggested that the internet over-using behavior should be a variant symptom of adolescent's depression. The comparison of the TCI profile among groups reveals that the lack of social motivations and the co-activated BAS/BIS temperamental templates contribute to the development of the internet addiction.

References:

- Young KS: The relationship between depression and internet addiction. *Cyberpsychol Behav* 1997; 4:25-28.

NR124 Monday, May 23, 9:00 a.m.-10:30 a.m.

Do Religious Beliefs About Terrorist Casualties Protect Israeli Rescue Workers From PTSD?

Zev J. Alexander, M.D., *Department of Epidemiological Research, Butler Hospital, 345 Blackstone Blvd., Providence, RI 02906*; Robert Kohn, M.D., Itzhak Levav, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the positive role that religion, faith, and ritual play for rescue workers who have been repeatedly exposed to gruesome trauma in maintaining their resilience against PTSD and to continue participating in their jobs.

Summary:

Objective: This study investigates the effects of repeated exposure to terrorist casualties on ultra-Orthodox Jewish volunteer rescue workers in Israel. Their task is part of a religious obligation

to ensure that all body parts of the victims and the suicide bombers are gathered for ritual burial. They have handled the remains of nearly 1100 victims from over 100 attacks in the past four years.

Methods: Risk for PTSD in 130 ultra-Orthodox male rescue workers will be compared with a control group from the secular Israeli police and fire departments that responded to the same bombings. The interview consists of three validated scales that measure PTSD symptoms, two validated scales that measure religious beliefs and coping strategies, as well as questions assessing exposure, drop-out rates, attitudes toward work, and quality of social functioning.

Results: Preliminary data suggest that greater religious coping leads to fewer PTSD symptoms and a lower drop-out rate. This is in marked contrast to the high rates of impairment found in the current literature on rescue workers following disasters.

Conclusions: Religious belief is a strong protective feature in maintaining resilience against PTSD while repeatedly being exposed to gruesome deaths during body handling.

References:

1. Bleich, Gelkopf, and Solomon: Exposure to terrorism, stress-related mental health symptoms, and coping behaviors among a nationally representative sample in Israel. *JAMA* 2003; 290(5):612-620.
2. Keller, Richard and Bobo, William: Handling human remains: exposure may result in severe psychological responses among rescue workers. *Psychiatric Annals* 2004; 34(8):635-640.

NR125 Monday, May 23, 9:00 a.m.-10:30 a.m.

Do Somatic Symptoms Predict Quality of Life in Primary Care?

Venugopal Duddu, M.R.C., *Department of Psychiatry, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL, United Kingdom*; Nusrat Husain, M.R.C., Chris Dickens, M.R.C.

Educational Objectives:

At the conclusion of the presentation, the participant should appreciate the complexity of factors that affect quality of life in primary care settings. The research teases out the relative impact of anxiety, depression, and somatic symptoms on QOL.

Summary:

Somatic symptoms are strongly associated with emotional distress. However, there is little research on the impact of somatic symptoms, anxiety, and depression on Quality of life(QOL).

Objectives: This study aimed to examine the associations of QOL in an urban general practice setting in the UK.

Methods: Ninety-one subjects were recruited from among patients attending a general practice in central Manchester. Subjects completed the Hospital Anxiety and Depression scale (HADS), Somatic symptoms checklist (from SCL-90) and a quality of life instrument (EQ-5D). A Physician encounter form (PEF) recorded whether the presenting symptoms were medically explained.

Results: A majority of the subjects was male (53%), married(52%), and employed(44%). 32% of the subjects had medically unexplained symptoms. The mean QOL valuation score was 0.686(SD: 0.37). On hierarchical multiple regression, anxiety (but not depression) accounted for 24%($p < 0.05$) of the variance in QOL. Somatic symptoms accounted for a further 14%($p < 0.05$) in the second block but the effect of anxiety was reduced but not eliminated. This suggests that somatic symptoms partially mediate the effect of anxiety on QOL. Whether symptoms were medically unexplained was not significant.

Conclusions: Somatic symptoms (whether medically explained or not) and anxiety are significant and partially independent factors affecting QOL.

References:

1. Kroenke K: Symptoms are sufficient. *Adv Mind Body Med* 2001; 17(4):244-9; 270-6.
2. Katon WJ, Walker EA: Medically unexplained symptoms in primary care. *J Clin Psychiatry* 1998; 59 Suppl 20:15-21.

NR126 Monday, May 23, 09:00 a.m.-10:30 a.m.

The Role of Depression and Anxiety in Functional Status in Patients With End-Stage Renal Disease

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Educational Objectives:

At the conclusion of this presentation, the participant will have a greater understanding of the relationship between somatic symptoms and psychological distress in individuals with ESRD.

Summary:

Introduction: Depression is the most common psychiatric problem seen in patients with end-stage renal disease (ESRD). This retrospective study was designed to evaluate the relationship between somatic symptoms and psychological distress in individuals with ESRD.

Methods: After IRB approval, we reviewed the records of 26 individuals with ESRD seen in psychiatry who completed routine self-report measures [Hospital Anxiety and Depression Scale (HADS), ISEL (Social Support), Dyspnea Scale, Daily Activities scale, self-report adherence scale]. Research indicates HADS scores are correlated with health perception, ability to attend to activities of daily living, fatigue, dyspnea, functional status, and social support.

Results: Patients with depressive and anxiety symptoms had more sleep disturbances ($p < .001$). HADS total scores were also negatively correlated with degree of religious involvement for those who endorsed a religious affiliation ($p < .05$) and amount of social support [$p < .05$]. Shortness of breath, sleep disturbance, and depression were not significantly correlated.

Conclusions: Results of the current study suggest religion and social support played a role in reducing level of depression and anxiety symptoms in patients with ESRD.

References:

1. Rodin G: Depression in patients with end-stage renal disease: psychopathology or normative response? *Adv Ren Replace Ther* 1994; 1(3):219-27. Review.
2. Finkelstein FO, Finkelstein SH: Depression in chronic dialysis patients: assessment and treatment. *Nephrol Dial Transplant* 2000; 15(12):1911-3. Review.

NR127 Monday, May 23, 9:00 a.m.-10:30 a.m.

Prognostic Validity of a Self-Report Scale to Identify Remission in Outpatients With Depression

Charlotte A.L. Rucker, *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street Suite 501, Providence, RI 02905*; Mark Zimmerman, M.D., Michael Posternak, M.D., Andrea Grenga

Educational Objectives:

At the conclusion of this presentation, the participant should be able to better understand the validity of using a self-report scale to identify remission from depression in depressed psychiatric outpatients.

Summary:

Objective: Previously, our group derived a cutoff on a self-report depression questionnaire corresponding to the most widely used definition of remission from depression (17-item Hamilton Rating Scale for Depression score = 7). In the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services project, we determined the validity of this self-report scale by examining whether it has prognostic significance among treatment responders.

Method: Ninety-six depressed psychiatric outpatients in ongoing treatment who responded to treatment completed the Clinically Useful Depression Outcome Scale (CUDOS). Using the previously validated cutoff score of 20 on the CUDOS to define remission, patients who were and were not in remission were compared in the rate of relapse of MDD six months after completing the scale.

Results: The majority (80%) of the treatment responders scored below 20 on the CUDOS and thus were considered the remitted group. At the six-month follow-up interval, approximately one-sixth of the patients had relapsed into an episode for MDD. The relapse rate was significantly lower in the remitted compared to the non-remitted patients (11.5% vs. 33.3%, $\chi^2 = 5.3$, $p < .05$).

Conclusions: These results support the validity of using a self-report scale to identify remission from depression among patients receiving treatment in a clinical outpatient setting.

References:

1. Zimmerman M, Posternak M, Chelminski I: Using a self-report depression scale to identify remission in depressed outpatients. *Am J Psychiatry* 2004; 161:1911-1913.
2. Paykel ES, Ramana R, Cooper Z, Hayhurst H, Kerr J, Barocka A. Residual symptoms after partial remission: an important outcome in depression. *Psychol Med* 1995; 25:1171-1180.

NR128 Monday, May 23, 9:00 a.m.-10:30 a.m. **Evaluating Comprehensive Community Services for Children and Families**

Hilary L. Copp, M.S.W., *School of Social Work, University of Georgia, 1000 University Center Lane, Lawrenceville, GA 30043*; Amy Traylor, M.S.W., Patrick Bordnick, Ph.D., Bruce Thyer, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the process of implementing a computerized assessment system of community-based mental health services for children and families.

Summary:

Objectives: To describe the utilization of a computerized assessment system to evaluate comprehensive community-based mental health services for children and families. We hypothesized that participating families would demonstrate improvement across a range of clinical indicators, specifically child and adolescent functioning in home, school, and community environments.

Methods: Families with children with serious emotional disturbances (SED) who met criteria were enrolled in a system of care between 2001-2004. A computerized assessment system was implemented to evaluate the impact of services upon family functioning. Interviews were conducted in the field at baseline and 6 months using laptop computers to collect demographic items and assessments of child behavior and family functioning.

Results: Our data indicate that a computerized assessment system is feasible for evaluating community-based services in the field. Evaluation data on 15 families who completed baseline and six-month interviews will be presented.

Conclusion: Our findings indicate that evaluation of comprehensive services using computer-based methods in the field is a viable

means of providing feedback to service providers. Additional information and suggestions for future large-scale program evaluations will be presented and discussed.

References:

1. Copp HL, Bordnick PS, Traylor AC, Thyer BA: Evaluating wrap-around services for seriously emotionally disturbed youth: preliminary outcomes in Georgia. Submitted for publication.
2. U.S. Department of Health and Human Services: Comprehensive Community Mental Health Services Program for Children and Their Families. Rockville, MD, 2004.

NR129 Monday, May 23, 9:00 a.m.-10:30 a.m. **Family Planning Needs and Contraceptive Use in Female Psychiatric Patients**

Kadriye Pehlivan, M.D., *1. Psikiyatri, Bakirköy Ruh ve Sinir Hastalıkları Hastanesi, Istanbul 34787, Turkey*; Nesrin B. Tomruk, M.D., Nesrin Karamustafalioğlu, M.D., Evrim E. Öztekin, M.D., Celal Calikusu, M.D., Nihat Alpay, M.D.

Educational Objectives:

In this study, attitudes and needs in family planning and contraceptive use have been evaluated in female psychiatric patients.

Summary:

The study was conducted in the outpatient clinic of Bakirkoy Neuropsychiatric Hospital. Schizophrenic, bipolar, and unipolar depressive patients in remission (50 patients in each group) have been compared with a control group of 50 healthy subjects. A semistructured questionnaire has been developed to collect the data regarding the sociodemographic characteristics.

The knowledge of family planning methods was inadequate in general but it was more pronounced in schizophrenic patients 82.5% Gynecological examination and discussing family planning with partner were infrequent in schizophrenic and bipolar patients. Gynecological examination in the last three years was 26.6% in schizophrenic and 37.5% in bipolar patients compared with 56% in healthy controls. Discussing family planning issues with partner was 40% in schizophrenic and 50% in bipolar patients compared with 90% controls. Although the patients reported high need for counseling in family planning (87%), they couldn't discuss these topics with their psychiatrists.

In summary, due to the fact that the course of illness overlaps with the reproductive period, especially schizophrenic and bipolar female patients are open to be affected deeply in the areas of family planning and contraceptive use. Therefore, psychiatric services should be enhanced to fulfill these basic primary healthcare needs.

References:

1. Miller LJ: Sexuality, reproduction, and family planning in women with schizophrenia. *Schizophr Bull* 1997; 23:623-35.
2. Coverdale JH, Turbott SH, Roberts H: Family planning needs and STD risk behaviours of female psychiatric outpatients. *Br J Psychiatry* 1997; 171:69-72.

NR130 Monday, May 23, 9:00 a.m.-10:30 a.m. **Rehospitalization Rates on Long-Acting Risperidone and Haloperidol Deconate**

Meera Narasimhan, M.D., *Department of Neuropsychiatry & Behavioral Science, USC School of Medicine, 3555 Harden Street, Suite 104-A, Columbia, SC 29203*; Christine Latham, R.Ph., Allison Clark, Pharm.D., Ronald Prier, M.D., Richard Harding, M.D.

Educational Objectives:

At the end of this presentation, participants will be able to evaluate the role of long-acting atypical antipsychotics and their role in relapse and adherence.

Summary:

Objective: The purpose of this study is to examine the rehospitalization rates in patients receiving long-acting risperidone or haloperidol decanoate who were discharged from a state psychiatric hospital.

Method: A retrospective analysis of 300 charts, pharmacy database examining the rehospitalization rate for all patients either on long-acting risperidone or haloperidol decanoate between December 2003 and June 2005 is being conducted. This study will also assess associated risk factors including age, sex, diagnosis, dose, noncompliance, concomitant medications, and substance abuse.

Results: Preliminary data from 89 patients discharged on long-acting risperidone and 100 on haloperidol shows a one-time readmission rate of 4.9% and 5.5% for long-acting risperidone and haloperidol deaconate treated patients, respectively. These preliminary data represent one rehospitalization after being on either of the two depot preparations and included patients on concomitant medications. 47.2% had schizophrenia, 28.8% had schizoaffective disorder and 11.6% had bipolar disorder.

Conclusions: This retrospective analysis compares rehospitalization with second-generation antipsychotic and a conventional depot preparation in a real-world clinical practice. Preventing relapse and enabling compliance are key to improving the overall outcome of schizophrenia. Results from this study may shed light on the role of long-acting, second-generation antipsychotics in relapse prevention.

References:

1. Conley RR, Kelly DL, Love RC, et al: Rehospitalization risk with second-generation and depot antipsychotics. *Ann of Clinical Psychiatry* 2003; 15(1):23-31.
2. Long-acting risperidone vs placebo in the treatment of hospital inpatients with schizophrenia. *Schizophrenia Res* 2005; 72(2-3):249-258.

NR131 Monday, May 23, 9:00 a.m.-10:30 a.m.

Parent/Child Interaction as a Function of Mood Episodes in Bipolar Disorder

Karen Yee, M.S.N., *Mood Disorders Unit, University Health Network, Toronto Western Hospital, 399 Bathurst Street, Toronto, ON M5T 2S8, Canada*; Vytus Velyvis, M.A., Stephanie Koenig-Noebert, B.S.C., Sagar V. Parikh, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should appreciate the relationship between parent-child interaction and mood episodes in bipolar disorder and recognize its implication on treatment.

Summary:

Objective: We interviewed patients with bipolar disorder (BD) to assess the relationship between mood symptom severity and quality of parent-child interactions. Although previous research has found that mood disorders are negatively related to parent-child interactions, these studies did not assess current levels of mood symptoms, nor did they investigate multidimensional aspects of parent-child interaction.

Method: Thirty-three subjects with BD were rated on the severity of their mood symptoms over a one-month period using the Longitudinal Interval Follow-Up Evaluation (LIFE); three dimensions of parent-child interaction were also rated over the same month using a modified version of the Social Adjustment Scale (Bauer, 2001)

including lack of involvement; impaired communication, and friction.

Results: Findings revealed that depressive symptoms in BD are highly correlated with lack of parental involvement as well as parent-child friction, but is not related to impaired communication. Surprisingly, no significant relationships were found between manic episodes and the three dimensions of parent-child interaction.

Conclusion: The apparently unique relationship between depression and parent-child interaction in BD as well as possible treatment implications will be discussed in the context of study limitations as well as other literature.

References:

1. Hay D, Vespo J, Zahn-Waxler C: Young children's quarrels with their siblings and mothers: links with maternal depression and bipolar illness. *British Journal of Developmental Psychology* 1998; 16(4):519-538.
2. Inoff-Germain G, Nottelmann ED, Radke-Yarrow M: Evaluative communications between affectively ill and well mothers and their children. *Journal of Abnormal Child Psychology* 20(2): 189-212.

NR132 Monday, May 23, 9:00 a.m.-10:30 a.m.

Early Sexual Maturity Risk Factors for Delinquency in Inner-City Adolescents

Mark J. Smith, M.D., *NPS Department, Riverside Hospital, 4460 MacArthur Boulevard NW, Washington, DC 20007*; M. Paula Gaudino, L.C.S.W., Sidney W. Binks, III, Ph.D., Pamela Blake, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the effect of puberty on psychiatric symptomatology in inner-city adolescent males.

Summary:

Objective: Externalizing behavior disorders in males clearly change from beginning toward the end adolescence. Attention-deficit/hyperactivity disorder (ADHD) decreases, whereas conduct disorder (CD) and substance abuse increase post-pubertally compared with pre-pubertally. These changes may be due to increasing age or to sexual maturation. We retrospectively reviewed charts of 12-15 year-old inner-city males hospitalized for disruptive behavior to determine if their degree of sexual maturity (as indicated by Tanner stage) affected externalizing behavior symptomatology.

Methods: Patients were grouped into those with a Tanner stage below (n=45, age = 13.45 yrs) or above (n=32, age = 13.52 yrs) the mean Tanner stage score for their age cohort. The following were compared: height, weight, diagnoses of substance abuse, CD and ADHD from MINI-KID interviews, Connors' Parents ADHD rating scale (short form), history of arrest, the Aggression and Delinquency sub-scales of the Child Behavior Checklist (CBCL), levels of gonadal steroids [dehydroandrosterone-sulfate, testosterone, bioavailable testosterone, dihydrotestosterone].

Results: Patients with higher Tanner scores were taller and heavier, had higher steroid levels, fewer diagnoses of ADHD and lower ADHD symptom scores, more diagnoses of substance abuse, CD, more arrests, and higher CBCL scores.

Conclusion: Externalizing behavior symptomatology in inner-city adolescent boys may be linked to sexual maturation.

References:

1. Scerbo AS, Kolko DJ: Salivary testosterone and cortisol in disruptive children: relationship to aggressive, hyperactive, and

internalizing behaviors. *J Am Acad Child Adolesc Psychiatry* 1994; 33(8):1174-84.

2. Valois RF, MacDonald JM, Bretous L, Fischer MA, Drane JW: Risk factors and behaviors associated with adolescent violence and aggression. *Am J Health Behav* 2002; 26(6):454-64.

NR133 **Monday, May 23, 9:00 a.m.-10:30 a.m.**
Mortality Rates and Behavioral Health Risk Factors in Veterans With Chronic PTSD Versus Other Axis I Psychiatric Diagnoses

Oscar M. Villaverde, *Department of Psychiatry, Miami VAMC and University of Miami, 2020 SW 104th Place, Miami, FL 33165*; Lester Hartswick, M.D., Daniella David, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should have a better understanding of behavioral risk factors and mortality rate in veterans with chronic PTSD vs. other chronic psychiatric disorders.

Summary:

Background: Chronic psychiatric disorders such as PTSD, major depression and schizophrenia have been associated with higher rates of self-reported poor health, morbidity, and mortality. The objective of this study is to compare mortality rates and behaviorally-related risk factors between two discrete veteran populations with chronic psychiatric disorders that completed residential rehabilitation treatment programs at a VA facility.

Methods: We are comparing two groups of male veterans admitted to two residential rehabilitation units between Jan 1999-Oct 2004, one for PTSD (PRRP) and one for psychosocial rehabilitation (PRRTP). Primary Axis I diagnoses were determined based on DSM-IV criteria as applied to patients' discharge summaries from their respective units. Patients in the PRRTP who met diagnostic criteria for PTSD were included in the PTSD group. Patients' medical records are currently being reviewed and mortality cases will be identified through the National Death Index. The information will then be categorized according to mortality rates, causes of death, demographic variables, and behaviorally-related health risk factors, such as smoking, hyperlipidemia, alcohol/drug abuse, and obesity. The study was approved by the Miami VAMC Institutional Review Board.

Results: We have identified 323 male veterans with a primary diagnosis of chronic PTSD (mean age 56.9 + 6.1, range 32-82 years old) and 243 male veterans with primary Axis I diagnoses of schizophrenia-spectrum and affective disorders (mean age 52.5 + 9.4, range 28-80 years) that completed one of the two residential programs in the above time period. Data are currently being run through the National Death Index and medical records are being reviewed.

Conclusions: Data will be analyzed to determine whether there is a significant difference in mortality rates and behavioral health risk factors between patients with a primary PTSD diagnosis and patients with other Axis I chronic psychiatric disorders.

References:

1. Drescher KD, Rosen CS, Burling TA, Foy DW: Causes of death among male veterans who received residential treatment for PTSD. *Journal of Traumatic Stress* 2003; 16:535-543.
2. David D, Woodward C, Esquenazi E, Mellman T: Comparison of comorbid physical illnesses among veterans with PTSD and veterans with alcohol dependence. *Psychiatric Services* 2004; 55:82-85.

NR134 **Monday, May 23, 9:00 a.m.-10:30 a.m.**

Marital Status, Parenthood, and Sexuality in Female Psychiatric Patients

Nesrin Karamustafalioglu, M.D., *Halkali Ca Tahsinbey #43/2, Yesilkoy, Istanbul 34800, Turkey*; Nesrin B. Tomruk, M.D., Kadriye Pehlivan, M.D., Celal Calikusu, M.D., Evrim E. Oztekin, M.D., Nihat Alpay, M.D.

Educational Objectives:

In this study, marriage, parenthood, and sexuality have been evaluated in female psychiatric patients.

Summary:

The study was conducted in the outpatient clinic of Bakirkoy Neuropsychiatric Hospital. Schizophrenic, bipolar, and unipolar depressive patients in remission (50 patients in each group) have been compared with a control group of 50 healthy subjects. A semistructured questionnaire has been developed to collect the data regarding the sociodemographic characteristics.

Lifetime marriage rates were similar in schizophrenia (64%), bipolar (76%), unipolar depression (82%) and control (84%) groups. Regarding marital status, the rate of being single, divorced and separated in all patient groups were significantly higher. Also psychopathology was more common in the partners of schizophrenic patients (29%).

The data related to menstruation, sexual intercourse; and masturbation in female patients were found to be similar to the control group. However, sexual abuse was more frequently reported in patient groups (schizophrenia 30%, bipolar 10%, unipolar depression 16%) especially in schizophrenic patients compared to controls (4%).

Schizophrenic and bipolar patients tended to seek more support or had to rely on their relatives and/or institutions for childrearing.

In summary, due to the fact that the course of illness overlaps with the reproductive period, especially schizophrenic and bipolar female patients are open to be affected deeply in the areas of sexuality and parenthood. Therefore psychiatric services should be enhanced to fulfill these basic primary health care needs.

References:

1. Miller LJ, Finnerty M: Sexuality, pregnancy, and childrearing among women with schizophrenia-spectrum disorders. *Psychiatr Serv* 1996; 47:502-6.
2. Nicholson J, Sweeney EM, Geller JL: Mothers with mental illness: I. The competing demands of parentig and living with mental illness. *Psychiatr Serv* 1998; 49:635-42.

NR135 **Monday, May 23, 9:00 a.m.-10:30 a.m.**

Risk Behaviors for Sexually Transmitted Infections in Female Psychiatric Patients

Nesrin B. Tomruk, M.D., *Sakayikaraligisok #4/4, Tesvikiye, Istanbul 80200, Turkey*; Nesrin Karamustafalioglu, M.D., Kadriye Pehlivan, M.D., Evrim E. Oztekin, M.D., Neslihan Cansel, M.D., Resit Kukurt, M.D.

Educational Objectives:

At the end of the presentation, the participant will have learned about high-risk behaviors in female psychiatric patients

Summary:

In this study, high-risk behaviors concerning sexually transmitted infections (STIs) and HIV/AIDS have been evaluated in female psychiatric patients. The study was conducted in the outpatient clinic of Bakirkoy Neuropsychiatric Hospital. Schizophrenic, bipolar, and unipolar depressive patients in remission (50 patients in each group) have been compared with a control group of 50 healthy subjects. A semistructured questionnaire has been devel-

oped to collect the data regarding the sociodemographic characteristics.

In schizophrenic patients, high-risk behaviors regarding STI and HIV/AIDS were reported frequently, hence lower than the literature. From these high-risk behaviors sexual intercourse during alcohol and substance use was 10%, sexual intercourse in return for shelter, alcohol and drug was 6% having a drug addicted partner was 4% and having multiple partners was 10%. Awareness and knowledge of STI and HIV/AIDS was also inadequate among this group. Media was the main source of information.

In summary, due to the fact that the course of illness overlaps with the reproductive period, especially schizophrenic and bipolar female patients are open to be affected deeply in the areas of high-risk behaviors concerning sexually transmitted infections and HIV/AIDS. Therefore, psychiatric services should be enhanced to fulfill these basic primary health care needs.

References:

1. Kalichman SC, Kelly JA, Johnson JR, Bulto M: Factors associated with risk for HIV infection among chronic mentally ill adults. *Am J Psychiatry* 1994; 151:221-7.
2. Coverdale JH, Turbott SH, Roberts H: Family planning needs and STD risk behaviours of female psychiatric outpatients. *Br J Psychiatry* 1997; 171:69-72.

NR136 Monday, May 23, 9:00 a.m.-10:30 a.m. **Course of Bipolar Disorder in Very Young (Three- to Seven Year-Old) Children**

Arman K. Danielyan, M.D., *Division of Psychiatry, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue, MLC 3014, Cincinnati, OH 45229*; Sanjeev Pathak, M.D., Sarah Arszman, B.A., Erin Johns, Pamela Campbell, M.D., Michael Sorter, M.D., Robert Kowatch, M.D.

Educational Objectives:

At the end of the presentation, the participant should be able to recognize presenting symptoms of bipolar disorder in very young (3-7 year old) children; will be familiar with the course of the illness, its recovery, and relapse rate.

Summary:

Objectives: To describe the course of bipolar disorder (BPD) in very young (3-7 year old) children.

Methods: We did a retrospective chart review of 26 children, treated as outpatients from 2000 to 2004. All children had diagnoses assigned by board-certified child and adolescent psychiatrists using DSM-IV-TR criteria.

Results: The most common diagnoses included BPD NOS (46.2%), BPD I (26.9%), BPD (15.4%) and mood disorder NOS (11.15%). Ten patients had at least one DSM IV axis I comorbid diagnosis, ADHD being the most common (30.8%). Five patients (19.2%) had two or more comorbid diagnoses. The most common symptoms at the initial presentation were aggression (88.5%), irritability (84.6%), decreased sleep (65.4%), increased energy (50%), and elated mood (30.8%). Twenty-five out of 26 patients were treated with psychotropic medications. Nineteen patients were treated with more than one medication. Ten out of 26 children had at least one relapse, defined as CGI-S score of > 3 for more than two weeks, during the course of treatment. Four subjects (15.4%) relapsed twice, and two subjects (7.7%) had three relapses during the course of treatment.

Conclusions: Diagnostic criteria for BPD in very young children are non-specific. The course of the illness is complex, characterized by one or more relapses.

References:

1. Geller B, Craney JL, Bolhofner K, Delbello MP, Williams M, Zimmerman B: One-year recovery and relapse rates of children

with a prepubertal and early adolescent bipolar disorder phenotype. *Am J Psychiatry* 2001; 158:303-305.

2. Rajeev J, Srinath S, Girimaji S, Seshadri SP, Singh P: A systematic chart review of the naturalistic course and treatment of early-onset bipolar disorder in a child and adolescent psychiatry center. *Comprehensive Psychiatry* 2004; 45:148-54.

NR137 Monday, May 23, 09:00 a.m.-10:30 a.m. **Source of Funding by Diagnosis in Clinical Trials in Psychiatry**

Megan F. Joseph, B.A., *Bipolar Clinic and Research Program, Massachusetts General Hospital, 50 Staniford Street, Suite 580, Boston, MA 02114*; Roy H. Perlis, M.D., Yelena P. Wu, B.A., Cindy H. Hwang, B.A., Andrew A. Nierenberg, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should understand the breakdown of industry, federal, and private funding support for clinical trials and the implications of these discrepancies.

Summary:

Introduction: The extent and impact of pharmaceutical industry funding for clinical trials has received increasing attention. We examined funding sources by diagnosis among clinical trials published between 2001 and 2003.

Methods: We conducted a Medline search using the term "clinical trial" limited to articles published in four widely-read psychiatric journals and supplemented this search with a manual review of the table of contents in these issues. Reviewers then used a standardized template to extract data on subjects' diagnoses and study funding sources.

Results: Of 209 randomized controlled trials identified, the most common diagnoses examined were major depressive disorder (MDD) (23%), anxiety disorders (20%), schizophrenia/psychosis (19%), bipolar disorder (8%), and substance-use disorders (7%). Within MDD, 79% reported industry support, 27% received NIH or other government support, and 10% received private support (some studies reported multiple funding sources). Patterns were generally similar among other disorders.

Discussion: In this sample of clinical trials published between 2001 and 2003, the majority received industry support. Given recent concern about the influence of industry funding on study design and outcomes, source of funding for clinical trials seems to be a relevant issue that warrants further investigation. Additionally, bipolar disorder appears to be underrepresented among clinical trials.

References:

1. Bekelman JE, Li Y, Gross CP: Scope and impact of financial conflicts of interest in biomedical research. *JAMA* 2003; (289)4:454-465.
2. Perlis RH, Wu YP, Hwang CH, Joseph MF, Perlis CS, Nierenberg AA: Conflict of interest in clinical trials in psychiatry, submitted.

NR138 Monday, May 23, 09:00 a.m.-10:30 a.m. **Comorbid Anxiety and Bipolar Disorder: Prevalence and Impact on Functioning**

Lisa Wygant, B.A., *Department of Psychiatry, Cambridge Health Alliance, Harvard Medical School, 1493 Cambridge Street, Cambridge, MA 02139*; S. Nassir Ghaemi, M.D., Gustavo Kinrys, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to have a better understanding of the impact of comorbid anxiety among bipolar disorder patients.

Summary:

Objective: To examine the prevalence and impact of anxiety comorbidity on functioning in a population of bipolar disorder patients.

Method: Retrospective chart review of 53 outpatients with a primary diagnosis of bipolar disorder. Clinical and demographic data was collected from STEP-BD baseline evaluation charts. A regression model correcting for confounding factors will be presented.

Results: Patients included 23 men and 30 women who had a mean (\pm SD) age of 44.9 ± 12.8 years. Thirty-one (58%) of the patients met DSM-IV criteria for at least one comorbid anxiety disorder, and 18 (34%) patients had at least two comorbid anxiety disorders. Twenty-three (43%) patients had generalized anxiety disorder, 14 (26%) panic disorder, 10 (19%) social anxiety disorder, six (11%) obsessive-compulsive disorder, and four (8%) post-traumatic stress disorder. Patients spent a mean (\pm SD) 38% (37) of the year anxious and had a mean \pm SD Beck Anxiety Inventory (BAI) score of 11.3 ± 11.7 . Patients with comorbid anxiety had significantly higher CGI-BP scores ($p < 0.001$) and significantly lower GAF scores ($p < 0.001$) than those with bipolar disorder alone.

Conclusion: Comorbid anxiety was highly prevalent and appears to have a significant impact on symptom severity and functioning in this group of bipolar disorder patients.

References:

1. Henry C, Van den Bulke D, Bellivier F, Etain B, Rouillon F, Leboyer M: Anxiety disorders in 318 bipolar patients: prevalence and impact on illness severity and response to mood stabilizer. *J Clin Psychiatry* 2003; 64:331-335.
2. Boylan KR, Bieling PJ, Marriott M, Begin H, Young LT, MacQueen GM: Impact of comorbid anxiety disorders on outcome in a cohort of patients with bipolar disorder. *J Clin Psychiatry* 2004; 65:1106-1113.

NR139 Monday, May 23, 9:00 a.m.-10:30 a.m. Temperament Characteristics and Behavioral Problems in Offspring With Bipolar Disorder

Diana Iorgova Simeonova, M.S., *Department of Child Psychiatry, Stanford University, 401 Quarry Road, Room 1105, Stanford, CA 94305*; Fiona Baumer, B.A., Hans Steiner, M.D., Kiki Chang, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand better the association between temperamental characteristics and behavioral problems in bipolar offspring with and at high risk for developing bipolar disorder.

Summary:

Objective: The purpose of this study was to investigate relationships between temperamental characteristics and behavioral problems in bipolar offspring with and at high risk for developing bipolar disorder (BD).

Methods: 50 children with BD (mean age = 12.8, 13 female) and 36 children with putative prodromal BD (mean age = 12, 13 female) completed the Dimensions of Temperament Survey-Revised (DOTS-R). Behavioral problems were assessed using the Child Behavior Checklist (CBCL).

Results: Internalizing Problems were negatively correlated with Adaptability and Mood scores in bipolar offspring with BD and

offspring with putative prodromal BD. Externalizing Problems were negatively correlated with Mood scores, and Attention Problems were positively correlated with Activity Level-General scores in offspring with putative prodromal BD.

Conclusions: Assessment of temperamental traits and behavioral problems may be useful in characterizing bipolar offspring with and at high risk for developing BD. The results of this study contribute to better understanding of associations between temperament and behavioral problems in this population and indicate directions for future research.

References:

1. Schmitz S, Fulker D, Plomin R, Zahn-Waxler C, Emde R, deFries J: Temperament and problem behaviour during early childhood. *International Journal of Behavioral Development* 1998; 23 (2):333-355.
2. Compas B, Connor-Smith J, Jaser S: Temperament, stress reactivity, and coping: implications for depression in childhood and adolescence. *Journal of Clinical and Child and Adolescent Psychology* 2004; 33(1):21-31.

NR140 Monday, May 23, 9:00 a.m.-10:30 a.m. Romantic Partner Interaction Reduces Endocrine and Autonomic Stress Responses in Women

Beate Ditzen, Ph.D., *Department of Clinical Psychology and Psychotherapy, University of Zurich, Zurichbergstr. 43, Zurich 8044, Switzerland*; Inga Neumann, Ph.D., Guy Bodenmann, Ph.D., Rebecca Turner, Ph.D., Ulrike Ehlert, Ph.D., Markus Heinrichs, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the role of partner interaction in stress protective mechanisms.

Summary:

Stable romantic partnerships are known to reduce suffering from chronic diseases and to increase health. This effect is suggested to be mediated by attenuated psychophysiological stress responses. Animal studies showed positive social interaction to increase the central nervous availability of the neuropeptide oxytocin, which was endogenously stimulated by warmth and massage during social interaction in animals. In humans, oxytocin was shown to reduce stress induced increases in cortisol.

The present study focuses on protective effects of instructed partner interaction in a standardized psychosocial stress situation. Seventy-five women participated in the standardized psychosocial Trier Social Stress Test TSST. Before stress, one-third of these women ($N = 25$) received social support from their partners. A second group ($N = 25$) received instructed shoulder-neck-massage from their partners, and the third group ($N = 25$) came alone with no intervention before the stress test. Blood samples were collected at three time points to analyze oxytocin levels. Subjective stress responses, salivary cortisol, and heart rate were repeatedly assessed in the course of the study.

The stressor induced an endocrine stress response in all groups. Most important, massage before stress exposure significantly reduced cortisol responses ($F = 3.06$, $p = .016$) and heart rate increases ($F = 4.33$, $p = .019$) compared with the social support and the alone group, which did not differ from one each other. The results are in line with animal studies about the stress ameliorating effect of oxytocin and oxytocin stimulating behavior. They demonstrate a protective role of touch and proximity on biological responses in stressful situations. They might, thus, explain the protective effects of stable romantic partnerships beyond cognitive variables.

References:

1. Heinrichs, et al: Biological Psychiatry, 2003.

NR141 Monday, May 23, 9:00 a.m.-10:30 a.m. **Impact of a Depression Intervention on U.S.-Born and Immigrant Latinos**

Francisco Velarde, M.D., LAC+USC Department of Psychiatry, University of Southern California, 2020 Zonal Ave., Los Angeles, CA 90033; Isabel T. Lagomasino, M.D., Jeanne Miranda, Ph.D., Cathy Sherbourne, Ph.D., Kenneth B. Wells, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the impact of a depression quality improvement intervention on depression care utilization and depression and employment outcomes for U.S.-born and immigrant Latinos in primary care settings.

Summary:

Objective: To examine whether a quality improvement (QI) intervention, with modest cultural adaptations, improved depression care and outcomes among US-born and immigrant Latinos.

Methods: Funded by AHRQ and NIMH, Partners in Care randomized 46 primary care practices to usual care or one of two QI programs with resources for medication management (QI-Meds) or cognitive-behavioral therapy (QI-Therapy). 1356 patients (including 398 Latinos) with probable depressive disorder enrolled; they and providers selected treatments. Multivariate logistic regressions adjusted for covariates and clustering effects.

Results: Among Latinos, 69.5% were U.S.-born. At six months, compared with usual care, US-born Latinos in QI-Meds and immigrants in both interventions had improved rates of appropriate care (medication or counseling). U.S.-born in QI-Therapy and immigrants in both interventions had improved depression outcomes. Immigrants in QI-Meds had worse employment outcomes than immigrants in usual care and QI-Therapy. There were no interaction effects between immigrant status and type of intervention on rates of care or depression outcomes, although U.S.-born Latinos in QI-meds had better employment outcomes than immigrants.

Conclusions: QI programs with modest accommodations can improve some but not all outcomes for immigrant as well as U.S.-born Latinos. Further analyses will examine the differential effects of interventions on Latino subgroups.

References:

1. Miranda J, Duan N, Sherbourn C, Schoenbaum M, Lagomasino I, Jackson-Triche M, Wells KB: Improving care for minorities: Can quality improvement interventions improve care and outcomes for depressed minorities? Results of a randomized, controlled trial. Health Services Research 2003; 38:613-630.
2. Wells KB, Sherbourne C, Shoenbaum M, Duan N, Meredith L, Unutzer J, Miranda J, Carney MF, Rubenstein LV: Impact of disseminating quality improvement programs for depression in managed primary care: a randomized controlled trial. JAMA 2000; 283(2):212-220.

NR142 Monday, May 23, 9:00 a.m.-10:30 a.m. **Religious Beliefs Among Psychiatric Outpatients: How Often Is It Incorporated Into Management?**

John R. Applegate, M.D., Department of Psychiatry, University of Pennsylvania, 3535 Market Street, Second Floor, Philadelphia, PA 19104; Claudia F. Baldassano, M.D., John O'reardon, M.D., Jeff Staab, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to evaluate religious beliefs among psychiatric outpatients and how this affects patient compliance and satisfaction with care.

Summary:

Introduction: Religious beliefs and spirituality is a topic that has received little attention in psychiatric outpatients. A good therapeutic relationship is an essential precursor to good treatment outcome. Although there is growing interest in the effects of spirituality on illness, there is little study on how it affects treatment course, outcome, and compliance.

Methods: To investigate whether patient's spiritual or religious beliefs are correlated with compliance to treatment and satisfaction with their therapeutic relationship, we plan to administer an adaptation of the self-administered Royal Free Interview for Spiritual/Religious Beliefs to 400 psychiatric outpatients in a general clinic. This will also be administered to the psychiatrists in the clinic. Patients will be queried about the extent to which they felt their psychiatrist incorporated their religious beliefs into illness discussion. Compliance will be measured by patient report, supplemented by chart review.

Results: Among 100 psychiatric outpatients, 79% endorsed religious and spiritual beliefs. Twenty-one percent reported having no religious affiliation, nor any spiritual beliefs. None of the treatment plans included any discussion of spiritual dimensions. Psychiatrist attitudes towards patient's religious beliefs and patients' attitudes towards how their providers incorporate their beliefs in their management will be analyzed.

Conclusion: Although the majority of our patients endorse a religious affiliation and spiritual beliefs, psychiatrists often neglect to incorporate these beliefs into illness management. Increasing awareness of the importance of religion in psychiatric patients may help psychiatrists form better therapeutic alliance with patients and therefore increase compliance to treatment.

References:

1. King M, Speck P, Thomas A: The Royal Free Interview for Spiritual and Religious Beliefs: development and validation of a self-report version. Psychol Med 2001; 31(6):1015-23.
2. King M, Speck P, Thomas A: Spiritual and religious beliefs in acute illness — is this a feasible area for study? Soc Sci Med 1994; 38(4):631-6.

NR143 Monday, May 23, 9:00 a.m.-10:30 a.m. **Dual Diagnoses in Acute Care Psychiatry: Patterns of Comorbidity**

Alexandru Trutia, M.D., Department of Psychiatry, Virginia Commonwealth University, 1300 East Marshall Street, Box 980710, Richmond, VA 23298-0710

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize unique demographics and patterns of psychiatric and medical comorbidity in dual-diagnoses patients.

Summary:

Background: A challenge on acute inpatient units is how best to treat dual-diagnoses (DD) patients. Rx groups need to be identified for optimal management.

Hypothesis: Distinct patterns of symptoms (Sx) and psychiatric/medical disorders exist in DD patients.

Method: Clinical & demographic data on all patients on the DD team at a University hospital, for 1 year was tabulated using ACCESS. Frequency & group differences were tested with SPSS by t-test & X².

Results: n=274. 176 males (64%), 98 females (36%). Age:37 yrs.; whites: 108 (40%); blacks:161 (59%).

Substance Abuse: 233 (86%) had a substance use Dx, with 181 polysubstance use & 52 monosubstance use. ETOH=148, cocaine=131 & opiates=67. We made groups based on the primary substance of abuse. ETOH=121 (44%), cocaine=71 (26%) & opiates=28 (10%). THC=57 but only nine used it as the primary substance & THC was often an adjunct substance. ETOH group was older than Cocaine group (38 yrs vs 34.5 years, t=1.86, p<.06). There were more males in the ETOH (70%) & Cocaine groups (65%) but not in opiate group. Significant differences in race ($X^2=64.5$, p<.00 with more whites in the ETOH group), psychiatric Sx ($X^2=26.3$, p<0.003, for suicide behavior), and psychiatric Dx ($X^2=23.3$, p<.02, more depression in opiate group & overall).

Psychiatric Sx: Suicidality = 187, psychosis=66, aggression=43. Suicidality was the commonest reason for admission - 82% in ETOH, 86% in cocaine and 100% in opiate group.

Psychiatric Dx: MDD = 146 (53%), SIMD = 49 (18%), psychotic Dx = 52 (19%). 76 (28%) had anxiety/adjustment/personality Dx. MDD was in 48% ETOH group, 47% cocaine group & 66% opiate group. Psychotic Dx was seen in 18% ETOH group, 15% cocaine group & 14% opiate group.

Medical Dx: 108 patients (39%) had one or more medical conditions. 65(24%) had one, 37 (13.5%) had two and six (2%) had 3 Dx. Common Dx were Sz, HTN, Hepatitis, HIV and Migraine. Medical Disorders were more common in ETOH group (44%) than cocaine group (22.5%).

Discussion: We studied comorbidity patterns on an acute DD team. More black men had DD. Polysubstance users exceeded mono substance users by >3:1. MDD exceeded psychosis 3:1. Cocaine group was younger than ETOH group and had more behavior disorder. This suggests that DD does not occur randomly and that there is a relation between the two disorders. This descriptive study cannot infer cause and effect. We did not study which disorder came first. However the findings may have Rx implications. For Ex: the ETOH group may need more medical care, and therapy aimed at vocational rehab and cocaine group may need help with impulse control and anger management.

Conclusion: There are distinct subgroups of patients with dual diagnoses. Treatment and programs should be customized to the identified needs of the subgroups rather than take a one size fits all approach.

References:

1. Havassy BE, et al: Comparisons of patients with comorbid psychiatric and substance use disorders: implications for treatment and service delivery. *Am J Psychiatry* 2004; 161(1):139-45.
2. Adrian M, Barry SJ: Physical and mental health problems associated with the use of alcohol and drugs. *Subst Use Misues* 2003; 38 (11-13):1575-614.

NR144 Monday, May 23, 9:00 a.m.-10:30 a.m.

An Open-Label Study to Evaluate Switching from an SSRI to Tiagabine to Alleviate SSRI Induced Sexual Dysfunction in Generalized Anxiety *Supported by Cephalon, Inc.*

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Schwartz, M.D., Mark Chilton, M.S., Francesca Bertone, B.A., Hari Kumaresan, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to (1) understand the pharmacology of both SSRI and Tiagabine, and (2) clinically apply this knowledge to treat sexual dysfunction in GAD patients.

Summary:

Background: Long-term use of benzodiazepines is a prevalent treatment for generalized anxiety disorder (GAD). Such use may be associated with the development of tolerance. Selective serotonin reuptake inhibitor (SSRI) and serotonin-norepinephrine reuptake inhibitor (SNRI) antidepressants are equally effective and safer, but are associated with sexual dysfunction as a major side effect. Tiagabine, FDA-approved for epilepsy, has been shown to facilitate GABA neurotransmission by blocking GABA re-uptake pumps, which does not promote tolerance, or addiction. It also is not associated with sexual dysfunction.

Methods: Eight GAD subjects were enrolled into an open-label study to see if a change from their SSRI/SNRI to Tiagabine would alleviate sexual dysfunction while maintaining a non-anxious state comparable to their SSRI/SNRI baseline. Subjects were tapered off their baseline drug and titrated onto Tiagabine (6-12mg/d) over four weeks. Subjects were followed for 14 weeks while sexual dysfunction was measured via the Arizona Sexual Experience Scale (ASEX) and anxiety was measured via the Hamilton Anxiety Scale (HAMA)

Results: Initial four week data show that sexual dysfunction was lowered by three points/15% on average (p=.07) and HAMA-anxiety symptoms were held in check (p = 0.18). Typical side effects included fatigue, GI upset, and headache.

Conclusions: Tiagabine appears to be more tolerable in that it may avoid sexual side effects and may be effective in maintaining a non-anxious state. Future controlled studies are warranted.

These are the four-week data set of a 14-week study due to be completed by April.

References:

1. Crane DL: Tiagabine, a selective GABA reuptake inhibitor for the treatment of anxiety. Presented at the 155th Annual Meeting of the American Psychiatric Association; May 18-23, 2002; Philadelphia, Pa.
2. Schwartz T: Tiagabine augmentation of SSRIs for treatment resistant anxiety. Poster presented May 2003 APA San Francisco Ca.

NR145 Monday, May 23, 9:00 a.m.-10:30 a.m.

Gender Differences in Service Utilization and Treatment for Bipolar Disorder

Supported by Ministry of Health and Long-Term Care, Province of Ontario, Canada

Ayal Schaffer, M.D., *Department of Psychiatry, Sunnybrook and WCHSC, 2075 Bayview Avenue, Room FG46, Toronto, ON M4N 3M5, Canada*; John Cairney, Ph.D., Amy H. Cheung, M.D., Scott Veldhuizen, B.A., Anthony J. Levitt, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be familiar with the effect of gender on determining the likelihood of patients with bipolar disorder seeking help, and the type of treatment that is provided to them.

Summary:

Objective: To determine the effect of gender on service utilization in a community sample of individuals with bipolar disorder (BD).

Methods: This study utilized data from the Canadian Community Health Survey Cycle 1.2 on Mental Health and Well-Being (CCHS 1.2). This survey, conducted by Statistics Canada between May and December 2002, involved 36,984 respondents aged 15 or older who were primarily interviewed in person. The overall response rate was 77.0%. For individuals diagnosed with BD, we determined the effect of gender on illness history, service utilization, and medication use.

Results: Men and women with BD had similar numbers of lifetime manic or depressive episodes, yet men with BD were significantly less likely than women with BD to have ever accessed mental health resources of any type ($p = 0.02$). There were no gender differences in likelihood of having experienced a depression in the past 12 months, but women were significantly more likely to have been prescribed an antidepressant medication during this time period ($p = 0.02$).

Discussion: Gender appears to play an important role in service utilization and medication use among this community sample of bipolar patients.

References:

1. Robb JC, Young LT, Cooke RG, et al: Gender differences in patients with bipolar disorder influence outcome in the medical outcome survey (SF-20) subscale scores. *J Affect Disord* 1998; 49:189-193.
2. Shulman KI, Schaffer A, Levitt A, et al: Effects of gender and age on the phenomenology and management of bipolar disorder. *World Psychiatric Association Series Evidence and Experience in Psychiatry: Volume 5 Bipolar Disorder*. Eds. Maj M, Akiskal HS, Lopez-Ibor JJ, Sartorius N. Wiley Publication, 2002.

NR146 Monday, May 23, 9:00 a.m.-10:30 a.m.

Insulin Resistance in Treatment-Naive Youngsters Treated With Novel Antipsychotics

Christoph U. Correll, M.D., *The Zucker Hillside Hospital-Psychiatry Res, Albert Einstein College of Medicine, 75-59 263rd Street, Glen Oaks, NY 11004*; Tahir Mughal, M.D., Umesh Parikh, M.D., Vladimir Olshanskiy, M.D., Meredith Moroff, M.D., John M. Kane, M.D., Anil K. Malhotra, M.D.

Educational Objectives:

At the end of the presentation, participants will be able to estimate the role of novel antipsychotics in the development of insulin resistance in children and adolescents.

Summary:

Objective: To assess the effect of novel antipsychotics (SGAs) on insulin resistance independent of past treatment.

Methods: 12-week naturalistic study in antipsychotic-naïve youths (4-19 years) with psychotic, mood, and aggressive disorders, treated with SGAs. At baseline and monthly, anthropometric measures, fasting glucose, insulin, and SGA levels were assessed.

Results: In 131 youngsters (mean age: 14.1 ± 3.5 years, 64.9% male, 49.6% Caucasian), who completed treatment with risperidone ($n=64$), olanzapine ($n=37$) quetiapine ($n=15$), or aripiprazole ($n=15$) for 8-14 (mean: 11.7 ± 1.6) weeks, fasting glucose ($p=.01$), and insulin resistance (homeostatic model=HOMA-IR) ($p=.04$) increased significantly. Only one pre-morbidly obese youngster (0.8%) developed diabetes. Medication differences were not significant regarding glucose ($p=.91$), insulin ($p=.22$), absolute ($p=.19$) or relative ($p=.41$) HOMA-IR changes. Analyzing each SGA separately, insulin and HOMA-IR increases remained significant only for olanzapine ($p=.02$, respectively). In a logistic regression model, glucose increase ($R^2=0.45$, $p<.0001$) was correlated with baseline glucose levels and male sex. Increases in insulin ($R^2=0.30$, $p<.0001$) and HOMA-IR ($R^2=0.31$, $p<.0001$) were correlated with weight gain, lower baseline insulin and HOMA-IR, Asian race, and higher baseline BMI percentile.

Conclusions: While early on in treatment with SGAs, frank diabetes is rare in youths, increasing insulin resistance by 10%-50% over three months is of concern.

References:

1. Casey DE, Haupt DW, Newcomer JW, Henderson DC, Sernyak MJ, Davidson M, Lindenmayer JP, Manoukian SV, Banerji MA, Lebovitz HE, Hennekens CH: Antipsychotic-induced weight gain and metabolic abnormalities: implications for increased mortality in patients with schizophrenia. *J Clin Psychiatry* 2004; 65 Suppl 7:4-18; quiz 19-20.
2. Ryan MC, Thakore JH: Physical consequences of schizophrenia and its treatment: the metabolic syndrome. *Life Sci* 2002; 71(3):239-57.

NR147 Monday, May 23, 9:00 a.m.-10:30 a.m.

Dyslipidemia in Treatment-Naive Youngsters Treated With Atypical Antipsychotics

Christoph U. Correll, M.D., *The Zucker Hillside Hospital-Psychiatry Res, Albert Einstein College of Medicine, 75-59 263rd Street, Glen Oaks, NY 11004*; Umesh Parikh, M.D., Tahir Mughal, M.D., Vladimir Olshanskiy, M.D., Zinoviy Gutkovich, M.D., John M. Kane, M.D., Anil Malhotra, M.D.

Educational Objectives:

At the end of the presentation, participants will be able to estimate the effect of novel antipsychotics on dyslipidemia in children and adolescents.

Summary:

Objective: To assess the effect of second-generation antipsychotics (SGAs) on lipid metabolism independent of past treatment effects.

Methods: 12-week naturalistic study in youths (4-19 years) with psychotic, mood, and aggressive disorders, treated with SGAs. At baseline and monthly anthropometric measures and fasting lipids were assessed.

Results: In 131 antipsychotic-naïve youngsters (mean age: 14.1 ± 3.5 years, 64.9% male, 49.6% Caucasian), treated with risperidone ($n=64$), olanzapine ($n=37$) quetiapine ($n=15$) or aripiprazole ($n=15$) for 8-14 (mean: 11.7 ± 1.6) weeks, fasting total cholesterol (6.9 ± 28.4 mg/dL, $p=.007$) and triglycerides (20 Analyzing changes for each SGA, lipid increases were significant only for olanzapine. Differences ± 56.2 mg/dL, $p<.0001$) increased significantly between medications were significant regarding total and LDL-cholesterol, with olanzapine causing greater increases than risperidone ($p<.05$). However, new-onset dyslipidemia (cholesterol >200 mg/dL and/or triglycerides >150 mg/dL) developed in 22.1% of youngsters (olanzapine: 29.7%, quetiapine: 26.7%, aripiprazole: 18.2%, risperidone: 17.2%, $p=.49$). Cholesterol increase ($R^2=0.27$, $p<.0001$) was correlated with low baseline cholesterol levels and weight gain. Increases in triglycerides ($R^2=0.30$, $p<.0001$) were correlated with weight gain, low baseline triglycerides, divalproex cotreatment, Asian and African-American ethnicity. New-onset dyslipidemia ($R^2=0.19$, $p<.0001$) was associated with weight gain, and cotreatment with divalproex.

Conclusions: New-onset dyslipidemia is a relevant side effect of SGA treatment in antipsychotic-naive youths.

References:

1. Casey DE, Haupt DW, Newcomer JW, Henderson DC, Sernyak MJ, Davidson M, Lindenmayer JP, Manoukian SV, Banerji MA, Lebovitz HE, Hennekens CH: Antipsychotic-induced weight gain and metabolic abnormalities: implications for increased mortality in patients with schizophrenia. *J Clin Psychiatry* 2004; 65 Suppl 7:4-18; quiz 19-20.
2. Wirshing DA, Boyd JA, Meng LR, Ballon JS, Marder SR, Wirshing WC: The effects of novel antipsychotics on glucose and lipid levels. *J Clin Psychiatry* 2002; 63(10):856-65.

NR148 Monday, May 23, 9:00 a.m.-10:30 a.m.

Searching for Prodromal Symptoms in Early-Onset Bipolar Disorder

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Educational Objectives:

At the end of the presentation, participants will be able to discuss the existence of a bipolar manic prodrome.

Summary:

Objective: The existence of a bipolar manic prodrome remains controversial.

Methods: 43 bipolar youngsters (confirmed by K-SADS (42.0%) or DSM-IVR criteria) and/or caregivers underwent a new, semi-structured interview, the Bipolar Prodrome Symptom Scale, for symptoms of >mild severity and >once weekly frequency.

Results: Youngsters (51.2% male, 69.8% White) were 16.0±2.9 years old and 3.2±2.3 years after their first manic episode. The mean manic prodrome duration was 17.5±19.8 (range: 1-96) months. Requiring two or three symptoms the duration was 11.0±14.6 (range: 0.25-60) and 7.3±9.2 (range: 0-48) months. The prodrome onset was slow with gradual deterioration (47.0%) or slow with quick worsening (39.4%), while rapid illness onset was rare (13.6%). Irritability (54.6%) and drop in school functioning (51.5%) were the most frequently reported symptoms and several others occurred at >40%: depressed mood, inattention, social isolation, mood swings, and racing thoughts. First noticeable symptoms were: social isolation (31.7%), depressed mood (31.2%), irritability (28.8%), mood swings (26.7%), anger (23.7%), anhedonia (22.7%), anxiety (21.3%), drop in school functioning (21.2%), increased energy (20.0%), and inattention (20.0%).

Conclusions: In early-onset bipolar disorder, prodromal manic symptoms develop over a considerable period of time. Research needs to confirm specific symptom constellations that will allow early identification and prevention.

References:

1. Cornblatt BA, Lencz T, Smith CW, Correll CU, Auther AM, Nakayama E: The schizophrenia prodrome revisited: a neurodevelopmental perspective. *Schizophr Bull* 2003; 29(4):633-51.
2. Kafantaris V, Coletti DJ, Dicker R, Padula G, Pollack S: Are childhood psychiatric histories of bipolar adolescents associated with family history, psychosis, and response to lithium treatment? *J Affect Disord* 1998; 51(2):153-64.

NR149 Monday, May 23, 9:00 a.m.-10:30 a.m.

Asialotransferrin: A Good Biomarker for Alcohol Abuse?

Raymund Schwan, Ph.D., *Department Psychiatry, University Hospital, rue Montalembert, Clermont-Ferrand 63003, France*; Franz Legros, Ph.D., Vincent Nuyens, M.B., Laurent Malet, M.A., Isabelle Chéreau-Boudet, M.A., Pierre-Michel Llorca, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the performance of asialotransferrin in the detection of alcohol misuse.

Summary:

Background: We evaluated accuracy of alcohol misuse and dependence detection based upon asialo- and disialotransferrin isoform.

Methods: A four-month trial was conducted on alcohol-abusing (N=85) and alcohol-dependent subjects (N=82), defined according to DSM-IV, and a control group moderately consuming ethanol (N=88). Asialo- and disialo-transferrin isoforms were measured by capillary zone electrophoresis. Serum transferrin isoforms were separated at 28 kV and monitored at 200 nm, using P/ACE MDQ equipment, fused silica-capillaries, and CEofix CDT reagent set. Levels of transferrin isoforms were expressed as percentages of total transferrin forms area under the peaks. Accuracies, sensitivities and specificities were compared by ROC analysis. The ?-CDT algorithm was also applied by inserting asialo- + disialotransferrin percentages as CDT.

Results: Asialotransferrin demonstrated a sensitivity of 0.34 and a specificity of 1.00 for alcohol abuse. The sensitivity of asialotransferrin increased to 0.57 in alcohol-dependent patients. Disialotransferrin discriminated moderate drinkers and alcohol dependent subjects with a sensitivity of 0.85 and a specificity of 0.97. Same results were obtained using GGT-CDT algorithm (ROC area 0.96; cutpoints 3.2 and 2.6).

Conclusions: Patients' selection governed by DSM-IV should be coupled to CZE percentages of disialylated transferrin in order to obtain accuracies higher than 80%.

References:

1. Schwan R, Albuissou E, Malet L, Loiseaux MN, Reynaud M, Schellenberg F, Brousse G, Llorca PM: The use of biological laboratory markers in the diagnosis of alcohol misuse: an evidence-based approach. *Drug Alcohol Depend* 2004; 74:273-9.
2. Legros FJ, Nuyens V, Baudoux M, Zouaoui Boudjeltila K, Ruelle JL, Colicis J, Cantraine F, Henry JP: Use of capillary zone electrophoresis for differentiating excessive from moderate alcohol consumption. *Clin Chem* 2003; 49:440-9.

NR150 Monday, May 23, 01:00 p.m.-02:30 p.m.

Personality Profiles as Predictors of Response for Fibromyalgia

Supported by GlaxoSmithKline

Heather W. Murray, M.S., *Department of Psychiatry, Thomas Jefferson University, 833 Chestnut East, Suite 210E, Philadelphia, PA 19107*; Ashwin A. Patkar, M.D., Kathleen Peindl, Ph.D., Stan Krulwicz, M.A., Eric Dube, Ph.D., Prakash S. Masand, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the importance of personality traits as possible clinical predictors of treatment outcome of fibromyalgia.

Summary:

Objective: We investigated whether personality traits predicted a change in severity of fibromyalgia symptoms for participants enrolled in a double-blind, randomized, placebo-controlled trial of paroxetine CR (12.5 mg-62.5 mg/day) for the treatment of fibromyalgia.

Methods: Pre-treatment assessment of personality was obtained using the Personality Disorder Questionnaire-Revised (PDQ-R) for 108 patients with a diagnosis of fibromyalgia randomized to paroxetine (N = 53) or placebo (N=55) for 12 weeks. Personality disorders were grouped as Clusters A (schizoid, schizotypal, paranoid), B (borderline, narcissistic, histrionic, antisocial), and C (avoidant, dependent, compulsive) (DSM-IV). Response was defined as a ≥25% reduction in scores on the fibromy-

algia Impact Questionnaire (FIQ) from randomization to the end of treatment.

Results: Our sample had high levels of disordered personality traits: Cluster A (28.6%), Cluster B (21.4%), and Cluster C (35.7%). These personality accounted for 15% of the variance in a change in FIQ scores, in particular Clusters A and B were significant contributors ($p = .04$ and $p = .000$ respectively). Personality traits contributed equally toward predicting response in both paroxetine CR and placebo groups.

Conclusions: Personality disturbances seem to be an important predictor of response in patients with fibromyalgia. A better understanding of personality traits in patients with fibromyalgia may help identify poor responders who may benefit from additional or alternative treatment approaches.

References:

1. Workman EA, Hubbard JR, Felker BL: Comorbid psychiatric disorders and predictors of pain management program success in patients with chronic pain. *Primary Care Companion J Clin Psychiatry* 2002; 4:137-140.
2. Skodol AE, Gunderson JG, McGlashan TH, et al: Functional impairment in patients with schizotypal, borderline, avoidant, or obsessive-compulsive personality disorder. *Am J Psychiatry* 2002; 159:276-283.

NR151 Monday, May 23, 01:00 p.m.-02:30 p.m. **Effects of Progressive Relaxation on Depression and Anxiety in COPD Patients**

Sermsak Lolak, M.D., *Department of Psychiatry, Inova Fairfax Hospital, 3300 Gallows Road, 3rd Floor Original Bldg., Falls Church, VA 22042*; Gerilynn Connors, RRT, Michael Sheridan, Sc.D., Judith Shumway, RRT, Sidney Hess, RRT, Susan Farrell, RRT

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the significance of anxiety and depression in patients with chronic pulmonary diseases; recognize the potential effectiveness of progressive muscle relaxation training on depression and anxiety in this patient population.

Summary:

Objectives: This prospective, RCT examined the effect of progressive muscle relaxation (PMR) training on anxiety and depression in outpatients receiving pulmonary rehabilitation (PR).

Methods: COPD patients entering the eight-week PR program were randomly assigned to a standard care or intervention group. The standard PR program included two days per week of exercise, education, and psychosocial support delivered by a multidisciplinary team. The intervention group received additional sessions of PMR training using a prerecorded tape for 20 minutes/week during weeks 2-8. Primary outcome measures were levels of anxiety and depression measured by the Hospital Anxiety and Depression Scales.

Results: Preliminary results ($N=56$) showed a statistically significant improvement in anxiety within each group over time ($p=0.008$), but no difference between groups despite lower scores in the intervention group for weeks 3-8. No statistically significant improvement in depression was seen within each group ($p=0.10$), although the trend in the intervention group was downward from weeks 2-8. However, a significant group-time interaction was found ($p=0.049$), with depression scores dropping in the intervention group between weeks 5-8, while rising in the standard group.

Conclusions: These preliminary findings suggest that adding structured PMR training to a PR program may help reduce depression in patients with COPD.

References:

1. Withers NJ, Rudkin ST, White RJ: Anxiety and depression in severe chronic obstructive pulmonary disease: the effects of pulmonary rehabilitation. *J Cardiopulm Rehabil* 1999; 19(6):362-365.
2. Renfro KL: Effect of progressive relaxation on dyspnea and state anxiety in patients with chronic obstructive pulmonary disease. *Heart Lung* 1988; 17(4):408-143.

NR152 Monday, May 23, 01:00 p.m.-02:30 p.m. **Emotional Aspects of Parkinson's Disease and Sleep Disorders: Preliminary Findings**

Leora L. Borek, M.D., *Department of Geriatric Psychiatry, Brown University, 345 Blackstone Boulevard, Providence, RI 02906*; Robert Kohn, M.D., Joseph H. Friedman, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that mood disorders are associated with sleep disturbances in patients with Parkinson's disease.

Summary:

Objectives: To determine whether depression and anxiety correlate with particular types of sleep disturbance in patients with Parkinson's disease (PD).

Methods: Subjects were consecutively recruited from a PD clinic in Rhode Island. The HAM-D, HAM-A and Covi anxiety rating scales assessed for depressive and anxiety symptoms, respectively. The Pittsburgh Sleep Quality Index and Epworth Sleepiness Scale evaluated sleep quality and daytime somnolence, respectively. Questions concerning REM sleep behavior disorder (RBD), nightmares, nightmare distress scale and a one month dream log were administered. The Hoehn-Yahr measured stage of PD.

Results: Mean age 70.8; 27% female, mean duration of PD 6.3 years, mean stage of PD 2.4; 62.5% had nightmares (56.7% of these had nightmares that began after onset of PD) and 33.3% had RBD. Depression, anxiety and duration of PD were correlated with poor sleep quality ($p<.05$) but not with disease severity. Nightmare were correlated with daytime somnolence ($p<.05$).

Conclusions: When evaluating patients with PD, it is important to take into consideration that depression and anxiety are associated with sleep disorders and that sleep disorders and that sleep disorders should not be attributed only to PD. Depression and anxiety impair quality of life and are treatable conditions.

References:

1. Thanvi BR: Neuropsychiatric non-motor aspects of Parkinson's disease. *Postgrad Med J* 2003; 79:561-565.
2. Friedman JH: Sleep and fatigue in Parkinson's disease. *Parkinsonism and Related Disorders* 2004; 10:S27-S35.

NR153 Monday, May 23, 01:00 p.m.-02:30 p.m. **Stress and Functional Gastrointestinal Symptoms**

Urs M. Nater, Ph.D., *Department of Clinical Psychology and Psychotherapy, University of Zurich, Zurichbergstr. 43, Zurich 8044, Switzerland*; Katharina Pinnekamp, B.S., Kerstin Suarez, B.S., Ulrike Ehler, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to identify stress factors as an important factor in the maintenance of functional gastrointestinal symptoms

Summary:

Functional gastrointestinal (FGI) symptoms are relatively prevalent in the normal and psychiatric population. Among others, stress factors have been discussed in the etiology and maintenance of FGI symptoms.

In the present study, we set out to examine what role stress factors play in FGI symptom manifestation. In a first step, we examined a total of 1901 subjects. Chronic stress, stress reactivity, and coping strategies were examined with regard to the existence of self-reported FGI symptoms. Logistic regression analysis results from this first part indicate that heightened stress reactivity is a major predictor for the occurrence of high self-reported FGI symptom load. In the second part of the study, 36 female subjects were identified from the total sample. All followed a diurnal cortisol assessment protocol. Subjects were compared with regard to FGI symptom load (high, N = 12, low, N = 12, no symptoms, N = 12). Post-hoc group comparison shows that subjects with high symptom load display a significant lower cortisol response to awakening ($p < .05$) than the two other groups. These results indicate that a higher stress reactivity might be a predisposing factor for the manifestation of FGI symptoms. Furthermore, HPA axis changes in FGI patients might be a consequence of symptom severity.

References:

1. Böhmelt AH, Nater UM, Franke S, Hellhammer DH, Ehler U: Basal and stimulated free salivary cortisol in patients with chronic functional gastrointestinal disorders and healthy controls. *Psychosomatic Medicine*, in press.

NR154 Monday, May 23, 01:00 p.m.-02:30 p.m. Analysis of Psychiatric Characteristics of Alopecia

Seong-Nam Jin, M.D., *Department of Neuropsychiatry, Chung-Ang University Hospital, 224-1, HeukSeokDong, DongjakGu, Seoul 156-756, South Korea*; Du-Byung Park, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to consider the correlation between alopecia and psychiatric variables, and that the psychiatric evaluation and management are needed in alopecia patients.

Summary:

Introduction: Numerous studies have shown controversial results about the role of psychological factors in the etiology and pathogenesis of alopecia. This study assessed the several psychiatric scales for the alopecia patients.

Methods: The subjects were 221 alopecia patients (127 alopecia areata, 52 androgenic alopecia, 21 alopecia universalis, 6 alopecia totalis, 13 other dermatologic diseases) with 100 controls were tested with MMPI, SCL-90-R, Toronto Alexythymia Scale-20 Korea, Beck Depression Inventory, State-Trait Anxiety Inventory, and Hamilton Depression Scale. In addition, the onset of alopecia, the age of first onset, the sociodemographic data, etc. were examined.

Results: Between the normal control group and alopecia group, there were significant differences in the subscales of SCL-90-R, and total score of BDI, STAI, HDS. In TAS-20K, the score of Factor I and Total in alopecia areata patients were higher than in normal healthy group. Among subtypes of alopecia, no difference existed.

Discussion: No difference among subtypes of alopecia in scales suggests that psychiatric conditions such as anxiety and depression could be either the etiology or the result of alopecia. Psychiatric evaluation and management should be needed for alopecia patients, and we need further examination of the effects of the psychiatric management of alopecia.

References:

1. Gulec At, Tanriverdi N, Duru C: The role of psychological factors in alopecia areata and the impact of the disease on the quality of life. *Int J Dermatol* 2004; 43(5):352-356.
2. Liakopoulou M, Alifiraki T, Katideniou A: Children with alopecia areata: psychiatric symptomatology. *J Am Acad Child Adolesc Psychiatry* 1997; 36(5):678-684.

NR155 Monday, May 23, 01:00 p.m.-02:00 p.m.

The Influence of Direct-to-Consumer Advertising on Patients' Attitudes Toward Their Psychiatric Medications

Manisha R. Punwani, M.D., *Department of Psychiatry, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, MA 01655*; Philip Burke, M.D., Kenneth Fletcher, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the effect direct-to-consumer advertising by pharmaceutical companies has on patients' attitudes toward their medications, and how this advertising can influence the interaction between the patient and prescriber.

Summary:

Objective: To determine how direct-to-consumer advertising influences the attitudes of patients toward their psychiatric medications and the interaction between patient and prescriber.

Methods: A 17-item questionnaire was developed to gather information about exposure to direct-to-consumer advertising, attitudes toward psychiatric medications, and the patient's interactions with the prescriber. It was distributed to 82 patients at a university-affiliated ambulatory psychiatry clinic.

Results: 50% of respondents reported that advertisements had caused them to wonder if a different medication might be better to treat their condition, and 63% of these respondents discussed this concern with their prescriber. Of these discussions, 50% resulted in a new medication being prescribed, and 31% of these new medications were the ones mentioned in the advertisements. Younger patients were more likely to wonder if a different medication might be better to treat their condition. (59% vs 41%, Fisher's $p = 0.031$) Female patients were more likely to discuss this concern with their prescriber. (79% vs 44%, Fisher's $p = 0.045$).

Conclusions: Direct-to-consumer advertising significantly affects the attitudes of patients toward their psychiatric medications and the interactions between patients and prescribers. Patient characteristics, such as age and gender, can affect the degree to which individuals are influenced by direct-to-consumer advertising.

References:

1. Bell RA: Direct-to-consumer prescription drug advertising and the public. *Journal of General Internal Medicine* 1999; 14(11):651-657.
2. Sumpradit N: Consumer's attitudes and behavior toward prescription drug advertising. *American Journal of Health Behavior* 2002; 26(1):68-75.

NR156 Monday, May 23, 01:00 p.m.-02:00 p.m.

The Impact of Aroma on the Perception of Age

Alan R. Hirsch, M.D., *Department of Psychiatry, Rush-Presbyterian, 845 North Michigan Avenue, Suite 990W, Chicago, IL 60611-2201*; Ying Ye

Educational Objectives:

At the conclusion of this presentation, participants should be able to recognize that the perceived rejuvenating effect of the grapefruit aroma may have utility in facilitating intergenerational communication or act as an adjuvant like botulism toxin, in cosmetic and pharmaceutical usage to impact perception of age.

Summary:

Introduction: While the determination of age has been primarily mediated visually, the ambient odor may also have an influence.

Methods: Thirty-seven subjects (age average of 28 years, ranging from 13 to 71 years) in a single blinded, randomized fashion, estimated the age of models in photographs while wearing either a blank mask or a grape, cucumber, or grapefruit aroma impregnated mask.

Results: The grape odor ($p = 0.198$) and the cucumber odor ($p = 0.244$) had no significant effects. The grapefruit aroma reduced subjects' perception of overall models' ages by an average of approximately three years ($p = 0.025$) and of female models' age by five years ($p = 0.053$).

Conclusion: Possible mechanisms whereby the grapefruit aroma created a rejuvenating effect with relationship to perceived age include induction of positive affect, sexual arousal, anxiety, change in cognitive set, and odor-induced visual distortion.

References:

1. Flemming KC, Evans JE, Chutkan DS: A cultural and economic history of old age in America. *Mayo Clinic Proc* 2003; 78:914-921.
2. Tefferi A, LaRusso NF: The "age" factor in adult medicine. *Mayo Clinic Proc* 2003; 78:913.

NR157 Monday, May 23, 01:00 p.m.-02:00 p.m.

Prescribing Habits Before and After the Introduction of Generic Fluoxetine

Robert McLay, M.D., *Department of Mental Health, Naval Medical Center San Diego, 34800 Bob Wilson Dr., San Diego, CA 92134*; Angelica Klinski, Pharm.D., Paulette Tucciarone, M.D., James Spira, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize how prescribing habits for SSRI changed at NMCS D with the introduction of generic fluoxetine; have an enhanced understanding of how marketing and pricing pressures influence doctor's prescribing habits.

Summary:

In 2001, the patent on Prozac (fluoxetine) expired, and generic fluoxetine became available. Prices for fluoxetine fell sharply, and marketing decreased. At Naval Medical Center San Diego (NMCS D) physicians were made aware of the cost savings, but were not compelled to use the cheaper medication when selecting an SSRI. We investigated how market share for fluoxetine changed with the introduction of the generic form. Prescribing information was obtained from the hospital's computerized pharmacy system, and tracked for the mental health (MH) and medicine (IM) clinics. Market share for fluoxetine among SSRIs was tracked for the 64 months surrounding the introduction and pattern of change examined by linear regression analysis.

Results: showed that in the 32 months before the introduction of the generic form, fluoxetine maintained a relatively steady share of total SSRI prescriptions. There was a trend toward fluoxetine becoming more popular among IM prescribers, but this did not quite reach the level of statistical significance ($p = 0.0742$). After the introduction of the generic form, fluoxetine steadily lost market share in both the IM ($p < 0.001$) and MH ($p < 0.05$) clinics over

time. Effects of pharmaceutical company representative visits and attempts to educate physicians are discussed.

References:

1. De Las Cuevas C, Sanz EJ, De La Fuente JA: Variations in antidepressant prescribing practice: clinical need or market influences? *Pharmacoepidemiol Drug Saf* 2002; 11(6):515-22.
2. Druss BG, Marcus SC, Olfson M, Pincus HA: Listening to generic Prozac: winners, losers, and sideliners: the market share of generic fluoxetine that of its brand-name counterpart, Prozac, at an unprecedented rate: within two weeks of the generic's introduction. *Health Aff (Millwood)* 2004; 23(5):210-6.

NR158 Monday, May 23, 01:00 p.m.-02:30 p.m.

Effects of Weather and Lunar Cycle on Psychiatric Emergency Evaluations

Robert McLay, M.D., *Department of Mental Health, Naval Medical Center San Diego, 34800 Bob Wilson Drive, San Diego, CA 92134*; Patcho Santiago, M.D., Amado Daylo, M.D., Paul Hammer, M.D.

Educational Objectives:

At conclusion of this presentation, the participant should be able to understand the relationship between weather and emergency psychiatric presentations.

Summary:

Objective: To examine effects of climate on psychiatric evaluations.

Background: Weather and lunar cycles previously have been suggested to influence patterns of emergency psychiatric presentations.

Methods: We studied such effects at Naval Medical Center, San Diego, a hospital located in a temperate climate and that serves a patient population with little secondary gain for coming in out of the elements. Over a one-year period, 1909 emergency psychiatric evaluations were examined.

Methods: Correlations were examined between number of evaluations per day, and data from the National Naval Observatory and National Weather Service.

Results: Higher temperatures were significantly ($p < 0.05$) associated with higher numbers of evaluations, whereas precipitation was significantly ($p < 0.01$) associated with fewer evaluations. Wind speed, cloud cover, and lunar cycle had no significant effect on number of evaluations. Examining the breakdown between those evaluations that required psychiatric admission, versus those evaluations where the individual was sent home, it was found that the significant correlations were always found among the non-admitted population.

Conclusions: Warmer, dryer days were associated with more emergency psychiatric evaluations, but this increase was mostly accounted for by patients not requiring admission.

References:

1. Modai I, Kikinzon L, Valevski A: Environmental factors and admission rates in patients with major psychiatric disorders. *Chronobiol Int* 1994; 11(3):196-9.
2. Vance DE: Belief in lunar effects on human behavior. *Psychol Rep* 1995; 76(1):32-34.

NR159 Monday, May 23, 01:00 p.m.-02:30 p.m.

The Monday Anomaly: An Evaluation of the Weekly Pattern of Anxiety Variation Within a Group Setting

Matthew Sager, M.D., *Department of Psychiatry, Rhode Island Hospital, 593 Eddy Street, Providence, RI 02906*; Rendueles Villalba, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the weekly variation of anxiety in the context of a group setting.

Summary:

Introduction: Hebdomadal patterns (seven day periodicities) have been reported in a variety of physiological, psychological, and social phenomena. The stock market is lower on Mondays than during the rest of the week. Absenteeism is higher on Mondays. Heart attacks, strokes and Sudden Infant Death Syndrome (SIDS) as well as cellular concentrations of chemicals vary on similar cyclical patterns: Speculation about these patterns has yielded two potential models: an endogenous model of physiologic stress, and an exogenous model related to human behavior such as substance abuse. The importance of the social environment as a determinant has received little examination. The stress of shifting from public to private life and vice versa clearly translates into weekly biologic rhythms. We propose that this pattern of variation is a result of interpersonal encounters through relationships within a group.

Methods: Subjects for this study were a heterogeneous population of acute psychiatric patients at the Rhode Island Adult Partial Hospitalization Program from July 2002 to September 2004. Individual anxiety levels were measured using the self-reported Beck Anxiety Inventory (BAI) prior to the start of daily treatment. Features of the social milieu were collected using the Group Climate Questionnaire (GCQ) at the end of daily interpersonal group sessions. Data were sorted by weekday and serial t-tests were performed to identify potential hebdomadal patterns. Individual and group variables were then compared.

Results: Data were collected from between 1206 to 1297 individuals per weekday using the BAI. Individuals reported higher anxiety levels on Mondays than other days of the week: 16.1 vs. 15.1. The P value was .006. The effect size was .08. The GCQ was collected from between 180 to 200 groups per weekday. The groups had lower engagement and higher avoidance scores on Mondays (and Tuesdays following a three day weekend) than the rest of the week: 3.44 vs. 3.71. The P value was .000025. The Effect size was 0.34.

Conclusion/Discussion: This study raises several questions about the hebdomadal pattern and the therapeutic group setting. Individual anxiety displays a small but statistically significant Monday peak. Group avoidance and engagement display important hebdomadal variations. Engagement in genuine therapeutic group participation displays a clear weekly trough on Mondays. Hebdomadal variation in the group measure entailed a substantially larger effect size than the individual measure of anxiety. This supports a prioritization of social determinants in accounting for various hebdomadal phenomena. This, in turn, may help explain physiological, social and psychological variations that occur in seven day patterns.

References:

1. Larsen J, Kasimatis M: Individual differences in entrainment of mood to the weekly calendar. *Journal of Personality and Social Psychology* 1990; 58(1):164-171.
2. Peters R, et al: Increased Monday incidence of life-threatening ventricular arrhythmias. *Circulation* 1996; 94, 1346-1349.

NR160 Monday, May 23, 01:00 p.m.-02:30 p.m. Compulsive Tanning in BDD

Michelle Conroy, M.D., *Brown University/ Butler Hospital, 345 Blackstone Boulevard, Providence, RI 02906*; Elizabeth R. Didie, Ph.D., William Menard, B.A., Maria E. Pagano, Ph.D., Risa B. Weisberg, Ph.D., Christina Fay, B.A., Katharine A. Phillips, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will be familiar with results from the first study of compulsive tanning in patients with body dysmorphic disorder.

Summary:

Background: No previous studies have addressed the frequency or clinical correlates of compulsive tanning in individuals with body dysmorphic disorder (BDD). It is important to investigate this behavior because of the well-known risks of tanning.

Methods: Subjects were 200 broadly ascertained individuals participating in a study of the course of BDD. Rates and clinical correlates of tanning were determined, and subjects were evaluated with a variety of reliable and valid measures.

Results: 50 subjects (25.0%; 95% CI=19% to 31%) reported past or current tanning. 78.0% of tanners were female, with a mean age of 34.5 + 10.7. Among tanners, the skin was the most common body area of concern (84.0%). 76.0% of tanners reported a history of suicidal ideation, and 26.0% had attempted suicide. 100% of tanners had experienced interference in social functioning, and 98.0% in work/academic functioning, due to BDD. 54% of tanners had sought dermatologic treatment, and 50% had received such treatment, which was usually ineffective for BDD symptoms. There were no significant differences between tanners and nontanners on the above variables. However, tanners were more likely to pick their skin (58.0% vs. 39.3%, p=.02) and to have a history of a substance-use disorder (70.0% vs. 40.7%, p=.0003) or an eating disorder (36.0% vs. 15.3%, p=.002).

Conclusions: A high proportion of individuals with BDD compulsively tan. Compared with nontanners, tanners were more likely to pick their skin and have a substance-use disorder or an eating disorder. It is important for clinicians to be aware that tanning may be sign of BDD.

References:

1. Phillips KA, Dufresne RG Jr, Wilkel C, Vittorio C: Rate of body dysmorphic disorder in dermatology patients. *J Am Acad Dermatol* 2000; 42:436-441.
2. Phillips KA: Body dysmorphic disorder, in *Somatoform and Factitious Disorders (Review of Psychiatry Series, Volume 20, Number 3; Oldham JM and Riba MB, series editors)*. Washington DC, American Psychiatric Publishing, 2001.

NR161 Monday, May 23, 01:00 p.m.-02:30 p.m. High School Students Seeking Help for Mental Illness

Candace L. Boley, B.S., *Department of Psychiatry, University of Michigan, 1021 Island Drive Court #105, Ann Arbor, MI 48105*; Heather Irish, B.A., Tuananh Nguyen, M.D., Stephanie Riolo, M.D., Cheryl A. King, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to identify predictors of help-seeking behavior and preferred sources of help among high school students with MI, recognize the need to improve help seeking attitudes among boys, understand the influence stigma and socioeconomic factors have on help seeking, recognize that peers are a major source of help for adolescents with MI.

Summary:

Objective: Identify predictors of mental health help-seeking behavior among high school students.

Method: 964 students from six Midwestern high schools were surveyed regarding their attitudes about mental illness (MI), self-perceived MI, and help-seeking behavior.

Results: 150/946 (15.9%) students self-identified MI. 129/946 (13.6%) students reported needing help. Of those who said they

needed help, 54.3% (70/129) reported seeking help or asking questions about MI. Female students were significantly more likely than males to seek help. Students attending schools in middle-income districts were significantly less likely to seek help than those in the highest and lowest income districts. Students who endorsed higher stigma were significantly more likely to report needing help, but they were less likely to seek help compared to those who endorsed lower stigma. There was no significant difference in the prevalence of help seeking by race/ethnicity. Parents were the most common source of help, regardless of demographic variables; however, white students were significantly less likely than black students to seek help from teachers/school sources. White and female students were significantly more likely to seek help/get information from friends.

Conclusions: Gender, perceived MI stigma, and income of school district were important factors for help-seeking behavior among high school students surveyed.

References:

1. Rickwood DJ, Braithwaite VA: Social-psychological factors affecting help-seeking for emotional problems. *Soc Sci Med* 1994; 39:563-572.
2. Saunders SM, Resnick MD, Hoberman HM, Blum RW: Formal help-seeking behavior of adolescents identifying themselves as having mental health problems. *J Am Acad Child Adolesc Psychiatry* 1994; 33:718-728.

NR162 Monday, May 23, 01:00 p.m.-02:30 p.m.

Demographic and Clinical Characteristics of Individuals With Undiagnosed Co-Occurring Substance Abuse and Mental Health Disorders Treated in the New Jersey Mental Health System

Frederick Y. Huang, M.D., *Institute for Health, Rutgers University, 30 College Ave., New Brunswick, NJ 08901*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to describe the demographic and clinical characteristics of co-occurring disordered patients who are typically not identified in the mental health system.

Summary:

Objective: Patients with co-occurring disorders are frequently not identified within the mental health system, but few studies have characterized this group of patients. This study describes the demographic and clinical characteristics of individuals treated in a statewide mental health system with undiagnosed co-occurring substance use disorders.

Methods: Administrative records of 67,590 patients with co-occurring disorders in all mental health agencies in New Jersey from 1994 to 1997 were systematically reviewed.

Results: A total of 32,013 (47.4%) mental health patients had a missed diagnosis of substance use disorder. Female patients had half the odds to be diagnosed with a co-occurring disorder. Psychotic patients had 0.61 the odds of being diagnosed with a co-occurring disorder as patients with depressive disorders. Undiagnosed co-occurring patients were older (mean 36.2 ± 11.9). Only 1,769 (5%) of the co-occurring disorder patients who were accurately identified were referred to discharge for further treatment at a substance abuse treatment center. Psychotic and bipolar disordered patients were less likely to be referred.

Conclusions: Patients with co-occurring substance use disorders who are undiagnosed in the mental health system tend to be female, have more severe psychiatric diagnoses, and are older.

References:

1. Havassy BE, Alvidrez J, Owen KK: Comparisons of patients with comorbid psychiatric and substance use disorders: impli-

cations for treatment and service delivery. *Am J Psychiatry* 2004; 161(1):139-45.

2. Kline A, Mammo A, Culleton R, Crowley C, Barton C: Treatment access and service utilization by clients in the substance abuse and mental health treatment systems. Research and Information Systems, New Jersey Department of Health and Senior Services, Division of Addiction Services, Trenton, NJ, September 2002.

NR163 Monday, May 23, 01:00 p.m.-02:30 p.m.

Childhood Predictors for Drunkenness Among Males: A Ten-Year, Population-Based, Follow-Up

Solja M. Niemelä, M.D., *Department of Psychiatry, Turku University, Malikkalankatu 3, Turku 20210, Finland*; Andre Sourander, Ph.D., Kari Poikolainen, Ph.D., Hans Helenius, M.S.C.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the possibilities of early prevention on childhood behavioral problems concerning alcohol abuse in late adolescence.

Summary:

Objective: To study childhood precursors of drunkenness frequency among 18-year-old boys in a representative nationwide 10-year follow-up study.

Methods: At age 8, information was collected from parents (Rutter A2 scale), teacher (Rutter B2 scale), and boys themselves (Child Depression Inventory). At age 18, drunkenness frequency during past six months was obtained from 78.3% (n=2306) of the original sample.

Results: After adjusting for other variables, family structure and teachers' estimate on child's conduct problems and hyperactivity at age 8 predicted frequent drunkenness in late adolescence.

Conclusions: Frequent drunkenness in late adolescence can be predicted as early as at age 8 by teachers' observations. Early interventions on children with conduct problems and hyperactivity are called for.

References:

1. Fergusson DM, Horwood LJ: Early conduct problems and later life opportunities. *J Child Psychol Psychiatr* 1999; 39:1097-1108.
2. Costello EJ, Erkanli A, Federman E, Angold A: Development of psychiatric comorbidity with substance abuse in adolescents: effects of timing and sex. *J Clin Child Psychol* 1999; 28:298-311.

NR164 Monday, May 23, 01:00 p.m.-02:30 p.m.

Dream Content Analysis of a Young Korean Population

Sok H. Chang, M.D., *Department of Psychiatry, Korean University Medical Center, 126-1, AnAm-Dong 5Ga, SeongBuk-Gu, Seoul 136-705, Korea*; Hyeong Song, M.D., Heon Lee, M.D., Leen Kim, M.D., Helen Chung, M.D.

Educational Objectives:

To demonstrate dream content of young Koreans and cross-cultural comparison with Americans.

Summary:

The aim of this study was to perform the analysis of dream content in a young Korean population. The most recent dream reports from 4,235 Koreans (male 2339, female 1,896; mean age=12.56, age range: 9-29) were collected and analyzed using Hall/

Van de Castle System. In 9-14 years old the differences between male and female were on "male, dead and imaginary and animal character," "aggressive behavior", "self-negative concept" ($P < 0.05$). In young adults (15-29), the differences were on self-negative concept, group character, dreamer-involved success. The difference of dream content between male and female begins before age 9. As age is increased, child dream content become similar to that of adult. Korean children dream content is more similar to that of Korean adults than that of American adults. These findings show similarities and differences between children and their young adult counterparts. Dream content analysis using most recent dream method may give us the understanding of psychosocial development.

References:

1. Avila-White D, Schneider A, Domhoff GW: The most recent dreams of 12-13 year-old boys and girls: a methodological contribution to the study of dream content in teenagers. *Dreaming* 1999; 9:163-171.
2. Hall C, Van de Castle R: *The Content Analysis of Dreams*. New York, Appleton-Century-Crofts, 1966.

NR165 Monday, May 23, 3:00 p.m.-5:00 p.m.

Trait Anxiety, But Not State Anxiety, Is Associated With Smoking

Daniele F. Zullino, M.D., *Department of Psychiatry, University of Lausanne, Site de Cery, Prilly-Lausanne 1008, Switzerland*; Emmanuelle Fresard, Miroslava Stankovic, Yasser Lhazaal, M.D., Josef Haettenschwiler, M.D., Francois Porgeat, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the importance of trait anxiety on the development and maintenance of smoking.

Summary:

Not only anxiety disorders, but also anxiety as a symptom has been associated with smoking. The objective of the present study was to assess state anxiety (a transitory emotional state of mind) and trait anxiety (a relatively stable personality characteristic) in subjects without history of psychiatric disorders and to compare smokers with nonsmokers.

Methods: 47 healthy subjects (25 smokers, 22 nonsmokers) were assessed with a self-administered questionnaire including sections on smoking status (Fagerstrom, stage of change algorithm, SOCRATES) and on anxiety (Spielberger's State-Trait Anxiety Inventory=STAI Y).

Results: Logistic regression analysis including STAI Y-A (State), STAI Y-B (Trait), sex, and age as covariates and smoking vs. nonsmoking as dependent variable indicated a significant effect only for the STAI Y-B score (OR 1.17; 95% CI 1.04 to 1.31). The mean (\pm SD) STAI Y-B scores were 40.2 ± 10.4 for smokers and 32.2 ± 6.9 for nonsmokers. Among smokers, no correlations were found between stage of change, Fagerstrom-scores or SOCRATES-scores on one hand, and STAI Y-A and STAI Y-B scores on the other hand.

Conclusions: Anxiety traits may increase the risk to initiate smoking but probably do not influence the severity of nicotine dependence and subject's motivation for smoking cessation.

References:

1. DeHaas RA, Calamari JE, Bair JP, Martin ED: Anxiety sensitivity and drug or alcohol use in individuals with anxiety and substance use disorders. *Addict Behav* 2001; 26 (6):787-801. 2001.
2. Zvolensky MJ, Feldner MT, Eifert GH, Brown RA: Affective style among smokers: Understanding anxiety sensitivity, emotional

reactivity, and distress tolerance using biological challenge. *Addict Behav* 26 (6):901-915, 2001.

NR166 Monday, May 23, 3:00 p.m.-5:00 p.m.

Long-Acting Stimulant Use in Patients With Depression

Angelo Fallu, M.D., *3120 Chemin Orr, Lennoxville, PQ J1M 2A3, Canada*

Educational Objectives:

At the conclusion of this session, the participants should be able to better understand responses of stimulant adjunctive therapy in patients with depression.

Summary:

Objective: To determine the effectiveness and safety of once-daily OROS® methylphenidate adjunctive therapy in adults with major depressive disorder (MDD).

Methods: This was a prospective, open-label trial of eight patients with DSM-IV-TR diagnosed MDD (based on clinical interview). Patients with an inadequate response to current antidepressant therapy of adequate dosage and duration, and with a score of ≥ 3 on the CGI-S were eligible to participate.

Results: Interim results of five patients on three months of adjunctive therapy demonstrated a mean improvement of 2.2 points in CGI-S from a baseline mean of 3.5. Patients were on citalopram or venlafaxine. OROS® methylphenidate was well tolerated with minimal side effects. All patients met criteria for functional remission.

Conclusion: These interim data suggest that adjunctive, once-daily formulation of OROS® methylphenidate is safe, well tolerated, and offers symptom control in patients with depression.

References:

1. Lavretsky H, Kumar A: Methylphenidate augmentation of citalopram in elderly depressed patients. *Journal of the American Association for Geriatric Psychiatry (United States) Summer 2001; 9 (3)p298-303, ISSN 1064-7881 Journal Code: 9309609*
2. Wallace A, Kofoed L, West A, Double-blind, placebo-controlled trial of methylphenidate in older, depressed, medically ill patients. *Am J Psychiatry* 1995; 152:6.

NR167 Monday, May 23, 3:00 p.m.-5:00 p.m.

Effects of COMT Polymorphism to Cognition and Aggression in Patients With Schizophrenia

Baik Seok Kee, M.D., *Department of Psychiatry, Chungang University Hospital, 224-1 Heukseokdong Dongjakgu, Seoul 156755, Korea*; Doug Hyun Han, M.D., Kyung Joon Min, M.D.

Educational Objectives:

At the conclusion of this session, we aimed to assess the relation of cognitive function, symptoms, and aggression with COMT polymorphism in schizophrenic patients.

Summary:

Introduction: Much research suggested that COMT Val158Met polymorphism was related to cognitive function, behaviors, and symptoms of schizophrenic patients. We aimed to assess the relation of cognitive function, symptoms, and aggression with COMT polymorphism in schizophrenia patients.

Methods: The subjects were 174 unrelated male schizophrenia or schizoaffective patients diagnosed according to DSM-IV. We checked symptoms with SAPS and SANS, cognition with Korean-WAIS, aggression with OAS, and COMT polymorphism with blood leukocyte.

Results: Digit Span score of COMT^H group was lower and Similarity score was higher than COMT^L group. Block design score of COMT^L allele was higher than COMT^H allele, alogia, attention, anhedonia, positive formal thought disorder, negative sum score of COMT^L group, and COMT^L allele was lower than COMT^H group and COMT^H allele. Aggression 1 and 4 score of COMT^L group was higher than COMT^H group. Aggression 4 score of COMT^L allele was higher than COMT^H allele.

Discussion: Our results supported the theory that COMT Met allele was related to increase of tonic dopamine activity and cognitive stability, which induced cognitive inflexibility. Furthermore, we suggest that high aggression of schizophrenia patients with COMT Met allele is related to cognitive stability.

References:

1. Nolan KA, Bilder R, Luchman HM, Volavka J: Catechol-o-methyltransferase val158 met polymorphism in schizophrenia: differential effects of val and met alleles on cognitive stability. *Am J Psychiatry* 2004; 161:359-361.
2. Tsai SJ, Hong CJ, Liao DL, Lai IC, Liou YJ: Association study of a functional catechol-o-methyltransferase genetic polymorphism with age of onset, cognitive function, symptomatology, and prognosis in chronic schizophrenia. *Biological Psychiatry* 2004; 49:196-200.

NR168 Monday, May 23, 3:00 p.m.-5:00 p.m.

Long-Term Depressive Symptom Improvement After Switch to Ziprasidone *Supported by Pfizer Inc.*

Nina R. Schooler, Ph.D., *Department of Psychiatry, State University of New York Downstate, 450 Clarkson Avenue, Box # 1203, Brooklyn, NY 11203*; Antony D. Loebel, M.D., Ruoyong Yang, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss the reported findings on long-term improvement and control of depressive symptoms in patients with schizophrenia who were switched to ziprasidone.

Summary:

Objective: To evaluate long-term improvement and control of depressive symptoms in schizophrenia patients switched to ziprasidone from other antipsychotics.

Methods: In six-week, open-label studies, stable outpatients were switched to flexible-dose (40-160 mg/d) ziprasidone from conventionals, olanzapine, or risperidone; completers entered one-year extensions. In pooled extension completers (n=63), we calculated change in MADRS Total and modified Total score from core baseline and responder rates ($\geq 50\%$ decrease in Total or modified Total score) from core baseline.

Results: Baseline MADRS scores for pooled completers were 8.2 for Total and 7.4 for modified Total. Significant improvements were observed in MADRS Total (-2.6 , $p < 0.005$) and modified Total (-2.9 , $p = 0.0001$) scores. More pronounced improvement (-4.4 in Total, -6.0 in modified Total) was observed in the limited number of patients (n=10) with baseline MADRS ≥ 14 (p=NS). Responder rates were 60% for Total score and 63% for modified Total.

Conclusions: Patients receiving long-term treatment with ziprasidone after switch from other antipsychotics demonstrated improvement in depressive symptoms and high rates of depressive symptom response. In the absence of a comparison group, these findings must be considered preliminary.

References:

1. Weiden PJ, Simpson GM, Potkin SG, O'Sullivan RL: Effectiveness of switching to ziprasidone for stable but symptomatic

outpatients with schizophrenia. *J Clin Psychiatry* 2003; 64:580-588.

2. Loebel A, Siu C, Romano S: Improvement in prosocial functioning after a switch to ziprasidone treatment. *CNS Spectr* 2004; 9:357-364.

NR169 Monday, May 23, 3:00 p.m.-5:00 p.m.

Comorbid Sexual Jealousy in Alcohol Dependence

Seong Bong Bahk, M.D., *Department of Psychiatry, Sanggye Park Hospital, Nowongu Sanggyedong, Seoul 139707, Korea*; Seong Keun Lee, Dong-Il Kwak, M.D., Je Wook Kang

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the comorbid sexual jealousy in alcohol dependence.

Summary:

Introduction: Comorbidity is defined as the presence of any co-occurring condition in a patient with an index disease. The concept of comorbid sexual jealousy covers a wide range of distressing, irrational thoughts, emotions, and unacceptable or bizarre overt behaviors that share a unifying dominant theme of preoccupation with the partner's sexual unfaithfulness.

Objective: This study was conducted to clarify the different manifestations of comorbid sexual jealousy in alcohol dependence.

Method: The manifestations of comorbid sexual jealousy were assessed in 343 male and 40 female patients with alcohol dependence using interviews with their spouses by the psychiatrist.

Results: A total of 25.6% (98 out of 383) of patients studied, suffered from comorbid sexual jealousy: 26.8% of male patients (92 out of 343) and 15% of female patients (6 out of 40).

Comorbid sexual jealousy in alcohol dependants had different manifestations: six patients had experienced sexual jealousy before the onset of alcohol dependence without exhibiting a delusion of infidelity. A total of 66 patients expressed it only when intoxicated, and 26 patients expressed it even when sober. Among those 26 patients, five patients exhibited delusions of infidelity, which were not well systematized.

Conclusion: Not only due to the high rate of comorbidity of alcohol dependence and sexual jealousy, but also because of the different manifestations of sexual jealousy, careful psychiatric assessment should be conducted routinely in patients being seen for alcohol treatment.

References:

1. Albert Michael, Sudeshni Mirza, KAH, Mirza VS, Babu, Empee Vithayathi Morbid jealousy in alcoholism *British Journal of Psychiatry* 1995; 167(5):668-72.
2. Kranzler HR, Rosenthal RN: Dual diagnosis: alcoholism and comorbid psychiatric disorders. *The American Journal on Addictions* 2003; 12:s26-s40.

NR170 Monday, May 23, 3:00 p.m.-5:00 p.m.

Economic Impact, Tolerability, and Effectiveness of Long-Acting Risperidone

Supported by Janssen-Ortho Inc.

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Summary:

Objectives: To evaluate the tolerability, effectiveness, and economic impact of long-acting risperidone microspheres in a difficult-to-treat patient population with schizophrenia from a large Canadian psychiatric facility.

Methods: Subjects who had been taking long-acting risperidone for at least three months were identified. Antipsychotic polypharmacy, side-effect medication administration, and ex-factory costs of previous and current therapies were evaluated.

Results: The demographics indicate a difficult-to-treat patient population with advanced age (mean = 40.39), large number of admissions (mean = 6), and a long duration of stay (mean = 327 days). Additionally, most were male (75%) and all subjects were diagnosed with schizophrenia. Antipsychotic polypharmacy decreased after treatment with long-acting risperidone to 31% from 63%. Co-administration of regularly dosed anticholinergic side-effect medication decreased to 12% from 47%. While the mean cost of medication was significantly higher after having switched to long-acting risperidone, this difference held true only when including oral risperidone, the least expensive atypical antipsychotic. After controlling for the cost effect of oral risperidone, differences became marginal.

Conclusions: Long-acting risperidone proved well tolerated and effective, and was largely cost neutral when compared with other atypical antipsychotics.

References:

1. Kane JM, Leucht S, Carpenter D, Doeherty JP: Expert consensus guideline series. Optimizing pharmacologic treatment of psychotic disorders. Introduction: methods, commentary, and summary. *J Clin Psychiatry*. 2003; 64 Suppl 12:5-19. Review.
2. Demovsek MZ, Prevolnik Rupel V, Rebolj M, Tavcar R: Quality of life and treatment costs in schizophrenic outpatients, treated with depot neuroleptics. *Eur Psychiatry* 2001; 16(8):474-82.

NR171 Monday, May 23, 3:00 p.m.-5:00 p.m.

Metabolic Syndrome Predicts Cardiovascular Disease and New-Onset Diabetes

Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co, Ltd.

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Educational Objectives:

At the conclusion of this session, participants will gain an understanding of the relationship between metabolic syndrome and the risk for development of new-onset diabetes and cardiovascular disease. Relevance to the schizophrenia population is discussed.

Summary:

Background: The cluster of risk factors constituting the metabolic syndrome (obesity, dyslipidemia, hypertension, and hyperglycemia) are twice as prevalent among schizophrenia patients as among the general population. Further, the FDA has expressed interest in data concerning drug-induced metabolic syndrome related to atypical antipsychotic use. The extensive published literature describing the relationship between the third Adult Treatment Panel—defined metabolic syndrome and diabetes/cardiovascular disease—affords the opportunity to quantitatively summarize the available evidence using systematic review.

Methods: We conducted a comprehensive search of MEDLINE for all relevant papers published since the definition of metabolic syndrome was released (September 2002) until September 2004.

Results: A total of nine primary studies comprising more than 50,000 patients were included in the systematic review. The median follow-up time was approximately five years. The overall risk for cardiovascular disease (fatal or non-fatal myocardial infarction, coronary death) was double for patients with metabolic syndrome. The risk for new-onset diabetes was tripled.

Conclusions: Metabolic syndrome confers an independent, clinically relevant risk for diabetes and cardiovascular disease. Exacerbation of the syndrome by use of certain atypical antipsychotic agents among schizophrenia patients warrants serious consideration by treating physicians.

References:

1. American Diabetes Association. Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. *Diabetes Care* 2004; 27(2):596-601.
2. Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults - Adult Treatment Panel III. National Institutes of Health, 2001; No 01-3670.

NR172 Monday, May 23, 3:00 p.m.-5:00 p.m.

Diabetes Risk Differs According to Atypical Antipsychotic Use: A Review

Supported by Bristol-Myers Squibb and Otsuka Pharmaceuticals Co, Ltd

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Educational Objectives:

At the conclusion of this session, participants will gain an understanding of the relationship between the use of atypical antipsychotics and the risk for development of new-onset diabetes among the major atypicals.

Summary:

Objective: The extensive published literature describing the relationship between atypical antipsychotic use and diabetes affords the opportunity to quantitatively summarize the available evidence using meta-analytic methods.

Methods: We conducted a comprehensive search of electronic databases (MEDLINE, Current Contents®) for all relevant papers published from January 1, 1990, to September 9, 2004. Studies with at least one atypical treatment for schizophrenia qualified. Summary Odds Ratios (SOR) were computed from reported ORs for four atypicals (clozapine, olanzapine, risperidone, quetiapine) with two referent groups: (1) conventional antipsychotics; and (2) no treatment. Mantel-Haenzel fixed-effects models were used to compute weighted SORs.

Results: A total of 16 primary studies comprising 272,955 patients were included. SORs for the association between diabetes and clozapine use was 7.4 (95% CI:1.6-34.7) versus no treatment, and 1.4 (95% CI:1.3-1.5) versus conventionals. For olanzapine use, SORs were 2.3 (95% CI:1-5.5) versus no treatment and 1.3 (95% CI:1.1-1.5) versus conventionals. Quetiapine use tended toward an association versus conventionals (1.2 (95% CI:0.9-1.6) only). Risperidone use exhibited the smallest association with diabetes in either referent category: 1.2 (95% CI:0.5-2.9) versus no treatment, and 1.1 (95% CI:1-1.3) versus conventionals.

Conclusions: Results suggest differential risk for diabetes differs among atypical agents. Consideration of these differential risks should be included in therapeutic decisions for this patient population.

References:

1. Keefe RS, Silva SG, Perkins DO, Lieberman JA: The effects of atypical antipsychotic drugs on neurocognitive impairment in schizophrenia: a review and meta-analysis. *Schizophrenia Bulletin* 1999; 25:201-222.

- Muench J, Carey M: Diabetes mellitus associated with atypical antipsychotic medications: new case report and review of the literature. *J Am Board Fam Pract* 2001; 14:278-282.

NR173 **Monday, May 23, 3:00 p.m.-5:00 p.m.**

Validation of a Weight-Related Quality of Life Measure in Schizophrenia

Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co, Ltd.

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Educational Objectives:

To have increased knowledge of the extent of obesity in patients being treated with atypical antipsychotics for schizophrenia, and gain a better understanding of the relationship between obesity and quality of life in patients with schizophrenia.

Summary:

Objective: Weight gain is associated with several atypical antipsychotic medications. In addition to negative health consequences of excess weight, studies have reported decreased quality of life (QOL) linked to obesity. This study reports on validation and use of a weight-related measure of QOL in individuals with schizophrenia.

Methods: Individuals with schizophrenia (n=111) were recruited from outpatient programs (mean age 43.5 years; 42% women; 60% Caucasian; 82% obese) to complete the Impact of Weight on Quality of Life-Lite measure (IWQOL-Lite). The IWQOL-Lite is a validated self-report measure of weight-related QOL, providing a total score and domain scores on physical function, self-esteem, social life, public distress, and work.

Results: The IWQOL-Lite domains and total score were reliable, with internal consistency ranging from 0.87 to 0.97 and test-retest reliability ranging from 0.79 to 0.93. The IWQOL-Lite demonstrated significant (p<0.01) correlations with body mass index (BMI) and discrimination across BMI categories (p<0.05). Patients were impaired in relation to community norms but similar to obese samples. Gender, age, or ethnicity did not affect findings.

Conclusions: Obesity is an area of concern for many patients with schizophrenia. The IWQOL-Lite is a valid and useful measure of weight-related quality of life in persons with schizophrenia.

References:

- American Diabetes Association, et al: Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. *Diabetes Care* 2004; 27(2):596-601.
- Kolotkin RL, Crosby RD, Kosloski KD, Williams GR: Development of a brief measure to assess quality of life in obesity. *Obes Res* 2001; 9:102-111.

NR174 **Monday, May 23, 3:00 p.m.-5:00 p.m.**

Discontinuation Rates Among Treated Schizophrenia Patients in Managed Care

Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co, Ltd.

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Educational Objectives:

At the conclusion of this session, participants should be able to better understand the relationship between treatment discontin-

uation and effectiveness, and recognize differences in adherence rates for conventional and second-generation antipsychotics.

Summary:

Objective: Treatment discontinuation has been associated with negative health outcomes in patients with schizophrenia. We studied the effect of specific antipsychotic agents on discontinuation rates in a large managed care database.

Methods: Treated patients with schizophrenia or schizoaffective disorder, ≥18 years, were included in the study (n=2947). Treatment discontinuation was defined as a gap in a patient's index medication of ≥15 days. Hazard ratios (HR) for time-to-treatment-discontinuation were estimated using Cox regression, controlling for age, gender, region, and physician specialty.

Results: Compared with patients treated with conventional antipsychotics, aripiprazole-treated patients exhibited the lowest risk for discontinuation (HR=0.60, 95% CI: 0.50-0.72), followed by users of other atypicals (HR, 95% CI: olanzapine = 0.83, 0.70-0.99; quetiapine = 0.67, 0.56-0.80; risperidone = 0.79, 0.67-0.95; ziprasidone = 0.74, 0.60-0.91).

Conclusions: Patients treated with second-generation antipsychotics (SGAs) exhibit lower real world discontinuation rates versus conventionals, and these rates differ according to the SGA used. Because adherence to therapy is linked with treatment effectiveness, substantial clinical and economic benefits may be realized by using medications with lower discontinuation rates.

References:

- Lindstrom E, Binge K: Patient compliance with drug therapy in schizophrenia: Economic and clinical issues. *Pharmacoeconomics* 2000; 18(2):106-124.
- Weiden PJ, Olfson M: Costs of relapse in schizophrenia. *Schizophrenia Bulletin*, 1995; 21 (3):419-429.

NR175 **Monday, May 23, 3:00 p.m.-5:00 p.m.**

Hyperlipidemia Following Treatment With Antipsychotic Medications

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Educational Objectives:

At the conclusion of this session, the participant should be able to describe the relative risks of developing hyperlipidemia following treatment with various antipsychotic medications.

Summary:

Objective: Previous studies suggest an association between certain second-generation antipsychotics (SGAs) and hyperlipidemia. Data on the newer agents, aripiprazole and ziprasidone, are lacking. This study assesses development of hyperlipidemia following treatment with all approved SGAs and conventional antipsychotics.

Methods: A case-control study using California Medicaid (Medi-Cal) patients, ages 18-64, with schizophrenia or affective psychoses. Cases were matched by age, sex, race, and diagnosis. Use of antipsychotics was assessed during 60 days prior to index date. Logistic regression was performed controlling for number of antipsychotic prescriptions 60 days prior to index date and antipsychotic treatment ≥12 months prior to index date.

Results: A total of 5,316 incident cases of hyperlipidemia were matched to 31,338 controls. Compared with the referent group of conventional antipsychotics, aripiprazole patients exhibited a comparable risk of developing hyperlipidemia (Odds Ratio [OR]: 0.80, 95% CI: 0.60-1.07). Ziprasidone patients were also similar to conventionals (OR: 0.97, 95% CI: 0.84-1.12). Clozapine (OR:

1.69, 95% CI: 1.39-2.05), quetiapine (OR: 1.16, 95% CI: 1.04-1.29), risperidone (OR: 1.14, 95% CI: 1.03-1.27), and olanzapine (OR: 1.12, 95% CI: 1.01-1.23) were each associated with a significantly elevated risk for hyperlipidemia compared with conventional agents.

Conclusions: These findings suggest that aripiprazole, ziprasidone, and conventional agents are less likely to promote hyperlipidemia than other antipsychotic medications.

References:

1. Koro CE, Fedder DO, L'Italien GJ, Weiss S, Magder LS, Kreyenbuhl J, Revicki D, Buchanan RW: An assessment of the independent effects of olanzapine and risperidone exposure on the risk of hyperlipidemia in schizophrenic patients. *Arch Gen Psychiatry* 2002; 59:1021-6.
2. American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity: Consensus development conference on antipsychotic drugs and obesity and diabetes. *Diabetes Care* 2004; 27:596-601.

NR176 Monday, May 23, 3:00 p.m.-5:00 p.m.

Computerized Cognitive Performance Varies With Acute Alcohol Consumption

Supported by Hebrew University and Institute for the Study of Aging

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Educational Objectives:

At the conclusion of this session, the participant should be able to appreciate the ability of a set of computerized cognitive tests to measure performance changes related to acute alcohol consumption.

Summary:

Objective: To assess the ability of Mindstreams computerized cognitive tests to measure changes in cognitive function related to acute alcohol consumption.

Method: Cognitively healthy participants ($N=42$; age: 25.9 ± 2.5 ; years of education: 14.5 ± 1.7) completed alternate forms of a Mindstreams® (NeuroTrax Corp., NY) battery administered at baseline, at peak alcohol level (target breath alcohol concentration [BrAC] = 70mg%), and when BrAC dropped below 20mg% (several hours after alcohol consumption). Within-subjects analysis of variance included alcohol condition as a repeated measure. Outcomes were age- and education-normalized memory, executive function, visual spatial, and motor index scores, and a Global Cognitive Score (GCS).

Results: Performance shifts attributable to alcohol consumption were found for memory ($F[2,80] = 6.58, p=0.002$), executive function ($F[2,82] = 11.56, p<0.001$), visual spatial ($F[2,76] = 19.48, p=0.002$), and motor ($F[2,80] = 6.58, p=0.002$) index scores and the GCS ($F[2,80] = 12.06, p<0.001$). Performance was poorest at peak and best at baseline for all but the visual spatial index score for which performance was best at peak and worst several hours after alcohol consumption. There were no differences for the attention ($F[2,74] = 6.58, p=0.522$) index score.

Conclusions: Mindstreams tests are sensitive to shifts in cognitive function attributable to acute alcohol consumption. Future work should evaluate sensitivity to other external agents and additional populations.

References:

1. Dwolatzky T, Whitehead V, Doniger GM, Simon ES, Schweiger A, Jaffe D, et al: Validity of a novel computerized cognitive battery for mild cognitive impairment. *BMC Geriatr* 2003; 3:4.

2. Elstein D, Doniger GM, Guedalia J, Simon ES, Antebi V, Arnon Y, et al: Computerized cognitive testing in patients with type I Gaucher disease: effects of enzyme replacement and substrate reduction. *Genet Med*, in press.

NR177 Monday, May 23, 3:00 p.m.-5:00 p.m.

Validity of Mindstreams Tests for Cognitive Assessment in Schizophrenia

Michael Ritsner, M.D., Faculty of Medicine, Technion Israel Institute of Technology, Shaar Menashe Mobile Post Hefer, Hadera 38814, Israel; Haya Blumenkrantz, M.D., Tatyana Dubinsky, M.D., Glen M. Doniger, Ph.D., Ely S. Simon, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to appreciate the validity of Mindstreams tests for examination of cognitive impairment in schizophrenia.

Summary:

Objective: To evaluate the correspondence between Mindstreams and CANTAB computerized cognitive batteries.

Method: Stable schizophrenia patients ($N=24$; age: 34.8 ± 9.3 ; years of education: 11.4 ± 2.4 ; illness duration: 11.3 ± 7.7 years) completed the Mindstreams® Global Assessment Battery (NeuroTrax Corp., NY) and the Cambridge Neuropsychological Test Automated Battery (CANTAB). Validity of memory tests was evaluated by correlating Mindstreams Non-Verbal Memory with CANTAB Pattern Recognition Memory (PRM) test performance. Validity of executive function tests was examined by correlating Mindstreams Go-NoGo and Catch Game with CANTAB Intra/Extra Dimensional Set Shift (IED) and Spatial Working Memory (SWM) tests.

Results: In the memory domain, Mindstreams Non-Verbal Memory test total accuracy was highly correlated with CANTAB PRM percent correct ($r=0.75, p<0.001$). In the executive function domain, Mindstreams Go-NoGo reaction time was highly correlated with CANTAB IED latency, all stages ($r=0.74, p<0.001$) and Mindstreams Catch Game Total Score was correlated with CANTAB SWM ($r=-0.67, p<0.001$).

Conclusions: These preliminary findings suggest that Mindstreams tests are a valid tool for examination of cognitive impairment in schizophrenia.

References:

1. Dwolatzky T, Whitehead V, Doniger GM, Simon ES, Schweiger A, Jaffe D, et al: Validity of a novel computerized cognitive battery for mild cognitive impairment. *BMC Geriatr* 2003; 3:4.
2. Pantelis C, Barnes TR, Nelson HE, Tanner S, Weatherley L, Owen AM, et al: Frontal-striatal cognitive deficits in patients with chronic schizophrenia. *Brain* 1997; 120:1828-1843.

NR178 Monday, May 23, 3:00 p.m.-5:00 p.m.

Risk of Rehospitalization in Antipsychotic-Treated Schizophrenia Patients

Supported by Bristol-Myers Squibb and Otsuka Pharmaceuticals Co, Ltd

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Educational Objectives:

At the conclusion of this session, participants should be able to better understand the relationship between treatment discontinuation and relapse, and recognize differences in rehospitalization rates for conventional and second-generation antipsychotics.

Summary:

Objective: Research demonstrates that antipsychotic tolerability impacts adherence to therapy and that non-adherence is linked to rehospitalization. We studied the effect of specific antipsychotic agents on rehospitalization rates in a large managed care database.

Methods: Analysis of patients with schizophrenia, ≥ 18 years, who were hospitalized between May 2002 and May 2004, receiving antipsychotic monotherapy ($n = 576$) post-discharge. Patients were followed from discharge until rehospitalization, loss to follow-up, or end of study. Hazard ratios (HR) for time to rehospitalization were estimated between antipsychotic agents using first-generation antipsychotics (FGAs) as referent.

Results: Risk of rehospitalization was significantly lower for patients treated with second-generation antipsychotics (SGAs) aripiprazole (HR=0.27, 95% CI: 0.08-0.91) and olanzapine (HR=0.41, 95% CI: 0.20-0.84) compared with FGAs. Lower risk for rehospitalization was observed for risperidone (HR=0.53, 95% CI: 0.27-1.05), quetiapine (HR=0.63, 95% CI: 0.31-1.27), and ziprasidone (HR=0.76, 95% CI: 0.37-1.58) treated patients vs. FGAs; however, these differences were not statistically significant.

Conclusions: Patients treated with SGAs exhibit lower real-world rates of rehospitalization versus conventional agents. Patient rehospitalization in schizophrenia produces an enormous clinical, social, and economic burden on providers and families. The use of agents that reduce this burden is warranted.

References:

1. Valenstein M, Copeland LA, Blow FC, McCarthy JF, Zeber JE, Gillon L, Bingham CR, Stavenger T: Pharmacy data identify poorly adherent patients with schizophrenia at risk for admission. *Medical Care* 2002; 40:630-639.
2. Rabinowitz J, Lichtenberg P, Kaplan Z, Mark M, Nahon D, Davidson M: Rehospitalization rates of chronically ill schizophrenic patients discharged on a regimen of risperidone, olanzapine, or conventional antipsychotics. *Am J Psychiatry* 2001; 158(2):266-269.

NR179 Monday, May 23, 3:00 p.m.-5:00 p.m. Six-Month Incidence of Diabetes Among Patients With Schizophrenia in Belgium

Supported by Bristol-Myers Squibb and Otsuka Pharmaceuticals Co, Ltd

Linda Hanssens, M.S.C., *Department of GEOR, Bristol Myers Squibb Braine-1 Alleud, Parc De L'Alleud, Braine L'Alleud, Belgium*; Marc De Hert, M.D., Erik Thys, M.D., Dominique Van Eyck, M.D., Martine Wampers, Ph.D., Andre Scheen, Ph.D., Gilbert L'Italien, Ph.D.

Educational Objectives:

At the conclusion of this study, participants will gain an understanding of the rates of new-onset diabetes among treated schizophrenia patients followed with extensive metabolic screenings for six months.

Summary:

Objective: The issue of metabolic risk among patients with schizophrenia has received growing attention in recent years, and antipsychotic therapies have been implicated. Although a number of retrospective, observational studies suggest an elevated rate of diabetes and glucose abnormalities in these patients, endpoint definition has been varied and often inaccurate. We sought to accurately measure the incidence of diabetes in a prospective, clinic-based cohort using carefully measured laboratory metabolic parameters.

Methods: A total of 200 schizophrenia (DSM-IV) patients free of glucose abnormalities were enrolled in the ongoing cohort and

followed for six months. Data collection included general clinical and demographic data and extensive metabolic screening (fasting glucose, insulin, and oral glucose tolerance tests). Data were collected at baseline, six weeks, three months, and six months. Diabetes was defined as either a fasting glucose ≥ 126 mg/dl or OGTT glucose ≥ 200 mg/dl at 120 minutes.

Results: The mean age of the cohort was 37.2 years and 68% were male. The mean duration of illness was 14.1 years. The majority of patients were treated with clozapine (29.7%), olanzapine (29.2%), risperidone (20.8%) or quetiapine (12%). The six month incidence of diabetes was 4% (95% CI: 1.3%-6.7%). Among a subset of naïve patients treated at baseline and follow-up, the six month incidence was 6% (95% CI: 0.1%-12.5%). This is considerably greater than the age-adjusted incidence of diabetes in the general population (0.29%).

Conclusion: The incidence of confirmed new-onset diabetes among schizophrenia patients previously free of glucose abnormalities is much greater than that for the general population. Consideration of metabolic risks in schizophrenia patients is warranted and requires careful management.

References:

1. Center for Disease Control, Incidence of Diabetes per 1000 population Aged 18-79 Years, by Age, United States, 1997-2002 [on line] www.cdc.gov/diabetes/statistics/incidence/fig3.htm. Accessed November, 29, 2004.
2. American Diabetes Association, Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. *Diabetes Care* 2004; 27(2): p. 596-601.

NR180 Monday, May 23, 3:00 p.m.-5:00 p.m.

Diabetes in Second-Generation, Antipsychotic-Treated Schizophrenia Patients

Supported by Bristol-Myers Squibb and Otsuka Pharmaceuticals Co, Ltd

Linda Hanssens, M.S.C., *Department of GEOR, Bristol Myers Squibb Braine-1 Alleud, Parc De L'Alleud, Braine L'Alleud, Belgium*; Marc De Hert, M.D., Dominique Van Eyck, M.D., Martine Wampers, Ph.D., Andre Scheen, Ph.D., J. Peuskens

Educational Objectives:

At the conclusion of this study, participants will gain a better understanding of the course of glucose metabolism dysfunction and onset of diabetes in schizophrenia patients prescribed second-generation antipsychotic agents.

Summary:

Objective: Second-generation antipsychotics (SGA) have demonstrated increased risk of diabetes in schizophrenia patients. This study identifies the potential effects of different SGAs on the glucose metabolism.

Methods: An exploratory evaluation of glucose metabolism in a subset of patients ($n=50$) receiving an initial prescription for an SGA or switching SGAs, from a naturalistic, one-year prospective study. All patients received an oral glucose tolerance test (OGTT) at baseline, six weeks and 12 weeks including a full lipid profile.

Results: All patients had abnormal OGTT at baseline. Six percent ($n=3$) of patients developed diabetes within 12 weeks; another 12% ($n=6$) developed impaired glucose tolerance. Diabetes was remitted in two of the three patients after switching to a different SGA. The third patient was treated with oral anti-diabetic medication.

Conclusion: Our data suggest that diabetes can occur rapidly after initiating SGAs. If detected early, diabetes can be reversed by switching to a SGA with a better metabolic safety profile. The study highlights the relevant predictive value of metabolic screening early in the course of SGA treatment.

References:

1. Melkersson K, Dahl M-L: Adverse metabolic effects associated with atypical antipsychotics. *Drugs* 2004; 64(7): 701-723.
2. American Diabetes Association, Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. *Diabetes Care* 2004; 27(2): 596-601.

NR181 Monday, May 23, 3:00 p.m.-5:00 p.m.

Can Hemoglobin (HbA 1c) Be Used to Screen for Diabetes in Patients With Schizophrenia?

Supported by Bristol-Myers Squibb and Otsuka Pharmaceuticals Co, Ltd

Erik Thys, M.D., *Department of Psychiatry, University Sintjozef, Leuvensesteenweg 517, Kortenberg 3070, Belgium*; Linda Hanssens, M.S.C., Marc De Hert, M.D., Martine Wampers, Ph.D., Dominique Van Eyck, M.D., Andre Scheen, Ph.D., J. Peuskens

Educational Objectives:

At the conclusion of this study, participants will gain an understanding of types of screening tests used to detect impairment of glucose metabolism in patients with schizophrenia and support use of the HB1Ac for screening in this population.

Summary:

Objective: Schizophrenia patients treated with atypical antipsychotics show an increased risk of diabetes. Observational studies reveal a need for screening methods to detect undiagnosed diabetes. HbA1c is an accepted index for blood glucose in diabetic patients but is not used for screening. We therefore aim to evaluate the use of HbA1c in screening for diabetes among schizophrenic patients.

Methods: Using a cohort of schizophrenia patients with extensive metabolic data (including both Glucose Tolerance Tests [OGTT] and HbA1c), diagnosis of glucose abnormalities were based on American Diabetic Association (ADA) criteria.

Results: Three hundred fifty patients were enrolled, providing 632 OGTT's and HbA1c for evaluation. According to ADA criteria, 7.9% of OGTT met the definition for diabetes. Impaired glucose tolerance (IGT) was present in 9.5% and impaired fasting glucose (IFG) in 11.9% of OGTT. In the overall study population, mean HbA1c-values differed significantly between 3 patient groups: patients suffering from diabetes, patients diagnosed with glucose abnormalities (IFG or IGT) and patients without any glucose abnormalities (p value ≤ 0.001).

Conclusion: Large inter-individual differences in HbA1c values were observed in each patient group, rendering it impossible to accurately categorize individual patients based on HbA1c alone.

References:

1. Marder SR, et al: Physical health monitoring of patients with schizophrenia. *American Journal of Psychiatry* 2004; 161(8): 1334-1349.
2. American Diabetes Association, Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. *Diabetes Care* 2004; 27(2): 596-601.

NR182 Monday, May 23, 3:00 p.m.-5:00 p.m.

Metabolic Syndrome in Schizophrenia Patients Treated With Antipsychotics

Supported by Bristol-Myers Squibb and Otsuka Pharmaceuticals Co, Ltd

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Belgium; J. Peuskens, Marc De Hert, M.D., Dominique Van Eyck, M.D., Martine Wampers, Ph.D., Andre Scheen, Ph.D.

Educational Objectives:

At the conclusion of this study, participants will gain a better understanding of the prevalence of metabolic syndrome and its components in a naturalistic study of patients with schizophrenia.

Summary:

Objective: Epidemiological studies have demonstrated increased risk of metabolic abnormalities in schizophrenia patients treated with second-generation antipsychotics (SGAs). This study evaluates the frequency of the metabolic syndrome (Met-S) in treated schizophrenic patients.

Methods: Evaluation of baseline metabolic data, including oral glucose tolerance, serum lipids, and weight in patients participating in a one-year naturalistic study. Metabolic syndrome was defined as the presence of three of five NCEP risk factors.

Results: Baseline data on 200 schizophrenia patients (mean age 37 years), stable on medication (88.5% on atypical antipsychotics) for one-year was assessed. Thirty-eight percent of patients were classified as overweight with 20.5% obese. Metabolic syndrome was present in 27% of patients. This value is double that of the general population, adjusting for age. Prevalence of individual metabolic risk factors were: 44% hypertriglyceridemia, 39% increased waist circumference, 29.5% low HDL, 42.5% hypertension, 6.5% impaired fasting glucose. Elevated cholesterol was present in 53.5% of patients. Three out of five patients with lipid assessments met criteria for statin treatment.

Conclusion: Adverse metabolic effects associated with antipsychotic treatment are more prevalent than in general populations. To prevent serious long-term health consequences, adverse metabolic events need to be recognized early and appropriately treated.

References:

1. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III).
2. Ford et al: *JAMA* 2002; 287:356.

NR183 Monday, May 23, 3:00 p.m.-5:00 p.m.

Antipsychotic Treatment of Obesity and Metabolism in Schizophrenia

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Educational Objectives:

At conclusion of this session, the participant should be able to recognize the metabolic and obesity effects of antipsychotic treatment in schizophrenia.

Summary:

Introduction: Atypical antipsychotic treatment is associated with increased prevalence of obesity and metabolic dysfunction in schizophrenia. We report the longitudinal effects of antipsychotic treatment in clinically stable chronic schizophrenia.

Methods: 55 chronic, independent living schizophrenia patient from urban VA day treatment program were enrolled for a two-year study. Patients received stable treatment regimen during the study period. There were 37 typical and 18 atypical antipsychotic treated patients. Assessments included body weight and metabolic profile at 6, 12, and 24 months of treatment. Self-administered Behavior and Symptom Identification Scale (BASIS-32),

Three Factor Questionnaire, and Positive and Negative Symptom Scale (PANSS) were administered to assess psychopathology.

Results:

1. Both typical and atypical antipsychotic medication groups gained weight and developed metabolic abnormalities.
2. Atypical group had a significantly greater weight gain and metabolic disturbance after six months of treatment, which peaked at 12 months and maintained during the second year.
3. No significant difference in the positive and negative psychopathology between the typical and atypical groups, but obese patients in both groups showed greater depression and functional impairment.

Conclusion: Atypical antipsychotic group had significantly greater obesity and metabolic disturbances. This metabolic effect was significant after six months of treatment and peaked at one year. No significant difference in the psychotic symptom profiles between groups, but the obese patients in both group had greater depression and functional impairments.

References:

1. Kornegay CJ, et al: Incidence of diabetes associated with antipsychotic use in the United Kingdom general practice research database. *J Clin Psychiatry* 2002; 63(9):758-62.
2. Wirshing DA, et al: Novel antipsychotics and new onset diabetes. *Biol Psychiatry* 1998; 44:778-783.

NR184 Monday, May 23, 3:00 p.m.-5:00 p.m.

Schizophrenia: Relationship Between Body Mass Index and Quality of Life

Supported by Bristol-Myers Squibb and Otsuka Pharmaceuticals Co, Ltd

Patricia K. Corey-Lisle, Ph.D., *Department of Epidemiology, Bristol Myers Squibb, 5 Research Parkway, Wallingford, CT 06492*; Ronette L. Kolotkin, Ph.D., Ross D. Crosby, Ph.D., Vickie V. Tuomari, M.S., William H. Carson, Jr., M.D., John W. Newcomer, M.D., Gilbert L'Italien, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to have increased knowledge of obesity in patients being treated with atypical antipsychotics for schizophrenia, and gain a better understanding of the relationship between obesity and quality of life in patients with schizophrenia.

Summary:

Objective: Weight gain is associated with several atypical antipsychotic medications. This study examines the relationship between body mass index (BMI) and quality of life (QOL) in patients with schizophrenia.

Methods: Individuals with schizophrenia (n=111) were recruited from outpatient programs. Assessments included height, weight, and the Impact of Weight on Quality of Life-Lite measure (IWQOL-Lite). The IWQOL-Lite is a validated self-report measure of weight-related QOL, providing a total score and domain scores on physical function, self-esteem, social life, public distress, and work. Higher scores are indicative of better QOL. Scores were compared for participants by BMI classification.

Results: Eighty-two percent (82%) of all participants were found to be overweight/obese. BMI ranges (18-24.9, 25-29.9, 30-34.9, 35-35.9, ≥ 40 kg/m²) correlated significantly ($r=-0.503$, $p<0.001$) with IWQOL-Lite total scores, and increasing BMI was associated with decreasing QOL scores (81.5, 84.9, 67.4, 55.0, and 42.8, respectively). Eta-square for BMI on the total score was 0.335, indicating that 33.5% of the variance was attributable to BMI classification.

Conclusions: Obesity is an area of concern for patients with schizophrenia, and may impact compliance with treatment. Physi-

cians prescribing atypical antipsychotics should be aware of both health risks and quality-of-life implications for these patients.

References:

1. American Diabetes Association, et al: Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. *Diabetes Care* 2004; 27(2):596-601.
2. Kolotkin RL, Crosby RD, Kosloski KD, Williams GR: Development of a brief measure to assess quality of life in obesity. *Obes Res* 2001; 9:102-111.

NR185 Monday, May 23, 3:00 p.m.-5:00 p.m.

Olanzapine/Risperdal Treatment of Marijuana and/or Cocaine Abuse Among Patients With Schizophrenia Supported by Eli Lilly and Company

Evaristo O. Akerele, M.D., *Department of Psychiatry, Columbia University, 1051 Riverside Drive, New York, NY 10032*; Frances R. Levin, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to (1) recognize and diagnose people with schizophrenia and substance use disorders; (2) recognize that pharmacological treatment is available for this population; (3) understand the future directions in medical development for individuals with schizophrenia and substance use disorders.

Summary:

Introduction: A significant number of patients with schizophrenia continue to use substances and this in long term compromises their recovery. There are some data that suggest risperidone and olanzapine might be helpful in reducing both marijuana/cocaine craving and use in individuals with schizophrenia/schizoaffective disorder. If one or both of these medications is shown to be useful we can then make them first choice for substance dependent individuals with schizophrenia and significantly improve the overall prognosis of this illness. In this project, we will determine if olanzapine (5-20 mg/day) is more effective than risperidone (3-6 mg/day) for the treatment of marijuana and/or cocaine abuse among psychiatrically stable schizophrenia patients.

Method: Twenty-nine patients meeting DSM-IV criteria for schizophrenia, cocaine, and/or marijuana use disorder were randomized to olanzapine/risperidone in a 14-week, double-blind study that consisted of three phases: (1) two-week assessment phase when baseline data were collected while patients were maintained on their prescribed medication, (2) two-week cross-taper phase where patients were tapered off their previously prescribed medication and onto the study medication (either olanzapine or risperidone), and (3) 10-week period where patients were maintained on either olanzapine or risperidone.

Results: Preliminary data analysis suggests a reduction in craving within groups. There appears to be no difference between groups for marijuana craving/use. Whereas there is a significant difference between the groups for cocaine craving/use ($p=.01$). The retention rates were high; 79% completed the study.

Conclusion: These results suggest that neuroleptics are promising for individuals with schizophrenia who abuse marijuana and/or cocaine.

References:

1. Akerele E, Levin F: Substance use among schizophrenic individuals. *Journal of Psychiatric Practice* 2002; 8(2) 70-80.
2. Akerele E, Vosburg SK, Gill K, Levin F: Efficacy of atypical neuroleptics in treatment of substance use among schizophrenic individuals. *College on Problems of Drug Dependence (CPDD)*, Quebec, Canada, 2002.

NR186 Monday, May 23, 3:00 p.m.-5:00 p.m.

Assessment of Antipsychotic Diabetes Risk: Sensitivity to Study Design

Supported by AstraZeneca Pharmaceuticals

Frank D. Gianfrancesco, Ph.D., *Hecon Associates, 9833 Whetstone Drive, Montgomery Village, MD 20886*; Jacqueline Pesa, Ph.D., Ruey-Hua Wang, M.S., Henry Nasrallah, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the impact study design has on estimating the risk of diabetes associated with antipsychotic medications and understand that the risk of drug-induced diabetes is not necessarily consistent among different antipsychotics.

Summary:

Objective: To determine the impact of study design on findings regarding diabetes risk associated with antipsychotics.

Methods: Data were analyzed for >100,000 Ohio Medicaid patients with psychoses treated or untreated with antipsychotics. Odds ratios (ORs) for patients treated with antipsychotics versus untreated patients were estimated varying these criteria: screening for preexisting diabetes, identifying diabetes using prescription claims only, and antipsychotic monotherapy. Logistic regression controlled for patient characteristics. Selection bias was also assessed.

Results: Under the weakest design (no prescreening, identification using medical or prescription claims, no monotherapy requirement), all antipsychotics were associated with statistically significant ($P<0.05$) higher ORs relative to nontreatment. Under the strongest design (screening eight months before observation, using prescription claims only, antipsychotic monotherapy) ORs relative to no antipsychotic treatment were significant for clozapine (1.484, 95% CI:1.138-1.934) and olanzapine (1.149, 1.001-1.319) but nonsignificant for quetiapine (0.998, 0.834-1.195), risperidone (1.124, 0.983-1.284), ziprasidone (0.717, 0.415-1.239), and conventional antipsychotics (1.025, 0.885-1.187). Selection bias favored olanzapine, but not risperidone or quetiapine.

Conclusions: Study design affects estimated diabetes risks associated with antipsychotics. A rigorous design found diabetes risk significantly greater with clozapine and olanzapine than with no antipsychotic treatment. These results were obtained despite evidence indicating selection bias favoring olanzapine and disfavoring risperidone and quetiapine.

References:

1. Wirshing DA, Spellberg BJ, Erhart SM, Marder SR, Wirshing WC: Novel antipsychotics and new onset diabetes. *Biol Psychiatry* 1998; 44:778-783.
2. Gianfrancesco FD, Grogg AL, Mahmoud RA, Wang RH, Nasrallah HA: Differential effects of risperidone, olanzapine, clozapine, and conventional antipsychotics on type 2 diabetes: findings from a large health plan database. *J Clin Psychiatry* 2002; 63:920-930.

NR187 Monday, May 23, 3:00 p.m.-5:00 p.m.

Risks and Costs of Hospitalization During Antipsychotic Treatment

Supported by AstraZeneca Pharmaceuticals

Frank D. Gianfrancesco, Ph.D., *Hecon Associates, 9833 Whetstone Drive, Montgomery Village, MD 20886*; Ruey-Hua Wang, M.S., Jacqueline Pesa, Ph.D., Henry Nasrallah, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that relative risk of hospitalization among patients with

schizophrenia can vary among antipsychotics and to recognize the effect of hospitalization risk on patient outcomes and costs

Summary:

Objective: To compare hospitalization risk and inpatient costs in patients with schizophrenia treated with antipsychotics.

Methods: Relative risks (hazard ratios) of hospitalization for mental illness between Ohio Medicaid enrollees with schizophrenia receiving antipsychotic monotherapy were assessed. Cox proportional hazard regression controlled for age, gender, diagnosis, prior hospitalization/ER use, substance dependence/abuse, dose, other psychotropics, other health needs, and coverage type. Length of stay and inpatient costs were assessed. A threshold of $P<0.05$ determined statistical significance.

Results: Patients taking quetiapine had 33% lower hospitalization risk than patients taking typical antipsychotics (HR .672, $P=0.0413$), with expected inpatient charges \$389 lower per patient per year. Other hospitalization risk comparisons were not significant. Risperidone had significantly longer stays than typical antipsychotics (1.78 days, $P=.0301$) and olanzapine (1.88 days, $P=.006$) with higher expected inpatient charges (\$303 and \$320 more than typical antipsychotics and olanzapine, respectively). Other length-of-stay differences were not significant.

Conclusion: This claims-based review determined that schizophrenia patients taking quetiapine had lower hospitalization risk vs patients taking typical antipsychotics, and subsequently lower inpatient costs. While risperidone had a 22% lower hospitalization risk than typical antipsychotics ($P=.0932$), length of stay was significantly longer, with higher inpatient costs. Risperidone also had significantly longer length of stay than olanzapine, and possibly ziprasidone (3.61 days, $P=.0619$).

References:

1. Csernansky JG, Schuchart EK: Relapse and rehospitalization rates in patients with schizophrenia effects of second generation antipsychotics. *CNS Drugs* 2002; 16:473-484
2. Lewis M, McCrone P, Frangou S: Service use and costs of treating schizophrenia with atypical antipsychotics. *J Clin Psychiatry* 2001; 62:749-756.

NR188 Monday, May 23, 3:00 p.m.-5:00 p.m.

Compliance With Atypical or Typical Antipsychotics in Patients With Schizophrenia

Supported by AstraZeneca Pharmaceuticals

Krithika Rajagopalan, Ph.D., *Health Economics, AstraZeneca LP, 1800 Concord Pike, Wilmington, DE 19850*; Frank D. Gianfrancesco, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the components of antipsychotic treatment adherence and their measurement with prescription claims data.

Summary:

Objective: To assess treatment compliance and continuation in patients with schizophrenia taking atypical or typical antipsychotics.

Methods: We reviewed a large commercial health claims database (1999-2003) to identify 7,216 antipsychotic monotherapy treatment episodes for patients with schizophrenia. Assessments included treatment compliance (measured with the "medication possession ratio") and continuation (duration of treatment). Antipsychotics included atypicals (risperidone, olanzapine, quetiapine, ziprasidone) and typicals (haloperidol, perphenazine, thioridazine, thiothixene).

Results: Compliance was significantly greater with all atypical versus typical antipsychotics and was highest with quetiapine,

significantly ($P < 0.05$) greater than with risperidone or olanzapine (by 6% and 4%, respectively). Compliance with olanzapine and typical antipsychotics was negatively associated with dose, suggesting dose-related adverse events. No atypical antipsychotic had significantly longer continuation than typical antipsychotics, but risperidone and olanzapine had longer continuation than quetiapine (by 7% and 10%, respectively). After terminating treatment, patients ceased therapy altogether or switched to another psychotropic; switching significantly predicted shorter continuation. Ziprasidone alone showed significantly greater likelihood of switching.

Conclusions: Although all atypical antipsychotics showed better compliance than typical antipsychotics, quetiapine showed significantly better compliance than olanzapine or risperidone. Quetiapine had shorter treatment continuation than risperidone and olanzapine, which was not associated with greater likelihood of switching to other psychotropics.

References:

1. Dolder CR, Lacro JP, Dunn LB, et al: Antipsychotic medication adherence: is there a difference between typical and atypical agents? *Am J Psychiatry* 2002; 159:103-8.
2. Svarstad BL, Shireman TI, Sweeney JK: Using drug claims data to assess the relationship of medication adherence with hospitalization and costs. *Psychiatr Serv* 2001; 52:805-11.

NR189 Monday, May 23, 3:00 p.m.-5:00 p.m.

Gender Differences in Pain Processing During Protracted Opiate Abstinence

Matthew Steinfeld, B.A., *Department of Psychiatry, Beth Israel Medical Center, 1st Avenue and 16th Street - 6Karpas, New York, NY 10003*; Lauren Kunik, B.A., Igor I. Galynker, M.D., Lisa J. Cohen, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to appreciate that there are gender differences in the interaction between pain processing and divided attention in opiate abusers in protracted abstinence.

Summary:

Background: Detoxified opiate abusers demonstrated functional impairment in regions of the anterior cingulate gyrus, which mediate the emotional aspects of pain and divided attention. Recent literature has demonstrated gender differences in pain processing. The purpose of this ongoing study is to assess the impact of gender on pain processing, divided attention, and the relationship between the two in opiate abusers.

Methods: The TSA-II NeuroSensory Analyzer, a computerized, quantitative, thermal sensory testing device, was used to assess pain processing. Performance on the Stroop CW test during painful vs. non-painful conditions was compared in 20 Methadone-Withdrawn (MW) abstinent opiate addicts (13 males, 7 females), and 22 healthy controls (13 males, 9 females).

Results: Surprisingly, Stroop performance improved under painful vs. non-painful conditions. The mean improvement in Stroop performance for MW subjects was 12.40 ± 11.53 (17.08 ± 11.8 for males, 3.72 ± 10.6 for females), and for controls was 4.77 ± 9.78 (8.23 ± 9.7 for males, $-.022 \pm 7.9$ for females). There was a marginally significant group effect ($F(1,41) = 3.83$, $p = .058$), and a significantly sex effect ($F(1,41) = 11.15$, $p = .002$), but the interaction effect was not significant.

Conclusion: There may be a significant gender difference in the relationship between pain processing and attention in former opiate abusers in protracted abstinence.

References:

1. Zubieta JK, Smith YR, Bueller JA, Xu Y, Kilbourn MR, Jewett DM, Meyer CR, Koeppe RA, Stohler CS: mu-opioid receptor-mediated antinociceptive responses differ in men and women. *The Journal of Neuroscience* 2002; 15; 22(12):5100-7.
2. Paulson PE, Minoshima S, Morrow TJ, Casey KL: Gender differences in pain perception and patterns of cerebral activation during noxious heat stimulation in humans. *Pain*; 1998 76(1-2):223-9.

NR190 Monday, May 23, 3:00 p.m.-5:00 p.m.

Comorbid Psychiatric Diagnosis and Substance Abuse in Pathological Gamblers: A Preliminary Gender Comparison Study

Pinhas N. Dannon, M.D., *Community Mental Health Clinic, Ness Ziona Medical Center, Remez St. 80, Rehovot 76449, Israel*; Katherine Lowengrub, M.D.

Educational Objectives:

The different patterns of psychiatric comorbidity seen in our male vs female PGs is questioning the possibility that underlying etiopathology in PG may differ between men and women.

Summary:

Background: Pathological gambling (PG) is a highly prevalent and disabling impulse control disorder. Recent studies have consistently shown that PG patients have responded well to treatment with SSRIs, mood stabilizers, and opioid agonists. These findings have supported the observation that PG is strongly associated with both mood and anxiety disorders as well as substance abuse. The aim of the study is to evaluate the comorbid psychiatric diagnoses in our sample.

Methods: Thirty-six female, and 42 male PGs were enrolled in our study. A comprehensive psychiatric diagnostic evaluation was performed on all patients, and patients were screened for symptoms of depression and anxiety using the Hamilton Depression Rating Scale, the Hamilton Anxiety Rating Scale, the Yale-Brown Obsessive Compulsive Scale, and the Frost Multidimensional Perfectionism Scale. In addition, the patients completed self-report questionnaires about their demographic status, and substance abuse.

Results: The majority of patients were married with full or part-time employment. The study results demonstrated that male PG is correlated with substance and alcohol abuse. Diagnoses, which were prevalent among our cohort of female PGs included major depression, affective disorders, anxiety disorders, and eating disorders.

Conclusion: The different patterns of psychiatric comorbidity seen in our male versus female PGs is questioning the possibility that underlying etiopathology in PG may differ between men and women.

References:

1. Crockford DN, El-Guebaly N: Psychiatric comorbidity in pathological gambling: a critical review. *Canadian Journal of Psychiatry* 1998; 43: 43-50.
2. Cunningham-Williams et al: Problem gambling and comorbid psychiatric and substance use disorders among drug users recruited from drug treatment and community settings. *Journal of Gambling Studies* 2000; 16(4): 347-376.

NR191 Monday, May 23, 3:00 p.m.-5:00 p.m.

Topiramate Versus Fluvoxamine in the Treatment of Pathological Gambling: A Randomized, Blind-Rater Comparison Study

Pinhas N. Dannon, M.D., *Community Mental Health Clinic, Ness Ziona Medical Center, Remez St. 80, Rehovot 76449, Israel*; Katherine Lowengrub, M.D., Moshe Kotler, M.D.

Educational Objectives:

Topiramate and fluvoxamine monotherapy may be effective in the treatment of pathological gambling.

Summary:

Background: Pathological gambling (PG) is a highly prevalent and disabling impulse control disorder. Recent studies have demonstrated that PG patients respond well to treatment with SSRIs, mood stabilizers, and opioid antagonists. These findings support the idea that PG and other disorders of impulse control may be conceptualized as part of the obsessive-compulsive spectrum disorders. Pilot studies have shown topiramate to be effective in the treatment of specific disorders of impulse control. The aim of the study is to compare the effectiveness of topiramate versus fluvoxamine in the treatment of PG.

Methods: Thirty-one male PGs were assigned in a randomized fashion to receive either topiramate (15/31) or fluvoxamine (16/31) pharmacotherapy for 12 weeks. A comprehensive psychiatric diagnostic evaluation was performed on all patients, and all patients were evaluated for symptoms of gambling, depression, and anxiety using the South Oaks Gambling Screen, the Hamilton Depression Rating Scale, the Hamilton Anxiety Rating Scale, the Yale-Brown Obsessive Compulsive Symptoms Scale, and the Clinical Global Impression-Improvement Scale. The rating scales were administered at baseline and at the 12-week endpoint. In addition, the patients completed self-report questionnaires about their demographic status.

Results: 12/15 patients from the topiramate group completed the 12-week treatment. 9/12 topiramate completers reported full remission of gambling behavior, and three completers had a partial remission. The CGI-improvement score was significantly better for the topiramate group at the 12-week visit as compared with baseline ($F=10.5$, $p<0.01$, $df=2,31$). In the fluvoxamine treatment group, 8/16 patients completed the study. 6/8 fluvoxamine completers reported a full remission and the remaining 2/8 fluvoxamine completers reported a partial remission. The fluvoxamine group showed improvement in the CGI-improvement score at week 12, although this difference was not significant ($F=3.7$, $p<0.08$, $df=2,31$).

Conclusion: Topiramate and fluvoxamine monotherapy may be effective in the treatment of pathological gambling.

References:

1. Bechara A: Risky business: emotion, decision making, pathological gambling, and addiction. *Journal of Gambling Studies* 2003; 19:23-51.
2. Blanco C, Petkova E, Ibanez A, et al: A pilot placebo controlled study of fluvoxamine for pathological gambling. *Annals of Clinical Psychiatry* 2002; 14:9-15.

NR192 Monday, May 23, 3:00 p.m.-5:00 p.m.

Impact of the A1 Allele of the DRD2 on Alcohol Craving

Emmanuel B. Pinto, M.D., *Department of Psychiatry, Universite de Liege, Chu Sart Tilman B35, Liege 4000, Belgium*; Philip Gorwood, M.D., Jean Reggers, Dolores Vaira, Sonia Fuchs, William Pitchot, M.D., Marc Ansseau, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand that alcohol craving may be influenced by genetic parameters.

Summary:

Introduction: Significant association has been reported between the D2 dopamine receptor (DRD2) minor Taq 1A (A1) allele and substance misuse, while dopamine hypo functioning seems as well involved in substance craving. Our goal was to study the putative link between the A1 allele of the DRD2 and alcohol craving.

Methods: 60 male DSM-IV alcohol-dependant patients were included and hospitalized for withdrawal. Alcohol craving was monitored weekly throughout their four-week stay and twice in two months after they were discharged, using the Obsessive Compulsive Drinking Scale (OCDS). Genomic DNA was extracted from peripheral leukocytes. Polymerase Chain Reactions (PCR) amplifying Taq 1 polymorphisms of the DRD2 were performed. The impact of DRD2 (A1 or A2 alleles) on alcohol craving was assessed by ANOVAs.

Results: While the A1 allele of the DRD2 didn't influence OCDS scores during the hospitalization, a statistically significant difference was found two months after discharge between carriers and non-carriers of the A1 allele. Patients with the A1 allele exhibited higher OCDS scores than homozygous patients for the A2 allele (5.81 ± 5.06 versus 0.3 ± 0.67 , $F = 12.262$, $p = .004$). This difference was also observed with the Obsessive Thinking subscale of the OCDS (3.8 ± 3.34 versus 0.2 ± 0.42 , $F = 12.103$, $p = .004$) and with the Compulsion subscale of the OCDS (2.0 ± 1.87 versus 0.1 ± 0.31 , $F = 10.499$, $p = .006$).

Conclusions: Alcohol craving may be influenced by genetic differences in alcohol-dependant patients. However, carrying the A1 allele of the DRD2 increases craving only when patients are no longer hospitalized, suggesting that this influence is exerted on individuals subjected to usual drinking cues they didn't experience during their hospitalization.

References:

1. Verheul R, Van den Brink W, Geerlings P: A three-pathway psychobiological model of craving for alcohol. *Alcohol* 1999; 2:197-222.
2. Young McD R, Lawford BR, Nutting A, Noble EP: Advances in molecular genetics and the prevention of substance misuse: Implications of association studies of the A1 allele of the D2 dopamine receptor gene. *Addictive Behavior* 2004; 29:1275-1294.

NR193 Monday, May 23, 3:00 p.m.-5:00 p.m.

Electronic Monitoring of Antipsychotic Adherence of Outpatients With Schizophrenia and Schizoaffective Disorders: An Evaluation of the Association With Symptoms, Quality of Life, and Cognition Supported by Janssen-Cilag Medical Affairs

Matthew J. Byerly, M.D., *University of Texas Southwestern Psychiatry, 6363 Forest Park Road, Ste 651, Dallas, TX 75235*; Ann Thompson, Ph.D., Thomas Carnody, Thomas Erwin, B.A., Rhiannon Bugno, B.A., A. John Rush, M.D.

Educational Objectives:

At the conclusion of this session, the participant should understand the relationship between electronic-monitored adherence and the clinical outcome of schizophrenia.

Summary:

Objective: Evaluate the relationship between electronically-determined antipsychotic adherence rates with (1) various baseline

patient characteristics, and (2) symptom severity, quality of life (QoL), and cognition measured prospectively for six months.

Methods: Adult outpatients with DSM-IV diagnosis of schizophrenia or schizoaffective disorder, taking a single oral antipsychotic were eligible. Adherence was collected via electronic monitored medication vial caps, prescriber report, patient self-report, and research assistant report. Symptom severity (PANSS) and QoL (SQLS, LOF, and PSP) were collected at baseline and monthly for six months. A single cognition (BACS) assessment was performed.

Results: Sixty-one patients (mean age 44.39 ± 1 years; 51% female; illness duration 21.2 ± 10.7 years) were included. Poorer mean adherence over the six-month study period was associated with baseline characteristics of less than high school education ($p < .0001$), non-Caucasian race ($p = .001$), and more severe symptoms ($p < .001$). Lower mean adherence rates during the six-month study period were also associated with worse mean six-month symptom (PANSS total; $p < 0.002$) and one of three QoL (SQLS; $p < 0.03$) ratings. No relationship was found between adherence and cognition.

Conclusion: Results suggest non-adherence with antipsychotic medication therapy is associated with worse symptoms, poorer QoL, less than high-school education, and non-Caucasian race in patients with schizophrenia and schizoaffective disorder.

References:

1. Diaz E, Levine HB, Sullivan MC, Sernyak MJ, Hawkins KA, Cramer JA, Woods SW: Use of the Medication Event Monitoring System to estimate the medication compliance in patients with schizophrenia." *J Psychiatry Neuroscience* 2001; 25(4):325-9.
2. Diaz E, Neuse E, Sullivan MC, Pearsall HR, Woods SW: Adherence to conventional and atypical antipsychotics after hospital discharge. *J Clinical Psychiatry* 2004; 65(3):354-60.

NR194 Monday, May 23, 3:00 p.m.-5:00 p.m.

Atypical Switching: Interim Results From a Naturalistic Schizophrenia Study *Supported by Eli Lilly and Company*

Jamie Karagianis, M.D., *Eli Lilly Canada Inc., 3650 Danforth Ave, Toronto, ON M1N2E8, Canada*; Janaki Srinivasan, M.D., Gerald Gray, M.D., Pramil Tahlan, M.D., Rodrigo Juarez, M.S.C., Laura M. Chapman, M.D., Ruth Dickson, M.D., Roger Simoneau, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to demonstrate an understanding of the outcomes for outpatients with psychotic disorders following a change in antipsychotic in the Canadian community setting, and be able to discuss the value of observational studies in providing real-life information.

Summary:

Objective: To describe the demographic, clinical, and functional status of outpatients switched to second-generation antipsychotics, and evaluate their treatment.

Methods: This is an interim analysis of the health outcomes of a Canadian community cohort study, examining outcomes associated with antipsychotic treatment for schizophrenia or related psychotic disorders (DSM-IV). Outpatients were assessed every three months up to 12 months.

Results: Patients were, on average, aged 41.6 ± 11.1 years (mean \pm SD), mildly ill (mean \pm SD BPRS total score 30 ± 17), male 52% ($n = 130$), with a diagnosis of schizophrenia (56%, $n = 140$). Many patients had long duration illnesses: 26% ($n = 65$) had received treatment for 10-20 years, with a further 24% ($n = 60$) having had in excess of 20 years of treatment. Olanzapine was prescribed

to 53% ($n = 132$) of patients. Of the non-olanzapine treatment group, risperidone (22%, $n = 55$) and quetiapine (23%, $n = 58$) accounted for almost all of prescriptions, with only three patients (1%) prescribed clozapine. Patients prescribed olanzapine were significantly more likely to maintain their original antipsychotic for a period of 12 months than those prescribed other second-generation antipsychotics, (64.9% [$n = 85$] for olanzapine, 40.0% [$n = 22$] quetiapine, 45.1% [$n = 23$] risperidone, and 0% clozapine, $p = 0.001$).

Conclusions: Olanzapine therapy was associated with treatment maintenance at one year in this population.

References:

1. Canadian Clinical Practice Guidelines for the Treatment of Schizophrenia. *Can J Psychiatry* 1998; 43 (Suppl. 2 — revised), November, 25S-S40S. Working group for the Canadian Psychiatric Association and the Canadian Alliance for Research for Schizophrenia.
2. American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edn. American Psychiatric Press, Washington, DC., 1994.

NR195 WITHDRAWN

NR196 Monday, May 23, 3:00 p.m.-05:00 p.m. **Effectiveness of an Integrated Treatment Program for Dually Diagnosed Veterans**

Patricia I. Ordorica, M.D., *University of South Florida, Tampa VAMC, Room 116A, 13000 Bruce B. Downs Boulevard, Tampa, FL 33612*; Cheryl Gonzales, M.D.

Educational Objectives:

At the conclusion of this session, the participant will recognize that integrated concurrent treatment for co-occurring disorders, substance-use disorders, and other mental disorders is significantly more effective in a Veteran population.

Summary:

Patients who are dually diagnosed are more likely to have poorer outcomes with increased hospitalizations, higher utilization of high cost services, and more severe psychiatric symptoms. A recent task force report commissioned by the Secretary of Veterans' Affairs, "Availability of and Access to Mental Health and Substance Abuse Services for Veterans: A Review and Recommendations," highlighted the large number of underserved veterans with dual diagnosis. We set forth a rigorous program evaluation to study the effectiveness of an evidence-based, integrated clinical treatment program for the dually-diagnosed veteran, Dual Diagnosis Treatment Program (DDTP). This ongoing study investigates the effectiveness of the DDTP program measured by the following: (1) inpatient utilization and health care costs, (2) percentage of negative drug urine screens (UDS), (3) use of positive coping strategies, (4) severity of psychiatric symptoms, and (5) quality of life (QOL) scores. Repeated clinical and research measures were collected at intake, three weeks, six weeks, 20 weeks, and 32 weeks, corresponding to phases in the DDTP. Preliminary data analyses demonstrate DDTP's clinical and cost-effectiveness, including significant decrease in health care costs, decrease in numbers of inpatient admissions, significant increase in negative drug screens, increased use of positive coping strategies on the Coping Responses Inventory (CRI), and increased quality of life (QOL) scores. Preliminary analyses in this report include over 100 veterans with co-occurring substance dependence and another major psychiatric disorder.

References:

1. Drake RE, et al: Three-year outcomes of long-term patients with co-occurring bipolar and substance disorders. *Biol Psychiatry* 2004; 56(10):749-56.
2. Tsuang J, Fong TW: Treatment of patients with schizophrenia and substance abuse disorders. *Curr Pharm Des* 2004; 10(18):2249-61.

NR197 Monday, May 23, 3:00 p.m.-05:00 p.m. **Obsessive Compulsive Symptoms With Atypical Antipsychotic Use**

Rathi Mahendran, M.B.B.S., *Department of General Psychiatry, Institute of Mental Health, 10 Buangkok View, Singapore 539747, Singapore*; Emily Liew, B.S.C., Yu-Jin Quek

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the de novo emergence of OC symptoms with atypical antipsychotic treatment, create awareness and close monitoring for treating patients with schizophrenia.

Summary:

Introduction: There are several reports of atypical antipsychotics inducing or exacerbating OC symptoms in patients with schizophrenia. The extent of the problem has not been established. In this study, schizophrenia patients without history of OC disorder or symptoms treated with atypical antipsychotics were examined for emergence of OC symptoms. Also excluded were those with an Axis II OC personality disorder or traits.

Methodology: The study was approved by the ethics committee and informed consent was taken from patients. During the study period, 958 outpatients received atypical antipsychotics (clozapine 138, olanzapine 99, quetiapine 99, risperidone 622). The YB-OCS Checklist and Scale were used.

Findings: 303 patients were recruited (123 males, 181 females). 57 received clozapine, 48 olanzapine, 30 quetiapine, and 169 risperidone. OC symptoms emerged in 11 patients (4 on clozapine, 2 olanzapine, 2 quetiapine, and 3 risperidone). Three developed either obsessions or compulsions, and 8 had both symptoms. OC symptoms emerged at varying intervals after starting atypical antipsychotics.

Conclusions: The study of OC symptoms in schizophrenia is confounded by under-recognition and similarities in psychopathology. 3.6% of schizophrenic patients treated with atypical antipsychotics developed OC symptoms de novo. This review highlights the need for clinical awareness and close monitoring for OC symptoms when treating schizophrenia patients with atypical antipsychotics.

References:

1. Lykouras L, Alevizos B, Michalopoulou P, Rabavilasa A: OC symptoms induced by atypical antipsychotics. A review of reported cases. *Prog Neuropsychopharmacol Biol Psychiatry* 2003; 27(3):333-46.

NR198 Monday, May 23, 3:00 p.m.-5:00 p.m. **Risperidone Consta Decreases Number of Hospitalizations Among Patients With Schizophrenia Supported by Janssen-Cilag Latvia**

Elmars Rancans, M.D., *Department of Psychiatry, Stradinsh University, Tvaika Street 2, Riga LA 1005, Latvia*

Educational Objectives:

Treatment with long-acting risperidone injection substantially decreases frequency of rehospitalizations and duration of stay in hospital among schizophrenia patients.

Summary:

Objectives: Analyze the impact of long-term risperidone injection therapy on frequency and duration of rehospitalizations among schizophrenia patients in Latvia.

Methods: Retrospective analysis of medical records from schizophrenia patients treated with Risperdal Consta during open-label observational study. Comparison of mean number of hospital bed-days two years before and during this study was made.

Results: Thirty-four patients (66.7% females) with history of previous relapses were treated with Risperdal Consta. Completers (88%) were previously treated with classical antipsychotics in 50%, with risperidone in 40% and olanzapine in 10% of cases. They were hospitalized on average for 1.5 times and 70.3 days per year. After an average duration of treatment with Risperdal Consta for 284.2 ± 94.5 days, mean number of hospitalizations decreased by 1.2 episodes and 82.2 days per patient treatment year ($p < 0.001$). Patients received Risperdal Consta with a mean dose of 31.8 ± 5.8 mg every two weeks. Therapy with 25 mg of Risperdal Consta was prescribed for 51.2% of patients. Tolerability of treatment was very good and no significant side effects were observed.

Conclusions: Treatment with long-acting risperidone injection substantially decreases frequency of rehospitalizations and duration of stay in hospital among schizophrenia patients.

Study supported by Janssen Cilag Latvia

References:

1. Hamann J, Leucht S, Kissling W: Are the second-generation antipsychotics cost-effective? A critical review on the background of different health systems. *Pharmacopsychiatry* 2003; 36:18-26.
2. Harrison TS, Goa KL: Long-acting risperidone: a review of its use in schizophrenia. *CNS Drugs* 2004; 18:113-132.

NR199 Monday, May 23, 3:00 p.m.-5:00 p.m. **Effect of Naltrexone on Subjective Acute Alcohol Effects in Social Drinkers**

Sung-Gon Kim, M.D., *Department of Psychiatry, Pusan National University, 1-GA 10, Ami-dong, Seo-gu, Pusan 602-739, Korea*; Jong-Hyun Kim, M.D., Je-Min Park, M.D., Myung-Jung Kim, M.D., Sung-Hyun Shin, M.D.

Educational Objectives:

Naltrexone is believed to have triple actions, attenuating the stimulatory effect, intensifying the sedative effect, and blocking alcohol-induced alcohol craving.

Summary:

Introduction: The effects of naltrexone, stimulatory and sedative, on acute alcohol response in healthy Korean social drinkers, based on 0.6 mg/kg of alcohol intake, were investigated.

Methods: Twenty-four healthy male medical students voluntarily participated. The experimental method was cross-over design. The subjects received 25 or 50 mg/day of naltrexone on the experimental days. Biphasic alcohol effect scale (BAES), alcohol craving, and blood alcohol concentration (BAC) were measured before drinking and at 15, 30, 45, 60, 90, and 120 minutes after drinking.

Results: When the scores on the stimulatory subscale of the BAES were compared between the naltrexone and the control group, the scores were found to be significantly lower in the naltrexone group at 15 and 90 minutes after drinking ($p < 0.05$). The alcohol-induced sedative effect was significantly higher in the naltrexone group at 90 minutes after drinking ($p < 0.05$). Alcohol-induced alcohol craving at 45 and 60 minutes after drinking was significantly less in the naltrexone group than in the control ($p < 0.05$).

Conclusion: Naltrexone is believed to attenuate the stimulatory effect, to intensify the sedative effect, and to block alcohol-induced alcohol craving. These triple actions might be utilized in the prevention of alcohol-dependence relapses.

References:

1. Volpicelli JR, Watson NT, King AC, Scherman CE, O'Brien CP: Effect of naltrexone on alcohol "high" in alcoholics. *Am J Psychiatry* 1995; 152:613-615.
2. Swift RM, Whelihan W, Kuznetsov O, Buongiorno G, Hsu H: Naltrexone-induced alterations in human ethanol intoxication. *Am J Psychiatry* 1994; 151:1463-1467.

NR200 Monday, May 23, 3:00 p.m.-5:00 p.m.

Validation of the CAGE Questionnaire in Patients With Schizophrenia

Alain Dervaux, M.D., *Department of Psychiatry, Hopital Sainte Anne, Shu, 1 Rue Cabanis, Paris F-75014, France*

Educational Objectives:

At the conclusion of this session, the participant should be able to assess alcohol use disorders in schizophrenic patients.

Summary:

Objective: To assess the face validity of the CAGE questionnaire in schizophrenia patients with alcohol use disorders and a group of patients without substance abuse.

Method: The CAGE questionnaire, the PANSS, and the psychoactive substance-use disorder section of the Composite International Diagnostic Interview (CIDI) for the DSM-III-R diagnosis of abuse of or dependence on alcohol and other substances were used in 114 subjects meeting the DSM-III-R criteria for schizophrenia or schizoaffective disorder.

Results: 29.8% (n=34) of the subjects in the study presented comorbidity of lifetime alcohol abuse (n=4) or dependence (n=30). There were no significant differences in the PANSS total mean scores between the groups of patients with or without alcohol use disorders. With a cutoff score of 1 or more, the sensitivity of the CAGE questionnaire was 0.91 and the specificity was 0.83. With a cutoff score of 2 or more, the sensitivity of the CAGE questionnaire was 0.82 and the specificity was 0.94. The kappa value was 0.768 p<0.0001.

Conclusions: The sensitivity and the specificity of the CAGE questionnaire are consistent with previous studies assessing these measures in samples of patients without schizophrenia. As in the general population, the CAGE questionnaire can be reliably used to assess alcohol-use disorders in schizophrenic patients.

References:

1. Ewing JA: Detecting alcoholism: the CAGE questionnaire. *JAMA* 1984; 252:1905-1907.
2. Fiellin DA, Reid MC, O'Connor PG: Screening for alcohol problems in primary care: a systematic review. *Arch Internal Med* 2000; 160:1977-1989.

NR201 Monday, May 23, 3:00 p.m.-5:00 p.m.

Dropouts and Retention at a University Substance Abuse Treatment Program in Brazil

Ana C. Saad, M.D., *PROJAD, UFRJ, Rua Bogari 15, AP 501, Rio De Janeiro, RJ 22471-340, Brazil*; Marcelo S. Cruz, M.D., Nilzete R. Costa, Ana C. Mathias, Marcio M. Barbeito, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize a Brazilian substance abuse program with its cultural specificity; demonstrate in this program the differences between

the retention and dropout groups in matters of socio-demographic data and the history of drug abuse.

Summary:

Objective: To identify the differences between patients who stayed in treatment (retention) for six months or more with those who dropped out (dropouts) before six months in their sociodemographic characteristics, previous treatments, and drug used.

Methods: The two groups of patients were compared (n= 90 patients): 41 from the group who abandoned treatment and 49 who did not. We compared proportions using the chi-square and Fisher Exact test; *t Student* test for mean age and *Mann-Whitney* for time of treatment; p=0,05 was considered statistically significant.

Results: The sample was majority male (80%) who lived by themselves (74.4%). The age ranged from 18 to 68 years old, mean age 38.39; 38.9% had an elementary school education; 34.1% had a legal problem. Alcohol was the drug most used, followed by cocaine and marijuana. About 78% of the patients had had a previous treatment.

There were statistically significant differences between the two groups on the variables of age and educational level. There were no statistically significant differences between the two groups on the other variables.

Conclusion: The youngest people leave treatment more frequently and are at risk for intense drug use. It is very important for substance-abuse programs to direct treatment toward this population.

References:

1. Passos SRL, Camacho LAB: I Características da clientela de um centro de tratamento de dependência de drogas. *Revista de Saúde Pública* 1998; 32 (01):64-71.
2. Vaughn T, Sarrafin MV, et al: Participation and retention in drug abuse treatment services research. *Journal of Substance Abuse Treatment* 2002; 23 (4):387-397.

NR202 Monday, May 23, 3:00 p.m.-5:00 p.m.

Optimized Long-Acting Risperidone Maintenance Therapy

Supported by Janssen Medical Affairs

Stephen C. Rodriguez, M.S., *Janssen Medical Affairs, 1125 Trenton-Harbourton Road, Titusville, NJ 08560*; Robert Lasser, M.D., Ibrahim Turkoz, M.S., Atul R. Mahabeshwarkar, M.D., Georges M. Gharabawi, M.D., Heeree Chung, Ph.D., George M. Simpson, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the relationship between long-acting, injectable risperidone dosing and clinical outcomes, including relapse rate, efficacy, and safety.

Summary:

Objective: Examine long-term outcomes in patients with psychotic disorders transitioned from oral antipsychotics to long-acting risperidone.

Method: Symptomatically stable patients were randomized to long-acting risperidone 25 or 50 mg every two weeks in a 52-week, double-blind, multicenter study. Relapse assessments, PANSS scores, and CGI-C ratings were performed. Safety data were collected via ESRs/AIMS and adverse event (AE) reporting.

Results: This study included 323 stable patients; 166 (51%) completed the study. Relapse occurred in 35 (21.6%) receiving 25 mg and 24 (14.9%) receiving 50 mg long-acting risperidone (P=0.131 time-to-relapse). Mean total PANSS scores decreased significantly (P<0.001 vs. baseline) and comparably (P=0.371 be-

tween-group comparison) for both doses. The percentage rated on the CGI-C as minimally to very much improved at endpoint also was comparable: 25 mg, 92 (59.4%); 50 mg, 91 (58.7%). The most common AEs (=10%) occurred at a similar rate in each dose group (25 mg, 50 mg): insomnia (25%, 30%), headache (21%, 16%), anxiety (18%, 15%), and psychosis not otherwise specified (23%, 18%). Few movement disorder AEs were reported for either dose group, with significant improvement in movement disorder rating scales.

Conclusions: Both doses of long-acting risperidone were well tolerated, provided symptomatic improvements, and had high proportions of relapse-free patients.

References:

1. Marder SR, Conley R, Ereshefsky L, Kane JM, Turner MS: Clinical guidelines: dosing and switching strategies for long-acting risperidone. *J Clin Psychiatry* 2003; 64(suppl 16):41-6.
2. Schooler NR: Relapse and rehospitalization: comparing oral and depot antipsychotics. *J Clin Psychiatry* 2003; 64(suppl 16):14-17.

NR203 Monday, May 23, 3:00 p.m.-5:00 p.m.

Cognitive and Functional Improvement With Long-Acting Risperidone Treatment

Supported by Janssen Medical Affairs

Robert Lasser, M.D., *CNS Medical Affairs, Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200*; Gahan J. Pandina, Ph.D., Robert Bilder, Ph.D., Philip D. Harvey, Ph.D., Stephen C. Rodriguez, M.S., Ibrahim Turkoz, M.S., Heeree Chung, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the relationship between cognitive and functional improvements in patients with schizophrenia receiving long-acting injectable risperidone.

Summary:

Objective: Schizophrenia patients receiving atypical antipsychotics, including risperidone, have shown improved cognition and independent role functioning. These outcomes may *not* be related. This preliminary report examines interim cognitive and functioning results from a 12-month study of long-acting risperidone.

Method: Clinically stable adults (N=323) with schizophrenia received a computer-administered cognitive assessment of attention, motor, verbal/visual learning, working memory, and executive functioning, and measures of functioning (Strauss-Carpenter Level of Functioning [LOF] scale, Personal and Social Performance scale, Schizophrenia Quality of Life Scale) were performed at baseline, three, six, and 12 months. Interim blinded six-month data were analyzed.

Results: Significant improvements were noted in four of seven cognitive domains. These included attention (flanker correct incongruent mean change=2.9; $P=.001$), verbal learning (word list memory: total learning mean change=3.1, $P=.0003$), working memory (object working memory [LOCF]: matching total correct mean change=0.3, $P=.0231$), and executive function (strategic target detection test: total errors mean change=-3.0, $P=.0637$). Exploratory analyses combining cognitive data and functioning measures revealed several significant, modest correlations (eg, total errors on an executive function test correlated at -0.36 [$P<.001$] with the LOF symptomatology subscale).

Conclusion: Cognitive functioning improved in patients treated with long-acting risperidone. Modest correlations were found between some measures of cognition and functioning at six months. Further analysis will use 12-month data.

References:

1. Addington J, Addington D: Neurocognitive and social functioning in schizophrenia: a 2.5 year follow-up study. *Schizophr Res* 2000; 44:47-56.
2. Meltzer HY, McGurk SR: The effects of clozapine, risperidone, and olanzapine on cognitive function in schizophrenia. *Schizophr Bull* 1999; 25:233-255.

NR204 Monday, May 23, 3:00 p.m.-5:00 p.m.

Characterizing the Remitted Patient With Schizophrenia

Supported by Janssen Medical Affairs

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand newly proposed remission criteria and the characteristics of patients who meet these criteria.

Summary:

Objective: The Remission in Schizophrenia Working Group proposed standard remission criteria (components = symptom severity and time) to evaluate long-term outcomes (Andreasen et al, in press). A previous report applied these criteria to a database and identified a population of remitted patients (Lasser et al). This analysis further characterizes those remitted patients.

Method: In a 50-week, open-label trial, stable patients with schizophrenia/schizoaffective disorder received long-acting injectable risperidone every two weeks. Remission criteria were applied (PANSS = 1[absent] to 3[mild] on eight core symptoms ≥ 6 months, absent at baseline). PANSS, patient-rated mental health status (SF-36), and Drug Attitude Inventory (DAI) were measured.

Results: Among 82 patients who achieved remission, mean scores for each of the 30 PANSS items were rated as absent to minimal/mild at endpoint. An "interpersonal" cluster of items (including social/emotional withdrawal, blunted affect, social avoidance) represented those items rated the highest, although mean item ratings were each only minimal/mild. Remitted patients experienced substantial improvements in self-rated mental health status (SF-36), with a significant improvement in mean DAI score at endpoint ($P < .001$).

Conclusions: Remitted patients had very low symptom ratings and significant improvements in patient-rated drug attitude and health status. These findings warrant further study and may provide important new information on the course of remission in schizophrenia.

References:

1. Andreasen NC, Carpenter W, Kane JM, et al: Remission in schizophrenia: proposed criteria and rationale for consensus. *Am J Psychiatry*, in press.
2. Fleischhacker WW, Eerdeken M, Karcher K, et al: Treatment of schizophrenia with long-acting injectable risperidone: a 12-month open-label trial of the first long-acting second-generation antipsychotic. *J Clin Psychiatry* 2003; 64(10):1250-7.

NR205 Monday, May 23, 3:00 p.m.-5:00 p.m.

Functioning and Quality of Life During Long-Acting Risperidone Maintenance Treatment

Supported by Janssen Medical Affairs

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Stephen C. Rodriguez, M.S., Julie C. Locklear, M.B.A., Atul R. Mahableshwarkar, M.D., Georges M. Gharabawi, M.D., Hearee Chung, Ph.D., David Feifel, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand patient functioning and quality of life during one year of maintenance treatment with long-acting, injectable risperidone.

Summary:

Objective: This analysis examined functioning and quality of life (QoL) during maintenance therapy with long-acting, injectable risperidone in previously symptomatically stable patients with schizophrenia or schizoaffective disorder.

Methods: Patients were randomized to long-acting risperidone 25 or 50 mg every two weeks in a 52-week, randomized, double-blind, multicenter study. Functioning and QoL were assessed using the Personal and Social Performance Scale (PSP), the Strauss-Carpenter Level of Functioning (LOF), and the Schizophrenia Quality of Life Scale (SQLS).

Results: Of 323 stable patients, 166 (51%) completed the study. The mean \pm SD PSP score improved significantly from baseline to endpoint: 62.1 ± 14.2 to 64.1 ± 14.0 ($P=0.003$). Patients who completed the study improved to a greater degree: 68.7 ± 11.8 ($P<0.001$ vs. baseline). LOF baseline to endpoint assessments indicated more patients having a greater frequency of social contacts (+4.6%), increased quality of relationships (+6.2%), greater fullness of life (+5.8%), and better overall level of function (+4.2%). LOF improvements were greater for patients who completed the study. The SQLS indicated QoL was maintained, with some non-significant trends toward improvement.

Conclusions: One-year maintenance treatment with long-acting risperidone improved functioning and maintained QoL in stable patients with schizophrenia or schizoaffective disorder.

References:

1. Morosini PL, Magliano L, Brambilla L, Ugolini S, Pioli R: Development, reliability and acceptability of a new version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) to assess routine social functioning. *Acta Psychiatr Scand* 2000; 101(4):323-329.
2. Nasrallah HA, Duchesne I, Mehnert A, Janagap C, Berdekens M: Health-related quality of life in patients with schizophrenia during treatment with long-acting, injectable risperidone. *J Clin Psychiatry* 2004; 65(4):531-536. Erratum in *J Clin Psychiatry*. 2004; 65(8):1150.

NR206 Monday, May 23, 3:00 p.m.-5:00 p.m.

Patient Acceptance and Long-Acting Risperidone: Start Program, Gain Approach

Supported by Janssen Medical Affairs

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the importance of acceptance of and adherence to maintenance schizophrenia treatment and the newly developed structured clinical discussion tool, GAIN, to support use of antipsychotic therapy.

Summary:

Objective: This study evaluated a novel psychosocial tool (GAIN Acceptance Approach) to support schizophrenia treatment decisions.

Method: The START Study compared GAIN with Approach As Usual (AAU) in supporting acceptance of long-acting risperidone in patients with schizophrenia. Using a six-week psychosocial approach phase and a 12-week treatment phase, U.S. sites were randomly assigned to GAIN or AAU. The proportion of patients who accepted treatment over the 12-week treatment phase, clinician satisfaction, and illness severity (per Clinical Global Impression scale) were evaluated.

Results: 655 outpatients participated across 268 sites (141 GAIN, 127 AAU). Data indicated high treatment acceptance across both groups: GAIN, 93.9%; AAU, 89.9%. Analysis of available data indicates that completion rates were equivalent across both groups; however, almost twice as many patients in the AAU group discontinued as a result of withdrawing consent or refusing treatment (GAIN 13.1%; AAU 25.8%). Clinicians found GAIN to be quite a bit/extremely effective overall (58.9%) were highly satisfied with GAIN (62.8%), and found it quite a bit/extremely easy to implement (69.6%).

Conclusion: The GAIN approach, an easily implemented tool, provides an effective method of building clinician and patient relationships, and supports acceptance of long-acting risperidone treatment.

References:

1. Kemp R, Hayward P, Applewhaite G, Everitt B, David A: Compliance therapy in psychotic patients: randomised controlled trial. *BMJ*. 1996; 312:345-349.
2. Miller WR: Motivational interviewing: research, practice, and puzzles. *Addict Behav* 1996; 21:835-842.

NR207

Monday, May 23, 3:00 p.m.-5:00 p.m.

Ramelteon (TAK-375) and Triazolam in Humans: Behavioral Effects and Abuse Potential

Roland R. Griffiths, Ph.D., *Behavioral Pharmacology Research Unit, Johns Hopkins Bayview Medical Center, 5510 Nathan Shock Drive, Baltimore, MD 21224*; Patricia Suess, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that ramelteon, a novel selective melatonin MT1/MT2 receptor agonist under development for the treatment of insomnia, shows no abuse potential as measured by multiple rating scales widely used and accepted for abuse liability testing in novel compounds.

Summary:

Objective: Ramelteon is a novel selective melatonin MT1/MT2 receptor agonist under development for insomnia treatment. This study evaluated behavioral effects and abuse potential of ramelteon and triazolam, a classic benzodiazepine sedative-hypnotic, in subjects with histories of sedative drug abuse.

Methods: In this double-blind, crossover study, 14 experienced drug users received one oral dose/day of ramelteon (16mg, 80mg, 160mg), triazolam (0.25mg, 0.5mg, 0.75mg), or placebo. Abuse potential was inferred from widely used subjective effect questionnaires. Behavioral and cognitive performance were also assessed.

Results: Compared with placebo, ramelteon (16mg, 80mg, 160mg) showed no significant effect on primary outcome questionnaire item "drug liking" at any time point (0.5-24 hours postdose) or on items "drug strength," "drug liking," "good effects," and "street value" at 24 hours postdose. Similarly, ramelteon had no effect on Word Recall/Recognition Task, Enter and Recall Task, Balance Task, Digit Symbol Substitution Task, and Circular Lights

performance at any dose compared with placebo. In contrast, triazolam (0.5 and 0.75mg) showed dose-related effects on all these subjective and behavioral measures, consistent with its profile as a sedative drug with known abuse potential.

Conclusion: Rameelteon demonstrated no abuse potential or behavioral impairment under these study conditions at doses up to 20 times the anticipated therapeutic dose.

References:

1. Griffiths RR, Bigelow GE, Ator NA: Principles of initial experimental drug abuse liability assessment in humans. *Drug Alcohol Depend* 2003; 70(3 Suppl):S41-S54.
2. Rush CR, Frey JM, Griffiths RR: Zaleplon and triazolam in humans: acute behavioral effects and abuse potential. *Psychopharmacology* 1999; 145:39-51.

NR208 Monday, May 23, 3:00 p.m.-5:00 p.m.

Differences Among Antipsychotics in Routine Care of Schizophrenia and Schizoaffective Patients

Atilla Soykan, M.D., *Department of Psychiatry, Yesilyurt sok. 23/6, Ayranci, Ankara 06100, Turkey*; Aysegül Yılmaz Dileköz, M.D., Elif Sultangül, M.D., Meram Saka, M.D.

Educational Objectives:

At the conclusion of the presentation, the participants should be able to; think about differences among clozapine, risperidone, olanzapine, quetiapine and classical antipsychotics in terms of add-on depot antipsychotic and anticholinergic use, and switching off rates; understand the significant impacts of inclusion/exclusion criteria on the results of naturalistic studies.

Summary:

Introduction: The aims of this naturalistic retrospective study are to compare (1) classical (C-APs) and atypical antipsychotics (A-APs) (2) risperidone, olanzapine, quetiapine, and clozapine, in routine care of schizophrenia and schizoaffective disorder inpatients.

Method: We examined schizophrenia and schizoaffective disorder inpatients (n=787) with regard to use of antipsychotics (AP). Information concerning sociodemographic and baseline clinical data, AP medication use and study outcome measures for patient was obtained from the charts. The use of anticholinergics (A-CH), add-on depot antipsychotics (D-AP) and switching off the index medication prior to discharge were our principal outcome measures.

Results: It is important to note that, if add-on D-APs patients were not included in analyses, A-CH use would have been lowest for clozapine (13%) and quetiapine (23%) treated patients. Treatment change occurred in 20% of our A-APs population. The switch rate was highest for quetiapine (25%) and lowest for clozapine (7%) treated patients (F=12.6.3, p<.007). It is important to note that, if add-on D-APs patients were not included in analyses, as was done in similar studies, A-CH use would have been lowest for clozapine (13%) and quetiapine (23%) treated patients. Treatment change occurred in 20% of our A-APs population. The switch rate was highest for quetiapine (25%) and lowest for clozapine (7%) treated patients (F=12.6.3, p<.007).

Conclusion: Overall assessments of the results imply different outcomes among A-APs in terms of add-on A-CH and D-APs, and switching off rate in routine care. Additionally, we observed that if we had used similar inclusion/exclusion criteria with industry-supported, naturalistic studies and exclude some cases, it was very possible to report results favoring a particular atypical antipsychotic as were in such studies.

References:

1. Taylor DM, Wright T, Libretto SE: Risperidone olanzapine drug outcomes studies in schizophrenia (RODOS) U.K. Investigator

Group. Risperidone compared with olanzapine in a naturalistic clinical study: a cost analysis. *J Clin Psychiatry* 2003; 64(5):589-97.

2. Dossenbach M, Erol A, Kessaci MM et al: Effectiveness of antipsychotic treatments for schizophrenia: interim 6-month analysis from a prospective observational study (IC-SOHO) comparing olanzapine, quetiapine, risperidone, and haloperidol. *J Clin Psychiatry* 2004; 65(3):312-21.

NR209 Monday, May 23, 3:00 p.m.-5:00 p.m.

New Approach in the Treatment of Motor Disturbances in Acute Psychosis: The VILAN Method®

Vera Ilankovic, Ph.D., *Belgrade, Yugoslavia*; Tanja Lakovic, M.D., Andrej Ilankovic, M.D., Lana Marija Ilankovic, M.A.

Educational Objectives:

At the conclusion of this session the participants should understand the effects of use of new neurorehabilitation method "VILAN" in early treatment of motor disturbances in acute psychotic patients.

Summary:

Purpose: Evaluation of effects of early treatment (rehabilitation) of motor disturbances by acute psychotic patients.

Methods: In clinical study of 30 patients with acute psychotic future (schizophrenia spectrum), we investigated the motor disturbances with clinical rating scales for: Abnormally Involuntary Movement Scale (AIMS, Gay), Depressive (psychomotor) Retardation Scale (DRS, Widlocher), Praxia Scale (Brown), L-R Orientation Test and Simultaneous Movement Test (TSM, V. Ilankovic, 1995). In treatment with VILAN method, we divided the patients into two subgroup: (1) the treatment of motor deficits and movement disorders was with typical neuroleptics + VILAN rehabilitation method, and (2) with atypical neuroleptic + VILAN method. The first assessment of effects of treatment was after four weeks.

Results: We found a deep psychomotor regression and serious psychomotor disturbances (movement disorders & motor deficits) in all patients. Dominant disturbances were: abnormality of - tonus (100%), posture and postural reflexes (100%), voluntary movements (95%), disorders in speech production (95%) and involuntary movements (70%).

Based on these findings, we applied (as augmentation the pharmacotherapy) our original program of rehabilitation, the "VILAN" method (V.a&N.ilankovic, 1997.)

Our results were in one group: reduction of - dyspraxio for 86%, disorders of simultan movements for 64%, depressive retardation for 48%, speech for 32%, and abnormal movements for 24%. In 2. group: reduction of - dyspraxio for 90%, disorders of simultan movements 78% (p<0.01), depressive retardation for 72% (p<0.001), speech 48% (p<0.01) and abnormal movements for 46% (p<0.001).

Conclusions: (1) Most of patients with acute psychotic future (Sch spectrum) had a deep level of psychomotor regression and serious motor disturbances. (2) The applying of early motor rehabilitation (VILAN method) in integrative treatment of psychotic disorders is obligatory for functional recovery and quality of life. (3) The basic pharmacotherapy with atypical neuroleptics resulted with higher improvement of simultan movements and speech, and significant reduction of depressive retardation and abnormal movements. (4) The early (and continuous) motor rehabilitation by acute psychotic illnesses is a good chance to prevent (diminish) the late psychomotoric deficits by psychiatric patients.

References:

1. Ilankovic Vera: "Motor deficits in psychotic residual states." Ph.D. Thesis, University Belgrade, 1994.

2. Ilankovic V, Ilankovic N: The psychomotor rehabilitation in psychiatry - the VILAN method", Bgd, 1997.

NR210 Monday, May 23, 3:00 p.m.-5:00 p.m.
Disorders of the Sleep-Wake Cycle, Depression, and Addiction by Youth

Andrej Ilankovic, M.D., *Belgrade, Yugoslavia*; Tanja Lakovic, M.D.

Educational Objectives:

At the conclusion of this session, the participants should understand the correlations between sleep disorders, depression, and drug addiction by youth.

Summary:

Objective: Our investigation is a comparative analysis between two groups of students in their sleep and wake behavior, depression, and drug abuse.

Methods: In the first group were 35 students from high school (16-17 years old) without data of drug abuses. In the second group were 35 students, older (20-27 years old), with clear addiction (heroin). For assessment we used: (1) the scale for assessment of sleep-wake behavior, (2) the Hamilton Depressive Scale (HAMD), and (3) the Zung scale for self-measurement of depression. The statistical analysis was made with > Mc Pearson test of linear correlation, with Student t-test and with linear regression.

Results: (1) The linear correlation (Mc Pearson) is very high and statistically very significant ($p < 0.0001$) between delay of sleeping time (after midnight), depression score (HAMD and Zung), and tendency to drug abuse.

(2) The predictive models (made with linear regression) as risk factors for addictive behavior point out: smoking, night life, different pains, abuses of analgetics drugs, delay of time going to sleep (to the morning!), and very high score of depressivity.

Conclusions: The disorders of circadian sleep and wake cycles by school children, students, and other young people is a big risk to develop depression and addiction disorders.

References:

1. Ilankovic N, et al.: Consciousness, sleep and dreams. Medical faculty, Belgrade, 1999.
2. Ilankovic A, et al.: Sleep disorders and depression by students, M.Sc. Thesis, Medical faculty, Belgrade, 2002.

NR211 Monday, May 23, 3:00 p.m.-5:00 p.m.
Health Services, Education, and Community Action: Preventing Drug Abuse in Turkey

Nesrin Dilbaz, M.D., *Department of Psychiatry, Ankara Numune Hastanesi, ANEAH II Psikiyatri Klinigi Samanpazari, Ankara 06, Turkey*; Tuncer Okay, M.D., Ozlem Aki, M.D., Cem Sengul, M.D., Gurhan Pocan, M.D., Ali Turkoglu, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to learn more about drug using patterns in a developing country and which substances were more problematic for a developing country.

Drug abuse and dependence is on the rise in Turkey like many other developing countries. Ankara, the capital of Turkey, has a population of approximately 4 million individuals. In this study we interviewed with 71 key informants in their locale 8 sampling sites. Key informants' occupational groups are doctor, health worker, local councilor, teacher, social worker, police officer, and ex drug user. 47 of (%66) key informants are male and 24 (%34) were female. Key informants were asked about the frequency of use of each drug group considered by the study in their locale. Inhal-

ants were the substance most often reported to be commonly used in Ankara. After inhalants, cannabis and benzodiazepines were reported as two most commonly used substances, respectively. Other substances seem to be at lower rates in almost every locale. The use of inhalants, ecstasy, cannabis, and benzodiazepines were on the rise. Increased availability and low prices are the most important cause of increase. The average age at first use of inhalants is 11.5 years old. Ecstasy is first used in earlier ages. Cannabis and benzodiazepines are first used in early adulthood.

References:

1. Botvin GJ: Preventing drug abuse in schools: social and competence enhancement approaches targeting individual-level etiologic factors. *Addict Behav* 2000; 25(6):887-97.
2. Bullock B Preventing drug abuse. *Tex Med*: 1990; 86(12):87-8.

NR212 Monday, May 23, 3:00 p.m.-5:00 p.m.
Sexual Dysfunction-Related Neural Circuits in Male Patients With Schizophrenia

Bum Seok Jeong, M.D., *Department of Psychiatry, Eulji University Hospital, 1306 Dunsan-Dong, Seo-Gu, Daejeon, NE 302830, Korea*; Jee Wook Choi, M.D., Sun Woo Lee, M.D., Ji-Woong Kim, M.D., Sung Kyun Hong, M.D.

Educational Objectives:

To explore the neural correlates of sexual dysfunction in antipsychotic medicated schizophrenics, functional MRI was performed with visual erotic stimuli.

Summary:

Introduction: Sexual dysfunction in schizophrenia, especially sexual arousal dysfunction, lack of sexual desire, is well-known. But there is no functional neuroimaging study to explore sexual dysfunction in schizophrenia.

Methods: To explore sexual arousal-related neural circuits in schizophrenics and to examine possible mechanism of sexual arousal dysfunction in schizophrenia using functional magnetic resonance imaging, we evaluated 12 schizophrenics and 12 healthy controls. Subjects underwent fMRI at 3 T while passive visualization of erotic arousal pictures.

Results: Schizophrenics showed more erectile and ejaculatory dysfunction, and higher levels of prolactin than healthy controls. The subjective response to sexual arousal was not significantly different between groups. Schizophrenics had less activation in right cerebellar tonsil and more activation in the right supplementary motor area and right precentral gyrus. AnCova with prolactin level failed to show the difference of activation in right cerebellar tonsil between group.

Discussion: Failure to activate at right tonsil in schizophrenics indicates neural correlates of sexual dysfunction in medicated schizophrenia and may be related with antipsychotics induced sexual dysfunction.

References:

1. Culter AJ: Sexual dysfunction and antipsychotic treatment. *Psychoneuroendocrinology* 2003;69-8216.
2. Mouras H, et al: Brain processing of visual sexual stimuli in healthy men: a functional magnetic resonance imaging study. *Neuroimage* 2003;855-869.

NR213 Monday, May 23, 3:00 p.m.-5:00 p.m.
Lamotrigine for Bipolar Disorder and Stimulant Dependence

E. Sherwood Brown, M.D., *Department of Psychiatry, University of Texas Southwestern Medical Center, 5323 Harry Hines*

Boulevard, Dallas, TX 75390-8849; Dana Perantie, B.S., Nafisa Dhanani, B.A., Laura Beard, M.D., Paul Orsulak, Ph.D., A. John Rush, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to treat persons with bipolar disorder and substance abuse with lamotrigine.

Summary:

Background: Bipolar disorder (BPD) is associated with high rates of substance abuse. Our group previously reported favorable results with lamotrigine in 30 patients with BPD and cocaine dependence. This report examines lamotrigine in 32 additional cocaine-dependent patients to replicate the findings, and extends the findings by combining data from both groups, including participants with amphetamine misuse.

Method: Participants received a baseline evaluation and assessment for up to 36 weeks with the Hamilton Rating Scale for Depression (HRSD-17), Young Mania Rating Scale (YMRS), Brief Psychiatric Rating Scale (BPRS-18), and Cocaine Craving Questionnaire (CCQ) while receiving open-label lamotrigine add-on therapy. Urine samples were collected and self-reported drug use quantified.

Results: In the replication sample (n=32), significant improvements were observed in the HRSD-17, YMRS, BPRS-18, CCQ, and dollars/week spent on cocaine. In the extension study, the original sample (n=30) and replication sample (n=32) were combined, and participants with amphetamine use (n=7) were included for 69 in the evaluable sample. HRSD-17, YMRS, BPRS-18, and CCQ scores, days of stimulant use and dollars spent on cocaine or amphetamines decreased significantly.

Conclusion: Lamotrigine treatment was associated with improvement in mood, and drug craving/use. Controlled trials are needed.

References:

1. Brown ES, Nejtek VA, Perantie DC, Orsulak PJ, Bobadilla L: Lamotrigine in patients with bipolar disorder and cocaine dependence. *Journal of Clinical Psychiatry*, 2003; 64:197-201.
2. Brown ES, Suppes T, Adinoff B, Thomas NR: Drug abuse and bipolar disorder: comorbidity or misdiagnosis? *Journal of Affective Disorders* 2001; 65:105-115.

NR214 Monday, May 23, 3:00 p.m.-5:00 p.m.

Outcome of Two Medication Strategies in First-Onset Schizophrenia: The Mesifos RCT

Alexander Wunderink, M.D., *Department of Psychiatry, Groningen University Medical Center, PO Box 30.001, 9700 RB Groningen, Netherlands*; Durk Wiersma, Ph.D., Pieter de Wit, M.D.

Educational Objectives:

At the conclusion of the presentation, the participants (visitors) should have been informed about factors influencing outcome of first episode psychoses, including the assignment to targeted or maintenance strategies, in our epidemiological catchment area study.

Summary:

Introduction: Trials on relapse rates after first psychotic episodes support long-term antipsychotic treatment. However, relapse prevention is not the sole contributor to quality of life. The Mesifos RCT is designed to compare outcome of targeted versus maintenance treatment in stably remitted patients after a first psychotic episode.

Methods: From October 2001 until January 2003, we included all first psychotic episode patients (n=157) fulfilling trial criteria in

a 3.2 million inhabitant catchment area. Patients (n=131) who remitted within six months and remained stable for another six months were assigned to either maintenance or targeted treatment. First nine months of treatment according to both strategies have been completed.

Results: Duration of untreated psychosis (DUP) was significantly related to time to remission (TTR), a finding reported by several but not all studies. Is DUP an independent predictor of outcome? The analysis focuses on (1) prediction of TTR by DUP and conceivable confounders: duration of prodromal symptoms, diagnosis, gender, age of onset, family history, substance abuse, pretreatment functioning and sociodemographic factors; and (2) prediction of 15 months-outcome after nine months of either maintenance or targeted treatment strategy by DUP, covariates and treatment strategy.

Funded by ZON-mw, Eli Lilly and St. tot Steun.

References:

1. Chan SSM, Ungvari GS: Maintenance therapy in schizophrenia: A critical comment. *International Journal of Neuropsychopharmacology* 2002; 5(3):277-281.

References:

2. Gaebel W, Janner M, Frommann N, Pietzcker A, Kopcke W, Linden M, Muller P, Muller SF, Tegeler J: First vs multiple episode schizophrenia: two-year outcome of intermittent and maintenance medication strategies. *Schizophrenia Research* 2002; 53(1-2):145-159-2.

NR215 Monday, May 23, 3:00 p.m.-5:00 p.m.

Correlation of Serum Gamma-Glutamyl Transferase With Alcohol Consumption

Peter R. Martin, M.D., *Division of Addiction Medicine, Department of Psychiatry, Vanderbilt University Medical Center, 1601 23rd Avenue South, Nashville, TN 37232-8650*; John Loewy, Ph.D., Song Liou, M.S., Bernard Silverman, M.D., Elliot Ehrlich, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that gamma-glutamyl transferase levels corroborate changes in drinking behavior in alcohol dependent patients.

Summary:

Objective: Assess the relationship of an objective laboratory measure of alcohol intake, serum gamma-glutamyl transferase, (GGT) with subjectively reported alcohol consumption in actively drinking patients.

Methods: N=624 DSM-IV alcohol-dependent adults were enrolled in a multi-center, randomized, double-blind, placebo-controlled study: 205 patients received long-acting naltrexone (LA-NTX) 380mg, 210 patients received LA-NTX 190mg, and 209 patients received placebo microspheres monthly for a total of six doses over the 24-week study period. Alcohol consumption was recorded throughout the study using the Timeline Followback (TLFB) method. GGT was collected prestudy and at four-week intervals during the study.

Results: In all groups, decreases in GGT concentrations occurred throughout the observation period, consistent with reduced drinking. Patients in the LA-NTX treatment groups had greater decreases in GGT from baseline at 28, 56, and 84 days compared with placebo-treated patients (P<0.05). An overall treatment effect (reduction in GGT) was observed with LA-NTX (geometric mean ratio LA-NTX vs. Placebo, P<0.05). There was a positive correlation (r=0.282, P<0.0001) between change from prestudy log-transformed GGT test results and change in reported number of drinks per day.

Conclusion: Reduction in reported alcohol consumption with LA-NTX assessed by TLFB correlated with and was corroborated by a reduction in GGT.

References:

1. Sobell LC, Sobell MB: Timeline Followback: a technique for assessing self-reported ethanol consumption. In: Allen J, Litten RZ, eds. Measuring alcohol consumption: psychosocial and biological methods. Totowa, N.J.: Humana Press, 1992: pp.41-72.

NR216 Monday, May 23, 3:00 p.m.-5:00 p.m. **Weight Gain in Psychotic Patients Positive to Cannabis in Admission and Treated With High Doses of Antipsychotic Medication**

Maria Isaac, M.D., *Maudsley Trust - Gresham - PICU, Bethlem Royal Monas, Orchard Road, Beckenham Kent BR3 3BX, United Kingdom*; Michael Isaac, M.D.

Educational Objectives:

The relevance of this study contributes to the growing acknowledgement of the importance of cannabis in psychosis, and illustrates the severity of disturbance associated with cannabis as reflected in the high total doses of medication. Rapid weight gain can cause cardiac failure in psychotic disturbed patients abusing cannabis and in a high carbohydrate (high GI) diet. It also points to the importance of metabolic monitoring in the acute psychiatric setting.

Summary:

Objective: Severely disturbed behavior is a psychiatric emergency. Despite the extensive use of antipsychotic medication to control disturbed behavior, very few studies have considered the metabolic, and cardiac implications of using this medication in high doses over weeks instead of days.

Methods: Open-label, naturalistic study of male patients in psychiatric intensive care. Eleven bedded male psychiatric intensive care unit (PICU) patients have the same diet and opportunities for exercise. We documented each patient's psychiatric history, BPRS, doses of medication, drug abuse, and weight every week for six weeks.

Results: Rapid weight increase caused by the combination of high carbohydrate, high GI diet (64% of the calories, lack of exercise, cannabis abuse, and antipsychotic treatment can cause cardiac failure. There were differences in the percentage of increase in body mass index (BMI) among patients with a history of cannabis abuse as early as the first week of admission (1.04% versus 2.93%) and up to six weeks (-0.91% versus 10.48%). There were correlations between number of incidents and doses of antipsychotic medication.

Conclusion: Patients positive to cannabis at admission required higher total doses of antipsychotic medication due to their aggressive and threatening behavior. The patients positive to cannabis gained weight more rapidly.

Relevance to practice: The relevance of this study contributes to the growing acknowledgement of the importance of cannabis in psychosis, and illustrates the severity of disturbance associated with cannabis as reflected in the high total doses of medication. Rapid weight gain can cause cardiac failure in psychotic disturbed patients abusing cannabis and in a high carbohydrate (high GI) diet. It also points to the importance of metabolic monitoring in the acute psychiatric setting.

References:

1. Marder SR, Essock SM, Miller AL: Physical health monitoring of patients with schizophrenia. *Am J Psychiatry* 2004; 161:1334-1349.

2. Allison DB, Mentore JL, Heo M, Chandler LP, Cappelleri JC, Infante MC, Weiden PJ: Antipsychotic-induced weight gain: a comprehensive research synthesis. *Am J Psychiatry* 1999; 156:1686-1696.

NR217 Monday, May 23, 3:00 p.m.-5:00 p.m. **A Study of Personality Disorder of Methamphetamine Abuse or Dependent Patients in Korea**

Dohoon Kwon, M.D., *Department of Psychiatry, Bugok National Mental Hospital, Bugok-Ri Bugok-Myon, Changnyung-Gun, Gyeongsangnam-635890, Korea*; Sungnam Cho, M.D., Soyoung Kim, M.D., Jungjae Lee, M.D., Jeonghyun Park, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the relationship between methamphetamine use disorder and personality disorders in Korea.

Summary:

Objectives: The purpose of this study was to examine the prevalence of personality disorders between normal control group and hospitalized methamphetamine abuse or dependent patients and, among the latter, the influence of comorbid personality disorder on their global assessment function and general characteristics.

Methods: Subjects were 50 non-methamphetamine abuse or dependent persons in the general population group and 50 methamphetamine abuse or dependent patients admitted to the psychiatric hospital. Methamphetamine abuse or dependence and the global assessment function were diagnosed according to DSM-IV, and the presence of personality disorder was assessed with the PDQ-4+.

Results: In the normal control group, 34% of subjects had at least one personality disorder and the average number of personality disorder was 3.94 per person. In the methamphetamine abuse or dependent group, 64% of the patients had at least one personality disorder and the average number of personality disorder was 4.72 per patient. The presence of comorbid personality disorder was not associated with onset age, dosage, and the number of admissions or arrests among the methamphetamine abuse or dependent group. But, when methamphetamine abuse or dependent patients had more than three personality disorders, the global assessment function was impaired.

Conclusion: In our study, substance-use disorder patients had the higher possibility of comorbid personality disorder in Korea, and among substance use disorder patients, those with comorbid personality disorders were associated with the greater global impairment.

References:

1. Andrew ES, John MO, Peggy EG: Axis II comorbidity of substance use disorders among patients referred for treatment of personality disorders; *Am J Psychiatry* 1999; 156:733-8.
2. Kleinman PH, Miller AB, Woody GE, Todd T, Kemp J, Lipton DS: Psychopathology among cocaine abusers entering treatment. *J Nerv Ment Dis* 1990; 178(7):442-7.

NR218 Monday, May 23, 3:00 p.m.-5:00 p.m. **Acamprosate Is Safe and Well Tolerated for the Treatment of Alcohol Dependence**

Richard N. Rosenthal, M.D., *Department of Psychiatry, St. Luke's Roosevelt Hospital Center, 1090 Amsterdam Avenue, 16th Floor, Suite G, New York, NY 10025*; Allyson Gage, Ph.D., James Perhach, Ph.D., Anita Goodman, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to: (1) Evaluate the safety and tolerability of acamprosate for the treatment of alcohol-dependence, (2) recognize treatment emergent adverse effects in alcohol-dependent patients associated with acamprosate treatment.

Summary:

Introduction: Acamprosate, with adjunctive psychosocial support, has been shown to be effective for the maintenance of abstinence in alcohol-dependent patients.

Methods: Acamprosate safety was assessed in 4,234 alcohol-dependent patients in 13 short-term (≤ 26 weeks) and long-term (≥ 48 weeks) randomized, double-blind, placebo-controlled studies (U.S. and Europe). Eleven studies recorded adverse events (AEs) by spontaneous report from 3,725 alcohol-dependent patients including 2019 treated with acamprosate (1332-3000 mg/day) and 1,706 treated with placebo. Clinical laboratory tests and vital signs were recorded for all groups.

Results: Overall incidence of AEs was 61% for acamprosate compared with 56% with placebo. The majority of AEs in all groups were considered "mild" or "moderate" in severity, with discontinuation rates due to AEs comparable in all groups. The most commonly reported AE ($\geq 3\%$ in either treatment group) was diarrhea (16% acamprosate vs. 10% placebo). All AEs, including diarrhea, had the highest incidence in the first four weeks of treatment and subsequently declined markedly to reach placebo levels. No clinically meaningful between-group differences were reported for any laboratory or vital sign parameters.

Conclusion: Acamprosate is a safe and well tolerated medication for the maintenance of alcohol abstinence in patients with alcohol dependence.

References:

1. Pelc I, Verbanck P, Le Bon O, et al: Efficacy and safety of acamprosate in the treatment of detoxified alcohol-dependent patients. A 90-day placebo-controlled dose-finding study. *Br J Psychiatry* 1997; 171:73-77.
2. Sass H, Soyka M, Mann K, et al: Relapse prevention by acamprosate. Results from a placebo-controlled study on alcohol dependence. *Arch Gen Psychiatry* 1996; 53:673-680.

NR219 Monday, May 23, 3:00 p.m.-5:00 p.m. Topiramate Added to Clozapine: Metabolic Effects, Antipsychotic Augmentation, Safety, and Tolerability: A 12-Week, Open Study

Tony A. Cohn, M.B., *Schizophrenia Program, Centre for Addiction and Mental Health, 1001 Queen Street West, Toronto, Ontario M5S2M8, Canada*; Daniel Bois, R.N., Gary Remington, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to appreciate the benefits and risks of topiramate augmentation in clozapine treated patients.

Summary:

Clozapine therapy all too often results in a partial treatment response and metabolic side effects. The goal of this naturalistic study was to examine the tolerability, and effect on psychotic symptoms and metabolic parameters, of adding topiramate to clozapine.

Method: Twenty clozapine treated patients, including five with type II diabetes, were titrated up to 200 mg/day of topiramate and evaluated over three months. Dose of concomitant medication was kept stable and subjects were on no other antipsychotic medications.

Results: Four patients did not complete the study. One experienced persistent nausea and vomiting that resolved with topiramate discontinuation. Another had worsening of psychotic symptoms and became noncompliant. In 16 remaining subjects, including five diabetics, there was a reduction in weight (2.6 ± 3.7 kg, $p = .015$) and 15% drop in the total BPRS (6.1 ± 8.1 pts, $p = .009$), mostly accounted for by a reduction in anxiety, tension, suspiciousness, and excitement. However, there were no changes in fasting or 2-hr glucose, HbA1c, fasting insulin, insulin sensitivity (Homa - IR) or fasting lipids. Ten experienced paraesthesia. In five this resolved or improved with dose reduction. There were no further changes in weekly hematological measures and repeat measures of liver function (ALT, AST), UKU, Calgary Depression, Barnes, Simpson Angus and AIMS scales.

Conclusion: The addition of topiramate, evaluated over 12 weeks, is a reasonable and safe treatment strategy that results in modest weight loss and symptom reduction in diabetic and non-diabetic clozapine treated patients.

References:

1. Chong SA, Remington G: Clozapine augmentation: safety and efficacy. *Schizophr Bull* 2000; 26(2):421-40.16
2. Henderson DC, Cagliero E, Gray C, et al: Clozapine, diabetes mellitus, weight gain, and lipid abnormalities: A five-year naturalistic study. *Am J Psychiatry* 2000; 157(6):975-81.

NR220 Monday, May 23, 3:00 p.m.-5:00 p.m. First-Episode and Neuroleptic-Free Schizophrenia Patients Have Reduced Insulin Sensitivity: A Minimal Model Analysis

Tony A. Cohn, M.B., *Schizophrenia Program, Centre for Addiction and Mental Health, 1001 Queen Street West, Toronto, Ontario M5S2M8, Canada*; Daniel Bois, R.N., Gary Remington, M.D., Thomas Wolever, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate that patients with schizophrenia are vulnerable to insulin resistance and associated metabolic disturbances such as diabetes. Understand that this vulnerability is present prior to antipsychotic treatment.

Patients with schizophrenia have an increased prevalence of diabetes. While much research attention is being paid to the effects of atypical antipsychotic medication on glucose homeostasis, an equally important area of investigation is whether patients with schizophrenia are prone to diabetes independent of antipsychotic treatment. There is limited evidence in this regard. We are not aware of published studies using rigorous and validated measures of insulin sensitivity and pancreatic beta cell function in neuroleptic free patients with schizophrenia. To investigate this issue, we studied nine patient with schizophrenia prior to antipsychotic treatment and nine healthy controls matched by age, BMI, ethnicity, gender and smoking status using Bergman's Minimal Model Analysis of the Frequently Sampled Intravenous Glucose Tolerance Test.

Compared with controls, subjects (age 26.5 ± 8.8) had significantly reduced insulin sensitivity (Si) (0.498 ± 0.234 versus 0.866 ± 0.373 , $p=0.023$) and a tendency for reduction in Disposition Index (DI) (1370 ± 872 versus 2019 ± 744 , $p = 0.108$) whereas Acute insulin response to glucose (AIRG) was similar. The reduced insulin sensitivity in the subjects was also reflected in a tendency for increased Homa IR ($0.95 \pm .44$ versus 0.18 ± 0.06 , $p=0.089$). These data suggest that, independent of antipsychotic treatment, schizophrenia is associated with insulin resistance. In addition, compensation in insulin secretion is incomplete. The findings are consistent with an increased prevalence of diabetes

in schizophrenia and should be taken into account in evaluating the effect of antipsychotic medication on glucose regulation.

References:

1. Dixon L, Weiden P, Delahanty J, Goldberg R, Postrado L, Lucksted A et al: Prevalence and correlates of diabetes in national schizophrenia samples. *Schizophr Bull* 2000; 26(4):903-12.
2. Thakore JH: Metabolic disturbance in first-episode schizophrenia. *Br J Psychiatry Suppl* 2004; 47:S76-9.

NR221 Monday, May 23, 3:00 p.m.-5:00 p.m.

Alcohol Abuse in Occupational Groups in Iceland

Kristinn Tomasson, M.D., *Department of Research, Administration OHS, Bildshofda 16, Reykjavik 110, Iceland*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate the variation in the prevalence of alcohol abuse among different occupational groups.

Summary:

Introduction: Occupational health-based substance abuse prevention actions need to be based on the prevalence of alcohol and substance abuse related problems in different occupational groups.

Methods: Data were collected in a survey of 4,000 individuals in Iceland in December 2001, aged 18-75 years, selected at random. The response rate was 63.6%. The analysis focuses on those who are on the job market in eight major occupational groups.

Results: A total of 5.1% of the respondents claimed that alcohol consumption or its consequences had adversely affected, their work, work opportunity or studies in the past year. This was insignificantly most common among heavy manual workers (8.8%). In terms of problems associated with medication abuse, 2.1% of the respondents claimed to have had such history. This was most common among heavy manual labor workers (6.0%) and sailors (5.2%). In terms of cannabis use, 24.5% claimed to have used or tried cannabis in their lifetime ranging from 13.4% among farmers to 34.5% among sailors.

Conclusion: Significant variation in alcohol and illegal substance use between occupational group is apparent in accordance with previous studies. Companies' substance-abuse prevention actions should put their main focus on alcohol use prevention strategies.

The study was funded in part by the Icelandic Alcohol and Substance Abuse council

References:

1. Hemmingsson T, Ringback Weitof G: Alcohol-related hospital utilization and mortality in different occupations in Sweden in 1991-1995. *Scandinavian Journal of Work, Environment & Health* 2001; 27:412-9.
2. Mandell W, Eaton WW, Anthony JC, Garrison R: Alcoholism and occupations: a review and analysis of 104 occupations. *Alcoholism: Clinical & Experimental Research* 1992; 16:734-46.

NR222 Monday, May 23, 3:00 p.m.-5:00 p.m.

Investigator Assessment of Clinical Parameters After Initiating Aripiprazole Therapy

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Pharm.D., Taro Iwamoto, Ph.D., Miranda Pans, M.S.C., William H. Carson, Jr., M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand how the effectiveness of aripiprazole can be assessed in a general psychiatric setting.

Summary:

Objective: To determine the effectiveness of initiating aripiprazole therapy in a naturalistic setting as evaluated by investigator assessment of clinical parameters.

Methods: The IAQ is a 12-item, five-point instrument used to record investigators' assessments of patient responses to study medication, including changes in positive and negative symptoms, cognition, mood, energy, somnolence, weight gain, EPS, and akathisia. In an eight-week, naturalistic study, aripiprazole therapy was initiated in 1,295 patients with schizophrenia or schizoaffective disorder requiring change in treatment based on efficacy or tolerability issues.

Results: At endpoint, the majority of aripiprazole-treated patients were rated as doing better than before receiving aripiprazole on positive symptoms (65%), negative symptoms (72%), somnolence (70%), weight (60%), cognition (63%), energy level (75%), and mood (67%). Other items indicated that the majority of patients were rated to be at least the same or better before receiving aripiprazole. A greater proportion of patients who changed medication due to prolactin elevation, EPS, or akathisia improved on these particular symptoms (55%, 72%, and 64%, respectively), compared with the overall patient population.

Conclusions: In this trial, conducted in the general psychiatric setting under naturalistic conditions, the effectiveness of aripiprazole was demonstrated by investigators' assessment of 12 groups of efficacy and tolerability parameters.

References:

1. Goodnick PJ, Jerry JM: Aripiprazole: profile on efficacy and safety. *Expert Opin Pharmacother* 2002; 3(12):1773-81.
2. Gómez JC, Sacristán JA, Hernández J, Breier A, Ruiz Carrasco P, Antón Saiz C, Fontova Carbonell E: The safety of olanzapine compared with other antipsychotic drugs: results of an observational prospective study in patients with schizophrenia (EFESO Study). *Pharmacoepidemiologic study of olanzapine in schizophrenia. J Clin Psychiatry* 2000; 61:335-43.

NR223 Monday, May 23, 3:00 p.m.-5:00 p.m.

Increased Depressive Symptoms Are Associated With Worse Functional Outcomes in Patients Diagnosed With Schizophrenia or Schizoaffective Disorder

Glenn A. Phillips, Ph.D., *Outcomes Research, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Haya Ascher-Svanum, Ph.D., Lei Chen, M.A., Bruce J. Kinon, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the link between greater severity of depressive symptoms of schizophrenia and poorer functional outcomes.

Summary:

Objective: To assess relationships between depressive symptoms and functional outcomes in the treatment of patients diagnosed with schizophrenia or schizoaffective disorder.

Methods: This was a post-hoc analysis of a randomized, double-blind, 24-week study of antipsychotic treatment for patients with schizophrenia or schizoaffective disorders with prominent depressive symptoms (N=394). Measures included the SCAP Health Questionnaire for functional outcomes and the Montgomery-Asb-

erg Depression Rating Scale for depressive symptoms. Associations between depressive symptoms at baseline and functional outcomes at baseline and 24 weeks (LOCF) were evaluated controlling for severity of schizophrenia symptoms (measured with the PANSS) and extrapyramidal symptoms measured with the Barnes Akathisia, the Simpson-Angus Scales, and the AIMS.

Results: At baseline, greater severity of depressive symptoms significantly correlated with a higher likelihood of violent behaviors, suicidal ideations, suicide attempts, and substance use (all $p < .050$). Baseline severity of depressive symptoms was significantly associated with poorer mental health functioning, increased likelihood of suicidal ideations and substance use at endpoint (all $p < .050$). At baseline, depressive symptoms were significantly correlated with positive symptoms and general psychopathology ($p < .001$), but not negative symptoms.

Conclusions: Depressive symptoms in schizophrenia or schizoaffective disorder are associated with worse functional outcomes, both concurrently and after 24 weeks of antipsychotic medication treatment.

References:

1. Lancon C, Auquier P, et al: Relationships between depression and psychotic symptoms of schizophrenia during an acute episode and stable period. *Schizophrenia Research* 2001; 47(2-3): 135-40.
2. Sands JR, Harrow M: Depression during the longitudinal course of schizophrenia. *Schizophrenia Bulletin* 1999; 25(1):157-71.

NR224 Monday, May 23, 3:00 p.m.-5:00 p.m. **Direct Transition to RLAI in Patients Treated With Various Antipsychotics**

Hans-Juergen Moeller, M.D., *Department of Psychiatry, University of Munich, Nussbaumstrasse 7, Munich 80336, Germany*, Pierre-Michel Llorca, M.D., Emilio Sacchetti, M.D., Stephen Martin, M.D., Rossella Medori, M.D., Eduard Parellada, M.D.

Educational Objectives:

This poster shares the information gained from a large international clinical trial investigating the efficacy and safety of a novel treatment in a variety of patients. The analysis of the outcome helps creating realistic and therefore applicable guidance for the transition from one substance or formulation to another.

Summary:

Objective: To study efficacy and safety of risperidone long-acting injectable given to patients with psychotic disorders without an oral risperidone run-in.

Methods: Clinically stable patients received risperidone long-acting injectable 25 mg (increased to 37.5 mg or 50 mg, if necessary) every 14 days for six months.

Results: A total of 1,876 patients (63% male) were included; 74% completed the study. By DSM-IV, 81% of patients had schizophrenia (mainly paranoid). Previous medications (mono- plus polytherapies; monotherapies only) were atypical antipsychotics (54%; 40%), depot (43%; 30%) and conventional oral neuroleptics (14%; 5%). Noncompliance with previous regimen (38%), insufficient efficacy (33%) and side effects (26%) prompted medication change. The total mean PANSS score was reduced significantly at treatment endpoint, as were all PANSS subscales ($p < .001$). At endpoint, 38% of patients had improvement $\geq 20\%$ in PANSS total score. Significant improvements were also seen in the CGI-Severity, GAF scores, all factors of the SF-36, and in patient satisfaction with treatment. Significant improvements in ESRS scores were noted throughout the trial.

Conclusion: In clinically stable psychotic patients with a wide variety of baseline characteristics, symptom control, functioning, as well as quality of life and tolerability improved significantly following direct transition to risperidone long-acting injectable.

References:

1. Fleischhacker WW, Eerdeken M, Karcher K et al: Treatment of schizophrenia with long-acting injectable risperidone: a 12-month open-label trial of the first long-acting second-generation antipsychotic. *J Clin Psychiatry* 2003; 64:1250-7.
2. Kane JM, Aguglia E, Altamura AC, Ayuso Gutierrez JL, Brunello N, Fleischhacker WW, et al: Guidelines for depot antipsychotic treatment in schizophrenia. European Neuropsychopharmacology Consensus Conference in Siena, Italy. *Eur Neuropsychopharmacol* 1998; 8:55-66.

NR225 Monday, May 23, 3:00 p.m.-5:00 p.m. **Patients Previously Treated With Atypical Monotherapy Improve With RLAI**

Per Glue, M.D., *Psychiatric Team, Vestfyn, Sygehus Fyn, Oestre Hougvej 70, Middelfart DK-5500, Denmark*; Wlodzimierz Chrzanowski, M.D., Werner Kissling, M.D., Domenico Buccomino, M.D., Andreas Schreiner, M.D., Rossella Medori, M.D., Eduard Parellada, M.D.

Educational Objectives:

This poster was written to share the knowledge gained from a clinical trial in stable patients suffering from schizophrenia and schizoaffective disorder treated with oral atypical antipsychotics who were switched directly to an injectable long-lasting antipsychotic formulation.

Summary:

Objective: To investigate the efficacy and safety of direct transition to risperidone long-acting injectable in psychotic patients on oral atypical antipsychotics requiring a treatment change.

Methods: Patients with unchanged symptoms on atypicals for \geq one month were switched to risperidone long-acting (25 mg, increased to 37.5 mg or 50 mg, if necessary) injected every 14 days for six months.

Results: Included were 754 patients (61% male) of mean age 38 years; 73% completed the study. Previous treatments were risperidone ($n=572$), olanzapine ($n=119$), amisulpride ($n=37$), quetiapine ($n=22$) and ziprasidone ($n=4$). Mean total PANSS score was significantly reduced from baseline to treatment endpoint (71.8 vs 61.6, $p < .001$), as were all PANSS subscale and symptom factor scores. At endpoint, 39% of patients had a $\geq 20\%$ improvement from baseline in PANSS total score. Significant improvements were also seen in CGI (Disease Severity), Global Assessment of Functioning, all factors of the SF-36 and patient satisfaction with treatment. The ESRS total score was reduced significantly ($p < .001$) from baseline to one month, and these improvements continued until endpoint.

Conclusion: Risperidone long-acting injectable significantly improved symptom control and functioning in schizophrenic patients previously considered clinically stable on monotherapy with an atypical antipsychotic, when directly transitioned without an oral risperidone run-in.

References:

1. Kane JM, Leucht S, Carpenter D, Docherty JP: Expert consensus guideline series. Optimizing pharmacologic treatment of psychotic disorders. Introduction: methods, commentary, and summary. *J Clin Psychiatry* 2003; 64(Suppl 12): 5-19.
2. Kane JM, Aguglia E, Altamura AC, Ayuso Gutierrez JL, Brunello N, Fleischhacker WW, et al: Guidelines for depot antipsychotic treatment in schizophrenia. European Neuropsychopharmacology Consensus Conference in Siena, Italy. *Eur Neuropsychopharmacol* 1998; 8:55-66.

NR226 Monday, May 23, 3:00 p.m.-5:00 p.m.

Sensitivity to Heat Stimuli in Schizophrenia

Gregory Dalack, M.D., *Department of Psychiatry, VA Ann Arbor Healthcare System, 3717 Creekside Court, Ann Arbor, MI 48105-9570*; James Meador-Woodruff, M.D., Kenneth Casey, M.D., Scott Langenecker, Ph.D., Mona Goldman, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to: (1) describe the use of a rigorous methodology to measure heat/pain sensitivity; (2) describe differences in sensitivity between people with schizophrenia and medical controls; (3) describe the relationship between temperature sensitivity and symptom severity and cognitive functioning.

Summary:

Objective: To provide a rigorous characterization of heat sensitivity in schizophrenia in order to determine its utility as a potential biomarker.

Methods: A precise, computer-controlled device was used to produce highly repeatable, graduated heating pulses via a thermode placed on the subject's forearm. Thresholds for warm sensation (WS), heat-pain (HP), and heat tolerance (HT) were compared in 17 individuals with schizophrenia and 20 medical controls. Visual analog scales (VAS) were used to compare subject ratings of intensity and unpleasantness at five different temperatures. Symptom severity was rated with standard scales.

Results: WS thresholds were significantly higher in individuals with schizophrenia compared with controls and correlated positively with negative symptoms. In contrast, HT thresholds were lower in those with schizophrenia and there was no significant difference in HP thresholds. Neither HT nor HP correlated with symptom severity. VAS scores were higher for individuals with schizophrenia at all temperatures examined, but none of these differences attained statistical significance.

Conclusions: Real differences in warmth and pain sensation exist between schizophrenia subjects and controls, but the relationship is complex. The thermal paradigm may be useful in identifying a subset of patients with schizophrenia who might benefit from targeted pharmacologic interventions.

References:

1. Dworkin RH: Pain insensitivity in schizophrenia: A neglected phenomenon and some implications. *Schizophrenia Bulletin* 1994; 20:235-248.
2. Hooley JM, Delgado ML: Pain insensitivity in the relatives of schizophrenia patients. *Schizophrenia Research* 2001; 47:265-273.

NR227 Monday, May 23, 3:00 p.m.-5:00 p.m.

IPSE Project: Use of Inpatient and Outpatient Services and Clinical Features of Schizophrenic Patients Included in Clinical Case Management Programs in Madrid, Spain

Maria Fe Bravo, M.D., *Department of Psychiatry (UAM), Fuencarral Community Mental Health Center, Amado Nervo 3-5-C, Madrid 28007, Spain*; Alberto Fernandez-Liria, M.D., Carlos Gonzalez-Juarez, Ana Belen Santos-Olmo, Maria Alonso, Manuel Muñoz, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate the impact of Clinical Case Management in resource use in schizophrenia patients.

Summary:

The present study is about the differential clinical characteristics and their relationship with use of inpatient services of schizophrenia patients included in three clinical case management (CCM) programs in two catchment areas of Madrid (Spain).

It is part of an effectiveness study of this case management programs (Project IPSE) in schizophrenia patients that have been treated in three CMHC in two catchment areas in Madrid. In this areas there exists a psychiatric case register (PCR) since 1985 that includes information about admissions, emergencies and outpatient care. There have been carried out a differential analysis of the clinical characteristics of the patients included in the programs with those that have not been included.

There have been studied 744 patients diagnosed with schizophrenia according to criteria CIE-10 and that have been attended from January, 2002 to October, 2003 in three CMHC (corresponding to a population of 552.000 inhabitants). Of them 267 were included in programs of CCM with different components (professional caseload, keyworker assignment, written individualized plan, team work, domiciliary visits and control of drop out).

The assessment instruments that have been used are: Positive and Negative Syndrome Scale (PANSS) (Kay SR, Opler LA, Lindenmayer JP., 1989); World Health Organization Disability Assessment Schedule (WHO DAS); Global Assessment of Functioning Scale (DSM-IV); adherence to treatment, and data of admissions, emergencies and outpatient care in PCR.

This research has being supported by the Department of Health.

References:

1. Marshall M, Lockwood A: Assertive community treatment for people with severe mental health disorders in Schizophrenia Module of the Cochrane Database systematic Reviews. Edited by C. Adams and C. Anderson & De Jesus Mari, London: The Cochrane Library. BMJ Publishing Group, 1998.
2. Thornicroft G, Strathdee G, Phelan M, Holloway F, Wykes T, Dunn G, McCrone P, Leese M, Johnson S, Szmukler G: Rationale and design. PRISM Psychosis Study 1. *British Journal of Psychiatry* 1998; 173:363-370.

NR228 Monday, May 23, 3:00 p.m.-5:00 p.m.

Association of Prolactin and Estrogen Levels With Cognitive Function in Women With Chronic Schizophrenia

Won Seung-Hee, M.D., *Department of Psychiatry, Daegu Catholic Medical Center, 3056-6 Daemyung 4 Nam-Gu, Daegu 705-718, South Korea*; Kyung-Phil Kwak, M.D., Kyung-Hee Lim, M.A., Im-Hee Shin, Ph.D., Jong-Hun Lee, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the loss of menses in a chronic schizophrenic woman treated with long-lasting prolactin elevating medications because hyperprolactinemia and secondary hypogonadal status may have associations with some domains of cognitive problems.

Summary:

Objective: To examine the effects of prolactin and estrogen(E2) levels on cognitive functioning in female with chronic schizophrenia.

Method: In naturalistic, cross-sectional study, 30 female (under 45 years) outpatients with chronic schizophrenia were enrolled in this study. All patients were medicated by same antipsychotics

for at least one year as per physician's choice; 15 risperidone (prolactin-elevating potential) and 15 olanzapine (prolactin-sparing potential) patients. Serum prolactin, E2 levels were measured in the midluteal phase of the menstrual cycle, the neuropsychological battery was also assessed at same day.

Results: In comparison between two groups, the olanzapine group presented significant lower mean prolactin ($p=0.000$), higher mean E2 levels ($p=0.025$) and higher scores in verbal fluency ($p=0.028$) than the risperidone group. In partial correlation coefficients, mean prolactin levels showed significant negative correlation with total memory quotients ($r=-0.4701$) and weak negative correlations with verbal memory ($r=-0.3538$), spatial memory ($r=-0.3523$). There was positive correlation between mean E2 levels and continuous attention ($r=0.4121$). Correlations of hormonal levels with executive function, verbal fluency were nonsignificant.

Conclusions: Higher E2 and lower prolactin levels in female patients with chronic schizophrenia are associated with better outcome in some domains of cognitive ability. These results suggest that elevated prolactin levels may have direct and indirect negative effects on ameliorating some domains of cognitive function.

References:

1. Hoff AL, Kremen WS, Wieneke MH, Lauriello J et al: Association of estrogen levels with neuropsychological performance in women with schizophrenia. *Am J Psychiatry* 2001; 158:1134-1139.
2. Rao ML, Kolsch H: Effects of estrogen on brain development and neuroprotection-implications for negative symptoms in schizophrenia. *Psychoneuroendocrinology* 2003; 28:83-96.

NR229 Monday, May 23, 9:00 a.m.-10:30 a.m. **Predictors of Withdrawal and Relapse in Alcohol Dependence**

Laurent Malet, M.D., *Department of Psychiatry B, CHU Clermont Ferrand, Rue Montalembert BP 69, Clermont Ferrand 63000, France*; Pierre-Michel Llorca, M.D., Olivier Blanc, Michel Reynaud, M.D., Bruno Falissard, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to improve management of alcohol dependence.

Summary:

Objectives: Main predictors of relapse in alcohol dependence are age, gender, marital status, and motivational factors. Our objective was to identify (and to compare) predictors of withdrawal.

Method: The study is naturalistic and prospective during 18 months. 135 DSM-IV alcohol dependent patients were followed-up by their usual general practitioners. Clinical and social data were collected on each consultation with standardized questionnaires. Analysis was conducted with Cox's model considering censored data.

Results: 80 withdrawals and 40 relapses occurred during 12 months. Results concerned 875 consultations. Positive predictors of occurring withdrawal were frequency of consultations and alcohol consumption advice (even in a non-structured way). Negative predictors were severity of alcohol dependence (according to DSM IV criteria) and life events (according to axis 4 of DSM IV). Age, gender, marital status, occupational status, earlier withdrawal, duration of alcohol misuse and prescriptions were not linked to withdrawal.

Conclusion: Quantitative management by general practitioners seems to be important in evolution of alcohol dependence. Simple warning and advice about alcohol consumption, frequently repeated, appear to increase maturation and can lead to abstinence. It might be a part of motivational factors. The importance of life

events confirm also the need of a medico-psychosocial management in alcohol dependence.

References:

1. Schuckit MA, Tipp JE, Smith TL, Bucholz KK: Periods of abstinence following the onset of alcohol dependence in 1,853 men and women. *J Stud Alcohol* 1997; 58(6):581-9.
2. Cunningham JA, Lin E, Ross HE, Walsh GW. Factors associated with untreated remissions from alcohol abuse or dependence. *Addict Behav.* 2000 Mar-Apr; 25(2):317-21.

NR230 WITHDRAWN

NR231 Monday, May 23, 9:00 a.m.-10:30 a.m. **The Burden of Depressive Symptoms in the Long-Term Treatment of Patients With Schizophrenia**

Robert R. Conley, M.D., *Spring Grove Hospital Grounds, Maryland Psychiatric Research Center, Maple and Locust Streets, P.O. Box 21247, Baltimore, MD 21228*; Haya Ascher-Svanum, Ph.D., Baojin Zhu, Ph.D., Douglas E. Faries, Ph.D., Qin Jiang, M.S., Bruce J. Kinon, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that people with schizophrenia and concurrent depressive symptoms are prone to have poorer long-term functional outcomes compared with people who are not depressed, with greater use of relapse-related mental health services and higher risk of involvement with law enforcement agencies.

Summary:

Objective: To assess the relationships between depressive symptoms and functional outcomes in the long-term treatment of patients with schizophrenia.

Methods: We used data of a prospective naturalistic study of schizophrenia patients treated in the U.S. Subjects who were depressed at enrollment (scored = 16 on the Montgomery-Asberg Depression Rating Scale) were compared with non-depressed subjects on several functional domains. Outcomes were assessed with patient-reported and clinician-rated measures. Group comparisons were performed at enrollment, at each following year of the study, and across the three-year study, adjusting for various patient characteristics.

Results: At enrollment, 40% of the subjects were depressed. Compared with non-depressed ($N=1351$), the depressed ($N=877$) were more likely to use relapse-related mental health services, to be of greater safety concern in the community, have greater substance-related problems, and have significantly poorer life satisfaction, quality of life, mental health functioning, family relationships, and medication adherence. Findings were similar during each of the three years following enrollment and across the three-year study.

Conclusions: Patients with schizophrenia and depressive symptoms are prone to have poorer long-term functional outcomes compared to patients who are not depressed, characterized by greater use of relapse-related mental health services and higher risk of involvement with law enforcement agencies.

References:

1. Tollefson GD, Andersen SW, Tran PV: The course of depressive symptoms in predicting relapse in schizophrenia: a double-blind, randomized comparison of olanzapine and risperidone. *Biol Psychiatry* 1999; 46:365-373.
2. Lancon C, Auquier P, Reine G, Bernard D, Addington D: Relationships between depression and psychotic symptoms of

schizophrenia during an acute episode and stable period. *Schizophr Res* 2001; 47:135-40.

NR232 **Monday, May 23, 3:00 p.m.-5:00 p.m.**
Substance Use in Schizophrenia: Impact on Effectiveness Trial Attrition

David A. Smelson, Psy.D., *MHBS, VA/University of Medicine and Dentistry, 151 Knollcroft Road, Building 143, Lyons, NJ 07939*; Allen W. Nyhuis, M.S., Douglas E. Faries, Ph.D., Sandra L. Tunis, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the impact of substance use on schizophrenia treatment outcomes.

Summary:

Introduction: Clinical trials involving individuals with schizophrenia often exclude those with co-occurring substance abuse, which is unfortunate given the high rate of comorbidity and negative consequences associated with use. This presentation reports on rates of trial discontinuation among individuals with schizophrenia, with and without co-occurring substance use.

Methods: In a randomized, open-label, one-year effectiveness trial, 236 individuals used substances at baseline, while 394 did not. Patients were further subgrouped by substances of abuse, and compared on time to trial discontinuation using survival analyses adjusted for demographics and baseline covariates.

Results: Substance users were more often male, younger, with shorter psychiatric history than non-substance users. With and without adjustment for baseline group differences, substance users had statistically significantly shorter times to study discontinuation than non-users across abused substances ($p < .001$). Among specific substance use groups, those using cocaine had the highest six-month discontinuation where as cannabis had the highest one-year rates.

Discussion: Individuals with co-occurring substance use appear to have a differential response to treatment with greater discontinuation. Given the need to improve outcomes for this population, which was highlighted in the Presidents Freedom Commission Report on Mental Health, future studies should examine whether particular medications are associated with less attrition.

References:

1. Drake RE, Muser KT: Managing Comorbid Schizophrenia and Substance Abuse, *Curr Psychiatry Rep* 2001; 3:418-422.
2. Havassy BE, Shopshire MS, Quigley LA: Effects of Substance Dependence on Outcomes of Patients in a Randomized Trial of Two Management Models, *Psychiatr Serv* 2000; 51:639-644.

NR233 **Monday, May 23, 3:00 p.m.-5:00 p.m.**
Psychiatric Hospitalizations and Violent Behaviors in the Long-Term Naturalistic Treatment of Patients With Schizophrenia With Olanzapine or Quetiapine

Douglas E. Faries, Ph.D., *Department of Health Outcomes, Eli Lilly, Lilly Corporate Center, Indianapolis, IN 46285*; Haya Ascher-Svanum, Ph.D., Baojin Zhu, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that in the long-term treatment of schizophrenia in usual care settings, olanzapine treatment was associated with a reduced risk of psychiatric hospitalization and a lower likelihood of violent behaviors as compared to quetiapine.

Summary:

Objective: To assess the long-term risk of psychiatric hospitalizations and violent behaviors among schizophrenia patients treated with olanzapine or quetiapine in usual care.

Methods: Analyses included data of patients treated predominantly with olanzapine ($n = 559$) or quetiapine ($n = 111$) in a prospective naturalistic, three-year study of schizophrenia. Medical records provided information about psychiatric hospitalizations, number of admissions, and hospitalized duration. Violent behaviors and medication adherence were assessed with a patient-reported measure. Statistical analyses used Marginal Structural Models, adjusting for patient characteristics and time-dependent illness severity markers at the beginning of each assessment period.

Results: Across the three-year study, quetiapine-treated patients were twice as likely to be hospitalized ($p = .002$), and had approximately 50% more admissions per six-month treatment period ($p = .001$) compared to olanzapine-treated patients. Treatment groups did not differ on total hospitalized duration among hospitalized patients ($p = .644$). Olanzapine-treated patients had a reduced risk of violent behaviors ($p = .011$) and a greater likelihood of medication adherence than quetiapine-treated patients ($p = .028$).

Conclusions: In the long-term treatment of schizophrenia, olanzapine treatment was associated with a reduced risk of psychiatric hospitalization and a lower likelihood of violent behaviors compared to quetiapine. Results may be due to better medication adherence observed during treatment with olanzapine.

References:

1. Swanson JW, Swartz MS, Elbogen EB: Effectiveness of atypical antipsychotic medications in reducing violent behavior among persons with schizophrenia in community-based treatment. *Schizophr Bull* 2004; 30 (1).
2. Ascher-Svanum H, Zhu B, Faries D, Ernst F: A comparison of olanzapine and risperidone on the risk of psychiatric hospitalization in the treatment of patients with schizophrenia. *Annals of General Hospital Psychiatry* 2004; 3:11 <http://www.general-hospital-psychiatry.com/content/3/1/1116>.

NR234 **Monday, May 23, 3:00 p.m.-5:00 p.m.**
Dopamine D3 Receptor Gene and Olanzapine Response in Schizophrenia

John P. Houston, M.D., *Department of Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Sandra Kirkwood, Ph.D., Dong-Jing Fu, Ph.D., David Adams, Ph.D., Mark Farnen, Ph.D., Ann Catherine Downing, Pharm.D., Nitai Mukhopadhyay, Ph.D., Alan F. Breier, M.D.

Educational Objectives:

At the conclusion of the session, the participant should be able to discuss differences in response by DRD-3 genotype to acute olanzapine treatment of patients with schizophrenia.

Summary:

Introduction: Several single nucleotide polymorphisms (SNPs) for dopamine D3 receptor gene (DRD-3) have been associated with differential anti-psychotic response, including ser-9-gly (rs6280).

Method: We assessed response in 82 patients with schizophrenia retrospectively genotyped for SNPs of neuroreceptor genes associated with olanzapine activity. Baseline-to-endpoint reduction in Positive and Negative Schizophrenic Syndrome (PANSS)-positive sub-scores over six weeks of olanzapine treatment was assessed by repeated measures ANOVA. Categorical response was an endpoint rating of mild or minimal or less on each PANSS-positive item.

Results: PANSS-positive reduction for 3 DRD-3 SNPs differed significantly by allelic and genotypic analyses respectively at chromosome 3 positions rs 1800828 ($p=.238$ and $.0130$), rs6280 ($p=.022$ and $.0045$), and rs3732790 (dbSNP) ($p=.0006$ and $.0130$). For each SNP, one homozygous genotype was associated with greatest response ($N=10, 24,$ and $42,$ respectively) compared with the rest of the 82 patients. Of patients homozygous for the more responsive ser-9-gly SNP vs. others, 45.8% vs. 17.24% ($p=.0116$) had at most minimal PANSS-positive symptoms, and 79.2% vs. 58.6% ($p=.127$) had at most mild PANSS-positive symptoms at endpoint.

Conclusions: DRD-3 receptor gene SNPs predicted statistically and clinically significant acute positive symptom reduction with olanzapine in substantial subsets of patients with schizophrenia.

References:

1. Mancama D, Arranz MJ, Kerwin RW: Genetic predictors of therapeutic response to clozapine. *CNS Drugs* 2002; 16(5):317-324.
2. Staddon S, Arranz MJ, Mancama D, Mata I, Kerwin RW: Clinical applications of pharmacogenetics in psychiatry. *Psychopharmacology* 2002; 162:18-23.

NR235 Monday, May 23, 3:00 p.m.-5:00 p.m.

Type of Symptom Remission and Treatment Outcomes in the Long-Term Treatment of Patients With Schizophrenia

John M. Kane, M.D., *Department of Psychiatry, Zucker Hillside Hospital, 75-59 263rd Street Kaufmann Boulevard, Glen Oaks, NY 11004-1150*; Haya Ascher-Svanum, Ph.D., Baojin Zhu, Ph.D., Douglas Faries, Ph.D., Bruce Kinon, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify the best predictors of future nonadherence with antipsychotic medication in the treatment of schizophrenia patients in usual care.

Summary:

Objective: To prospectively examine the relationships between type of symptom remission and type of treatment outcomes during the long-term treatment of patients with schizophrenia.

Methods: Data from a three-year, prospective, naturalistic study of schizophrenia patients were used to identify four mutually exclusive patient groups based on their type of symptom remission: (1) remission of psychotic symptoms, (2) remission of depressive symptoms, (3) remission of psychotic and depressive symptoms, and (4) non-remitted status on depressive and psychotic symptoms. Outcome domains were assessed with validated measures. Effect sizes assessed the differential impact of each remission type relative to the non-remitted group on each outcome variable.

Results: Across the three-year study, remission of psychotic and depressive symptoms was accompanied by best treatment outcomes. Compared with remission of psychotic symptoms, remission of depressive symptoms was more related to specific outcomes, including a lower risk of being violent, suicidal, or using emergency services. Remission of psychotic symptoms was more related to higher functional levels, and better quality of life.

Conclusions: Remission of specific symptom domains appears to differentially contribute to distinct treatment outcomes. Treatments that are able to improve both psychotic and depressive symptoms may provide greater therapeutic benefits and to impact more outcome domains.

References:

1. Kane JM, Krystal J, Correll CU: Treatment models and designs for intervention research during the psychotic prodrome. *Schizophr Bull* 2003; 29:747-756.

2. Kane J: Progress defined-short-term efficacy, long-term effectiveness. *Int Clin Psychopharmacol* 2001; 16 Suppl 1:S1-8.

NR236 Monday, May 23, 3:00 p.m.-5:00 p.m.

Executive Functions Among First-Degree Relatives of Patients With Schizophrenia and Controls

Andrea Cesareni, M.D., *Department of Psychiatry, University of Brescia, P.le Spedali Civili 1, Brescia 25100, Italy*, Paolo Bonacina, M.D., Daniela Borda, M.D., Cesare Turrina, M.D., Larry J. Seidman, Ph.D., Emilio Sacchetti, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize some specific neuropsychological impairment in first-degree relatives of schizophrenia patients.

Summary:

Objectives: The aim of the study was to compare executive functions between non-psychotic, first-degree relatives of schizophrenia subjects and controls.

Methods: We compared a randomized group of first-degree relatives of patients with schizophrenia and healthy controls with a negative family history of psychosis. Inclusion criteria were age between 18 and 40, $IQ>70$, a negative history of substance and alcohol abuse or CNS diseases. Executive functions were assessed with the Object Alternation Test.

Results: Twenty relatives (mean age 26.3 years, 40.0% males, mean IQ 99.1) and 40 controls (mean age 25.6 years, 35% males, mean IQ 102.8) were tested. The two groups were comparable for age, sex and IQ. Significant differences were found in Total Errors (15.4 vs. 7.3, $t=2.5$, $p<.02$) and Total Perseverations (4.2 vs. 1.8, $t=2.2$, $p<.05$). Test Criterion was met by 75.0% of relatives and 95.0% of controls ($\chi^2=3.4$, $p<.03$).

Conclusion: First-degree relatives performed significantly worse in some variables of the Object Alternation Test. This could suggest a vulnerability trait in at-risk subjects, in keeping with recent literature on schizotaxia.

References:

1. Seidman LJ, Oscar-Berman M, Kalinowski AG, Ajilore O, Kremen WS, Faraone SV, Tsuang MT: Experimental and clinical neuropsychological measures of prefrontal dysfunction in schizophrenia. *Neuropsychology* 1995; 9:481-490.
2. Faraone SV, Seidman LJ, Kremen WS, Toomey R, Pepple JR, Tsuang MT: Neuropsychologic functioning among the nonpsychotic relatives of schizophrenic patients: the effect of genetic loading. *Biological Psychiatry* 2000; 48:120-6.

NR237 Monday, May 23, 3:00 p.m.-5:00 p.m.

Risperidone Long-Acting Injectable Functioning in French Patients

Charles-Siegfried Peretti, M.D., *Service du Pr. Ferreri, Hôpital St Antoine, 184, Faubourg St Antoine, Paris 75571, France*; Pierre-Michel Llorca, M.D., Marie-Bénédicte Girard, M.D., Yves Delaunay, M.D., Philippe Durst, M.D., Philippe Bouhours, M.D., Veronique Moreau-Mallet, M.D.

Educational Objectives:

This poster will inform the participants about the impact of a direct treatment change to an injectable long-acting antipsychotic on symptoms, GAF, SF-36 and patient satisfaction in schizophrenia patients in France.

Summary:

Objective: To investigate the effect of a direct transition to risperidone long-acting injectable on patient functioning.

Methods: Adults with schizophrenia or other psychotic disorders who were clinically stable for \geq one month but required a change of treatment, received risperidone long-acting injectable (25 mg, increased to 37.5 mg or 50 mg, if necessary) every 14 days for six months.

Results: Of 202 patients (70% male) with mean age 38 ± 12 years, the majority (86%) had DSM-IV schizophrenia (mainly paranoid). Previous treatments were atypical antipsychotics (64%), depot (34%) and oral (8%) conventional neuroleptics. The mean total PANSS score was significantly reduced from baseline to treatment endpoint (79.4 vs 68.3, $p < 0.001$), as was the score for the General Assessment of Functioning (54.3 vs 61.1). There were significant improvements ($p < 0.05$) from baseline to endpoint in mean scores for all factors of the SF-36, except Bodily Pain. Patient satisfaction with treatment also improved significantly ($p < 0.001$), with 31% rating it as 'very good' at endpoint compared with 8% at baseline.

Conclusion: Risperidone long-acting injectable significantly improved patient functioning, health-related quality of life, and treatment satisfaction. It therefore provides a useful option for the management of patients with psychotic disorders.

References:

1. Lindenmayer JP, Eerdeken E, Berry SA, Eerdeken M: Safety and efficacy of long-acting risperidone in schizophrenia A 12-week, multicenter, open-label study in stable patients switched from typical and atypical oral antipsychotics. *J Clin Psychiatry* 2004; 65:1084-1089.
2. Harrison TS, Goa KL: Long-acting risperidone: a review of its use in schizophrenia. *CNS Drugs* 2004; 18:113-32.

NR238 Monday, May 23, 3:00 p.m.-5:00 p.m.

Tolerability of Risperidone Long-Acting Injectable in French Patients

Pierre-Michel Llorca, M.D., *Psychiatrie B, Service Hospitalier Universitaire, Rue Montalembert, BP 69, Clermont-Ferrand Cedex 1 63003, France*; Charles-Siegfried Peretti, M.D., Pierre Murry, M.D., Christian Guggiari, M.D., Jean-Christophe Loirat, M.D., Philippe Bouhours, M.D., Veronique Moreau-Mallet, M.D.

Educational Objectives:

The participants will learn about the tolerability and safety profile of an injectable long-acting antipsychotic medication directly administered without an oral run-in period to schizophrenia patients in France.

Summary:

Objective: The tolerability of a direct transition to risperidone long-acting injectable in adults with schizophrenia or other psychotic disorders requiring a change of treatment.

Methods: Patients clinically stable for \geq one month received risperidone long-acting injectable (25 mg, increased to 37.5 mg or 50 mg, if necessary) every 14 days for six months.

Results: 202 patients were included in the study (70% male) of mean age 38 ± 12 years. 86% of patients suffered from DSM-IV schizophrenia. 22% needed a treatment change due to adverse events. Previous treatments were atypical antipsychotics (64%), depot (34%) and oral (8%) conventional neuroleptics. The ESRS total score was reduced significantly from baseline (7.4) to one month (5.3), and further until treatment endpoint (3.4) as was the Parkinsonism subscale score: Baseline (5.8); one month (4.1); endpoint (2.6) ($p < 0.001$ throughout). The most frequent treatment-emergent adverse events ($>5\%$) were anxiety (15.3%), insomnia (8.9%) and weight gain (8.9%). Only two injection-site related events were reported and one glucose-related event. Mean weight gain at endpoint was 0.5 kg (N.S.) and there was no significant

change from baseline to endpoint in mean BMI (26.0 vs 26.2 kg/m²).

Conclusion: Direct transition to risperidone long-acting injectable was well tolerated and significantly improved movement disorders.

References:

1. Eerdeken M, Van Hove I, Remmerie B, Mannaert E: Pharmacokinetics and tolerability of long-acting risperidone in schizophrenia. *Schizophrenia Research* 2004; 70:91-100.
2. Chue P: Risperidone long-acting injection. *Expert Rev Neurotherapeutics* 2003; 3:435-46.

NR239 Monday, May 23, 3:00 p.m.-5:00 p.m.

Olanzapine Versus Risperidone: One-Year Results in Positive Symptoms in Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participant should know that these results contribute information regarding the efficacy of olanzapine in residual positive symptoms compared with risperidone in outpatients with schizophrenia.

Summary:

Objective: To evaluate the efficacy in residual positive symptoms of olanzapine (Olz) compared with risperidone (Ris) after one year of treatment in outpatients with schizophrenia with prominent negative symptoms.

Methods: This was a one year, multi-center, randomized, open-label, parallel, dose-flexible study. Prominent negative symptoms were defined as a SANS Global score > 10 . The efficacy measure of positive symptoms was the SAPS Global score. The response rate was defined as a 30% of improvement in the SAPS Global score.

Results: Mean \pm SD dose was 12.2 ± 5.8 mg/day for Olz and 4.9 ± 2.0 mg/day for Ris. There were no baseline-significant differences in SAPS Global score ($p = .116$) in Olz-treated patients (mean \pm SD 6.7 ± 3.8) and Ris-treated patients (6.0 ± 3.5) or in CGI-S ($p = .564$) in Olz-treated patients (4.4 ± 0.7) and Ris-treated patients (4.4 ± 0.8). At one year, Olz-treated patients showed significantly higher improvement than Ris-treated patients on the SAPS Global ($p = 0.021$), and CGI-S ($p = 0.008$) scores. The response rate was greater in Olz-treated patients (65.0%) than the Ris-treated patients (53.9%) although this difference was not significant ($p = 0.08$).

Conclusions: Olanzapine-treated patients showed a significant better improvement in residual positive symptoms measured by SAPS Global than risperidone-treated outpatients with schizophrenia with prominent negative symptoms after one year of treatment.

References:

1. Andreasen NC: Negative Symptoms in Schizophrenia. Definition and reliability. *Arch Gen Psychiatry* 1982; 39:784-788.
2. Tran PV, Hamilton SH, Kuntz AJ, Potvin JH, Andersen SW, Beasley C jr, Tollefson GD: Double-blind comparison of olanzapine versus risperidone in the treatment of schizophrenia and other psychotic disorders. *J Clin Psychopharmacol* 1997; 17:407-418.

NR240 Monday, May 23, 03:00 p.m.-05:00 p.m.

Cognitive Benefits of Quetiapine Versus Risperidone in Schizophrenia

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Educational Objectives:

At the conclusion of the presentation, participants should understand that although both quetiapine and risperidone improve cognitive function in patients with schizophrenia, quetiapine may offer advantages over risperidone with regards to working and verbal memory, as well as an improved EPS profile.

Summary:

Objective: This randomized, double-blind study compared the effect of quetiapine and risperidone on cognitive function in patients with schizophrenia.

Method: Patients (n=44) with predominantly negative symptoms were randomized to quetiapine (400-800 mg/day) or risperidone (4-8 mg/day) for 12 weeks. Cognitive function (reaction time and quality; executive function; working, verbal and visual memory) was assessed at baseline, Week 6 and Week 12. Between-group differences at Week 6 were analyzed using t-tests. The incidence of extrapyramidal symptoms (EPS) was also assessed.

Results: Patients had mild cognitive impairment at baseline. Twenty-five patients completed the study. At Week 6, 19 patients in the quetiapine group and 15 in the risperidone group had cognitive data available for analysis. Mean modal doses at Week 6 were 566.7 mg/day for quetiapine and 4.9 mg/day for risperidone. Cognitive scores improved from baseline to Week 6 in both groups. However, improvements in working and verbal memory were significantly greater with quetiapine ($p < 0.01$ and $p < 0.05$ vs risperidone, respectively). EPS and anticholinergic medication requirement were significantly lower in the quetiapine group.

Conclusions: Although both quetiapine and risperidone improved cognition, quetiapine produced significantly greater improvements in working and verbal memory, with fewer EPS.

References:

1. Kasper S, Resinger E: Cognitive effects and antipsychotic treatment. *Psychoneuroendocrinology* 2003; 28 Suppl 1: 27-38.
2. Velligan DI, Prihoda TJ, Sui D, Ritch JL, Maples N, Miller AL: The effectiveness of quetiapine versus conventional antipsychotics in improving cognitive and functional outcomes in standard treatment settings. *J Clin Psychiatry* 2003; 64: 524-531.

NR241 Monday, May 23, 03:00 p.m.-05:00 p.m.

Fasting Plasma Glucose Levels in an Early Psychosis Program

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Educational Objectives:

At the conclusion of the presentation, the participant should be able to: (1) recognize fasting plasma levels associated with impaired fasting glucose and diabetes mellitus, (2) recognize that elevated fasting plasma glucose is prevalent in the early psychosis population, and (3) demonstrate an awareness that screening for impaired fasting glucose and diabetes in this population might be advisable.

Summary:

Introduction: Literature on fasting plasma glucose (FPG) among early psychosis patients is scarce, despite widespread concern regarding metabolic deterioration associated with second-generation antipsychotic medications.

Objectives: To describe FPG distribution, and prevalence of impaired fasting glucose (IFG, $FPG = 6.1-6.9$ mmol/L, $FPG = 110-125$ mg/dL) and diabetes (DM, $FPG \geq 7.0$ mmol/L, $FPG \geq 126$ mg/dL), among individuals with early psychosis in Calgary, Canada.

Methods: This ongoing cross-sectional survey invites participation of individuals aged 18+ attending a population-based early psychosis program serving outpatients taking antipsychotics for <40 months. A precision-based target sample size of 200 was determined. Data collected include age, sex, ethnicity, body mass index (BMI), and fasting (10-16 hours) glucose.

Results: The sample size after nine months was 101 of the 138 invited (male:female=67:34). Age range was 18-57 (mean=29.3, SD=10.1); 73% were white. The BMI range was 17.3-41.9 (mean=27.6, SD=4.7). FPG ranged from 4.1-6.5 mmol/L (mean=5.0, SD=0.45, median=4.8). Four individuals had IFG (4.0%, 95%CI=1.1-9.8%); none had DM. Those with IFG either had BMI>30, or had age>=45 with BMI>27.

Conclusions/Discussion: Those working with this population should consider the possibility of elevated FPG, in spite of the generally young age and early stage of psychiatric illness. It may be prudent to screen all such patients for IFG and DM.

References:

1. Ryan MC, Collins P, Thakore JH: Impaired fasting glucose tolerance in first-episode, drug-naive patients with schizophrenia. *Am J Psychiatry* 2003; 160(2):284-9.
2. Subramaniam M, Chong SA, Pek E: Diabetes mellitus and impaired glucose tolerance in patients with schizophrenia. *Can J Psychiatry* 2003; 48(5):345-7.

NR242 Monday, May 23, 3:00 p.m.-5:00 p.m.

Prevalence of the Metabolic Syndrome in Patients With Schizophrenia

Jonathan M. Meyer, M.D., *Department of Psychiatry, VA San Diego Healthcare Systems, 3350 La Jolla Village Dr. (116-A), San Diego, CA 92161*; Catherine Loh, Ph.D., Donna Wirshing, M.D., Susan Leckband, R.Ph., Jennifer Boyd, Pharm.D.

Educational Objectives:

At the conclusion of this presentation, the participant will have a greater understanding of the high prevalence of the metabolic syndrome among patients with schizophrenia, and the need for monitoring waist circumference, serum glucose and lipids, and blood pressure in these patients.

Summary:

The metabolic syndrome has become a focus of clinical attention due to its high prevalence in the United States (23.7%), and impact on cardiovascular risk, yet limited data exist on the prevalence of this syndrome among patients with schizophrenia.

Methods: A sample of convenience of patients diagnosed with schizophrenia or schizoaffective disorder was recruited from inpatient units and outpatient clinics at Veterans Affairs medical centers in San Diego and Los Angeles.

Results: This sample of 84 individuals was predominantly male (92.5%), of mean age 49.7 years, and predominantly white (58.3%), with 26.2% black, 8.3% Hispanic, and 7.2% from other ethnic groups. The age-adjusted prevalence of the metabolic syndrome was 51.24%, more than twice the age-adjusted U.S. prevalence. Additionally, the mean fasting glucose of 105 mg/dL falls in the range of impaired fasting glucose (100-125 mg/dL), implying that many of these patients are prediabetic.

Conclusions: The metabolic syndrome is highly prevalent in this sample of schizophrenia patients and represents an enormous source of cardiovascular risk. Clinicians who treat patients with schizophrenia must monitor for the parameters that define the metabolic syndrome as part of the ongoing management of patients on atypical antipsychotics.

References:

1. Ford ES, Giles WH, Dietz WH: Prevalence of the metabolic syndrome among US adults: findings from the third national health and nutrition examination survey. *JAMA* 2002; 287: 356-59.
2. Heiskanen T, Niskanen L, Lyytikäinen R, et al: Metabolic syndrome in patients with schizophrenia. *J Clin Psychiatry* 2003; 64: 575-9.

NR243 Monday, May 23, 3:00 p.m.-5:00 p.m.

Prevalence of the Metabolic Syndrome Among Patients in the CATIE Schizophrenia Trial

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Educational Objectives:

At the conclusion of this presentation, the participant will be knowledgeable about the prevalence of the metabolic syndrome in patients with schizophrenia, the subgroups at highest risk, and the parameters to be monitored as part of routine clinical care.

Summary:

The metabolic syndrome (MS) is a significant risk factor for cardiovascular mortality, yet limited data exist on MS prevalence among patients with schizophrenia, a group at risk for cardiovascular disease.

Method: Using baseline data from the multisite CATIE Schizophrenia Trial, assessment of MS prevalence was performed using the NCEP definition, and an updated definition with lower fasting glucose threshold (100 mg/dl). Only subjects with fasting laboratory measurements (=8 hours since last meal) were included in the analysis.

Results: Among 689 subjects with fasting laboratory measurements (73.9% male, mean age 40.4 years), the crude MS prevalence was 40.9% and 42.7%, respectively, using the NCEP and updated definitions, nearly twice the prevalence for the US population ages 40-49. The MS prevalence was greater among females (NCEP: 51.6% vs. 36.0% for males; $\chi^2=13.46$, $p=.0002$; Updated: 54.2% vs. 36.6% for males; $\chi^2=13.18$, $p=.0003$), but lower among African Americans (NCEP: 29.6% vs. 44.2% for whites $\chi^2=12.86$, $p=.0003$; Updated: 31.5% vs. 47.4% for whites; $\chi^2=14.83$, $p=.0001$). 76.3% of females met the waist circumference criterion compared to 35.5% of males.

Conclusions: The metabolic syndrome is prevalent in this large cohort of schizophrenia patients, especially among females, and represents a significant source of cardiovascular risk.

References:

1. Heiskanen T, Niskanen L, Lyytikäinen R, Saarinen PI, Hintikka J: Metabolic syndrome in patients with schizophrenia. *Journal of Clinical Psychiatry* 2003; 64(5):575-9.
2. Basu R, Brar JS, Chengappa KNR, John V, Parepally H, Schlicht P, Kupfer D: The prevalence of the metabolic syndrome in patients with schizoaffective disorder-bipolar subtype. *Bipolar Disorders* 2004; 6(4):314-8.

NR244 Monday, May 23, 03:00 p.m.-05:00 p.m.

Cognitive Function in Schizophrenia: Effects of Quetiapine and Risperidone

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the relationship between improvements in cognitive functioning following treatment with atypical antipsychotics, such as quetiapine and risperidone, and improved social skills.

Summary:

Objectives: Quetiapine has been reported to have beneficial effects on cognitive functioning in patients with schizophrenia. As part of an efficacy and tolerability study, the effects of quetiapine or risperidone treatment on cognitive functioning and social skills performance were examined in patients with schizophrenia.

Methods: This was an eight-week, double-blind, flexible-dose, parallel study. Patients with schizophrenia were randomized to quetiapine (200-800 mg/day) or risperidone (2-8 mg/day). Cognitive assessments (attention, memory, verbal fluency and executive function) and a social skills performance-based measure were conducted at baseline and endpoint.

Results: Of 673 patients randomized, 134 quetiapine- and 155 risperidone-treated patients had data available at both baseline and endpoint. The mean modal dose (SD) was 530 (288) mg/day and 5 (2) mg/day for quetiapine and risperidone, respectively. A multivariate analysis of variance found both medications were associated with overall improvements in cognitive functioning ($p<0.01$) versus baseline, with no significant differences between the two treatments ($p=0.84$). Significant improvements in social skills performance in both groups ($p<0.01$) were correlated with improvements in executive functioning (quetiapine $r=0.33$, risperidone $r=0.36$; both $p<0.01$)

Conclusions: Treatment with either quetiapine or risperidone is associated with improvement in social skills performance. Furthermore, these improvements were linked to improvements in cognitive functioning.

References:

1. Purdon SE, Malla A, Labelle A, Lit W: Neuropsychological change in patients with schizophrenia after treatment with quetiapine or haloperidol. *J Psychiatry Neurosci* 2001; 26:137-149.
2. Velligan DI, Newcomer J, Pultz J, Csernansky J, Hoff AL, Mahurin R, Miller AL: Does cognitive function improve with quetiapine in comparison to haloperidol? *Schizophr Res* 2002; 53:239-248.

NR245 Monday, May 23, 03:00 p.m.-05:00 p.m.

Economic Burden of Lost Productivity Due to Schizophrenia in the U.S.: 2002

Lizheng Shi, Ph.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Eric Q. Wu, Ph.D., Howard Birnbaum, Ph.D., Ronald Kessler, Ph.D., Lizheng Shi, Ph.D., Daniel Ball, Ph.D., Haya Ascher-Svanum, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand the lost productivity costs of schizophrenia in the United States in 2002. Participants should also be able to understand and identify the indirect cost components that contribute substantially to the economic burden of the disease.

Summary:

Objectives: This study aims to quantify national costs of productivity loss among U.S. patients with schizophrenia in 2002.

Methods: Annual costs were estimated separately for four distinct components of productivity loss: unemployment, reduced workplace productivity, premature mortality from suicide, and family caregiving. Each component was estimated using a human capital approach based on market wages. Schizophrenia prevalence was based on concurrent analysis of the National Comorbidity Survey Replication (NCS-R). A comprehensive literature review was conducted to provide all other information for calculating costs of productivity loss.

Results: The total costs of productivity loss due to schizophrenia were estimated to be over \$30 billion. Unemployment resulted in a cost of over \$20 billion, and was the largest contributor of the total costs. Additionally, lost productivity costs due to reduced work place productivity, premature mortality, and caregiving were approximately \$1 billion, \$1 billion, and \$8 billion, respectively.

Conclusions: Schizophrenia is a debilitating illness resulting in substantial costs due to lost productivity. The magnitudes of these cost estimates suggest the existence of large potential cost savings from more effective management of the illness and more targeted interventions on improving productivity within the schizophrenia population.

References:

- Wyatt RJ, Henter I, Leary MC, Taylor E: An economic evaluation of schizophrenia — 1991. *Soc Psychiatry Psychiatric Epidemiology* 1995; 30:196-205.
- Rice DP, Miller LS: The economic burden of schizophrenia: conceptual and methodological issues, and cost estimates, In *Handbook of Mental-Health Economics and Health Policy*, Volume 1, Schizophrenia. Edited by Moscarelli M, Rupp A, Sartorius N. New York, John Wiley & Sons, 1996, pp321-334.

NR246 Monday, May 23, 3:00 p.m.-5:00 p.m.

Olanzapine in Young Patients With Schizophrenia: Effects on Prolactin Levels

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to rely on more solid safety data including prolactin levels when treating young patients with olanzapine.

Summary:

Background: This study assessed efficacy and safety of olanzapine in young patients with schizophrenia (DSM-IV). Here, we report on prolactin levels.

Methods: Patients received open-label olanzapine for six weeks (5>20mg/day), responders continued for additional 18 weeks. Prolactin levels were measured throughout the study and evaluated by gender. Primary study endpoint was the change in Brief Psychiatric RS (BPRS-6) scores to week 6 (response: 30% reduction).

Results: 100 patients entered the trial (12-21 years), 96 received olanzapine, 80 reached week 6, 34/60 responders completed 24 weeks. Mean maximum dose was 16.7 mg/day. At baseline, the mean prolactin level was 16.9±16.4 ug/l (n=91), for males 12.7±7.5 ug/l (n=66), for females 28.3±25.9 ug/l. By week 6 (LOCF), there were increases in prolactin both for males (p<0.001) and females (p=0.057). Maximum single levels were 58 ug/l (males) and 104 ug/l (females). One female dropped out early because of galactorrhea. BPRS-6 scores at week 6 had de-

creased by 17.0±14.4 points (p<0.001), 62.5% (N=60/96) of the patients were responders.

Conclusions: These young patients experienced increases in prolactin levels that were associated with one early dropout. Clinical efficacy and response rate were very good.

References:

- Dittmann RW: Olanzapine in the treatment of children and adolescents with pervasive developmental disorders. *16 Child & Adolescent Psychopharm News* 2000; 5 (2):1-416.
- Dittmann RW, Junghanß, J: Olanzapin in der Behandlung jugendlicher psychotischer Patienten. *Psychopharmacotherapie* 2001; 8, (2):71-75.

NR247 Monday, May 23, 3:00 p.m.-5:00 p.m.

Validation of a Brief Instrument to Monitor Cocaine Craving

Bradley D. Sussner, Ph.D., *Mental Health and Behavioral Sciences, Department of Veterans Affairs NJ Healthcare System, 151 Knollcroft Road, Building 143 (116A), Lyons, NJ 07939*; Stephanie Rodrigues, B.S., Steven Maslany, M.D., Jeffrey Berman, M.D., Douglas Ziedonis, M.D., David Smelson, Psy.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the utility of a brief, comprehensive and psychometrically sound instrument to measure cocaine craving over the course of psychiatric treatment.

Summary:

Introduction: Although researchers have suggested that substance abusers with a mental illness exhibit persistent cocaine craving that jeopardizes recovery, there are no brief, comprehensive and valid instruments to measure craving as part of a routine substance abuse assessment. The 45-item Cocaine Craving Questionnaire-Now (CCQ-Now) is the most widely used measure to assess current craving, but its length makes its use in clinical work impractical. The 10-item CCQ-Brief has been derived from the full measure, but its psychometric properties have not been established.

Method: 247 cocaine abusers completed the CCQ-Now, the CCQ-Brief, the Addiction Severity Index (ASI), the Beck Depression Inventory-II (BDI-II) and the Beck Anxiety Inventory (BAI). The ASI was included to confirm the validity of the CCQ-Brief and the BAI and the BDI were included due to the relationships among craving, anxiety, and depression.

Results: The CCQ-Brief correlated with the CCQ-Now (r=.65, p<.01), BDI-II (r=.37, p<.01), BAI (r=.34, p<.01), and ASI Psychiatric Status subscale (r=.20, p<.01). The CCQ-Brief correlated with recent drug use (r=.17, p=.01). Internal consistency (alpha=.78) and test-retest reliability (r=.51, p=.02) were strong.

Discussion: The CCQ-Brief is a valid and reliable instrument that clinicians can easily use to monitor cocaine craving over the course of treatment.

References:

- Tiffany ST, Singleton E, Haertzen CA, Henningfield JE: The development of a cocaine craving questionnaire. *Drug and Alcohol Dependence* 1993; 34: 19-28.
- Carol G, Smelson DA, Losonczy MF, Ziedonis D: Alcohol & drug abuse: a preliminary investigation of cocaine craving among persons with and without schizophrenics. *Psychiatric Services* 2001; 52(8): 1029-1031.

NR248 Monday, May 23, 3:00 p.m.-5:00 p.m.

Antipsychotic Treatment Change: 24-Month Results From the SOHO Study

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the frequency, patterns, and reasons of antipsychotic treatment change among patients participating in SOHO during the first two years of follow up.

Summary:

Objective: To report the frequency and patterns of antipsychotic treatment change in outpatients with schizophrenia and how they vary among medications.

Methods: SOHO is a prospective, observational study of outpatient treatment for schizophrenia. Patients were enrolled if they had antipsychotic initiation or change. Treatment was at the discretion of the psychiatrist. Medication change was defined as initiating a new antipsychotic and/or stopping the medication prescribed at baseline. Since the objective was to compare olanzapine with the other antipsychotics, 50% of the sample started olanzapine treatment at baseline. The analysis includes 6801 patients that were assessed at two years.

Results: Overall, 41% of patients changed medication (10% added another antipsychotic, 13% stopped their baseline medication and 18% switched medication). 63% of patients prescribed quetiapine at baseline had switched medication; this proportion for patients initiating clozapine or olanzapine at baseline was 36%. Reasons for change were lack of effectiveness (53%), patient's request (24%), intolerability (20%) and lack of compliance (16%).

Conclusions: Rate of medication change varied among medications. Limitations: (1) due to the sampling strategy, we have more power to detect differences between olanzapine and other cohorts than between the other cohorts, (2) participating psychiatrists may have tended to enrol compliant patients.

References:

1. Haro JM, Edgell ET, Jones PB, Alonso J, Gavart S, Gregor KJ, Wright P, Knapp M, on behalf of the SOHO Study Group: SOHO Study; rationale, methods and recruitment. *Acta Psychiatrica Scandinavica* 2003; 107(3):222-32.
2. Haro JM, Edgell ET, Frewer P, Alonso J, Jones PB on behalf of the SOHO Study Group: The European Schizophrenia Outpatient Health Outcomes Study: baseline findings across country and treatment. *Acta Psychiatr Scand* 2003; 107(Suppl 416):1-9.

NR249 Monday, May 23, 3:00 p.m.-5:00 p.m.

Symptomatic Remission and Social Functioning: 24-Month Results From the SOHO Study

Diego Novick, M.D., *Eli Lilly and Company Limited, Earl Wood Manor, Sunninghill Road, Windlesham GU20 6PH, United Kingdom*; J.M. Haro, M.D., D. Suarez, M.D., S. Tziveleakis, M.D., J.P. Lepine, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the factors that influence symptom remission and adequate social functioning in the outpatient setting.

Summary:

Objectives: To report predictors of symptomatic remission (SR) and adequate social functioning (ASF) of previously untreated schizophrenic patients after two years of antipsychotic treatment.

Methods: SOHO1, 2 is a prospective, observational study of antipsychotic treatment.

SR was defined as a rating of no worse than mild (< 3) for the CGI-severity overall and positive symptoms score and a rating of no worse than moderate (< 4) for the CGI-severity negative symptoms score for six months or longer.

ASF was defined as being employed and having social interactions for six months or longer.

Results: 1,009 monotherapy never-treated patients were enrolled at baseline; 763 were evaluated at 24 months. Seventy-eight % of the sample (585) achieved SR, whereas 47 % (333) achieved ASF. Baseline predictors of higher SR were: lower BMI (0.890;0.842-0.942), living in Northern countries (Germany, UK & Netherlands) vs. Italy and France {(0.328;0.184-0.585)& (0.411;0.191-0.887) respectively} and have started olanzapine at baseline instead of typicals (0.364;0.160-0.826) Baseline predictors of good ASF were: being Employed (13.483;6.412-28.353), living in a Northern countries vs. Spain (0.314;0.62-0.611) and have started Olanzapine instead of risperidone at baseline (0.545;0.303-0.982)

Conclusions: Substantial SR and moderate ASF was achieved after 24 months. Country, treatment, and working status predict SR and ASF.

References:

1. Haro JM, Edgell ET, Jones PB, Alonso J, Gavart S, Gregor KJ, Wright P, Knapp M, on behalf of the SOHO Study Group: SOHO Study: rationale, methods and recruitment. *Acta Psychiatrica Scandinavica* 2003; 107(3):222-32.
2. Haro JM, Edgell ET, Frewer P, Alonso J, Jones PB on behalf of the SOHO Study Group: The European Schizophrenia Outpatient Health Outcomes Study: baseline findings across country and treatment. *Acta Psychiatr Scand* 2003; 107(Suppl 416):1-9.

NR250 Monday, May 23, 3:00 p.m.-5:00 p.m.

Treatment Continuation as a Measure of Effectiveness Among Antipsychotics

Bruce J. Kinon, M.D., *Lilly Research Lab, Eli Lilly And Company, Lilly Corporate Center, Indianapolis, IN 46285*; Hong Liu-Seifert, Ph.D., David Adams, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to discuss differences in treatment discontinuation rates between olanzapine and other atypical antipsychotic medications and the reasons for this difference.

Summary:

Objective: Antipsychotic treatment discontinuation may be used to measure overall treatment effectiveness. Few studies systematically assess early treatment discontinuation differences among antipsychotics. We investigate olanzapine discontinuation compared to other atypical antipsychotics.

Methods: A post hoc, pooled analysis of four randomized, 24-28 week, double-blind clinical trials included 822 olanzapine-treated and 805 risperidone-, quetiapine-, or ziprasidone-treated patients. Discontinuation rates and the probability of staying in treatment were compared between olanzapine and the other atypicals combined.

Results: Poor response/symptom worsening was the primary reason for discontinuation regardless of medication. There was a significant treatment difference in the rate of discontinuation due

to poor response/symptom worsening (olanzapine 14.23% vs. other atypicals 24.60%, $p < .001$). There was no treatment difference in the rate of discontinuation due to medication intolerability (olanzapine 5.60% vs. other atypicals 7.45%, $p = .13$). Olanzapine-treated patients were significantly more likely to complete treatment (53.9% vs. 39.3%, $p < .001$) and stayed in treatment longer (19.1 vs. 16.1 weeks, $p < .001$) than other atypical-treated patients.

Conclusions: The predominant reason for difference in early discontinuation between olanzapine and other antipsychotics was higher dropouts due to poor response/symptom worsening with other antipsychotics. Treatment discontinuation may be an important gauge of relative treatment effectiveness among antipsychotics.

References:

1. Santarlasci B, Messori A: Clinical trial response and dropout rates with olanzapine versus risperidone. *Ann Pharmacother* 2003; 37(4):556-63.
2. Stroup TS, McEvoy JP et al. The National Institute of Mental Health Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) project: schizophrenia trial design and protocol development. *Schizophr Bull* 2003; 29(1):15-31.

NR251 Monday, May 23, 3:00 p.m.-5:00 p.m.

Predictors of Pretreatment Attrition From a Drug Treatment Wait List Program

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Educational Objectives:

At the conclusion of the presentation, the participant should be able to better recognize individuals who are at a greater risk of failing to engage in treatment once placed on a residential substance abuse treatment waitlist program.

Summary:

Introduction: The imbalance between the number of people seeking residential substance abuse treatment and the availability of treatment slots has necessitated the use of waiting lists. Though almost 70% of those placed on waiting lists fail to follow up with treatment, little is known about the predictors of pre-treatment attrition.

Method: 589 people placed on a waiting list at the VA-New Jersey and given a future appointment for admission completed the Addiction Severity Index (ASI) and the Abstinence Self-Efficacy Scale (ASE). The ASI provided information about recent drug use and psychosocial variables and the ASE measured confidence in the ability to remain abstinent and temptation to use substances.

Results: The ASE-Confidence ($p = .03$) and Temptation subscales ($p < .01$); and the ASI alcohol use ($p < .01$), employment ($p < .01$), and drug use ($p = .03$) subscales were significant predictors of treatment engagement.

Discussion: Individuals with little confidence in their ability to remain abstinent and strong temptations to use substances are at greater risk of failing to engage in treatment after placement on a waiting list. Recent substance use and employment problems also increase the likelihood of pre-treatment attrition. Clinicians may consider prioritizing at-risk clients for residential admission, or instituting targeted brief transitional interventions to promote treatment engagement.

References:

1. Donovan D, Rosengren D, Downey L, Cox G, Sloan K: Attrition prevention with individuals awaiting publicly funded drug treatment. *Addiction* 2001; 96: 1149-1160.
2. Parker J: A brief telephone intervention targeting treatment engagement from a substance abuse program wait list. *Journal of Behavioral Health Services and Research* 2002; 29: 288-303.

NR252 Monday, May 23, 3:00 p.m.-5:00 p.m.

Overall Treatment Effectiveness Measured by Time Continuing on Antipsychotic Therapy

Charles M. Beasley, M.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; V.L. Stauffer, Pharm.D., C.P. Mitchell, Ph.D., H. Liu-Seifert, Ph.D., J.M. Davis, M.D., E. Dunayevich, M.D.

Educational Objectives:

At the end of this presentation, the participant should be able to recognize the importance of continuation on antipsychotic therapy in the treatment of schizophrenia and understand how olanzapine compares with other antipsychotics along this measure.

Summary:

Objective: Examine continuation on therapy in double-blind, randomized studies of olanzapine versus other antipsychotics.

Methods: Seventeen double-blind, randomized studies met inclusion criteria (>12 weeks duration; >20 patients/arm; no mandatory discontinuation before 12 weeks; diagnosis: schizophrenia, schizophreniform, or schizoaffective disorders). Weighted mean hazard ratios (HRs) and 95% confidence intervals (CIs) of continuation time were calculated (greater HRs indicate greater risk of discontinuation). When >2 studies met inclusion criteria for a comparator, a meta-analysis was conducted. [numbers of these studies and combined N's: 5, olanzapine ($n=537$) vs. haloperidol ($n=439$); 5, olanzapine ($n=421$) vs. risperidone ($n=426$); 2, olanzapine ($n=550$) vs. ziprasidone ($n=525$); 3, olanzapine ($n=201$) vs. clozapine ($n=202$)]. When only one study met inclusion criteria for a comparator, it was analyzed separately: [olanzapine ($n=30$) vs. fluphenazine ($n=30$); olanzapine ($n=23$) vs. perphenazine ($n=23$); olanzapine ($n=139$) vs. amisulpride ($n=70$); olanzapine ($n=171$) vs. quetiapine ($n=175$)].

Results: HRs (CIs) for comparators included in meta-analyses versus olanzapine were: haloperidol=1.4 (1.2-1.7) ($p < 0.0001$); clozapine=1.2 (0.9-1.6) ($p = 0.312$); risperidone=1.3 (1.1-1.6) ($p = 0.0047$); ziprasidone=1.6 (1.4-2.0) ($p < 0.0001$). HRs (CIs) for single-study comparators versus olanzapine were: fluphenazine=1.82 (0.78-4.27) ($p = 0.169$); perphenazine=1.06 (0.47-2.42) ($p = 0.88$); amisulpride=1.10 (0.77-1.57) ($p = 0.60$); and quetiapine=1.41 (1.06-1.89) ($p = 0.02$).

Conclusions: Treatment continuation appears significantly longer with olanzapine than haloperidol, risperidone, ziprasidone, and quetiapine, but not clozapine.

References:

1. Herz MI, Glazer WM, Mostert MA, et al: Intermittent vs maintenance medication in schizophrenia. *Arch Gen Psychiatry* 1991; 48:333-339.
2. Stroup TS, McEvoy JP, Swartz MS, et al: The National Institute of Mental Health Clinical Antipsychotic trials of intervention effectiveness (CATIE) project: Schizophrenia trial design and protocol development. *Schizophr Bull* 2003; 29:15-31.

NR253 Monday, May 23, 3:00 p.m.-5:00 p.m.

Quality of Life of Minimally Symptomatic Patients Continued on Olanzapine Treatment

Charles M. Beasley, M.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Virginia K. Sutton, Ph.D., Cindy C. Taylor, Ph.D., Gopalan Sethuraman, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that patients taken off active drug treatment after psychotic symptoms are under control do not necessarily function better in terms of QOL than those who are maintained on treatment, even if symptoms do not worsen among those patients discontinuing medication.

Summary:

Objective: To assess whether maintenance treatment with antipsychotics positively or negatively influences quality of life (QOL) among patients with schizophrenia.

Methods: In this post-hoc analysis of our double-blind relapse prevention trial, baseline-to-endpoint mean change on the Heinrichs-Carpenter Quality of Life scale (QLS) were collected from stabilized, minimally symptomatic patients with schizophrenia who had been treated with olanzapine (10-20 mg/day; N=212) or placebo (N=92). Data were analyzed for relapsing, nonrelapsing, and "non-exacerbating" (<10% baseline-to-endpoint PANSS Total worsening) patients.

Results: Significant QLS Total improvements from baseline were observed during treatment with olanzapine (4.3 ± 10.6) compared with placebo (-7.1 ± 14.6 ; $p=0.001$). All QLS between-treatment comparisons were significant for non-relapsing patients, but not for relapsing or non-exacerbating (QLS Total, $p=0.07$) patients. For all patients and for non-relapsing patients in both treatment groups, increases (worsenings) in PANSS Total or Negative scores were associated with decreases (worsenings) in QLS Total (Pearson's correlations from -0.1 to -0.6 , $p<0.05$). Path analysis revealed a direct treatment effect of 20%-30% on QLS Total and subscales after adjusting for changes in psychopathology (PANSS scores).

Conclusions: These data suggest that olanzapine treatment has a positive and partial direct influence on QOL among stable, minimally symptomatic patients with schizophrenia, supporting continuation of antipsychotic treatment even after psychotic symptoms are controlled.

References:

1. Beasley CM, Sutton VK, Hamilton SH, et al.: A double-blind, randomized, placebo-controlled trial of olanzapine in the prevention of psychotic relapse. *J Clin Psychopharmacol* 2003; 23:582-594.
2. Bosveld-van Haandel LJ, Slooff CJ, van den Bosch RJ: Reasoning about the optimal duration of prophylactic antipsychotic medication in schizophrenia: evidence and arguments. *Acta Psychiatrica Scand* 2001; 103:335-346.

NR254 Monday, May 23, 3:00 p.m.-5:00 p.m.

The Ventromedial Striatum in Schizophrenia: An MRI Study

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Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the importance of the nucleus accumbens,

which is relevant for both reward-guided behavior and for the expression of psychosis in schizophrenia, and be able to identify the core structural components that form the limbic frontal-striatal thalamocortical loop.

Summary:

Introduction: The ventromedial striatum (VMS), or the limbic striatum, includes the nucleus accumbens, and the rostral, ventral caudate, and putamen. It is an important component in frontal-subcortical circuitry. It receives afferent innervation from medial orbital and anterior cingulate prefrontal cortex and it projects to other structures which, in turn, project back to these same cortical structures via the thalamus. Additionally, the VMS is further modulated by input from amygdala and hippocampus limbic structures and midbrain DA neurons. It is believed that these brain structures, which are linked via the frontal striatal thalamocortical circuits, are relevant both for reward-guided behaviors, and for the expression of psychosis. We, thus, hypothesized that the VMS may be abnormal in schizophrenia. Hence, using MRI, we assessed the volume of the VMS in schizophrenia and NCLs.

Methods: We measured the VMS, using 1.5 Tesla MRI scans in seven right-handed male, chronic, medicated schizophrenic subjects, and in seven NCLs. We used 1.5 mm SPGR images for absolute volume region of interest measurements and, to correct for head size and calculate relative volumes, we used 3mm spin echo double axial images for whole brain measurements. All SPGR scans were realigned and resampled yielding isotropic voxels. The VMS was defined as striatal tissue inferior to an oblique line formed by the connection between defined points at the inferior-lateral border of the putamen and the medial border of the caudate.

Results: Using Mann-Whitney tests, we found mean left and right absolute (1.66 vs. 1.55 ml, $p<0.75$; 1.56 vs. 1.18 ml, $p=0.11$) and relative (0.114 vs. 0.102%, $p<0.41$; 0.107 vs. 0.078 %, $p=0.064$) VMS volumes were larger in schizophrenics than in NCLs.

Conclusions: Our results are consistent with prior reports of striatal enlargement associated with neuroleptic treatment and suggest this effect of neuroleptics occurs for both ventral and dorsal striatal structures although whether the degree of this effect is similar, or not, requires further research. Future work will further refine volumetric MRI measurement issues regarding this important but challenging structure to assess. It will also account for neuroleptic status and correlate VMS volume with treatment outcome and psychopathological symptoms in schizophrenia.

References:

1. Levitt JJ, McCarley RW, Dickey CC, Vogimaier MM, Niznikiewicz MA, Seidman LJ, Hirayasu Y, Ciszewski AA, Kikinis R, Jolesz FA, Shenton ME: MRI study of caudate nucleus volume and its cognitive correlates in neuroleptic-naïve patients with schizotypal personality disorder. *Am J Psychiatry* 2002; 159:1190-1197.
2. Wise RA: Brain reward circuitry: insights from unsensed incentives. *Neuron* 2002; 36(2):229-40.

NR255 Monday, May 23, 03:00 p.m.-05:00 p.m.

Predictors of Patient Satisfaction With Medication in Patients With Schizophrenia

George Awad, M.D., *Chief of Psychiatry, Humber River Regional Hospital, 2175 Keele Street, Suite #243A, Toronto M6M 3Z4, Canada*; Andrew Greenspan, M.D., Colette Kosik-Gonzalez, M.A., Marcia Rupnow, Ph.D., Amir Kalali, M.D., Jacquelyn McLemore, M.D., Georges Gharabawi, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to assess possible predictors of medication satisfaction in patients with schizophrenia.

Summary:

Background: In a recent placebo-controlled trial of atypical antipsychotics in patients with recently exacerbated schizophrenia, patient-reported satisfaction with their medication was significantly greater with risperidone than with quetiapine or placebo. This report explored whether predictors of medication satisfaction could be identified.

Methods: Multiple hierarchical linear regression models explored the association between medication satisfaction and treatment outcomes (via measures of psychopathology and of adverse events) in recently exacerbated patients with schizophrenia receiving monotherapy with risperidone (N=152), quetiapine (N=156), or placebo (N=71) for two weeks. Patient-rated satisfaction was measured with the Medication Satisfaction Questionnaire (MSQ).

Results: PANSS score emerged as the only significant factor in the models. Greater improvement in symptoms (as measured by the PANSS) was associated with significantly greater medication satisfaction (as measured by the MSQ; $P < 0.001$). Categorical distribution of MSQ scores showed that patients with a 30% or greater PANSS improvement at endpoint were significantly more satisfied with the medication compared with those with <30% improvement ($p < 0.001$). These findings will be discussed in the context of previous research regarding predictors of patient satisfaction with medication.

Conclusion: In this study of patients with schizophrenia, improvement in psychopathology was strongly associated with medication satisfaction. Measures of adverse events did not emerge as significant factors in patient-rated medication satisfaction.

References:

1. Greenspan A, Kosik-Gonzalez C, Bossie C, et al: Readiness to discharge among inpatients with schizophrenia: effects of risperidone, quetiapine, and placebo. Presented at the XXIVth Collegium Internationale Neuro-Psychopharmacologicum Congress, June 20-24, Paris, France.
2. Awad AG, Voruganti LN: New antipsychotics, compliance, quality of life, and subjective tolerability— are patients better off? *Can J Psychiatry* 2004; 49:297-302.

NR256 Monday, May 23, 03:00 p.m.-05:00 p.m. Effects of Lead-in Drinking/Treatment Goal With Long-Acting Naltrexone

Stephanie S. O'Malley, Ph.D., *Department of Psychiatry, Yale University Medical School CMHC, 34 Park Street, Room S202, New Haven, CT 06519*; Ari Illeperuma, M.S., John Loewy, Ph.D., Elliot Ehrich, M.D., Bernard Silverman, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the effects of lead-in drinking and a treatment goal of abstinence on heavy drinking outcomes.

Summary:

Objective: Determine the predictive value of lead-in drinking and a treatment goal of abstinence in heavy drinking outcome; assess interaction with naltrexone.

Methods: A 24-week multicenter, double-blind study. DSM-IV alcohol-dependent patients (N=624) were randomized to long-acting naltrexone (LA-NTX) 380mg, LA-NTX 190mg, or placebo injections monthly for six doses and psychosocial support (BRENDA).

Results: Eighty patients abstinent for the four days before treatment had a 72% greater reduction in heavy drinking relative to patients who had any lead-in drinking. The 380mg treatment effect relative to placebo was 74% in the subgroup without lead-in drink-

ing vs. 19% in patients with lead-in drinking. Patients with no lead-in drinking were more likely to be abstinent (38% vs. 11%).

The 270 patients who had a treatment goal of total abstinence had a 39% greater reduction in heavy drinking during the study vs. patients who had other goals. Estimate of the 380mg dose treatment effect relative to placebo was slightly higher in the subgroup with a goal of total abstinence (28%) vs. patients without a goal of total abstinence (22%).

Conclusion: Abstinence was more likely in LA-NTX-treated patients with lead-in abstinence. Both lead-in abstinence and a goal of total abstinence were associated with better outcomes overall.

References:

1. Volpicelli JR, Pettinati HM, McLellan AT, O'Brien CP: Combining medication and psychosocial treatments for addictions: the BRENDA approach. New York: The Guilford Press; 2001.

NR257 Monday, May 23, 3:00 p.m.-5:00 p.m. Factors Related to Suicidal Risk in Patients With Schizophrenia

Sung-Wan Kim, M.D., *Department of Psychiatry, Chonnam National University Medical School, 5 Hak-Dong, Dong-Gu, Kwangju 501-746, South Korea*; Jin-Sang Yoon, M.D., Bo-Hyun Yoon, M.D., Woong-Jang Kim, M.D., Jeong-Hoon Kim, M.D., Michael Y. Hwang, M.D., Moo-Suk Lee, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the factors that could predict and prevent suicide attempt in patients with schizophrenia in clinical practice.

Summary:

Objective: This study aimed to comprehensively investigate clinical variables related to suicidal risk in patients with schizophrenia.

Method: Study sample consisted of 84 inpatients meeting the DSM-IV criteria for schizophrenia. Clinical Global Impression for Severity of Suicidality (CGI-SS) was modified to 7-point scale, and history of previous suicide attempt was gathered to evaluate suicidal risk. Socio-demographic and clinical variables were collected and the Positive and Negative Syndrome Scale, Beck Depression Inventory, Calgary Depression Scale for Schizophrenia (CDSS), Simpson-Angus Rating Scale, Scale to Assess Unawareness of Mental Disorder, Fagerstrom Test for Nicotine Dependence, and Alcohol Use Disorders Identification Test were assessed to identify factors associated with suicidal risk.

Results: Forty-three subjects (51.2%) reported present clear suicide idea. The subjects with past history of suicide attempt with serious method (n=19) had a significantly higher frequency of present suicide idea ($p < 0.01$). The CGI-SS was significantly correlated with age, age at onset, higher education, severe depressive symptom, and higher insight level. Among those factors, depressive symptom measured by the CDSS was independently associated with the CGI-SS in multivariate analysis.

Conclusion: Our study suggests that assessment of depressive symptom by an objective and specific tool is important to predict and prevent suicidal risk in patients with schizophrenia.

References:

1. Altamura AC, Bassetti R, Bignotti S, Pioli R, Mundo E: Clinical variables related to suicide attempts in schizophrenic patients: a retrospective study. *Schizophr Res* 2003; 60, 47-55.
2. Potkin SG, Alphas L, Hsu C, Krishnan KR, Anand R, Young FK, Meltzer H, Green A, InterSePT Study Group: Predicting suicidal risk in schizophrenic and schizoaffective patients in a prospective two-year trial. *Biol Psychiatry* 2003; 15; 54:444-52.

NR258 Monday, May 23, 3:00 p.m.-5:00 p.m.

Comparison of Clinical Characteristics Between Primary and Secondary Alcoholism in Dually-Diagnosed Alcoholics

Seok Woo Moon, M.D., *Department of Psychiatry, Konkuk University Hospital, 620-5 Kyohyun-2-dong, Chungju-si, Chungcheongbuk-do 380-704, South Korea*; Beom Woo Nam, M.D., Jeong Seok Seo, M.D.

Educational Objectives:

This study was carried out to compare the clinical characteristics between primary psychiatric disorder and secondary alcoholism (hereinafter PPSA) and primary alcoholism and secondary psychiatric disorder (hereinafter PASP) group. So authors aimed to establish the therapeutic plan and method of approach for dually diagnosed patients through understanding the differences of the clinical characteristics between two groups.

Summary:

Objectives: This study was carried out to compare the clinical characteristics between primary psychiatric disorder and secondary alcoholism (PPSA) and primary alcoholism and secondary psychiatric disorder (PASP) group. Authors aimed to establish the therapeutic plan and method of approach for dually-diagnosed patients through understanding the differences of the clinical characteristics between two groups.

Methods: The subjects consist of 128 male and female inpatients who met criteria for dual diagnosis of alcoholism and other mental disorders consecutively admitted to this mental hospital from February 1 to June 30, 2003. The questionnaire included sociodemographic data, past alcohol history, family loading etc. Also, the subjects were screened by NAST (National Alcoholism Screen Test) and CAGE scales. A dual diagnosis was made by charge doctors and chart review including past alcohol history.

Results: (1) There were no differences in demographic characteristics between two groups but over the half of them were lower socioeconomic status. (2) PPSA group had a preference for low degree alcohol beverage, less recognized their addiction severity, more frequently violent behavior and involuntary admission than PASP group ($p < 0.001$). (3) PPSA group were mainly occupied with schizophrenia (39.1%), mood disorder (21.7%), and major depressive disorder (17.4%), but PASP group were mainly occupied with major depressive disorder (40.7%), personality disorder (30.5%), and anxiety disorder (6.8%).

Conclusion: There were many clinical differences between PPSA and PASP group of recognition of addiction severity, violent behavior, mode of admission, and history of suicide. Two groups were dually-diagnosed alcoholics and mentally ill patients, but PPSA group, which have primary psychiatric disorder, were more treatment resisted and complicated "highly risk" group than PASP group which have primary alcohol dependence. Therefore, it is required that therapists consider more intensive evaluation and treatment approach according to their function in dually-diagnosed psychiatric patients.

References:

1. Dixon L, McNary S, Lehman A: One year follow-up of secondary versus primary mental disorder in persons with comorbid substance use disorder. *Am J Psychiatry* 1997; 154(11):1610-1612.
2. Wu LT, Kouzis AC, Leaf PJ: Influence of comorbid alcohol and psychiatric disorders on utilization of mental health services in the national comorbidity survey. *Am J Psychiatry* 1999; 156:1230-1236.

NR259 Monday, May 23, 3:00 p.m.-5:00 p.m.

A Review of the Evidence for Somnolence With Quetiapine Treatment

Jeffrey M. Goldstein, Ph.D., *AstraZeneca, 1800 Concord Pike, PO Box 15437, Wilmington, DE 19850-5437*; Björn Paulsson, M.D., Dennis Sweitzer, M.D., Kate Zhong, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the putative mechanisms involved in somnolence as a side effect of antipsychotic treatment and evaluate the available data on somnolence associated with quetiapine. The participant will gain an improved knowledge of the nature and extent of this effect in patients with schizophrenia.

Summary:

Objective: Quetiapine has high affinity for histamine (H1) receptors, which is associated with somnolence; however, tolerance to this side effect develops rapidly. This analysis assesses the incidence, severity, and duration of somnolence with quetiapine and its possible effect on response to treatment.

Methods: We analyzed somnolence adverse event data from 7,894 patients in 77 quetiapine clinical trials, retrospectively. Sub-analysis of a recent schizophrenia trial versus risperidone was also undertaken.

Results: Overall, 25.5% of patients reported somnolence at least once; in 95% of these, somnolence was mild or moderate. Median duration was eight days, in 19.4% somnolence lasted one day. Only 99/7,894 patients (1.3%) withdrew due to somnolence. An eight-week study comparing quetiapine and risperidone found 26.3% quetiapine- versus 19.8% risperidone-treated patients experienced somnolence. Somnolence with quetiapine was more common at Week 1 (20.4%) than at Week 8 (8.4%). There was no statistically significant association between somnolence on or before a visit and response to treatment with quetiapine (whether defined as $\geq 40\%$ improvement in PANSS or any, much or very much CGI global improvement).

Conclusions: Somnolence with quetiapine is usually mild or moderate, tends to occur early in treatment, is not often persistent, and does not affect response to treatment.

References:

1. Richardson GS, Roehrs TA, Rosenthal L, Koshorek G, Roth T: Tolerance to daytime sedative effects of H1 antihistamines. *J Clin Psychopharmacol* 2002; 22:511-515.
2. Zhong KX, Sweitzer D, Russo J, Potter L, Mullen J: A comparison of the efficacy and safety of quetiapine and risperidone. Poster presented at the 16th Congress of the European College of Neuropsychopharmacology, Prague, Czech Republic, 20-24 September 2003.

NR260 Monday, May 23, 3:00 p.m.-5:00 p.m.

Aripiprazole Reduces Agitation With Minimal Sedation in Special Populations

Maha Radhakrishnan, M.D., *Bristol-Myers Squibb, 777 Scudders Mill Road, Plainsboro, NJ 08536*; Margareta Nyilas, M.D., Owen Randall, M.D., Robert Berman, M.D., Sterling Hardy, M.D., Philippe Auby, M.D., Rene Swanink, M.S.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the need to dissociate antipsychotic efficacy from sedation effects when treating elderly demented patients and pediatric patients with conduct disorder. They will gain insight into how an atypical antipsychotic can reduce agitation without inducing excessive somnolence.

Summary:

Objective: To demonstrate the effectiveness of aripiprazole on agitation while producing minimal sedation in elderly and pediatric patients.

Method: Data were analyzed from two double-blind, randomized, 10-week psychosis in Alzheimer's dementia (AD) trials (institutional settings) and one open-label, 15-day, outpatient study of pediatric conduct disorder. AD trial-1 included flexibly-dosed aripiprazole 2-15 mg/d (n=131) versus placebo (n=125). AD trial-2 used fixed-dose aripiprazole: 2 mg/d (n=118), 5 mg/d (n=122), 10 mg/d (n=126) versus placebo (n=121). Agitation was evaluated using the Cohen-Mansfield Agitation Inventory (CMAI). The pediatric trial included 12 children and 11 adolescents on fixed-dose aripiprazole: 2 mg/d, 5 mg/d, 10 mg/d, assessed with the Ratings for Aggression Against People and Property (RAAPP) scale.

Results: Patients in AD trial-1 showed significant decreases in agitation (CMAI) at endpoint compared with placebo (-10.3 versus -6.2, $p<0.05$). Somnolence rates were aripiprazole 14%, placebo 4%. In AD trial-2, patients on aripiprazole 5 mg/d and 10 mg/d showed significantly decreased agitation across weeks 6-10 ($p<0.05$). Respective somnolence rates were: aripiprazole 2 mg/d=3%, 5 mg/d=10%, 10 mg/d=7%, placebo=3%. In the pediatric study, RAAPP scores shifted toward milder aggression by endpoint. Somnolence occurred in 6/12 children and 0/11 adolescents.

Conclusions: Aripiprazole demonstrated efficacy against agitation with mild to moderate sedation in elderly demented and pediatric conduct disorder patients.

References:

1. Streim JE, McQuade RD, Stock E, Goyvaerts H, Breder C, Iwamoto T, Yasuchika Y: Aripiprazole treatment of institutionalized patients with psychosis of Alzheimer's disease. Presented at the American College of Neuropsychopharmacology Annual Conference, 2003.
2. Findling RL, Blumer JL, Kauffman R, Batterson JR, Gilbert DL, Bramer S, Marcus R: Pharmacokinetic effects of aripiprazole in conduct disorder. Presented at the American Academy of Child and Adolescent Psychiatry Annual Conference, 2003.

NR261 Monday, May 23, 3:00 p.m.-5:00 p.m. Improvement of Hostility in Acute Mania: Data From Two Aripiprazole Trials

Judith Dogin, M.D., Bristol-Myers Squibb Co, PO Box 4500 MS 13-30, Princeton, NJ 08543-4500; Berit Carlson, Pharm.D., Raymond Sanchez, M.D., Andrei Pikalov, M.D., Elyse G. Stock, M.D., Phillipe Auby, Don Archibald, M.S.C.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to discuss the efficacy of aripiprazole in terms of reducing hostility symptoms in patients with an acute manic or mixed episode of bipolar disorder while producing minimal sedation.

Summary:

Objective: To evaluate the improvement in the Positive and Negative Symptom Scale Hostility (PANSS-H) subscale in patients with acute manic/mixed episodes, in a pooled analysis from two aripiprazole trials.

Methods: Data from 177 patients (aripiprazole, 78; placebo, 99) and 246 patients (124, 122) experiencing acute manic/mixed episodes from two three-week, double-blind, randomized, multicenter, placebo-controlled studies. The PANSS-H is comprised of four components: (P4=excitement, P7=hostility, G8=uncooperativeness, and G14=poor impulse control).

Results: As compared with placebo, significant decreases in the PANSS-H scores were shown in the aripiprazole group at

Week 3 (LOCF). These were in Trial 1 (n=177): aripiprazole, mean baseline, 10.8, mean decrease at Week 3, -1.6; placebo, mean baseline 12.3, mean decrease at Week 3, -0.5 ($p=0.01$). In Trial 2 (n=246): aripiprazole mean baseline, 10.6, mean decrease at Week 3, -2.2; placebo, mean baseline 10.7, mean decrease at Week 3, -0.8 ($p=0.01$). The mean incidence of treatment-emergent sedation was 20% in aripiprazole-treated patients and 8% with placebo.

Conclusion: These data demonstrate that in patients with an acute manic/mixed episode, symptoms of excitement, hostility, uncooperativeness, and poor impulse control can be improved during therapy with aripiprazole, an antipsychotic agent with a low incidence of sedation.

References:

1. Keck PE, Marcus R, Tourkodimitris S, Ali M, Liebeskind A, Saha A, Ingenito G, Aripiprazole study group: A placebo-controlled, double-blind study of the efficacy and safety of aripiprazole in patients with acute bipolar mania. *Am J Psychiatry* 2003; 160:1651-1658.
2. Shapiro DA, Renock S, Arrington E, Chiodo LA, Liu LX, Sibley DR, Roth BL, Mailman R: Aripiprazole, a novel atypical antipsychotic drug with a unique and robust pharmacology. *Neuropsychopharmacology* 2003; 28:1400-1411.

NR262 Monday, May 23, 3:00 p.m.-5:00 p.m. Long-Term Weight Change With Quetiapine in Schizophrenia: Data Review

Martin Brecher, M.D., AstraZeneca, 1800 Concord Pike, Wilmington, DE 19850-5437; Ronald Leong, M.D., Lisa Osterling-Koskinen, M.S.C., Martin Jones, M.S.C.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the available data on weight change in patients with schizophrenia treated in the long-term with quetiapine monotherapy, and will gain an improved understating of weight change with atypical antipsychotic treatment.

Summary:

Objective: Determine the magnitude and pattern of weight change in patients with schizophrenia receiving long-term quetiapine, because weight gain is associated with different atypical antipsychotics to varying extents.

Methods: Baseline and final visit weight data from patients with schizophrenia who received quetiapine monotherapy for ≥ 26 weeks in the AstraZeneca clinical trials program were analyzed retrospectively.

Results: Mean treatment duration was 17.8 months and mean modal dose 467mg/day (n=661). Mean and median weight changes were +2.3kg (95% CI 1.6, 3.0) and +1.5kg. Weight change was greatest in underweight patients and not statistically significant in obese patients: in baseline BMI category <18.5 (n=26), mean weight change was +4.0kg (95% CI 1.4, 6.7); $18.5-25$ (n=325), +3.3kg (95% CI 2.4, 4.2); $25-30$ (n=189), +1.6kg (95% CI 0.4, 2.9); and ≥ 30 (n=121) +0.4kg (95% CI -1.6, 2.4). Analysis by modal daily dose showed no relationship with weight change: at doses 300 mg/day or less (n=218), mean change was +2.1kg (95% CI 1.1, 3.2); $>300-500$ mg/day (n=172), +2.7kg (95% CI 1.4, 4.1); and >500 mg/day (n=271), +2.2kg (95% CI 1.0, 3.3).

Conclusions: Mean weight change during long-term (≥ 26 weeks) quetiapine treatment of patients with schizophrenia was +2.3kg. There was no apparent association between weight change and dose of quetiapine.

References:

1. Meyer JM: Effects of atypical antipsychotics on weight and serum lipid levels. *J Clin Psychiatry* 2001; 62(Suppl 27):27-34.

2. Brecher M, Rak IW, Melvin K, Jones AM: The long-term effect of quetiapine (Seroquel™) monotherapy on weight in patients with schizophrenia. *Int J Psychiatry Clin Pract* 2000; 4:287-291.

NR263 Monday, May 23, 3:00 p.m.-5:00 p.m.
Efficacy and Safety of Lower Doses of Aripiprazole

Ronald N. Marcus, M.D., *Department of Department of Neurosciences, Bristol-Myers Squibb, 5 Research Parkway, Wallingford, CT 06492*; Frank Yocca, Ph.D., Elyse G. Stock, M.D., Sterling Hardy, M.S., William H. Carson, Jr., M.D., Robert McQuade, Ph.D., Amy O'Donnell, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the effects of various doses of aripiprazole and about the dose-response effects of this agent in patients with acute exacerbations of schizophrenia.

Summary:

Objective: To obtain information on the effects of aripiprazole in patients with schizophrenia when administered at doses lower than those previously studied systematically.

Method: A double-blind, placebo-controlled, randomized, six-week, multicenter trial. 367 hospitalized patients in acute relapse of schizophrenia were randomized to placebo or one of the fixed doses (2, 5, and 10 mg/d) of aripiprazole. The primary efficacy outcome measure was the mean change from baseline to endpoint (Week 6 LOCF) in the PANSS Total score.

Results: The reduction in PANSS Total score was significantly greater among patients treated with aripiprazole 10 mg/day than among those treated with placebo from week 2 through endpoint (-11.3 vs -5.3, $p=0.030$ at endpoint). The 5 mg/d dose separated from placebo at weeks 3 through 5, but was only numerically superior to placebo at endpoint (-10.6, $p=0.058$). The 2 mg/d dose did not separate from placebo at any point during the trial. All doses of aripiprazole were well tolerated.

Conclusions: Aripiprazole 10 mg/d dose was efficacious for treatment of hospitalized patients with acute exacerbation of schizophrenia; the 5 mg/d dose may be effective for treatment of some patients, and the 2 mg/d dose seems to be lower than the minimally effective dose.

References:

1. Marder SR, McQuade RD, Stock E, Kaplita S, Marcus R, Saferman AZ, Saha A, Ali M, Iwamoto T: Aripiprazole in the treatment of schizophrenia: safety and tolerability in short-term, placebo-controlled trials. *Schizophr Res* 2003; 61(2-3):123-136.
2. Alexopoulos GS, Streim J, Carpenter D, Docherty JP: Expert Consensus Panel for Using Antipsychotic Drugs in Older Patients. Using antipsychotic agents in older patients. *J Clin Psychiatry* 2004; 65(Suppl 2):5-99

NR264 Monday, May 23, 3:00 p.m.-5:00 p.m.
Is Sedation Needed for Effective Reduction of Acute Schizophrenia Symptoms?

David Crandall, Ph.D., *Bristol-Myers Squibb, 777 Scudders Mill Rd, Plainsboro, NJ 08536*; Andrei Pikalov, M.D., Dusan Kostic, Ph.D., Stephen Kaplita, M.S., Robert Berman, M.D., Robert McQuade, M.D., Maha Radhakrishnan, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to appreciate the need to dissociate antipsychotic efficacy from sedation effects when treating patients with schizophrenia. They will gain an understanding of how an atypical antipsychotic

can produce rapid and sustained efficacy without inducing excessive somnolence.

Summary:

Objective: Evaluate the effect of aripiprazole on decreasing hostility and psychosis while producing minimal sedation in schizophrenia.

Methods: Data from six double-blind, randomized schizophrenia trials were included. Five 4-6 week acute inpatient trials were pooled (885 aripiprazole, 405 placebo), and PANSS scores, including the hostility/excitability factor were analyzed. The same measures were analyzed from a 52-week maintenance trial (861 aripiprazole, 433 haloperidol).

Results: In the acute trials, aripiprazole 5-30 mg/d showed significant decreases in PANSS Total, Positive, Negative, and Hostility/Excitability symptoms. Sedation was reported for 8% of the placebo-treated and 11% of aripiprazole-treated patients. Of note, 88% of the patients considered to have responded to therapy based on CGI-I or reduction in PANSS score did not experience sedation. The effects of aripiprazole on reduction of hostility symptoms were found to be independent of sedative effects. In the maintenance trial, aripiprazole 30 mg/d and haloperidol 10 mg/d showed similar reduction of overall symptomatology, as well as similar reduction in hostility/excitability symptoms. Somnolence rates across 52 weeks were 5% with aripiprazole and 8% with haloperidol.

Conclusions: Aripiprazole demonstrated significant improvements in positive, negative, and hostility symptoms with low incidence of sedation across schizophrenia trials. The response to aripiprazole therapy was not related to sedation.

References:

1. Daniel D, Stock E, Wilber R, Marcus R, Carson W, Manos G, Iwamoto T: Intramuscular aripiprazole in acutely agitated psychotic patients. Presented at the American Psychiatric Association 2004 Annual Conference.
2. Kasper S, Lerman MN, McQuade RD, Saha A, Carson W, Ali M, Archibald D, Ingenito G, Marcus R, Pigott T: Efficacy and safety of aripiprazole vs. haloperidol for long-term maintenance treatment following acute relapse of schizophrenia. *Int J Neuropsychopharmacol* 2003; 6:325-37.

NR265 Monday, May 23, 3:00 p.m.-5:00 p.m.
Effects of Long-Term (up to Five Years), Open-Label Treatment With Aripiprazole

William H. Carson, Jr., M.D., *Otsuka America Pharmaceutical Company, 100 Overlook Drive, Princeton, NJ 08540*; Mirza Ali, Ph.D., Anutosh Saha, Ph.D., Robert McQuade, Ph.D., Randall Owen, M.D., Elyse G. Stock, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to discuss the effects of long-term aripiprazole treatment (up to five years) on parameters of efficacy and tolerability in schizophrenic patients as derived from an analysis of open-label extension data.

Summary:

Objective: Pooled data from long-term, open-label extension trials were analyzed for effects of aripiprazole on measures of efficacy and tolerability in schizophrenia patients for periods of up to five years.

Method: Data from 639 patients (639 at one year, 484 at two years, 385 at three years, 209 at four years, and 55 at 5 years) in long-term, open-label extension trials with aripiprazole were pooled. Analysis was performed on efficacy (PANSS and CGI-

severity) and tolerability parameters, including weight and laboratory values.

Results: Efficacy was maintained over time, with improvement noted at each time point (PANSS total score: baseline = 73; improvement at one year = -11, two years = -13, three years = -13, four years = -15, five years = -32). There was minimal weight gain over time, varying from increases of 1.9 kg after one year to 6.7 kg after five years. There were no indications of increases in either total cholesterol or glucose levels over time, and no evidence of QTc prolongation emerged.

Conclusions: Long-term exposure to aripiprazole appeared to result in maintenance of effect, with improvement of symptoms over time. No late-emerging tolerability issues were identified and aripiprazole continued to be well tolerated.

References:

1. Kasper S, Lerman MN, McQuade RD, Saha A, Carson WH, Ali M, Archibald D, Ingenito G, Marcus R, Pigott T: Efficacy and safety of aripiprazole vs. haloperidol for long-term maintenance treatment following acute relapse of schizophrenia. *Int J Neuropsychopharmacol* 2003; 6:325-337
2. Sebastian CS, Glazer W, Buckley PF: Naturalistic studies of second generation antipsychotics in the treatment of schizophrenia. *Curr Med Chem* 2004; 11:329-342

NR266 Monday, May 23, 3:00 p.m.-5:00 p.m. **Individual Symptom Analysis in Pivotal Aripiprazole Schizophrenia Trials**

Randall Owen, M.D., *Bristol-Myers Squibb, 5 Research Parkway, Wallingford, CT 06492*; Robert Berman, M.D., Ashley Pereira, Pharm.D., Joseph Pultz, Ph.D., Andy Forbes, Ph.D., William H. Carson, Jr., M.D., Fred Grossman, D.O.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to gauge the impact of aripiprazole on specific symptom changes in patients with schizophrenia.

Summary:

Objective: To examine efficacy of aripiprazole for amelioration of individual symptoms in patients with acute exacerbation of schizophrenia.

Method: PANSS data were pooled from four 4-6 week acute schizophrenia registrational trials (aripiprazole doses: 5-30 mg/d; n=647 aripiprazole, n=370 placebo). PANSS Total, Positive, Negative, and General Psychopathology scales, as well as all 30 individual PANSS items, were analyzed using analysis of covariance (ANCOVA, controlling for baseline score and trial, LOCF method).

Results: Aripiprazole demonstrated statistically significant decreases compared with placebo on the PANSS Total (-13.5 vs. -3.1; p<0.001), Positive (-4.1 vs. -1.0; p<0.001), Negative (-3.1 vs. -0.8; p<0.001), and General Psychopathology (-6.2 vs. -2.3, p<0.001) scales. Patients on aripiprazole showed significant decreases in 27 of 30 symptoms compared to placebo (p<0.05), including positive symptoms of delusions, disorganization, hallucinations, excitement, grandiosity, suspiciousness, and hostility, negative symptoms of emotional withdrawal, poor rapport, apathetic withdrawal, difficult thinking, lack of spontaneity, and stereotyped thinking, and general symptoms of anxiety, tension, posturing, depression, motor retardation, uncooperativeness, unusual thought content, disorientation, poor attention, lack of judgement, disturbed volition, poor impulse control, preoccupation, and social avoidance.

Conclusions: Acute schizophrenia patients treated with aripiprazole experienced significant improvements in the majority of posi-

tive, negative, and general psychopathology symptoms measured by the PANSS.

References:

1. Kane JM, Carson WH, Saha AR, McQuade RD, Ingenito GG, Zimbroff DL, Ali MW: Efficacy and safety of aripiprazole and haloperidol versus placebo in patients with schizophrenia and schizoaffective disorder. *J Clin Psychiatry* 2002; 63:763-771.
2. Potkin SG, Marder SR: Aripiprazole, an antipsychotic with a novel mechanism of action, and risperidone vs placebo in patients with schizophrenia and schizoaffective disorder. *Arch Gen Psychiatry* 2003; 60:681-690.

NR267 Monday, May 23, 3:00 p.m.-5:00 p.m. **Aripiprazole Versus Olanzapine in Schizophrenia: A 52-Week, Open-Label Study**

Elyse G. Stock, M.D., *Department of Neurosciences Department, Bristol-Myers Squibb Company, 5 Research Parkway, Wallingford, CT 06492-7660*; Margaretta Nyilas, M.D., Robert McQuade, Ph.D., Ronald Marcus, M.D., Dusan Kostic, Ph.D., Anne Torbeyns, Ph.D., Amy O'Donnell, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to describe the long-term efficacy and safety of atypical antipsychotics, including their differing metabolic profiles in patients with acutely relapsing or chronic stable schizophrenia.

Summary:

Objective: Compare long-term efficacy, safety, and metabolic profile of aripiprazole with olanzapine in patients with acute relapsing or chronic stable schizophrenia.

Method: Patients (n=214) who completed (n=112) a 26-week, randomized, double-blind, placebo-controlled trial of aripiprazole in stabilized patients with chronic schizophrenia, or who relapsed (n=102) after at least two weeks of double-blind treatment, entered a randomized, open-label extension trial of aripiprazole (15-30 mg/day, n=104) vs olanzapine (10-20 mg/day, n=110) for up to 52 weeks.

Results: Improvement across all psychiatric scales was comparable with aripiprazole and olanzapine. Olanzapine led to significantly greater mean weight gain compared with aripiprazole (Week 52 (LOCF): 2.54 kg vs 0.04 kg; p<0.001). Significant differences favoring aripiprazole over olanzapine were observed in the mean changes from baseline to Week 52 (LOCF) for fasting total cholesterol (aripiprazole, 1.6 mg/dL; olanzapine, 17.2 mg/dL; p=0.009), fasting LDL (aripiprazole, -1.5 mg/dL; olanzapine, 13.9 mg/dL; p=0.006) and fasting HDL (aripiprazole, +1.1 mg/dL; olanzapine, -2.7 mg/dL; p=0.026).

Conclusions: In acutely relapsing and stable, chronic patients treated for up to 52 weeks, symptom improvement was comparable with aripiprazole and olanzapine. With regard to weight and metabolic factors, aripiprazole was consistently superior to olanzapine.

References:

1. Pigott TA, Carson WH, Saha AR, Torbeyns AF, Stock EG, Ingenito GG, Aripiprazole Study Group: Aripiprazole for the prevention of relapsed in stabilized patients with chronic schizophrenia: a placebo-controlled 26-week study. *J Clin Psychiatry* 2003; 64:1048-1056.
2. Allison DB, Casey DE: Antipsychotic-induced weight gain: a review of the literature. *J Clin Psychiatry* 2001; 62(Suppl 7):22-31.

NR268 Monday, May 23, 3:00 p.m.-5:00 p.m.

Overall Safety of Aripiprazole in Trials of Patients With Psychosis of Alzheimer's Dementia

Christopher Breder, M.D., *Department of Neurosciences Department, Bristol-Myers Squibb, 5 Research Parkway, Wallingford, CT 06492*; Dusan Kostic, Ph.D., Andy Forbes, Ph.D., Ronald Marcus, M.D., Harry Goyvaerts, M.S., Rene Swanink, M.S., William H. Carson, Jr., M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate understanding of safety and tolerability data from pooled clinical trials of aripiprazole-enrolling patients with psychosis of Alzheimer's dementia, including the occurrence of adverse events, with particular emphasis on cerebrovascular AEs.

Summary:

Objective: To describe the safety and tolerability of aripiprazole in patients with psychosis of Alzheimer's dementia (AD).

Method: To date, three placebo-controlled trials have evaluated aripiprazole for treatment of patients with psychosis of AD. Pooled safety data from a total of 938 patients were included in the analysis. In addition, the safety database was searched for occurrences of cerebrovascular adverse events (CVAEs).

Results: AEs led to discontinuation in 14.5% of patients treated with aripiprazole and 9.9% of those treated with placebo. The incidences of most AEs, including EPS, anticholinergic events, and orthostatic events, were similar among patients treated with aripiprazole and those treated with placebo. Somnolence occurred infrequently, but more commonly with aripiprazole (8.6%) than with placebo (2.9%). Of particular interest, CVAEs were reported in 1.3% of aripiprazole-treated and 0.6% of placebo-treated patients; all of the aripiprazole-treated patients experiencing CVAEs had one or more relevant risk factors.

References:

1. Tariot PN, Profenno LA, Ismail MS: Efficacy of atypical antipsychotics in elderly patients with dementia. *J Clin Psychiatry* 2004; 65(suppl 11):11-15.
2. DeDeyn PP, Jeste D, Aubey P, Goyvaerts H, Breder C, Schneider L, Mintzer J: Aripiprazole treatment for psychosis in patients with Alzheimer's disease. *Eur Neuropsychopharm* 2003; 13(suppl 4):S325.

NR269 Monday, May 23, 3:00 p.m.-5:00 p.m.

YMRS Line Analysis of Aripiprazole in Acute Mania: Pooled Data

Raymond Sanchez, M.D., *Bristol-Myers Squibb Company, PO Box 5100, 5 Research Parkway, Wallingford, CT 06492*; Berit Carlson, Pharm.D., Dusan Kostic, Ph.D., Andrei Pikalov, M.D., Taro Iwamoto, Ph.D., Linda Rollin, Ph.D., Judith Dogin, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to discuss the short-term efficacy of aripiprazole in patients with bipolar disorder according to the individual line items by the Young Mania Rating Scale pooled from two three-week, double-blind, multicenter studies.

Summary:

Objective: This pooled analysis of the Young Mania Rating Scale (YMRS) 11-line items evaluated the efficacy of aripiprazole in patients with acute manic or mixed episodes.

Method: Data from 513 patients (254, aripiprazole; 259, placebo) experiencing acute manic or mixed episodes from two three-week, double-blind, randomized, multicenter, placebo-controlled studies were included in this pooled analysis.

Results: In this population, aripiprazole led to significantly greater reduction in YMRS Total Score compared with placebo (endpoint: aripiprazole, -10.76; placebo, -5.52; $p < 0.001$). All YMRS line item scores, except for item 3 (Sexual Interest), demonstrated at endpoint a significant reduction in patients receiving aripiprazole (aripiprazole; placebo): item 1 (Elevated Mood) -1.09; -0.69, $p < 0.001$; item 2 (Increased Motor Activity-Energy) -1.02; -0.68, $p = 0.002$; item 3 (Sexual Interest) -0.54; -0.42, $p = 0.184$; item 4 (Sleep) -0.89; -0.55, $p = 0.001$; item 5 (Irritability) -1.30; -0.23, $p < 0.001$; item 6 (Speech) -1.86; -1.09, $p < 0.001$; item 7 (Language) -0.78; -0.53, $p = 0.003$; item 8 (Content) -1.92; -1.10, $p < 0.001$; item 9 (Disruptive-Aggressive Behavior) -0.79; 0.06, $p < 0.001$; item 10 (Appearance) -0.47; -0.17, $p < 0.001$; item 11 (Insight) -0.20; -0.02, $p = 0.006$.

Conclusion: This pooled analysis demonstrates that aripiprazole is effective in ameliorating the common symptoms experienced by patients with acute manic or mixed episodes of bipolar disorder.

References:

1. Keck PE, Marcus R, Tourkodimitris S, Ali M, Liebeskind A, Saha A, Ingenito G, Aripiprazole study group: A placebo-controlled, double-blind study of the efficacy and safety of aripiprazole in patients with acute bipolar mania. *Am J Psychiatry* 2003; 160:1651-1658.
2. Shapiro DA, Renock S, Arrington E, Chiodo LA, Liu LX, Sibley DR, Roth BL, Mailman R: Aripiprazole, a novel atypical antipsychotic drug with a unique and robust pharmacology. *Neuropsychopharmacology* 2003; 28:1400-1411.

NR270 Monday, May 23, 3:00 p.m.-5:00 p.m.

Nonmedical Prescription Stimulant Use in College Students

John Hall, M.D., *3713 North West 58th Place, Gainesville, FL 32653-0841*; Robert DuPont, M.D., Megan Moncur, M.S., Tavis Glassman, M.P.H., Maureen Miller, M.P.H.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to better understand the population at risk to abuse prescription stimulants and recognize the need for better education and awareness of the abuse of prescription stimulants.

Summary:

Objective: To study the patterns of non-medical prescription stimulant use in a population of college students.

Methods: A cross-sectional anonymous survey of non-medical use of prescription stimulants was conducted in a self-selected sample of college students attending a large Southeastern university; questions included past and current illicit drug use, reasons for use, route of administration, and types of prescription stimulants used non-medically. All participants had reported abuse of prescription stimulants in the past year.

Results: A total of 53 students participated in the survey. The vast majority preferred immediate-release (IR) amphetamine (73.5%) over both extended release (XR) amphetamine (20.4%) and methylphenidate (6.1%). Current polysubstance abuse was common (43.4%) among participants, with 32% smoking marijuana daily and near daily. Most (96.2%) had never been prescribed a stimulant. While studying was the primary reason for using (86%), use for partying was prevalent (24%).

Conclusions: College students reporting abuse of prescription stimulants used amphetamines, particularly IR formulations, more frequently than methylphenidate. Non-medical prescription stimulant users are likely to be polysubstance abusers. Most non-medical prescription stimulant use is as a performance-enhancing agent for studying. More research is needed to identify conse-

quences of use in the population and develop effective prevention programs.

References:

1. Johnston LD, O'Malley PM, Bachman JG, Schulenberg JE: Monitoring the Future national survey results on drug use, 1975-2003. Volume II: College students and adults ages 19-45 (NIH Publication No. 04-5508). Bethesda, MD: National Institute on Drug Abuse, 2004, pp. 267.
2. Low KG, Gendaszek AE: Illicit use of psychostimulants among college students: A preliminary study. *Psychology, Health, & Medicine* 2002; 7(3).

NR271 Monday, May 23, 3:00 p.m.-5:00 p.m. **Improved Quality of Life of Antipsychotic-Treated Patients Who Achieved Remission**

Eduardo Dunayevich, M.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Gopalan Sethuraman, Ph.D., Mark Enerson, M.S., Cindy C. Taylor, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that remission during antipsychotic treatment is an important alternative efficacy measure, which might predict the quality of life of patients with schizophrenia.

Summary:

Objective: To examine whether patients with schizophrenia who attain symptomatic remission during antipsychotic treatment experience greater improvements in quality of life than those who do not.

Methods: Data were retrospectively pooled from six double-blind olanzapine comparator clinical trials. Using severity criteria of two proposed definitions of remission, Kane's (scores of <3 concurrently on PANSS items P1, P2, P3, N1, N4, N6, G5, G9) and Lieberman's (50% reduction in BPRS Total score, scores of <3 concurrently on BPRS psychosis items and CGI-severity), mean changes in Heindrichs-Carpenter quality of life scale (QLS) total scores from baseline to 8, 16, and 24 weeks were analyzed for patients who met one (nonexclusive), both, or neither remission definition.

Results: At each visit, patients who met both or either one of the remission definitions attained significantly greater mean improvement in QLS scores than those who met neither ($p < 0.001$). At Week 24, mean QLS change from baseline was 20.6 ± 21.3 ($n=396$) for patients who met both definitions, 19.6 ± 20.9 ($n=456$) for Lieberman's, 15.4 ± 20.6 ($n=719$) for Kane's, and 3.8 ± 15.8 ($n=610$) for neither.

Conclusions: For patients with schizophrenia, attaining remission during antipsychotic treatment appears to be associated with improvements in quality of life.

References:

1. Kane JM, et al: Optimizing pharmacologic treatment of psychotic disorders: Introduction, methods, commentary, and summary. *J Clin Psychiatry* 2003; 64(Suppl 12):5-19
2. Lieberman JA, et al: Atypical and conventional antipsychotic drugs in treatment-naive first-episode schizophrenia: a 52-week randomized trial of clozapine vs chlorpromazine. *Neuropsychopharmacology* 2003; 28:995-1003

NR272 Monday, May 23, 3:00 p.m.-5:00 p.m. **Olanzapine Dose and Weight Gain**

Eduardo Dunayevich, M.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Gopalan

Sethuraman, Ph.D., Hank Wei, M.S., Venkatraman Prabhakar, M.S., Christopher Carlson, Ph.D., John Davis, M.D.

Educational Objectives:

At the conclusion of this presentation, participants will recognize that in these four fixed-dose clinical trials of olanzapine, there is no consistent dose-response relationship between weight gain and therapeutic doses of olanzapine. Furthermore, dosing effects on weight gain appear modest compared with the effects of age and baseline weight.

Summary:

Objective: To examine the relationship between therapeutic olanzapine doses and weight gain.

Methods: Data were pooled from four (24 to 52 weeks), double-blind, randomized, placebo- or active comparator-controlled clinical trials comparing fixed doses of 5, 10, 15, and 20mg/day olanzapine among patients with schizophrenia. Weight change from baseline was analyzed with a mixed model repeated measures method using treatment (olanzapine dose), week (4, 6, 8-10, 12-14, 16-18, 20-22, 24-26), treatment by week, gender, ethnicity, age, baseline weight, study, and region (North America or Europe) as independent variables. Weight gain during treatment with different olanzapine doses were compared using least square estimates from the model in all patients, and those who completed six and 26 weeks of therapy.

Results: In all patients and in patients that completed 26 weeks of therapy, treatment-emergent weight gain in patients receiving 15mg was significantly greater than patients receiving 5 or 10mg (all patients, $p=.02$ and $p=.01$, respectively; 26 week completers, $p=0.02$ and $p=0.05$, respectively). There were no significant differences between the 20mg group and any other dose group. Weight gain over time for each dose and least square means estimates, dose-weight gain curves for the individual studies and the pooled data will be presented.

References:

1. Kinon BJ, Ahl J, Stauffer VL, Hill AL, Buckley PF: Dose response and atypical antipsychotics. *CNS Drugs* 2004; 18(9):597-616.
2. Nemeroff CB: Dosing the antipsychotic medication olanzapine. *J Clin Psychiatry* 1997; 58(suppl 10):45-49.

NR273 Monday, May 23, 3:00 p.m.-5:00 p.m. **Remission in Acute Mania: Pooled Data From Two Aripiprazole Trials**

Berit Carlson, Pharm.D., *Bristol-Myers Squibb Company, 777 Scudders Mill Road, Plainsboro, NJ 08536*; Judith Dogin, M.D., Raymond Sanchez, M.D., William H. Carson, Jr., M.D., Ronald Marcus, M.D., Joseph Stringfellow, M.S., Robert McQuade, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to discuss the efficacy of aripiprazole in patients with bipolar disorder in terms of remission rates pooled from two three-week, double-blind, multicenter studies.

Summary:

Objective: A pooled analysis from two aripiprazole trials evaluated the remission rates of patients with acute manic or mixed episodes.

Method: Data from 513 patients (254, aripiprazole; 259, placebo) experiencing acute manic or mixed episodes from two three-week, double-blind, randomized, multicenter, placebo-controlled studies were included in this pooled analysis. (i.e. YMRS total score =12)

Results: The aripiprazole group demonstrated a significantly higher response rate (i.e. =50% decrease in the Young Mania Rating Scale [YMRS] total score from baseline) than placebo at all time points during the three-week trials ($p < 0.01$). Similarly, remission rates of the aripiprazole group were significantly greater than placebo at all time points during the three-week trials. These values are as follows (aripiprazole, placebo): Day 4: 15%, 7%, $p = 0.004$; Week 1: 26%, 17%, $p = 0.011$; Day 10: 36%, 21%, $p = 0.001$; Week 2: 39%, 22%, $p = 0.001$; Week 3: 42%, 24%, $p = 0.001$. These data show that within the aripiprazole responder groups, 74% were in remission on Day 4, and by Week 3, 87% of the responders were in remission.

Conclusions: This pooled analysis demonstrates that, as early as Day 4, remission in patients with an acute manic/mixed episode can be achieved with aripiprazole treatment.

References:

1. Keck PE, Marcus R, Tourkodimitris S, Ali M, Liebeskind A, Saha A, Ingenito G, Aripiprazole study group: A placebo-controlled, double-blind study of the efficacy and safety of aripiprazole in patients with acute bipolar mania. *Am J Psychiatry* 2003; 160:1651-1658.
2. Shapiro DA, Renock S, Arrington E, Chiodo LA, Liu LX, Sibley DR, Roth BL, Mallman R: Aripiprazole, a novel atypical antipsychotic drug with a unique and robust pharmacology. *Neuropsychopharmacology* 2003; 28:1400-1411.

NR274 Monday, May 23, 3:00 p.m.-5:00 p.m **Intramuscular Aripiprazole in Acute Schizophrenia: A Pivotal Phase-Three Study**

Frank Yocca, B.Ph., *Department of Neuroscience Biology, Bristol-Myers Squibb Company, PO Box 5100, 5 Research Parkway, Wallingford, CT 06492*; Ronald Marcus, M.D., Dan Oren, M.D., George Manos, Ph.D., William H. Carson, Jr., M.D., Taro Iwamoto, Ph.D., Elyse Stock, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to describe the use of intramuscular formulations of typical and atypical antipsychotics in acutely agitated patients with schizophrenia or schizoaffective disorder.

Summary:

Objective: Compare the efficacy of intramuscular (IM) aripiprazole and haloperidol IM with placebo in acutely agitated patients with schizophrenia or schizoaffective disorder.

Methods: In this double-blind trial, patients were randomized to IM aripiprazole 10 mg, IM haloperidol 6.5 mg or placebo in a 2:2:1 fashion. The first injection was followed by inpatient evaluation for 24 hours. If needed, a second injection was given >2 hours post-initial injection and a third injection, if needed >2 hours post-second injection. For patients randomized to placebo, the third dose contained 10 mg aripiprazole. Primary efficacy measure was the mean change from baseline to two hours (LOCF) post-initial IM injection in the PANSS Excited Component (PEC) score. Patients completing the 24-hour IM phase continued their blinded treatment with tablets/capsules for four days.

Results: Mean changes from baseline in PEC scores two hours post-initial IM injection were aripiprazole ($n = 173$), -7.3; haloperidol ($n = 184$), -7.8; placebo ($n = 88$), -4.8 ($p < 0.001$ for both drugs vs placebo). Mean CGI-I scores two hours post-initial IM injection were aripiprazole, 2.4; haloperidol, 2.4; placebo, 3.1 ($p < 0.001$ vs aripiprazole/haloperidol). Aripiprazole was well tolerated.

Conclusions: Aripiprazole IM shows greater efficacy than placebo and comparable efficacy to haloperidol IM in acutely agitated patients with schizophrenia or schizoaffective disorder.

References:

1. Gismondi R, Daniel D, Stock E, Wilber R, Marcus R, Carson W, Manos G, Iwamoto T: Intramuscular aripiprazole treatment for acute agitation in patients with psychosis *Neuropsychopharmacology* 2004; 14(suppl 3):S261.
2. Zimbroff DL: Management of acute psychosis: from emergency to stabilization. *CNS Spectr* 2003; 8(11 Suppl 2):10-15.

NR275 Monday, May 23, 3:00 p.m.-5:00 p.m. **Intramuscular Aripiprazole Versus Placebo for Agitation in Acute Mania**

Dan Oren, M.D., *Bristol-Myers Squibb, 5 Research Parkway, Wallingford, CT 06492*; Taro Iwamoto, Ph.D., Ronald Marcus, M.D., Simon Vanveggel, M.S.C., Robert McQuade, Ph.D., Elyse G. Stock, M.D., Frank Yocca, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to describe the intramuscular use of medications in acutely agitated patients with bipolar mania.

Summary:

Objective: To compare the efficacy of intramuscular (IM) aripiprazole and IM lorazepam with placebo in acutely agitated patients with a manic or mixed episode in bipolar 1 disorder.

Methods: This double-blinded, randomized, multicenter study compared two doses of IM aripiprazole (10 mg and 15 mg), lorazepam (2 mg), and placebo. The first injection was followed by inpatient evaluation for 24 hours. If needed, a second injection was given >2 hours post-initial injection and a third injection, if needed, >2 hours post-second injection. Primary efficacy measure was the mean change from baseline to two hours (LOCF), post-initial IM injection, in the PANSS Excited Component (PEC) score.

Results: Mean changes from baseline in PEC scores two hours post-initial IM injection were aripiprazole 10 mg ($n = 75$), -8.7; aripiprazole 15 mg ($n = 75$), -8.7; lorazepam 2 mg ($n = 68$), -9.6, placebo ($n = 73$), -5.8 (all active drugs $p < 0.001$ vs. placebo). Aripiprazole was well tolerated in this study.

Conclusion: Aripiprazole IM shows efficacy significantly improved over placebo and similar to that of IM lorazepam in the treatment of agitation in patients with bipolar I disorder, manic or mixed.

References:

1. Keck PE, Marcus R, Tourkodimitris S, Ali M, Liebeskind A, Saha A, Ingenito G: A placebo-controlled, double-blind study of the efficacy and safety of aripiprazole in patients with acute bipolar mania. *Am J Psychiatry* 2003; 160:1651-1658.
2. R Gismondi, D Daniel, E Stock, R Wilber, R Marcus, W Carson, G Manos, T Iwamoto: Intramuscular aripiprazole treatment for acute agitation in patients with psychosis *Neuropsychopharmacology* 2004; 14(suppl 3):S261.

NR276 Monday, May 23, 3:00 p.m.-5:00 p.m. **Acamprosate Efficacy in Alcohol-Dependent Patients: Summary of Three Pivotal Studies**

Allyson Gage, Ph.D., *Forest Laboratories, Inc., 909 Third Avenue, New York, NY 10022*; Sylvie Chabac, M.D., Anita Goodman, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to (1) recognize that acamprosate is an effective treatment for alcohol dependence, using the most stringent definition of "complete abstinence," (2) appreciate that acamprosate provides

incremental benefits to psychosocial support in reducing drinking among alcohol-dependent patients.

Summary:

Introduction: Acamprosate is indicated, in conjunction with psychosocial support, for the maintenance of abstinence in alcohol dependent patients. Data from three previously published trials have been re-analyzed, applying a consistent definition of "complete abstinence," the primary measure of efficacy.

Methods: Using uniform patient tracking and data recording methodology in the three double-blind, placebo-controlled, pivotal efficacy trials of acamprosate, the rate of complete abstinence, was re-assessed. Additional efficacy outcomes calculated in this re-analysis were the percent days abstinent and time to first drink. For all efficacy measures, dropouts were considered treatment failures. A total of 998 alcohol-dependent patients (623 treated with acamprosate 1332 or 1998 mg/day and 375 who received placebo) were included in the re-analysis.

Results: The efficacy of acamprosate was confirmed across all efficacy measures in all three pivotal studies. The rate of complete abstinence was statistically significantly higher with acamprosate 1998 mg/day (16%-38%) compared with placebo (9%-13%, $p < 0.05$). Both percent days abstinent and time to first drink were statistically significantly greater among acamprosate-treated patients compared with placebo ($p < 0.01$).

Conclusions: Re-analyses of three pivotal trials using a more stringent definition of abstinence confirmed that acamprosate is effective in the treatment of alcohol dependence.

References:

1. Paille FM et al: Double-blind randomized multicentre trial of acamprosate in maintaining abstinence from alcohol. *Alcohol* 1995; 30: 239-47.
2. Pelc I, et al: Efficacy and safety of acamprosate in the treatment of detoxified alcohol-dependent patients. A 90-day placebo-controlled dose-finding study. *Br J Psychiatry* 1997; 171: 73-7.

NR277 Monday, May 23, 3:00 p.m.-5:00 p.m. **Polypharmacy in Schizophrenia: Data From a Randomized, Double-Blind Study**

Marcia Rupnow, Ph.D., *Department of Outcomes Research, Janssen Medical Affairs, L.L.C., 1125 Trenton Harbourton Road, Titusville, NJ 08560*; Andrew Greenspan, M.D., Colette Kosik-Gonzalez, M.A., Cynthia Bossie, Ph.D., Young Zhu, Ph.D., Georges Gharabawi, M.D., Stephen Stahl, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the incidence and costs of polypharmacy in patients treated with antipsychotics.

Summary:

Background: The use and predictors of polypharmacy were examined in patients with an acute exacerbation of schizophrenia or schizoaffective disorder randomized to risperidone ($n=133$), quetiapine ($n=122$), or placebo ($n=53$).

Methods: In a double-blind study, a 14-day monotherapy phase was followed by a 28-day additive-therapy phase during which clinicians were allowed to add psychotropic medications. Risperidone and quetiapine doses were fixed by day 8. Predictors of polypharmacy were analyzed using multiple regression models.

Results: Mean \pm SD doses at monotherapy endpoint were 4.7 ± 0.9 mg/day of risperidone and 579.5 ± 128.9 mg/day of quetiapine. During the additive-therapy phase, additional psychotropics (including antipsychotics, mood stabilizers and antidepressants) were received by 36% of patients in the risperidone group and 53% in the quetiapine group ($P=.006$); 59% of placebo patients

received psychotropics. Additional antipsychotics were received by 33% and 53% of risperidone- and quetiapine-treated patients, respectively ($P < 0.005$); 57% of placebo patients received antipsychotics. Relative risk of antipsychotic polypharmacy (quetiapine vs risperidone) was 1.90 (95%CI 1.29-2.80). Among symptoms and other outcomes assessments, CGI-S, PANSS Hostility/Excitement factor, and patient satisfaction with medication were significantly associated with antipsychotic polypharmacy.

Conclusions: Quetiapine was associated with a significantly higher rate of polypharmacy than risperidone. Poorer overall clinical improvement and hostility/excitement symptoms were among the strongest predictors of antipsychotic polypharmacy use.

References:

1. Stahl SM, Grady MM: A critical review of atypical antipsychotic utilization: comparing monotherapy with polypharmacy and augmentation. *Curr Med Chem* 2004; 11:313-327.
2. Clark RE, Bartels SJ, Mellman TA, Peacock WJ: Recent trends in antipsychotic combination therapy of schizophrenia and schizoaffective disorder: implications for State mental health policy. *Schizophr Bull* 2002; 28:75-84.

NR278 Monday, May 23, 3:00 p.m.-5:00 p.m.

Reliability and Validity of the Readiness for Discharge Questionnaire in Schizophrenia

Marcia Rupnow, Ph.D., *Department of Outcomes Research, Janssen Medical Affairs, L.L.C., 1125 Trenton Harbourton Road, Titusville, NJ 08560*; Charles Ruetsch, Ph.D., Dennis Revicki, Ph.D., Colette Kosik-Gonzalez, M.A., Andrew Greenspan, M.D., Georges Gharabawi, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand the reliability and validity of Readiness for Discharge Questionnaire (RDQ), a new instrument to assess discharge readiness among inpatients with schizophrenia and understand the benefits of using the RDQ in clinical research of patients with schizophrenia.

Summary:

Background: This study evaluated the reliability and validity of the Readiness for Discharge Questionnaire (RDQ), a new research tool for inpatients with schizophrenia.

Methods: Using a Likert scale, the RDQ items assess suicidality/homicidality, control of aggression/impulsivity, activities of daily living, medication-taking, and delusions/hallucinations interfering with functioning. A final yes/no question assesses readiness for discharge. Data were derived from three studies. Analyses included inter-rater and test-retest reliability, content and construct validity, and responsiveness.

Results: The inter-rater reliability was high on all items of the RDQ (reliability coefficient > 0.9) and the readiness status (polychoric correlation $r=.81$). Test-retest reliability was also high on all items of the RDQ (reliability coefficient > 0.9) and the readiness for discharge status (tetrachoric correlation $r=.82$). Content validity was favorable. The RDQ was rated as a useful tool by 84% of the respondents. Evidence of good construct validity included significant correlations with PANSS total and factor scores, and a significant relationship with actual discharge. Significantly more patients with symptom improvement were ready for discharge (compared to those without symptom improvement), indicating that the RDQ was responsive to change over time.

Conclusions: The RDQ has favorable reliability and validity properties, and appears to be a useful tool for assessing the outcomes of interventions among inpatients with schizophrenia.

References:

1. Hogarty GE, Ulrich R: The discharge readiness inventory. Arch Gen Psychiatry 1972; 26(5):419-426.
2. Greenspan A, Kosik-Gonzalez C, Bossie C: Readiness to discharge among inpatients with schizophrenia: effects of risperidone, quetiapine, and placebo. Poster presented at the XXXIVth Collegium Internationale Neuro-Psychopharmacologicum Congress, June 20-24, 2004, Paris, France.

NR279 Monday, May 23, 3:00 p.m.-5:00 p.m.

Atypical Antipsychotics in Patients With Schizophrenia and Comorbid Substance Abuse

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the effects of comorbid substance abuse on treatment responses in patients with schizophrenia.

Summary:

Background: Substance abuse, reported in 20% to 40% of patients with schizophrenia, can complicate treatment regimens and their effectiveness. Treatment responses were evaluated in patients with schizophrenia and substance abuse in a six-week double-blind study. Each patient had recently experienced an acute exacerbation of psychosis that required hospitalization.

Methods: Patients with schizophrenia received risperidone, quetiapine, or placebo monotherapy for two weeks, followed by four weeks during which additional psychotropics were permitted. Efficacy data were analyzed from the two-week monotherapy phase comparing patients with and without substance abuse. Substance abuse=a positive urine drug screen (excluding benzodiazepines) or patients' self-report of prior substance abuse (alcohol, cocaine/amphetamines, marijuana, or opiates).

Results: Of the 382 patients, 111 were substance abusers; 51 received risperidone, 40 quetiapine, and 20 placebo. There were no significant differences in PANSS reductions at endpoint in substance abusers vs non-substance abusers in any of the treatment arms. Adjusted mean changes in PANSS total scores (2-week LOCF) in the substance abusers and the non-substance abusers were: -29.1 ± 3.0 and -26.1 ± 2.2 , risperidone; -23.7 ± 3.6 and -20.3 ± 2.4 , quetiapine; and -18.0 ± 3.5 and -19.4 ± 2.6 , placebo. Among all patients in the study, risperidone was associated with a greater PANSS reduction than quetiapine or placebo ($P < 0.001$).

Conclusion: In patients with a recent exacerbation of schizophrenia, substance abusers and non-substance abusers had similar treatment responses.

References:

1. Mueser KT, Yarnold PR, Levinson DF, et al: Prevalence of substance abuse in schizophrenia: demographic and clinical correlates. Schizophr Bull 1992; 16:31-56.
2. Tsuang J, Fong TW: Treatment of patients with schizophrenia and substance abuse disorders. Curr Pharm Des 2004; 10:2249-61.

NR280 Monday, May 23, 3:00 p.m.-5:00 p.m.

Durability of Effect of Long-Acting Injectable Naltrexone

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Commonwealth Avenue, Lower Level, Boston, MA 02115; Qunming Dong, Ph.D., John Loewy, Ph.D., Bernard Silverman, M.D., Elliot W. Ehrlich, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the durability of treatment effect achieved with long-acting naltrexone.

Summary:

Objective: To assess the durability of effect and tolerability of long-acting injectable naltrexone (LA-NTX) in a one-year extension study in patients with alcohol dependence!

Methods: A 24-week, multicenter, double-blind, placebo-controlled study evaluated the safety and efficacy of LA-NTX, a polylactide microsphere intramuscular formulation of naltrexone. DSM-IV alcohol-dependent patients (N=624) were randomized to six monthly injections of LA-NTX 380mg, LA-NTX 190mg, or placebo in combination with psychosocial support (BRENDA). 61% of patients completed the study, of whom 85% (N=332) enrolled in a one-year open-label extension. Alcohol intake was recorded in the base and extension studies by the Timeline Followback method.

Results: Patients randomized to 380mg in the base study continued to receive 380mg in the extension study (N=115). Mean percent heavy drinking days was similar in the base study (22.7%) and the extension (19.6%) study (P=NS). Patients treated with BRENDA and placebo injections who were switched to 380mg in the extension (N=60) showed significant reduction in percent heavy drinking days ($P < .01$). Once-monthly injections of LA-NTX were well tolerated.

Conclusions: Reduction in alcohol intake observed with LA-NTX and BRENDA during a 24-week double-blind study were durable and maintained during a one-year, open-label extension study.

References:

1. Volpicelli JR, Pettinati HM, McLellan AT, O'Brien CP: Combining medication and psychosocial treatments for addictions: the BRENDA approach. New York: The Guilford Press; 2001.
2. Sobell LC, Sobell MB: Timeline Followback: a technique for assessing self-reported ethanol consumption in Allen J, Litten RZ, eds. Measuring Alcohol Consumption: Psychosocial and Biological Methods. Totowa, NJ, Humana Press, 1992: pp.41-72.

NR281 Monday, May 23, 3:00 p.m.-5:00 p.m.

The Role of Internal and External Source Control Condition in Opioid Addicts

Mohamad R. Eskandari, M.D., *Department of Psychiatry, Zanjan University of Medical Sciences, Arq Square Beheshti Hospital, Zanjan 45136, Iran*; Soghra Karami, M.Psy.

Educational Objectives:

At the conclusion of the presentation, participant should be able to recognize that locus of control in opioid addicts may have important role in treatment outcome of these patients and increasing internal control of loci by psychotherapy may be helpful in these patients.

Summary:

Introduction: Addicts have two kinds of control factors: external locus of control and internal locus of control. Internal control factors depend on one's personality and causes internal control on addiction. By the external locus of controls patient believe in chance and luck. Patients with internal locus of control try more than other group to treat there addiction.

Method: This study was carried out on 62 addict (57 male and 5 female) admitted to hospital during one year and assessed by

two questionnaires including demographic information and second one was Rutter test.

Results: Mean age of smoking beginning was 18.3 and 24.7yr were mean age of onset of addiction. Loci of control in 41.96% of cases were internal and in 58.06% were external. In 62.9% of cases that friends reported as main cause of addiction, 60% had external locus of control these cases had less efforts to overcome psychological problem.

Conclusion: According to this study most of addicts have external locus of control such as their friends and treatment seeking is low in this patients. Administration of instructive method for increasing internal controls can be improving treatment outcome in opioids addicts.

References:

1. Magura S, Knight EL, Vogel HS, Mahmood D, Laudet AB, Rosenblum A: Mediators of effectiveness in dual-focus self-help groups. *Am J Drug Alcohol Abuse* 2003; 29(2):301-22.
2. Kostowski W: Drug addiction as drive satisfaction ("antidrive") dysfunction. *Acta Neurobiol Exp (Wars)* 2002; 62(2):111-7.

NR282 Monday, May 23, 3:00 p.m.-5:00 p.m.

Obesity in Severe Mental Illness: The Effect of Smoking

Supported by Eli Lilly and Company, NARSAD, Internal Funding and Roche Molecular Systems

Jose de Leon, M.D., Department of Psychiatry, University of Kentucky, 627 West 4th Street, MHRC 627, Lexington, KY 40508-1207; Margaret Susce, R.N., Francisco J. Diaz, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to demonstrate a better understanding of the role of tobacco smoking in obesity among severe mentally ill patients.

Summary:

Objective: This naturalistic, cross-sectional survey of patients with severe mental illnesses (SMIs) explores the association between important variables and obesity and extreme obesity. These analyses focus on the effects of tobacco smoking.

Method: Weight and height were obtained from 560 patients with SMI recruited at Central Kentucky inpatient and outpatient facilities to estimate their body mass index (BMI).

Results: When comparing the patients with Kentucky adults from the general population, the odds ratio (OR) of obesity (BMI ≥ 30 kg/m²) was 2.6 (95% confidence interval, CI, 2.2-3.0), and of current tobacco smoking was 5.0 (CI, 4.2-6.0). The psychiatric diagnosis or the current antipsychotic medication was not associated with obesity; however, early onset and long psychiatric medication duration were significantly associated with obesity, particularly in females. In males, substance-use disorders, including nicotine use, exhibited significant ORs of obesity lower than 1. Nicotine use was the only variable associated with extreme obesity among obese patients.

Conclusions: These results suggest a complex pattern of variables that may influence the development of obesity and its complications in patients with SMIs, but need replication. The importance of nicotine suggest that a better understanding of its pharmacological effects may help developing new pharmacological interventions.

References:

1. ADA, AACE, APA, NAASO: Consensus development conference on antipsychotic drugs and obesity and diabetes. *Diabetes Care* 2004; 27:596-601

2. Li MD, Parker SL, Kane JK: Regulation of feeding-associated peptides and receptors by nicotine. *Mol Neurobiol* 2000; 22:143-165

NR283 Monday, May 23, 3:00 p.m.-5:00 p.m.

Time to All Cause Discontinuation Following Randomization to Open-Label Olanzapine, Risperidone, or Conventional Antipsychotic Treatment for Schizophrenia

Haya Ascher-Svanum, Ph.D., Department of Outcomes Research, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Allen W. Nyhuis, M.A., Sandra L. Tunis, Ph.D., Michael Stevens, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the usefulness of "time to all-cause medication discontinuation" as an important measure of treatment effectiveness, and that olanzapine appears to be associated with significantly longer time to all-cause medication discontinuation compared to treatment with risperidone or conventional antipsychotics, regardless of potency level.

Summary:

Objective: To compare olanzapine, risperidone, and conventional antipsychotics on time to all-cause medication discontinuation in the treatment of schizophrenia.

Methods: Data were from a randomized, open-label, one-year effectiveness trial conducted in the U.S. between 5/1998 and 9/2002. Patients randomized to olanzapine (N=222), risperidone (N=217), or conventional antipsychotics (N=209) of low, medium, or high potency level were compared on time to all-cause medication discontinuation. Post hoc survival analyses were used to compare the treatment groups on time to all-cause medication discontinuation during the one year following randomization.

Results: The one-year survival rate was significantly higher for olanzapine (55%) than risperidone-treated patients (47%, $p=.006$). Survival rate for olanzapine-treated patients was significantly ($p<.001$) higher than conventional antipsychotics of high, medium, or low potency levels, and compared with perphenazine, a medium potency conventional antipsychotic (32%). Survival rate for risperidone-treated patients was significantly ($p<.01$) higher than conventionals of high or medium potency, but did not significantly differ from conventionals of low potency or perphenazine.

Conclusion: In this randomized, open-label study, patients randomized to olanzapine had significantly longer time to all-cause medication discontinuation compared to patients treated with risperidone or conventional antipsychotics, regardless of potency level. Findings suggest that atypical antipsychotics differ on this important effectiveness measure.

References:

1. Stroup TS, McEvoy JP, Swartz MS, Byerly MJ, Glick ID, Canive JM, McGee MF, Simpson GM, Stevens MC, Lieberman JA: The National Institute of Mental Health Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) project: schizophrenia trial design and protocol development. *Schizophr Bull* 2003; 29:15-31.
2. Hugenholtz GWK, Heerdink ER, Nolen WA, Egberts ACG: Less medication switching after initial start with atypical antipsychotics. *European neuropsychopharmacology* 2004; 14:1-5.

NR284 Monday, May 23, 3:00 p.m.-5:00 p.m.

Prevalence of Paroxysmal Perceptual Alterations With Antipsychotics

Monica Magarinos, M.D., Department of Psychiatry, Hospital Puerta Hierro, San Martin De Porres, 4, Madrid 280, Spain;

Juan J. Carballo, M.D., Pedro Garcia-Parajua, M.D., Santiago Ovejero, M.D., Belen Sanz-Aranguéz, M.D., Lucas Giner, M.D., Enrique Baca-García, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize and diagnose paroxysmal perceptual alterations in visual modality in patients under antipsychotic treatment.

Summary:

Introduction: It has been reported a prevalence of 3.25% of paroxysmal perceptual alterations (PPA) among Japanese patients under antipsychotic treatment. PPA consists of brief recurrent episodes characterized by hypersensitivity of visual perception. The aim of this study was to investigate the existence of PPA and estimate the prevalence among Caucasian patients.

Methods: 103 consecutive Caucasian patients under treatment with antipsychotics and diagnosed with schizophrenia, other psychotic disorders, mood disorders, neurotic, or personality disorders (ICD-10 criteria) were interviewed. To be classified as having PPA, the following criteria were required: (1) hypersensitivity of perception in the visual modality, (2) to be ego dystonic, (3) duration for few minutes up to few hours.

Results: Four patients had PPA, giving a prevalence in three months of 3.9%. Three of them had a schizophrenia and one a bipolar disorder. One patient with PPA had oculogyric crisis (OGC) in the past. No differences were found in age, global assessment functioning and daily dose of chlorpromazine equivalents between patient with or without PPA (Mann-Witney U test; $p>0.05$).

Conclusions: PPA could be an undesirable side effect of antipsychotics. We didn't find a clear similarity between PPA and OCG in terms of phenomenology as it has been reported elsewhere.

References:

1. Uchida H, Suzuki T, Tanaka KF, Watanabe K, Yagi G, Kashima H: Recurrent episodes of perceptual alteration in patients treated with antipsychotic agent. *J Clin Psychopharmacol* 2003; 23:496-499.
2. Higuchi H, Shimizu T, Hishikawa Y: Recurrent paroxysmal episodes characterized by perceptual, alteration in three schizophrenic patients on neuroleptic medication. *Psychiatry Clin Neurosci* 1997; 51:99-101.

NR285 Monday, May 23, 3:00 p.m.-5:00 p.m.

A Trial of Risperidone Long-Acting Injectable In First-Episode Psychosis

Robin A. Emsley, M.D., *Department of Psychiatry, University Stellenbosch, PO Box 19063, Tygerberg Cape Town 7505, South Africa*; Piet Oosthuizen, M.D., Liezl Koen, M.D., Rossella Medori, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should have an understanding of the safety and tolerability of risperidone long acting injectable in first episode schizophrenia.

Summary:

Objectives: Relapse prevention is the cornerstone of treatment of early psychosis. A long-acting injectable antipsychotic may be of benefit, as non-adherence to antipsychotic treatment is the strongest predictor of relapse. The objective of this study was to assess the safety of risperidone long acting injectable (RLAI) in first-episode psychosis in an open-label design.

Methods: This 12-week interim analysis was conducted on the first 20 subjects entered into the study. The sample comprised 11 women and 9 men, aged 26.9 ± 7 years, with a diagnosis of schizophreniform disorder ($n=11$) or schizophrenia ($n=9$). Partici-

pants received RLAI 25-50mg twice weekly after one week of risperidone oro-dispersible tablets.

Results: Eighteen subjects completed the 12 weeks of treatment (one withdrew consent at week 4, and one was lost to follow up at week 8). Endpoint doses were 25mg ($n=9$), 37.5mg ($n=8$) and 50mg ($n=1$). Adverse events ($n=14$) were mainly mild to moderate (96%) and judged unlikely related (not related, doubtful) to trial medication (84.9%). Two subjects developed mild parkinsonism, requiring anticholinergic medication. Median baseline and 12-week BMI's were, respectively, 21 and 23. However, seven patients were underweight (BMI = 18.5) at the trial start.

Conclusions: These preliminary data suggest that RLAI is well tolerated in first-episode psychosis.

References:

1. Schooler N, Rabinowitz J, Davidson M, Emsley R, Harvey P, Kopala L, McGorry P, Van Hove I, Eerdeken M, Swyzen W, De Smedt G, and Early Psychosis Global Working Group: Risperidone and haloperidol in first episode psychosis: a long-term randomized trial. *Am J Psychiatry*, in press.
2. Robinson DG, Woerner MG, Alvir JM, Geisler S, Koreen A, Sheitman B, Chakos M, Mayerhoff D, Bilder R, Goldman R, Lieberman JA: Predictors of treatment response from a first episode of schizophrenia or schizoaffective disorder. *Am J Psychiatry* 1999; 156:544-549.

NR286 Monday, May 23, 3:00 p.m.-5:00 p.m.

The Treatment of Psychotic Symptoms in Children and Adolescents With Bipolar Disorder

Joseph Biederman, M.D., *Department of Psychiatry, Massachusetts General Hospital, 55 Fruit Street, Warren Building 705, Boston, MA 02114*; Eric Mick, Sc.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the effectiveness of atypical antipsychotics in the improvement of psychotic behavior in youth with bipolar disorder.

Summary:

Introduction: Bipolar disorder in children is associated with greater severity of illness, more functional impairment, and high risk of comorbid psychosis. The objective of this study was to address the improvement of associated psychotic behavior, from our open-label trials of atypical antipsychotics in the treatment of youth with pediatric bipolar disorder.

Methods: This was a single-site, prospective, open-label, eight-week study of risperidone, olanzapine, or quetiapine monotherapy in the treatment of youth with mania. Psychotic symptoms were evaluated with the Brief Psychiatric Rating Scale, which was assessed at Week 0, 4, and 8.

Results: There were 70 males and 40 females with a mean age of 9.3 ± 2.7 years. There was a statically significant reduction of 10 points ($p<0.0001$) on the BPRS over the course of the trial that did not differ between study groups ($p=0.6$). There were significant improvements for the thought disorder ($p<0.001$), Anxiety/depression ($p<0.009$), and hostility ($p<0.001$) factors of the BPRS that did respond to one medication preferentially.

Conclusion: This study shows that, in addition to being effective in managing bipolar symptomatology, risperidone, quetiapine, and olanzapine may also be effective in treating psychotic symptomatology.

References:

1. Biederman J, Petty C, et al: Phenomenology of childhood-onset psychosis: Findings from a large sample of psychiatrically referred youth. *Journal of Nervous and Mental Disease* 2004; 192(9):607-614.

2. Pavuluri MN, Herbener ES, et al: Psychotic symptoms in pediatric bipolar disorder. *J Affect Disord* 2004; 80(1):19-28.

NR287 **Monday, May 23, 3:00 p.m.-5:00 p.m.**
Treatment of Preschoolers With Bipolar Disorder

Joseph Biederman, M.D., *Department of Psychiatry, Massachusetts General Hospital, 55 Fruit Street, Warren Building 705, Boston, MA 02114*; Erick Mick, Sc.D., Theresa Harpold, M.D., Paul Hammerness, M.D., Megan Aleardi, B.A., Meghan Dougherty, B.S., Chantal Menard, B.A.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that while treatment with risperidone and olanzapine can result in a rapid reduction of symptoms of mania in preschool children with bipolar disorder, substantial residual symptomatology and adverse effects are observed, and there is a need for identifying additional safe and effective treatments.

Summary:

Introduction: To evaluate the short-term safety and effectiveness of atypical antipsychotics in a single-site, prospective, open-label, eight-week study of risperidone and olanzapine monotherapy in preschoolers with bipolar disorder (BPD).

Methods: Risperidone was initiated at an open-label dose of 0.25 mg/day to be increased weekly according to response and tolerability to a maximum dose of 2.0mg/day. Olanzapine was initiated at 1.25 mg/day and increased to no more than 10 mg/day.

Results: Thirty-nine children aged 4-6 years were treated with olanzapine (N=17) or risperidone (N=22). At study endpoint (week 8 or LOCF), there was a 13.6±12.5 point reduction in risperidone-treated subjects and a 12.4±10.6 point reduction in YMRS scores in olanzapine-treated subjects (ns). According to the CGI, there was no difference in overall rate of improvement ("Much" or "Very Much" improved) in the risperidone (55%) and olanzapine (47%) groups.

Conclusion: This prospective, open study suggests that treatment with risperidone and olanzapine can result in a rapid reduction of symptoms of mania in preschool children with bipolar disorder. However, because of the substantial residual symptomatology and adverse effects observed, there is a pressing need for identifying additional safe and effective treatments for the management of bipolar disorder in this high-risk population.

References:

1. Frazier JA, Biederman J, et al: Olanzapine in the treatment of bipolar disorder in juveniles. American Psychiatric Association, Chicago, Illinois, 2000.
2. Frazier JA, Meyer MC, et al: Risperidone treatment for juvenile bipolar disorder: a retrospective chart review. *Journal of the American Academy of Child and Adolescent Psychiatry* 1999; 38(8): 960-5.

NR288 **Monday, May 23, 3:00 p.m.-5:00 p.m.**
Open-Label Study of OROS Methylphenidate in the Treatment of Adults With ADHD Not Otherwise Specified (NOS)

Joseph Biederman, M.D., *Department of Psychiatry, Massachusetts General Hospital, 55 Fruit Street, Warren Building 705, Boston, MA 02114*; Thomas Spencer, M.D., Craig Surman, M.D., Megan Aleardi, B.A., Meghan Dougherty, B.S., Karl Schweitzer, B.A., Eric Mick, Sc.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that treatment with OROS Methylphenidate is efficacious and safe in adults with ADHD NOS.

Summary:

Introduction: A sizeable number of adults are increasingly being recognized with a highly impairing current clinical picture of ADHD symptoms, but with insufficient childhood history and/or insufficient number of current ADHD symptoms to meet full diagnosis of ADHD.

Methods: We conducted a six-week, open-label treatment study with OROS® methylphenidate in subjects diagnosed with ADHD not otherwise specified (NOS) as defined by meeting full current diagnosis of DSM-IV ADHD, but with age of onset later than 12 years. Severity of symptoms was measured weekly using the ADHD rating scale (RS). Subjects were treated with OROS methylphenidate initiated at an open-label dose of 36mg/day to be increased weekly according to response and tolerability.

Results: Twenty-five subjects (35.4±15.0 years) completed six weeks of OROS methylphenidate treatment at a mean dose of 82.1±25.8 mg/day (range 36-144 mg/day). At study endpoint (week 6 or LOCF), there was a clinically and statistically significant reduction of ADHD symptoms as measured on the ADHD RS. Treatment with OROS methylphenidate was well tolerated.

Conclusion: These results suggest that treatment with OROS methylphenidate is efficacious and safe in adults with ADHD NOS, and support the need for further randomized, clinical trial assessment of its efficacy and tolerability.

References:

1. Kessler RC: Prevalence of adult ADHD in the United States: results from the national comorbidity survey replication (NCS-R). Annual Meeting of the American Psychiatric Association, New York, NY, American Psychiatric Association, 2004.
2. Spencer T, Biederman J, et al: Overview and neurobiology of attention-deficit/hyperactivity disorder. *Journal of Clinical Psychiatry* 2002; 63(Supp 12):3-9.

NR289 **Monday, May 23, 3:00 p.m.-5:00 p.m.**
Economic Impact of Adult ADHD

Joseph Biederman, M.D., *Department of Psychiatry, Massachusetts General Hospital, 55 Fruit Street, Warren Building 705, Boston, MA 02114*; Stephen Faraone, Ph.D.

Educational Objectives:

After reviewing this poster, the participant should be able to describe and appreciate the economic impact of attention-deficit/hyperactivity disorder (ADHD) on adults in the US.

Summary:

Objective: To estimate the economic impact of adult ADHD on employment and household income in adults with the disorder.

Method: A weighted sample of 500 ADHD adults and 501 gender- and age-matched controls that reflected the general U.S. population was obtained via telephone survey. Roper ASW conducted all interviews between April and May of 2003. Several different econometric models were used to estimate the impact of ADHD in 2003 U.S. dollars.

Results: A previous prevalence survey estimated that 4.3% of working-age adults in the U.S. have been diagnosed with ADHD. Adults with ADHD had a lower educational attainment and achievement than controls, which significantly impacted employment rates and income. Even when controlling for educational attainment and achievement, the average loss of household income per person with ADHD ranged from \$8,900 to \$15,400 per year, depending on the econometric model used. In aggregate,

this resulted in an annual loss in household income of 67 to 116 billion dollars.

Conclusion: ADHD has a substantial impact on the household income of those afflicted, making this disorder one of the costliest medical conditions in the U.S.

References:

1. Faraone SV, Biederman J: Controlled Study of Functional Impairments in 500 ADHD Adults. Presented at the 157th Annual Meeting of the American Psychiatric Association. New York; May 6, 2004.
2. Faraone SV, Biederman J: Prevalence of Adult ADHD in the United States. Presented at the 157th Annual Meeting of the American Psychiatric Association. New York; May 4, 2004.

NR290 Monday, May 23, 3:00 p.m.-5:00 p.m.

Does the Presence of Comorbid ODD Affect Responses to Atomoxetine?

Joseph Biederman, M.D., *Department of Psychiatry, Massachusetts General Hospital, 55 Fruit Street, Warren Building 705, Boston, MA 02114*; Thomas Spencer, M.D., Jeffrey Newcorn, M.D., Haitao Gao, Ph.D., Denai Milton, M.S., Peter Feldman, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the attendee should recognize that comorbid ODD does not appear to have a significant effect on the responsiveness of ADHD symptoms to treatment with atomoxetine.

Summary:

Objective: To determine the effect of the presence of comorbid oppositional defiant disorder (ODD) on clinical outcomes among pediatric patients being treated for attention-deficit/hyperactivity disorder (ADHD).

Methods: Acute-phase data were analyzed from the three double-blind studies in children and adolescents (ages 6-16) with ADHD who received once-daily treatment with atomoxetine (0.5-1.8 mg/kg/day, 6-8 weeks) or placebo. Patients met DSM-IV diagnostic/severity criteria for ADHD on the K-SADS-PL:Behavioral structured interview. ODD was diagnosed with the K-SADS-PL.

Results: Relative to placebo, atomoxetine treatment significantly reduced ADHD symptoms in both comorbid and non-comorbid patients. However, clinical and psychosocial responses (CPRS, ADHDRS-IV-Parent:Inv, CGI-ADHD-S, CHQ) to atomoxetine treatment compared with placebo were not significantly different between comorbid and non-comorbid patients. For ODD patients, changes in CPRS ADHD index and oppositional scores were highly correlated ($r=0.78$). Responses (25% reduction from baseline) within the ADHD and ODD domains of the CPRS were not significantly different ($p=.366$, McNemar), indicating a strong association between the improvements in patients' ADHD and oppositional symptoms.

Conclusions: Atomoxetine treatment significantly reduced ADHD symptoms in both comorbid and non-comorbid patients. The presence of comorbid symptoms of oppositionality does not appear to affect clinical outcomes of treatment of ADHD.

References:

1. Kuhne M, Schachar R, Tannock R: Impact of comorbid oppositional or conduct problems on attention-deficit hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 1997; 36(12):1715-1725.
2. Swanson JM, Kraemer HC, Hinshaw SP, Eugene AL, Conners CK, Abikoff HB, Clevenger W, Davies M, Elliott GR, Greenhill LL, Hechtman L, Hoza B, Jensen PS, March JS, Newcorn JH, Owens EB, Pelham WE, Schiller E, Severe JB, Simpson S,

Vitiello B, Wells K, Wigal T, Wu M: Clinical relevance of the primary findings of the MTA: success rates based on severity of ADHD and ODD symptoms at the end of treatment. *J Am Acad Child Adolesc Psychiatry* 2001; 40(2):168-179.

NR291 Monday, May 23, 3:00 p.m.-5:00 p.m.

Accuracy of the Diagnosis of Psychotic Depression at Four Academic Medical Centers

Anthony J. Rothschild, M.D., *Department of Psychiatry, University of Massachusetts Medical School, 361 Plantation Street, Worcester, MA 01605*; Jesse Winer, B.S., Alastair Flint, M.D., Barnett Meyers, M.D., Benoit Mulsant, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize and diagnose accurately major depression with psychotic features and be able to distinguish it from other psychiatric diagnoses.

Summary:

Major depression with psychotic features (psychotic depression) is a commonly misdiagnosed psychiatric disorder. With proper and timely diagnosis and treatment, morbidity and costs can be reduced while improving outcomes. This study ascertained the accuracy of the diagnosis of psychotic depression at four academic medical centers and explored whether the symptoms with which the patient presents, the setting of presentation, and level of training of the physician affected the accuracy of diagnosis. Clinical and research diagnoses were compared in 65 psychiatric inpatients who participated in the NIMH Study of the Pharmacotherapy of Psychotic Depression (STO-PD). Standardized forms were used to extract clinical diagnoses made in the emergency room and upon admission to the psychiatric unit, yielding 130 diagnoses. Psychotic depression was initially misdiagnosed in 27% of the study group. Diagnoses were more likely to be accurate on the inpatient unit than the ER (chi-squared = 11.13, $p<.005$), and more likely to be made accurately by resident psychiatrists than attending psychiatrists (chi-squared = 9.08, $p<.05$). Failure to make an accurate diagnosis of psychotic depression was more likely when the psychiatrist failed to note symptoms of depressed mood (chi-squared = 11.48, $p<.005$), hallucinations (chi-squared = 11.69, $p<.005$), or delusions (chi-squared = 19.48, $p<.001$) in the medical record.

Supported by the NIMH START-MH Program and NIMH grants MH62518, MH62446, MH62565, MH62624, and for the NIMH Study of the Pharmacotherapy of Psychotic Depression (STOP-PD)).

References:

1. Rothschild AJ: Challenges in the treatment of depression with psychotic features. *Biological Psychiatry*, 2003; 53:680-690.
2. Ohayon MM, Schatzberg AF: Prevalence of depressive episodes with psychotic features in the general population. *Am J Psychiatry* 2002; 159:1855-1861.

NR292 Monday, May 23, 03:00 p.m.-05:00 p.m.

Cognitive Effects of Ziprasidone in First-Episode Psychosis: An fMRI Study

Tonmoy Sharma, M.D., *CNRC, Department of Neuroscience Center, 7 Twisleton Center Priory Hill, Dartford DA1 2EN, United Kingdom*; Veena Kumari, Ph.D., Ravi Mehrotra, Ph.D., Anil Kumar

Educational Objectives:

At the conclusion of this session, the participant should be able to demonstrate knowledge of the effects of the antipsychotic

ziprasidone on attention and working memory of first-episode psychotic patients, and the role of fMRI in longitudinal assessment of psychopharmacological effects on cerebral physiology.

Summary:

Antipsychotic drug treatment of first-episode psychosis may be complicated by side effects of widespread dopaminergic antagonism, including exacerbation of negative and cognitive symptoms due to prefrontal hypodopaminergia. Cognitive deficits in first-episode psychosis have been well documented. Second-generation antipsychotic drugs have had a big impact on treatment of early psychosis due to lack of neurological side effects.

To elucidate the neural mechanisms of the effects of ziprasidone on attention and working memory in first-episode psychosis, this study examined behavioural performance and blood-oxygenation-level-dependent regional brain activity (BOLD), using functional magnetic resonance imaging (fMRI), during a procedural learning task in 10 subjects with first-episode psychosis who were treated with ziprasidone. They were compared with patients who had received conventional antipsychotics. Functional MRI was carried out in these two groups of patients at baseline and six weeks later.

The ziprasidone-treated group had significantly greater response at six weeks in inferior prefrontal cortex, thalamus and cerebellum ($p < 0.005$).

These data provide the first direct evidence for enhanced prefrontal cortical function in first-episode psychosis patients following treatment with ziprasidone, and indicate the potential value of fMRI as a tool for longitudinal assessment of psychopharmacological effects on cerebral physiology.

References:

1. Honey GD, Bullmore ET, Soni W, Varatheesan M, Williams SC, Sharma T: Differences in frontal cortical activation by a working memory task after substitution of risperidone for typical antipsychotic drugs in patients with schizophrenia. *Proc Natl Acad Sci U S A* 1999; Nov 9: 96(23):13432-7.
2. Lieberman JA, Tollefson G, Tohen M, Green AI, Gur RE, Kahn R, McEvoy J, Perkins D, Sharma T, Zipursky R, Wei H, Hamer RM; HGDH Study Group: Comparative efficacy and safety of atypical and conventional antipsychotic drugs in first-episode psychosis: a randomized, double-blind trial of olanzapine versus haloperidol. *Am J Psychiatry* 2003; 160(8):1396-404.

NR293 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Etanercept Improves Symptoms of Depression and Fatigue in Patients With Psoriasis

K. Ranga R. Krishnan, M.D., *Department of Psychiatry, Duke University Medical Center, Box 3950 DUMC, Durham, NC 27710*; David Cella, Ph.D., Michael Woolley, Ph.D., Deepa Lalla, Ph.D., Ralph Zitnik, M.D., David Brajac, B.S.C.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the (1) role of TNF in depression; (2) use of TNF antagonist to treat depression.

Summary:

Objective: To evaluate the effect of etanercept therapy on symptoms of depression and fatigue in patients with moderate-to-severe psoriasis.

Methods: 618 patients participating in a 12-week, double-blind, multi-center clinical trial of etanercept therapy were randomized to receive etanercept 50mg twice weekly or placebo. The Ham-D, BDI, and FACIT-Fatigue were used to assess symptoms of depression and fatigue.

Results: Mean baseline Ham-D and BDI scores show that on average patients with moderate-to-severe psoriasis are mildly de-

pressed (Ham-D=4.51, BDI=8.23). Compared with subjects on placebo, those receiving etanercept reported mean improvements in the Ham-D (1.5 vs. 0.4, $p < 0.0012$), the BDI (3.9 vs. 2.1, $p < 0.0001$) and the FACIT-F (5.0 vs. 1.9, $p < 0.0001$). These improvements were statistically significant by week 4 for the BDI and the FACIT-F. Patients on etanercept were also more likely to report a 50% improvement in the Ham-D (43% vs. 32%; $p < 0.0048$) and the BDI (55% vs. 39%; $p < 0.0001$).

Conclusions: Treatment of psoriasis with etanercept is associated with rapid and meaningful improvements in symptoms of depression and fatigue.

References:

1. Suarez EC, Krishnan RR, Lewis JG: The relation of severity of depressive symptoms to monocyte-associated proinflammatory cytokines and chemokines in apparently healthy men. *Psychosomatic Medicine* 2003; 65 (3):362-368.
2. Mease PJ, Goffe BS, Metz J, VanderStoep A, Finck B, Burge DJ: Etanercept in the treatment of psoriatic arthritis and psoriasis: a randomised trial. *Lancet* 2000; 356(9227):385-390.

NR294 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Blood Test for Bipolar Disorder Using Na Pump Regulation

Alagu P. Thiruvengadam, Ph.D., *University of Maryland School of Medicine, 11862 Farside Road, Ellicott City, MD 21042*; Krish Chandrasekaran, Ph.D., William T. Regenold, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to make the diagnosis of bipolar disorder.

Summary:

Introduction: El-Mallakh et al (1996) found that the membrane potentials of leukocytes from bipolar patients were hyperpolarized. However, Tamella et al (1996) measured the membrane potentials of cultured lymphoblasts and concluded that there was no significant difference in membrane potentials among bipolar patients, their siblings, and normal controls. Thiruvengadam (2001) calculated the potentials using Goldman-Hodgkin-Katz equation and showed that lithium would depolarize the membranes. These results led us to measure the membrane potentials of cultured lymphoblasts from bipolar patients, their siblings, and matched controls. The Na, K-ATPase activity was regulated by using different chemicals that alter the Na⁺ and K⁺ ionic gradients. This technique was able to differentiate lymphoblasts of bipolar patients from those of siblings and normals. We extended this technique to measure the membrane potentials of whole blood cells of four groups, including bipolar, unipolar, and schizophrenic patients, and matched controls through a clinical trial. The bipolar cells are significantly different from other types of cells.

Methods: Cultured lymphoblasts were obtained from Coriell Institute for Medical Research. Their membrane potentials were measured using a Hitachi 2500 Fluorescence Spectrophotometer. The cells were suspended in a buffer (5 mM KCl, 4 mM NaHCO₃, 5mM HEPES, 134 mM NaCl, 2.3 mM CaCl₂, and 5 mM glucose) during measurement. A lipid soluble fluorescent dye, dihexylcarboxylacetate (DiOC6(3)), was used. The membrane potentials in regular buffer were compared with those in K⁺-free buffer, which contained no potassium.

Results: The membrane potentials of bipolar lymphoblasts were significantly hyperpolarized when compared with those of siblings and controls. The ratio of potentials in K⁺-free buffer to the potentials in regular buffer of bipolar cells was significantly different from those of unaffected cells. The cells incubated in ethacrynate (30uM) showed significant differences between affected cells and unaffected cells. The cells incubated in monensin (10uM) and in

PMA (2uM phorbol myristate acetate) showed significant differences. Lithium also served as a medium to differentiate the affected from unaffected cells.

Encouraged by these results, we tested the whole blood samples from bipolar, unipolar, and schizophrenic patients and compared the results with normal controls through a clinical trial. The ratio of potentials of bipolar cells were significantly different from those of other types of cells ($P < 0.001$). The specificity and sensitivity of these tests compared well with the state of the art diagnostic techniques for various other diseases. These results indicate that the Na, K-ATPase regulation can be used as a diagnostic blood test to augment the DSM-IV for bipolar disorder.

References:

1. Living with bipolar disorder: How far have we really come? Constituency survey by National Depressive and Manic Depressive Assocn. Chicago, Illinois, 2001.
2. Looney SW, El-Mallackh RS: META-analysis of erythrocyte Na, K-ATPase activity in bipolar illness. *Depress Anxiety* 1997; 5: 53-65.

NR295 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Trail-Making Test in Schizophrenia and Bipolar Disorder: Implications in Functional Outcome

Supported by Janssen-Cilag Medical Affairs, Portugal

Vasco Dias, M.D., *Department of Neuropsychology, I.P.A.F., Rua Diogo Couto No. 1 9o Frt, Lisbon 1100-194, Portugal;* Sofia Brissos, M.D.

Summary:

Objectives: Our aim was to test Trail Making Test Part B (TMT-B) in detecting cognitive impairment in schizophrenic and bipolar patients.

Method: One hundred patients were evaluated; remission state was evaluated with the Clinical Global Impression Scale and cognitive function was assessed using the TMT-B.

Results: The sample comprised 45 women and 55 men, 50 patients were diagnosed schizophrenia, 18 patients bipolar I, and 32 patients bipolar II disorder. 91% of patients had some degree of cognitive impairment, and 76% of patients showed severe cognitive impairment. TMT-B performance was worse in bipolar II patients, followed by bipolar I and by schizophrenic patients.

Conclusions: All groups performed worse than normative data ($p < 0.001$), bipolar patients performing worse than schizophrenics on the TMT-B. Sustained attention deficit is present early in the course of bipolar disorder. Executive functions are shown to be much altered in bipolar patients and this might be important to target treatment interventions, since improvements in the domains tested by TMT-B might prove useful for maintaining functional status. We propose the utility of TMT-B to evaluate these patients' cognitive status, so that adequate treatment and rehabilitation programs can be delineated.

References:

1. Martinez-Aran A, Penades R, Vieta E, Colom F, Reinares M, Benerbarre A, Salamero M, Gasto C: Executive function in patients with remitted bipolar disorder and schizophrenia and its relationship with functional outcome. *Psychother Psychosom* 2002; 71(1):39-46.
2. Murray RM, Sham P, Van Os J, Zanelli J, Cannon M, McDonald C: A developmental model for similarities and dissimilarities between schizophrenia and bipolar disorder. *Schizophr Res* 2004; 71(2-3), 405-16.

NR296 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Internalizing Behaviors of Children Prenatally Exposed to SSRIs

Supported by British Columbia Medical Services Foundation and GlaxoSmithKline Inc., Canada

Shaila Misri, M.D., *Department of Psychiatry, University of British Columbia, 1081 Burrard Street, 2B Room 185, Vancouver, BC V6Z 1Y6, Canada;* Pratibha Reebye, M.D., Tim F. Oberlander, M.D., Diana Carter, M.S., Deirdre M. Ryan, M.B., Kristin Kendrick, B.A.

Educational Objectives:

At the conclusion of this presentation, participants will have an increased awareness of the long-term behavioral effects of prenatal psychotropic medication exposure.

Summary:

Objective: To prospectively investigate internalizing behaviors in four- and five-year-old children exposed prenatally to psychotropic medications.

Method: The internalizing behaviors (e.g., depression, anxiety, and emotional withdrawal) of children exposed to SSRIs plus clonazepam and SSRIs alone were compared with a control group of non-exposed, healthy children. The Child Behavior Checklist, the Caregiver-Teacher Report Form, and the Crowell procedure were used to measure behavioral characteristics, and the critical variable of maternal mood was controlled for in all analyses. Ordered logistic regressions, *t*-Tests and Chi-Square analyses were used to examine group differences.

Results: No statistically significant differences in the children's internalizing behaviors were found when comparing the exposed group of SSRIs and SSRIs plus clonazepam with the control group.

Conclusions: These findings suggest that SSRIs, with or without clonazepam exposure during pregnancy, do not appear to have long-term negative consequences on the internalizing behaviors of four- and five-year-old children. This study adds to existing data on the pharmacological treatment of mood and anxiety disorders during pregnancy, and addresses their long-term safety. More research is needed before definitive statements can be made.

References:

1. Reebye PN, Morison SJ, Panikkar H, Misri S, Grunau RE: Affect expression in prenatally exposed and nonexposed mother-infant dyads. *Infant Ment Health J* 2002; 23(4):403-416.
2. Nulman I, Rovet J, Stewart DE, Wolpin J, Pace-Asciak P, Shuhaiber S, Koren G: Child development following exposure to tricyclic antidepressants or fluoxetine throughout fetal life: a prospective, controlled study. *Am J Psychiatry* 2002; 159(11):1889-1895.

NR297 **WITHDRAWN**

NR298 **WITHDRAWN**

NR299 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Ziprasidone's Long-Term Efficacy in Subpopulations With Bipolar Mania

Supported by Pfizer Inc.

Lewis Warrington, M.D., *Medical Department, Pfizer Incorporated, 235 East 42nd Street, New York, NY 10017-5755;* Steven G. Potkin, M.D., Kathleen Ice, Ph.D., Cynthia Siu, Ph.D.

Educational Objectives:

At the conclusion of this session, the participants should understand ziprasidone's potential for improving long-term symptom severity in patients with bipolar disorder who experience either manic or mixed episodes, with or without psychosis.

Summary:

Objective: To evaluate ziprasidone's long-term efficacy in clinically relevant subpopulations with acute bipolar mania.

Methods: Ziprasidone-treated completers of a 21-day, placebo-controlled trial of acute bipolar mania (N=62) were enrolled in a 52-week, open-label extension of flexibly-dosed ziprasidone 40-160 mg/d. Efficacy measures included change from core baseline in Mania Rating Scale (MRS) and CGI-S, as well as MRS responder rates ($\geq 50\%$ change from core baseline), in subpopulations with manic (n=43) or mixed (n=19) episodes, with (n=37) or without (n=25) psychotic symptoms.

Results: Mean change in MRS at last visit (LOCF) was -24.7 ($P < 0.0001$) for manic and -20.8 ($P < 0.0001$) for mixed subjects (baseline 30.5 and 25.6, respectively). Respective CGI-S change scores were -2.5 ($P < 0.0001$) and -1.8 ($P < 0.005$) (baseline 5.1 and 4.7, respectively). MRS and CGI-S changes were comparable for subjects with and without baseline psychotic symptoms. Responder rates were 88% in manic, 79% in mixed, 84% in psychotic, and 88% in nonpsychotic subjects. Long-term improvement observed within subpopulations was comparable to that observed in overall study population. Overall median dosage was 130 mg/d.

Conclusion: In this long-term extension study of subjects with acute bipolar mania, ziprasidone demonstrated sustained and comparable improvements in symptoms and global illness severity whether baseline episode was manic or mixed or involved psychotic symptoms.

References:

1. Keck PE Jr, Versiani M, Potkin S, et al: Ziprasidone in the treatment of acute bipolar mania: a three-week, placebo-controlled, double-blind, randomized trial. *Am J Psychiatry* 2003; 160:741-748.
2. Keck PE Jr, Potkin S, Lombardo I, Bazar E: Efficacy and safety of ziprasidone in bipolar disorder: longterm data. Presented at the 56th Institute on Psychiatric Services, October 6-10, 2004, Atlanta, Georgia.

NR300 Tuesday, May 24, 12:00 p.m.-2:00 p.m. Quetiapine in Bipolar Depression: NNT and Time-to-Event Analyses

Supported by AstraZeneca Pharmaceuticals

John Cookson, M.B., *The Royal London Hospital, 85B Forest Road London, London E83BT, England*; Paul E. Keck, Jr., M.D., Terence A. Ketter, M.D., Wayne Macfadden, M.D., Margaret C. Minkwitz, Ph.D., Jamie Mullen, M.D.

Educational Objectives:

At the conclusion of this session, the participant should: (1) understand that quetiapine treatment is associated with rapid and superior response and remission rates in patients with bipolar depression; and (2) recognize that quetiapine is an effective and well tolerated treatment for patients with bipolar depression.

Summary:

Objective: Evaluate the efficacy and safety/tolerability of quetiapine monotherapy in bipolar depression.

Methods: 542 patients with bipolar I or II disorder exhibiting moderate to severe depression were randomized to an eight-week, double-blind treatment with quetiapine (600 or 300 mg/day) or placebo. Kaplan-Meier analysis and the log-rank, chi-squared test compared populations for time to response ($\geq 50\%$ reduction

from baseline in MADRS score) and time to remission (MADRS score ≤ 12).

Results: Mean time to response was significantly shorter with quetiapine 600 mg/day (25.50 days) and 300 mg/day (27.44 days) than placebo (37.05 days; log-rank $\chi=30.73$, df 2, $P < 0.001$). Mean time to remission was also significantly shorter with quetiapine 600 mg/day (30.92 days) and 300 mg/day (33.22 days) compared with placebo (41.24 days; log rank $\chi=29.93$, df 2, $P < 0.001$). Response rates at Week 8 were 58% for both quetiapine groups and 36% for placebo ($P < 0.001$). Remission rates were 53% for both quetiapine groups and 28% for placebo ($P < 0.001$). NNT analyses similarly suggested efficacy of quetiapine (600 and 300 mg/day) compared with placebo (NNT=5 for both response and remission).

Conclusion: Quetiapine (600 or 300 mg/day) significantly reduces time to response (by 31% and 26%, respectively) and remission (by 25% and 20%, respectively) compared with placebo, has favorable NNTs, and is well tolerated.

References:

1. Calabrese J, Macfadden W, McCoy R, Minkwitz M, Wilson E, Mullen J: Double-blind, placebo-controlled study of quetiapine in bipolar depression. Poster NR756 presented at the 156th meeting of the American Psychiatric Association, New York, May 1-6, 2004.
2. American Psychiatric Association. Practice guideline for the treatment of patients with bipolar disorder (revision). *Am J Psychiatry* 2002; 159(4 Suppl):1-50.

NR301 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Quetiapine Treatment of Rapid Cycling Bipolar Depression

Supported by AstraZeneca Pharmaceuticals

Eduard Vieta, M.D., *Department of Psychiatry, Hospital Clinic, Villarroel 170, Barcelona 08036, Spain*; Joseph R. Calabrese, M.D., Wayne Macfadden, M.D., Margaret C. Minkwitz, Ph.D., Jamie Mullen, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to (1) evaluate efficacy data for quetiapine in patients with bipolar depression and a rapid cycling course; and (2) use the analyses presented to inform clinical practice when using quetiapine for the management of bipolar depression.

Summary:

Objective: Evaluate the efficacy and tolerability of quetiapine monotherapy in the treatment of bipolar depression with a rapid cycling disease course.

Methods: 108 patients with bipolar I or II disorder, rapid cycling (DSM-IV), exhibiting moderate to severe depression, randomized to receive eight weeks of double-blind treatment with fixed-dose quetiapine 600 mg/day (n=31), quetiapine 300 mg/day (n=42) or placebo (n=35) were included in the efficacy analysis. Primary endpoint was change from baseline in MADRS total score. Safety assessments included change from baseline in YMRS total score.

Results: Patients treated with quetiapine (600 mg/day or 300 mg/day) had a significantly ($P < 0.01$) greater improvement in mean MADRS score at every assessment, from Week 1 to Week 8, compared with placebo (-17.68 , -18.57 , -9.87 , respectively). Minimal changes were noted on the YMRS throughout treatment, with no difference between-groups in mean change from baseline to Week 8 ($+0.1$, -1.1 , -0.8). The number of patients with treatment-emergent mania was low and similar in each group: quetiapine 600 mg/day (2), quetiapine 300 mg/day (2) or placebo (1). Common quetiapine adverse events were dry mouth, sedation, somnolence, constipation, and fatigue.

Conclusion: Quetiapine monotherapy (600 mg/day or 300 mg/day) is significantly more effective than placebo and is well tolerated for the treatment of patients with rapid cycling bipolar depression.

References:

1. Kupka RW, Luckenbaugh DA, Post RM, Leverich GS, Nolen WA: Rapid and non-rapid cycling bipolar disorder: a meta-analysis of clinical studies. *J Clin Psychiatry* 2003; 64(12):1483-94.
2. Vieta E, Parramon G, Padrell E, Nieto E, Martinez-Aran A, Corbella B, Colom F, Reinares M, Golkolea JM, Torrent C: Quetiapine in the treatment of rapid cycling bipolar disorder. *Bipolar Disord* 2002; 4(5):335-40.

NR302 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Depression in Patients With Chronic Illness: Differences of Physical Symptom Severity and Economic Burden

Kwang Soo Kim, M.D., *Department of Psychiatry, St. Mary's Hospital, 62 Yoidodong, Youngdeungpo-GU, Seoul 150-713, Korea*; Kyoung-UK Lee, Yumi Na, Pyoung-Soo Lee

Educational Objectives:

Early diagnosis and treatment of depression in patients with chronic illness is very important for their quality of life and economic burden.

Summary:

Objective: We screened the presence of depression in patients with chronic illness and compared the differences of the symptom severity and economic burden in the chronic illness patients with or without depression.

Method: The subjects were the patients (N=1155) in the medical department of St. Mary's Hospital, the Catholic University of Korea, who have been treated due to endocrine disease, cardiovascular disease, pulmonary disease, gastrointestinal disease, renal disease, or immunological disease over one year in 2003. The patients completed the Zung Self-rating Depression Scale and Patients Health Questionnaire (PHQ)-15(1). Also, we compared the difference of direct medical care costs, use of medical care, and days of total medical treatment of the patients with or without depression in 2003.

Results: The numbers of patients without depression, with mild depression, with moderate depression, and with severe depression by screening with Zung's scale were 662(57.3%), 254(22.0%), 149(12.9%), and 90(7.8%). The means of direct medical care costs of patients without depression, with mild depression, with moderate depression, and with severe depression were \$1896, \$2292, \$2411, and \$3005 in 2003. The means of medical treatment days of patients without depression, with mild depression, with moderate depression, and with severe depression were 430.5 days, 402.1 days, 465.8 days, and 555.0 days in 2003. The numbers of patients with under 5 of PHQ score, with 6-10 of PHQ score, with 11-15 of PHQ score, and with over 16 of PHQ score were 579(50.1%), 398(34.5%), 135(11.7%), and 43(3.7%). The numbers of patients without depression, with mild depression, with moderate depression and severe depression in patients(N=43) with high PHQ score(>16) were 4(9.3%), 5(11.6%), 12(27.9%), and 22(51.2%). The numbers of patients with more physical symptoms was higher in patients with severe depression(Table 1).

Conclusion: In this study, 42.7% of patients with chronic illness had depression. The economic burden in 2003 and the severity of symptoms of chronic illness patients with depression was higher than those of patients without depression. This study suggested that early diagnosis and treatment of depression in chronic illness

patients is very important for the quality of life and economy of patients.

References:

1. Kroenke K, Spitzer RL, Williams JBW: PHQ-15 Validity of a new measure for evaluating the severity of somatic symptoms. *Psychosomatic Medicine* 2002; 64(2):258-266.
2. Davis JM, Gershtein CM: Screening for depression in patients with chronic illness; why and How? *Dis Manage Health Outcome* 2003; 11(6):375-378.

NR303 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Adjunctive Treatment for Initial Mood Stabilization of Bipolar I Patients

Supported by GlaxoSmithKline

Theodore C. Spaulding, Ph.D., *Department of Department of Neuroscience, GlaxoSmithKline, 5 Moore Drive, Research Triangle Park, NC 27709*; Ronald E. Westlund, M.S., Thomas R. Thompson, M.D., Gary E. Evoniuk, Ph.D., Robert A. Leadbetter, M.D.

Educational Objectives:

At the conclusion of this session, the participant should understand that in bipolar I disorder, episodic symptom excursions of opposite polarity than the presenting episode can occur and additional treatment with anxiolytic/sedative/hypnotic therapy alone may help in the stabilization of these patients.

Summary:

Objective: Evaluate the effect of the addition of anxiolytic/sedative/hypnotic (ASH) drugs combined with lamotrigine (LTG) on mood stability in bipolar patients.

Methods: Subjects in the preliminary phase of combined studies GW605/2003 and GW606/2006 were classified post-hoc into those receiving LTG monotherapy throughout the preliminary phase (N=202; baseline HAMD-17=19.1±8.0, MRS-11=5.7±8.4) or LTG as adjunctive treatment (N=904; baseline HAMD-17=19.6±8.2, MRS-11=5.3±8.4). Subjects with depression (DEP) were evaluated for manic excursions and those with mania (MAN) for depressive excursions. An excursion was defined as a HAMD-17 or MRS-11 score increase ≥10 that returned to <10.

Results: Stabilization rate (randomization, SR) for LTG monotherapy was not significantly affected by symptom excursions with 57% SR in the group with no excursions compared with 58% SR in the group with at least one excursion (p=0.9). In the lamotrigine adjunctive treatment group, SR was significantly affected by symptom excursions with a 53% SR in the group with no excursions compared with 36% SR in the group with at least one excursion (p<0.001). The further addition of ASH alone significantly improved stabilization for subjects with (p=0.023) and without (p<0.008) symptom excursions.

Conclusion: Adjunctive treatment with ASH alone may be sufficient to stabilize mood in bipolar patients treated with lamotrigine.

References:

1. Calabrese J, Bowden C, Sachs G, Yatham L, et al for the Lamictal 605 Study Group: *Journal of Clinical Psychiatry* 2003; 64:1013-1024.
2. Bowden C, Calabrese J, Sachs G, Yatham L, et al for the Lamictal 606 Study Group: *Archives of General Psychiatry* 2003; 60:392-400.

NR304 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Randomized Trial of Oral Versus Injectable Antipsychotics in Bipolar Disorder

Supported by Janssen Ortho Inc.

Lakshmi N. Yatham, M.D., *Department of Psychiatry, University of British Columbia, 2255 Wesbrook Mall, Vancouver, BC V6T 2A1, Canada*; Carin Binder, M.B.A., Angelo Fallu, M.D.

Educational Objectives:

At the conclusion of this session, participants should be able to better understand issues in research design and clinical features of patients with bipolar disorder.

Summary:

Objective: Determine the safety of long-acting injectable(LAI) risperidone in stable bipolar subjects compared with usual care with oral atypical antipsychotics (AAPs) (olanzapine/risperidone/quetiapine).

Methods: Ongoing, randomized, stratified by antidepressant, multicenter study recruiting 40 bipolar subjects on oral AAP plus adjunct bipolar treatment (antidepressant, lithium, lamotrigine, or valproate) either continued on current oral AAP or switched to LAI risperidone (starting dose 25mg) and followed for six months. Adverse events, weight, BARS, SAS, and AIMS were collected.

Results: 15/40 subjects have been recruited with a treatment duration of seven days to six months. Adverse events (AEs) reported in 14 subjects. Six LAI risperidone subjects reported nine AEs vs 31 AEs in eight oral AAP subjects. Equal numbers of LAI risperidone and AAP subjects lost weight, two LAI risperidone subjects gained a mean of 1 kg compared with two subjects on AAP who gained a mean of 2.3 kg. The majority of subjects had very low EPS scores at baseline and remained unchanged or improved. Slight worsening of EPS scales occurred in three AAP vs two LAI patients. Symptom control was similar between groups.

Conclusion: These preliminary interim data suggest good tolerability of adjunctive LAI risperidone in subjects with bipolar disorder.

References:

1. Yatham, LN, Grossman F, Augustyns I, et al: An international, double-blind, randomized, controlled trial of mood stabilizers plus risperidone or placebo in the treatment of acute mania. *Brit J Psychiatry* 2003; 182:141-147.
2. Fleischhacker W, Eerdeken M, Yang X, Beauclair H, Sauret H, Chrzanowski W, Martin S, Gefvert O: Long-term safety of long-acting risperidone microspheres. *ACNP Scientific Abstracts* 2001:398.

NR305 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Popularity of Subsyndromal Symptoms in Bipolar Maintenance Studies

Supported by GlaxoSmithKline

Lakshmi N. Yatham, M.D., *Department of Psychiatry, University of British Columbia, 2255 Wesbrook Mall, Vancouver, BC V6T 2A1, Canada*; Charles L. Bowden, M.D., Bryan E. Adams, Ph.D., Joseph R. Calabrese, M.D., Angela M. Deveaugh-Geiss, M.S., Terence A. Ketter, M.D., Thomas R. Thompson, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize the relationship between polarity of index mood episode and the polarity of subsequent subsyndromal symptoms and the relationship between the polarity of subsyndromal symptoms and the polarity of subsequent mood episodes.

Summary:

Introduction: Subsyndromal symptoms (SSx) in bipolar disorder have been shown to increase risk of relapse. Polarity of SSx may

play an important role in predicting polarity of subsequent episodes and, therefore, timing and choice of treatment.

Objective: To retrospectively assess the onset and polarity of SSx in two large controlled trials, as well as their impact on the polarity of subsequent mood episodes.

Methods: Pooled data from two long-term maintenance trials (GW605/606) in bipolar I disorder were examined. The ratio of polarity of index episode (IE) to polarity of onset of SSx (depressed, manic, both) and the ratio of subsequent depressive to manic episodes were examined.

Results: Across all treatment groups, SSx of depression were 12.5-fold more frequent than manic SSx following an IE of depression, whereas SSx of mania were 1.4-fold more frequent than depressive SSx following an IE of mania. Patients with depressive SSx had a 3.90:1 ratio of subsequent depressive to manic episodes whereas patients with manic SSx had a 2.62:1 ratio of subsequent manic to depressive episodes.

Conclusions: Generally, polarity of IE and polarity of SSxs appear to be associated with a reoccurrence of a subsequent mood episode of the same polarity, especially for depression.

References:

1. Goodwin GM, Bowden CL, Calabrese JR, Grunze H, Kasper S, White R, Greene P, Leadbetter R: A pooled analysis of 2 placebo-controlled, 18-month trials of lamotrigine and lithium maintenance in bipolar I disorder. *J Clin Psychiatry* 2004; 65(3):432-41.
2. Marangell LB: The importance of subsyndromal symptoms in bipolar disorder. *J Clin Psychiatry* 2004; 65(Suppl 10):24-27.

NR306 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Lamotrigine as Monotherapy or Adjunctive Therapy for Depressive Symptoms

Supported by GlaxoSmithKline

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Educational Objectives:

At the conclusion of this session, the participant should be able to describe the effects of lamotrigine monotherapy or adjunctive therapy for acute depressive symptoms in patients with bipolar I disorder.

Summary:

Objectives: We assessed the effects of lamotrigine monotherapy and adjunctive therapy in bipolar I patients with acute depressive symptoms.

Methods: Data were combined from the 8-16 week, open-label preliminary phase of two lamotrigine maintenance trials for patients who were depressed (defined post-hoc as HAMD>18 and MRS<10). Patients received lamotrigine as monotherapy or concomitantly with other psychotropic medications for stabilization of acute symptoms.

Results: Of 1,305 enrolled patients, 897 had depressive symptoms and had efficacy assessments; 161 received lamotrigine monotherapy and 736 received lamotrigine as adjunctive treatment (most commonly antidepressants). Baseline HAMD-17 scores were similar for the monotherapy and adjunctive therapy groups (HAMD=22.7 and 23.0, respectively). Mean change HAMD-17 scores at the end of the preliminary phase for the monotherapy group were -18 (observed case [OC] analysis) and -15 (LOCF analysis) and were -13 (OC analysis) and -12 (LOCF analysis) for the adjunctive therapy group. Patients on monother-

apy had change scores that were statistically significantly greater ($p < 0.05$) than those for patients on adjunctive therapy at the following timepoints (OC analysis: Weeks 1-8, 11, end of preliminary phase; LOCF analysis: Week 1, 3-8).

Conclusions: Lamotrigine may be useful for stabilization of acute bipolar depressive symptoms when used as monotherapy or adjunctive therapy.

References:

1. Bowden CL, Calabrese JR, Sachs G, et al: A placebo-controlled 18-month trial of lamotrigine and lithium maintenance treatment in recently manic or hypomanic patients with bipolar I disorder. *Arch Gen Psychiatry* 2003; 60:392-400.
2. Calabrese JR, Bowden CL, Sachs G, et al: A placebo-controlled 18-month trial of lamotrigine and lithium maintenance treatment in recently depressed patients with bipolar I disorder. *J Clin Psychiatry* 2003; 64:1013-1024.

NR307 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

The International Lamotrigine Pregnancy Registry: 12-Year Interim Results

Supported by GlaxoSmithKline

Marianne Cunningham, Ph.D., *Department of Epidemiology, GlaxoSmithKline, Building H81 3rd Avenue, Harlow Essex CM195AW, United Kingdom*; John Messenheimer, M.D., Robert A. Leadbetter, M.D., Thomas R. Thompson, M.D.

Educational Objectives:

At the conclusion of this session, the participant should have an understanding of the lamotrigine pregnancy registry and the risk of major congenital malformations following lamotrigine monotherapy exposure.

Summary:

Objective: To monitor pregnancy outcomes in women exposed to lamotrigine.

Methods: The manufacturer of lamotrigine maintains a pregnancy registry to which physicians voluntarily report exposure and subsequent outcomes. Major congenital malformations (MCMs) are classified according to U.S. Centers for Disease Control criteria and are reviewed by a pediatrician. The percentage of MCMs is calculated for prospective first trimester lamotrigine monotherapy and polytherapy exposures. Conclusions are developed and endorsed by an independent scientific advisory committee.

Results: As of March 31, 2004, 12 MCMs were observed among 414 first trimester lamotrigine monotherapy exposures, risk=2.9% [95% CI (1.6%, 5.1%)]; compared with risks of 2-3% in the general population and 3.3-4.5% in women with epilepsy on AED monotherapy. The observed risk among 88 first trimester lamotrigine and valproate polytherapy exposures was 12.5% [95% CI (6.7%, 21.7%)] and was 2.7% [95% CI (1.0%, 6.6%)] among 182 first trimester lamotrigine polytherapy without valproate exposures. Although the registry is not powered to detect the risk of specific malformations, no consistent pattern of malformation types was observed.

Conclusions: The risk of MCMs following lamotrigine monotherapy exposure is similar to that in the general population, though the sample size is insufficient to allow definitive conclusions.

References:

1. Management of bipolar disorder during pregnancy and the postpartum period. *Am J Psychiatry* 2004; 161(4):608-20.
2. The international lamotrigine pregnancy registry update for the epilepsy foundation. *Epilepsia* 2004; 45(11):1468.

NR308 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Bipolar Patients Treated With Lamotrigine and Divalproex or Lithium

Supported by GlaxoSmithKline

James Redmond, M.D., *8245 Fredericksburg Road, San Antonio, TX 78229*; Katrina L. Jamison, B.S., Charles L. Bowden, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to better consider the use of lamotrigine in combination with other mood stabilizer medications for the management of patients with bipolar disorder.

Summary:

Introduction: A retrospective study examining patients treated with combinations of lamotrigine with either divalproex or lithium.

Method: Included in the study were patients (N=55) treated for bipolar I, II or not otherwise specified, who were treated with lamotrigine plus either divalproex or lithium. Patients were retrospectively classified as mixed, cycling, or predominantly depressed. Scores were retrospectively assigned on the Clinical Global Impression Scale for Bipolar Disorder (CGI-BP) at baseline and three months thereafter.

Results: Of patients treated with lamotrigine and divalproex (LTG/VPA), 74% completed three months of the combination, versus 56% of the lamotrigine and lithium (LTG/Li) treated patients. Due to adverse events, 13% of the LTG/VPA patients vs 31% of LTG/Li patients discontinued combination treatment. No patient had a treatment-emergent manic episode. Comparing "Change from Preceding Phase" scores for depression, mania, overall bipolar illness, patients rated as "much improved" or "very much improved" for LTG/VPA were 67%, 33%, and 67%, and for LTG/Li 44%, 44%, 63%, respectively.

Conclusions: The combinations of LTG/VPA or LTG/Li were valuable strategies for management of bipolar patients, and were generally well tolerated. Specifically LTG/VPA appeared to be particularly effective at improving depression, an often treatment-resistant part of these illnesses.

References:

1. Calabrese JR, et al: A double-blind, placebo-controlled, prophylaxis study of lamotrigine in rapid-cycling bipolar disorder. *Journal of Clinical Psychiatry* 2000; 61:0.
2. Calabrese JR, et al: A double-blind, placebo-controlled study of lamotrigine monotherapy in outpatients with bipolar I depression. *Journal of Clinical Psychiatry* 1999; 60:2.

NR309 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Efficacy of Switching to Extended-Release Carbamazepine in Bipolar Disorder

Supported by Shire US, Inc.

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to compare and contrast the efficacy of extended-release carbamazepine capsules (ERC-CBZ), as well as patients' former therapies, in the treatment of bipolar disorder previously.

Summary:

Objective: Evaluate the efficacy of ERC-CBZ in the treatment of patients switched from lithium, olanzapine, and valproate for the treatment of their bipolar disorder.

Method: This analysis pooled data from two randomized, placebo-controlled phase III trials of ERC-CBZ monotherapy in the treatment of bipolar disorder. Efficacy was assessed with the Young Mania Rating Scale (YMRS), the Clinical Global Impression-Severity (CGI-S) scale, the CGI-Improvement (CGI-I) scale, and the Hamilton Depression Rating Scale (HDRS).

Results: When compared with placebo, there were statistically different reductions in YMRS change in patients previously on lithium and valproate who were switched to ERC-CBZ. There were also significant reductions in HDRS change and CGI-S change versus placebo (and a trend toward significance for YMRS change) for those patients previously on olanzapine who were switched to ERC-CBZ. Clinical Global Impression-Improvement responder rates indicated trends toward significance for each of the three populations of patients (previously on olanzapine, lithium, or valproate) when compared with those patients on placebo, but were not significant.

Conclusion: These data suggest that ERC-CBZ is an effective therapy for patients (previously on valproate, lithium, and olanzapine) with bipolar disorder as evidenced by improvements in the YMRS, HDRS, and CGI-S rating scales.

References:

1. Weisler RH, Kalali AH, Ketter TA, the Carbatrol Study Group: A multicenter, randomized, double-blind, placebo-controlled trial of extended-release carbamazepine capsules as monotherapy for bipolar disorder patients with manic or mixed episodes. *J Clin Psychiatry* 2004; 65:478-484.
2. Ballenger JC, Post RM: Therapeutic effects of carbamazepine in affective illness: a preliminary report. *Commun Psychopharmacol* 1978; 2:159-175.

NR310 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Prevalence of Bipolar Spectrum Disorders in United Kingdom Adults Using the Mood Disorder Questionnaire

Supported by Johnson & Johnson

Robert M.A. Hirschfeld, M.D., *Department of Psychiatry & Behavioral Science, University of Texas Medical Branch, 301 University Boulevard 1.302RSH, Galveston, TX 77555-0188*; Allan H. Young, M.D., Karen D. Wagner, M.D., Theresa Frangiosa, Maneesha Mehra, Michael L. Reed, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should understand the prevalence and diagnosis rate for bipolar spectrum disorder (BSD) among United Kingdom (UK) adults.

Summary:

Background: A 2002 community survey in the United States estimated the prevalence of bipolar I and II disorder to be 3.7%.

Methods: The Mood Disorder Questionnaire (MDQ), a self-report screening instrument for bipolar I and II disorder, was mailed to a representative sample of 30,960 adults in the UK. Following two survey mailings, the MDQ was administered via phone interviews among a random sample of 1,202 adult non-responders.

Results: A total of 13,387 mail surveys were returned from the original mail-out, yielding a response rate of 43%. After weighting and adjusting for non-response bias, the estimated prevalence of MDQ positive cases was 2.72%. Only 14% of positive cases reported a previous diagnosis of bipolar disorder by a doctor, while 42% reported a diagnosis of unipolar depression only, and 44% had neither diagnosis.

Conclusions: Positive BSD cases in the UK totaled 2.72% (slightly less than the U.S. estimate but significantly more than historical estimates). The difference with U.S. prevalence may reflect cultural differences in symptom reporting.

References:

1. Hirschfeld RMA, Calabrese JR, Weissman MM, Reed ML et al: Screening for bipolar disorder in the community. *Journal of Clinical Psychiatry* 2003; 64:53-59.
2. Weissman MM, Bland RC, Canino GJ et al: Cross-national epidemiology of major depression and bipolar disorder. *JAMA* 1996; 276:293-299.

NR311 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Retrospective Review of Lamotrigine in Treatment-Resistant Depression

Supported by GlaxoSmithKline

Rosben L. Gutierrez, M.D., *PsyCare, Inc., 15525 Pomerado Road, Suite A-7, Poway, CA 92064*; Ruth Mc Kercher, Ph.D., Jason Galea, M.A., Katrina L. Jamison, B.S.

Educational Objectives:

At the conclusion of this session, the participant should be able to (1) increase clinician awareness about treatment-resistant depression. (2) increase awareness about the usefulness of lamotrigine augmentation in patients with treatment-resistant depression.

Summary:

Objective: To demonstrate that lamotrigine added to an antidepressant regimen reduces the symptoms of depression in treatment-resistant patients.

Methods: A retrospective chart review of 34 patients with a documented diagnosis of DSM-IV-TR major depressive disorder who received lamotrigine and met criteria for treatment-resistant depression was conducted. Data collection occurred at baseline and approximately 1, 3, 6, and 12 months between January 2000 and June 2004. A clinical data collection scale was used focusing on key study variables.

Results: Lamotrigine was initiated at 43mg/d at one month and titrated up to 113mg/d at 12 months. Results show a statistically significant reduction of scores as early as one month for the target symptoms of depressed mood, loss of interest, anxiety, irritability, (low) energy, and cognitive impairment. The difference from baseline remained statistically significant for these target symptoms at 3, 6, and 12 months (with the exception of irritability at six months). Additionally, the patient's response improved at all time points. Tiredness was the most common reason for discontinuation.

Conclusion: Lamotrigine added to an antidepressant regimen is an efficacious strategy for treating patients with treatment-resistant depression and has a tolerable side-effect profile.

References:

1. Amsterdam J, Hornig-Rohan M: Treatment algorithms in treatment-resistant depression. *Psychiatric Clinics of North America* 1996; 19(2):371-386.
2. Barbee JG, Jamhour NJ: Lamotrigine as an augmentation agent in treatment-resistant depression. *Journal of Clinical Psychiatry* 2002; 63(8):737-741.

NR312 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Validation of a Weight-Related Quality of Life Measure in Bipolar Depression

Supported by Bristol-Myers Squibb and Otsuka Pharmaceuticals Co, Ltd

Ronette L. Kolotkin, Ph.D., *QOL Consulting, 1004 Norwood Avenue, Durham, NC 27707*; Ross D. Crosby, Ph.D., Patricia K. Corey-Lisle, Ph.D., Hong Li, Ph.D., Gilbert L'Italien, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should have increased knowledge of the extent of obesity in treated patients with bipolar disorder, and gain a better understanding of the relationship between obesity and quality of life in patients with bipolar disorder.

Summary:

Objective: Patients with bipolar disorder have greater risk for obesity than the general population. Obesity may be due to illness-associated factors and/or medications used in treatment. This study describes validation of a weight-related measure of quality-of-life (QOL) for patients with bipolar disorder.

Methods: Individuals with bipolar disorder (n=100) were recruited from outpatient programs (mean age of 42.8 years; 66% women; 81% Caucasian; 86% overweight/obese) to complete the Impact of Weight on Quality-of-Life-Lite (IWQOL-Lite) measure. The IWQOL-Lite is a validated self-report measure of weight-related QOL, providing overall total score and domain scores on physical function, self-esteem; social life, public distress, and work.

Results: The internal consistency of the IWQOL-Lite domains and total score were reliable, ranging from 0.90 to 0.97, test-retest reliability ranged from 0.74 to 0.94. The IWQOL-Lite significantly (p<0.001) correlated with Body Mass Index (BMI) and discriminated across BMI categories (p<0.01). Bipolar patients were impaired in relation to community norms but similar to obese samples. All scores were significantly different between men and women (women had poorer quality-of-life).

Conclusions: Obesity is an area of concern for patients with bipolar disorder. The IWQOL-Lite is a valid and useful measure of weight-related quality of life in this population.

References:

1. Keck PE, McElroy SL: Bipolar disorder, obesity, and pharmacotherapy-associated weight gain. *J Clin Psych* 2003; 64(12):1426-1435.
2. Kolotkin RL, Crosby RD, Kosloski KD, Williams GR: Development of a brief measure to assess quality of life in obesity. *Obes Res* 2001; 9:102-111.

NR313 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Safety and Efficacy of Lamotrigine for Patients With Adult Bipolar Disorder

Supported by GlaxoSmithKline

Lawrence D. Ginsberg, M.D., *Red Oak Psychiatry, 17115 Red Oak Drive, Houston, TX 77090*

Educational Objectives:

At the conclusion of this session, the participant should be able to demonstrate knowledge of the role for lamotrigine in the treatment of bipolar disorder in adults, including its efficacy and safety profiles.

Summary:

Objective: To assess the effectiveness and safety of lamotrigine in the treatment of bipolar disorder.

Method: Chart reviews of 587 adult outpatients with DSM-IV bipolar disorder and treated with lamotrigine were conducted (mean age 37.6 ± 11.6 years; 72% female; 54.3% bipolar I, 28.3% bipolar II, 16.9% bipolar not otherwise specified, bipolar mixed, 0.5%). Charts of subjects who received lamotrigine in a private practice setting (LDG, Red Oak Psychiatry Associates, Houston, TX) between October 1998 and May 2004 were reviewed. Treatment response was assessed with the Clinical Global Impression-Improvement (CGI-I) scale (1 = very marked improvement, 2 = moderate improvement). Relapse was defined as a mood change

that occurs four weeks after initiation of medication or the return of symptoms from the original episode.

Results: Three hundred fifty-two subjects (59.9%) taking lamotrigine had marked to moderate improvement (CGI-I scores: 1, 20.6%; 2, 39.3%). Two hundred nineteen subjects (37.3%) relapsed during lamotrigine treatment (mean time to relapse = 207 days). The final mean lamotrigine dose was 120.4 ± 94.3 mg/d. Rash (12.6%) and headache (2.6%) were the most frequently reported side effects.

Conclusion: Lamotrigine appears effective in the treatment of bipolar disorder and was well tolerated.

References:

1. Calabrese JR, Kasper S, Johnson G, Tajima O, Vieta E, Yatham LN, Young AH: International Consensus Group on Bipolar I Depression Treatment Guidelines. *J Clin Psychiatry* 2004; 65(4):571-9.
2. Bowden CL, Asnis GM, Ginsberg LD, Bentley B, Leadbetter R, White R: Safety and tolerability of lamotrigine for bipolar disorder. *Drug Saf* 2004; 27(3):173-84.

NR314 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Safety and Efficacy of Lamotrigine for Patients With Pediatric Bipolar Disorder

Supported by GlaxoSmithKline

Lawrence D. Ginsberg, M.D., *Red Oak Psychiatry, 17115 Red Oak Drive, Houston, TX 77090*

Educational Objectives:

At the conclusion of this session, the participant should be able to demonstrate knowledge of the role for lamotrigine in the treatment of bipolar disorder in adolescents, including its efficacy and safety profiles.

Summary:

Objective: To assess the effectiveness and safety of lamotrigine in the treatment of pediatric patients with bipolar disorder.

Method: Chart reviews of 92 children and adolescents aged 7-17 years with DSM-IV bipolar disorder and treated with lamotrigine were conducted (mean age 15.2 ± 2.0 years; 66.3% female; 23.9% bipolar I, 42.4% bipolar II, 31.5% bipolar not otherwise specified, and 2.2% bipolar mixed). Charts of subjects who received lamotrigine in a private practice setting (LDG, Red Oak Psychiatry Associates, Houston, TX) between October 1998 and May 2004 were reviewed. Treatment response was assessed with the Clinical Global Impressions-Improvement (CGI-I) scale (1 = marked improvement, 2 = moderate improvement). Relapse was defined as a mood change that occurs four weeks after initiation of treatment medication or the return of symptoms from the original episode.

Results: Fifty-five subjects (59.8%) taking lamotrigine had marked to moderate improvement (CGI-I scores: 1, 16.3%; 2, 43.5%). Thirty-two patients (34.8%) relapsed during lamotrigine treatment (mean time to relapse = 143 days). The mean final lamotrigine dose was 100.54 ± 78.79 mg/d. Rash (14.13%) and headache (5.43%) were the most frequently reported side effects.

Conclusion: Lamotrigine appears effective in the treatment of pediatric patients with bipolar disorder and was well tolerated.

References:

1. Calabrese JR, Kasper S, Johnson G, Tajima O, Vieta E, Yatham LN, Young AH: International Consensus Group on Bipolar I Depression Treatment Guidelines. *J Clin Psychiatry* 2004; 65(4):571-9.
2. Bowden CL, Asnis GM, Ginsberg LD, Bentley B, Leadbetter R, White R: Safety and tolerability of lamotrigine for bipolar disorder. *Drug Saf* 2004; 27(3):173-84.

NR315 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

The Effectiveness of Switching to Extended-Release Carbamazepine in Bipolar Disorder

Supported by Shire US, Inc.

Lawrence D. Ginsberg, M.D., Red Oak Psychiatry, 17115 Red Oak Drive, Houston, TX 77090

Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss the efficacy of extended-release carbamazepine capsules (ERC-CBZ) in the treatment of patients with bipolar disorder previously on other chemotherapeutic agents.

Summary:

Objective: Evaluate the efficacy of ERC-CBZ in the treatment of patients switched from other chemotherapeutic agents for the treatment of their bipolar disorder.

Method: Data were obtained from the charts of 187 patients aged 5-70 years who met DSM-IV criteria for bipolar disorder. Clinical response to ERC-CBZ therapy was defined as a score of 3 or lower on the Clinical Global Impression-Improvement (CGI-I) scale. Relapse was defined as a change in CGI-I to 4 or greater in those subjects who had previously achieved clinical response.

Results: Data from patients switched to ERC-CBZ from lamotrigine, valproic acid, olanzapine, oxcarbazepine, lithium, and other formulations of CBZ (immediate-release [IR] CBZ, and extended-release [XR] CBZ) were analyzed. All groups of patients had mean CGI-S scores above 4.5 at initiation of ERC-CBZ treatment. CGI-I scores indicated that all groups of patients improved after the switch to ERC-CBZ; mean scores for all groups were 2.3 or lower. Interestingly, those patients previously on oxcarbazepine (mean CGI-S score: 5.1) improved dramatically in this analysis (mean CGI-I score: 2.1 [at best visit]).

Conclusion: ERC-CBZ are efficacious in the treatment of patients with bipolar disorder switched from other therapies, and may represent an important treatment option in this population.

References:

1. Weisler RH, Kalali AH, Ketter TA, the Carbatrol Study Group: A multicenter, randomized, double-blind, placebo-controlled trial of extended-release carbamazepine capsules as monotherapy for bipolar disorder patients with manic or mixed episodes. *J Clin Psychiatry* 2004; 65:478-484.
2. Ballenger JC, Post RM: Therapeutic effects of carbamazepine in affective illness: a preliminary report. *Commun Psychopharmacol* 1978; 2:159-175.

NR316 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Impact of Mood Stabilizers on Subsyndromal Symptoms in Bipolar Disorder

Supported by GlaxoSmithKline

Mark A. Frye, M.D., Department of Psychiatry, University of California at Los Angeles, 300 UCLA Medical Plaza, Suite 1544, Los Angeles, CA 90095-6968; Joseph R. Calabrese, M.D., Angela M. Deveaugh-Geiss, M.S., Charles L. Bowden, M.D., Bryan E. Adams, Ph.D., Lakshmi N. Yatham, M.D., Thomas R. Thompson, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the impact of lamotrigine, lithium, and placebo on subsyndromal symptoms in bipolar I disorder.

Summary:

Introduction: Subsyndromal symptoms in bipolar disorder can cause significant functional impairment and may increase the risk of relapse.

Objective: To assess the impact of mood stabilizer treatment on subsyndromal symptoms and subsequent mood episode.

Methods: Pooled data from two long-term maintenance trials (GW605/606) in bipolar I disorder were retrospectively examined to assess the impact of mood stabilizer treatment on subsyndromal symptoms and subsequent mood episode. Subsyndromal symptoms were defined as a HAM-D₁₇ score of 8 to 14 or an MRS₁₁ score of 8 to 13.

Results: Both lamotrigine and lithium significantly delayed the time from onset of first observed subsyndromal symptoms to intervention for any mood episode (lamotrigine vs. placebo, p=0.010, lithium vs. placebo, p=0.013). Median number of days (with 95% confidence intervals) from the onset of first subsyndromal symptoms to any mood episode were 72 (41, 154) for lamotrigine, 84 (57, 137) for lithium, and 43 (23, 78) for placebo.

Conclusions: Treatment with lamotrigine or lithium significantly delayed the time to intervention for a mood episode even after the onset of SSx.

References:

1. Goodwin GM, Bowden CL, Calabrese JR, Grunze H, Kasper S, White R, Greene P, Leadbetter R: A pooled analysis of 2 placebo-controlled 18-month trials of lamotrigine and lithium maintenance in bipolar I disorder. *J Clin Psychiatry* 2004; 65(3):432-41.
2. Marangell LB: The importance of subsyndromal symptoms in bipolar disorder. *J Clin Psychiatry* 2004; 65(Suppl 10):24-27.

NR317 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Ziprasidone Efficacy and Safety in Acute Bipolar Mania: 12-Week Study

Supported by Pfizer Inc.

Tatiana S. Ramey, M.D., Department of Department of Neuroscience, Pfizer, MS 8260-1413, Groton, CT 06320; Earl Giller, Jr., M.D., Patricia English, Ph.D., Robert Riesenber, M.D., Jitendra K. Trivedi, M.D., Vladimir A. Tochilov, M.D.

Educational Objectives:

At the conclusion of this presentation, participants should understand ziprasidone's efficacy and tolerability in the initial treatment of patients with acute bipolar mania and its long-term maintenance of effect and tolerability.

Summary:

Objectives: To establish ziprasidone's superior efficacy versus placebo in treatment of bipolar mania at three weeks and to evaluate 12-week maintenance of effect for ziprasidone and haloperidol.

Methods: 438 bipolar subjects, current episode manic or mixed, were randomized to three weeks of flexibly-dosed ziprasidone (40-80 mg BID), haloperidol (4-15 mg BID), or placebo. Placebo subjects were reassigned to ziprasidone after Week 3, and were evaluated for safety only. Subjects randomized to ziprasidone or haloperidol received treatment for ≤12 weeks. Primary efficacy measure: MRS mean change from baseline to Week 3. Maintenance of effect: percent of Week 3 responders who were Week 12 responders.

Results: Ziprasidone was superior to placebo at Week 3 in both LOCF (P<0.01) and OC (P<0.05) analyses of mean MRS change. Ziprasidone's effect was significant as early as Day 2, and was maintained to endpoint. 92.5% of Week 3 ziprasidone responders were still responders at Week 12 (equivalent to haloperidol). Ziprasidone group had lower rates of EPS at Week 12 and overall lower rates of adverse events versus haloperidol.

Conclusion: Ziprasidone effectively treated subjects with bipolar mania and maintained efficacy throughout 12-week study. Ziprasidone was safe and well tolerated, with lower rates of adverse events and EPS than seen with haloperidol.

References:

1. Keck PE, Versiani M, Potkin S et, al: Ziprasidone in the treatment of acute bipolar mania: a three-week, placebo-controlled, double-blind, randomized trial. *Am J Psychiatry* 2003; 160:741-748.
2. Weisler R, Warrington LE, Dunn J, Giller E, Mandel FS: Adjunctive ziprasidone in bipolar mania: long-term data. Presented at the 157th annual meeting of the American Psychiatric Association, May 1-6, 2004; New York, New York.

NR318 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Sildenafil: Improved Erectile Function Associated With Gains in Self-Esteem

Supported by Pfizer Inc.

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Educational Objectives:

At the conclusion of this session, the participant should understand the relationship between erectile function and psychosocial quality of life.

Summary:

Objectives: To determine associations between erectile function (EF) and psychosocial quality-of-life measured with the erectile dysfunction (ED)-specific Self-Esteem and Relationship (SEAR) questionnaire.

Methods: We pooled results from U.S. and international double-blind, placebo-controlled trials with identical protocols. Men (≥ 18 y) with ED were treated with flexible-dose sildenafil (25-100 mg) for 12 weeks. EF was categorized as normal, or as mild, mild-to-moderate, moderate, or severe ED by the EF domain of the International Index of Erectile Function. SEAR components (Overall score, Confidence and Sexual Relationship domains, Self-Esteem and Overall Relationship subscales) were scored on a 0 to 100 scale (higher scores more favorable).

Results: At end of treatment, 85% (217/256) of men receiving sildenafil versus 46% (118/254) receiving placebo had ED improve by ≥ 1 severity category, and 72% (184/256) versus 36% (91/254) had EF that was near normal (ie, mild ED) or normal. SEAR score improvement varied with ED improvement—for sildenafil, mean \pm SE change in SEAR scores across the 5 SEAR components ranged from 34 ± 2 to 42 ± 2 when ED improved ≥ 1 category, versus -3 ± 3 to 5 ± 4 when ED did not improve.

Conclusions: Most men with ED achieve normal or near normal EF scores after receiving sildenafil, accompanied by substantial improvements in self-esteem, confidence, and relationship.

References:

1. Althof SE, Cappelleri JC, Shpilsky A, Stecher V, Diuguid C, Weeney M, Duttagupta S: Treatment responsiveness of the Self-Esteem and Relationship Questionnaire in erectile dysfunction. *Urology* 2003; 61:888-892.
2. Cappelleri JC, Althof SE, Siefel RL, Shpilsky A, Bell SS, Duttagupta S: Development and validation of the Self-Esteem and Relationship (SEAR) questionnaire in erectile dysfunction. *IJIR* 2004; 16:30-38.

NR319 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Effects of Phosphodiesterase Type 5 Inhibitor Treatment of Erectile Function on Depression Severity in Men With Erectile Dysfunction *Supported by Pfizer Inc.*

Richard L. Siegel, M.D., *Department of Sexual Health, Pfizer Incorporated, 235 East 42nd Street, 235/4/1, New York, NY 10017*; H. George Nurnberg, M.D.

Educational Objectives:

At the end of this presentation, the attendee will understand the possible link between effective erectile dysfunction treatment with phosphodiesterase type 5 inhibitor (PDE5I) and improvements in depressive symptoms, as well as adherence to antidepressant medication.

Summary:

Objective: To determine if effective treatment of erectile dysfunction (ED) associated with depression, antidepressant medication, and other medical conditions, is associated with improvements in concurrent depressive symptoms.

Methods: Medline search identified six double-blind placebo-controlled studies of sildenafil treatment for ED in men with depression. Depressive symptoms were assessed using standardized measures (HAM-D, MADRS, CES-D).

Results: PDE5I sildenafil significantly improved erectile function (EF) and depression severity in men with ED associated with minor depression (Seidman, 2001) or SRI antidepressant treatment (Nurnberg et al. 2001, 2003). Sildenafil also improved EF with modest to significant improvements in depressive symptoms in men with residual ED following depression remission (Tignol, 2004), ED associated with SRI treatment (Fava, 2004), and chronic ED associated with congestive heart failure (Webster, 2004). These findings are consistent with two other PDE5I studies reporting significantly improved EF and depressive symptoms in men with ED and untreated major depression (Rosen, 2004), and in men with ED and depressive symptoms following prostatectomy (Brock, 2003).

Conclusions: These reports suggest that effective PDE5I ED treatment may be associated with improvements in symptomatic depression severity from 5% to 50% over baseline. Although direct antidepressant actions of PDE5Is have not been demonstrated, successful treatment of ED may be associated with improvements in depression and antidepressant medication adherence, which needs further study.

References:

1. Nurnberg HG, Hensley P, Gelenberg A, Fava M, Lauriello J, Paine S: Treatment of antidepressant-associated sexual dysfunction with sildenafil. *JAMA* 2003; 289:56-64.
2. Seidman S, Roose S, Menza M, Shabsigh R, Rosen R: Treatment of erectile dysfunction in men with depressive symptoms: results of a placebo-controlled trial with sildenafil citrate, *Am J Psychiatry* 2001; 158:1623-1630.

NR320 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Course of Depression and Lifestyle in Older Patients in Family Practice *Supported by Netherlands Heart Foundation*

Koen van der Kooij, M.S.C., *EMGO Institute, V U University, V.D. Boechorststraat 7, Amsterdam 1071VR, Netherlands*; Hein V. Hout, Ph.D., Aartjan Beekman, Ph.D., Harm V. Marwijk, Marten D. Haah, Ph.D.

Educational Objectives:

At the conclusion of this session, the participants should be able to recognize the changes in lifestyle in patients with a major depression.

Summary:

Objectives: Does change in lifestyle differ between depressed and non-depressed older family practice patients over a period of six months? Does a reduction of depressive symptoms have a positive effect on lifestyle?

Methods: The design is a case-control study with a six-month follow-up. In 14 family practices a baseline sample of 140 consecutively visiting major depression patients (age > 55 year) and 140 non-depressed controls matched on age and gender were recruited.

Demographic characteristics, psychiatric status, and lifestyle measures (e.g. smoking, drinking, sleeping) were assessed by means of a structured interview.

Results: The smoking status of the 140 depressed patients changed dramatically: 62 patients restarted and 22 stopped smoking, independent of mood change. In the non-depressed patients the smoking status changed of only 17 patients ($X^2=88$, $df=3$, $p < 0.001$) Improvement in mood was correlated with increased sleep quality ($R = 0.32$, $p < 0.001$) in both depressed and non-depressed patients. None of the other lifestyle indicators correlated with mood change over a period of six months.

Conclusion: Depressed patients dramatically restarted smoking independent of mood improvements over six months. Reduction in depressed mood was related to an increase in sleep quality.

Funded by the Netherlands Heart Foundation.

References:

1. Lemke MR, Puhl P, Broderick A: Motor activity and perception of sleep in depressed patients. *J Psychiatr Res* 1999; 33(3):215-24.
2. Wilhelm K, Mitchell P, Slade T, Brownhill S, Andrews G: Prevalence and correlates of DSM-IV major depression in an Australian national survey. *J Affect Disord* 2003; 75(2):155-62.

NR321 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Bipolar Disorder: Relationship Between Body Mass Index and Quality of Life

Supported by Bristol-Myers Squibb and Otsuka Pharmaceuticals Co, Ltd

Patricia K. Corey-Lisle, Ph.D., *Department of Epidemiology, Bristol Myers Squibb, 5 Research Parkway, Wallingford, CT 06492*; Ronette L. Kolotkin, Ph.D., Ross D. Crosby, Ph.D., Vickie V. Tuomari, M.S., John W. Newcomer, M.D., Gilbert L'Italien, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should have increased knowledge of the extent of obesity in treated patients with bipolar disorder and to gain a better understanding of the relationship between obesity and quality of life in patients with bipolar disorder.

Summary:

Objective: Patients with bipolar disorder (BPD) have greater risk for obesity than the general population. This study examines the relationship between weight and quality of life (QOL) in BPD.

Methods: Individuals with BPD ($n=100$) were recruited from outpatient programs. Assessments included height, weight and the Impact of Weight on Quality of Life-Lite (IWQOL-Lite) measure. The IWQOL-Lite is a validated self-report measure of weight-related QOL, providing overall total score and domain scores on physical function, self-esteem, social life, public distress, and

work. Higher scores are indicative of better QOL. Total and domain scores were compared for participants by body mass index (BMI) classification.

Results: Eighty-six percent (86%) of all participants were categorized as overweight/obese. BMI significantly ($p < 0.001$) correlated with IWQOL-Lite total score ($r = -0.691$) and all domain scores. Score decreases corresponded to increases in BMI (IWQOL-Lite total score/BMI category: 87.3/18-24.9; 82/25-29.9; 60.5/30-34.9; 58.1/35-39.9; 39.3/40+). Eta-square for BMI on the total score was 0.329, indicating that 32.9% of the variance was attributable to BMI classification.

Conclusions: Obesity is an area of concern for patients with bipolar disorder, highlighting the need for better preventative measures. Physicians should be aware of both health risks and quality-of-life implications when treating these patients.

References:

1. Keck PE, McElroy SL: Bipolar disorder, obesity, and pharmacotherapy-associated weight gain. *J Clin Psychiatry* 2003; 64(12):1426-1435.
2. Kolotkin RL, Crosby RD, Kosloski KD, Williams GR: Development of a brief measure to assess quality of life in obesity. *Obes Res* 2001; 9:102-111.

NR322 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Factors Influencing a CGI-S Evolution in Depressive Remitted Patient

Supported by Pfizer Inc.

Alain Gerard, M.D., *17 Rue des Marronniers, Paris 75016, France*; Bruno Falissard, M.D., Gwenaél Goussiaune, Veronique Millet, M.D.

Educational Objectives:

At the conclusion of this session, the participant should understand which is the optimal care management of remitted depressed patient in order to avoid any further recurrence.

Summary:

Objective: To present the variables that are correlated with a CGI-S score evolution (intermediate 6-month analysis) in remitted recurrent depressive patients.

Method: During 2003-2004, private psychiatrists have included and followed during one year patients who had been suffering from major depressive episode (DSM-IV) and were in complete or partial remission of their last episode. At six months, the CGI-S and the usual psychiatrist's practice have been assessed. Data of 453 patients related with 126 psychiatrists have been crossed by logistic regression (patient and psychiatrist personality [TCI], profiles and medical care).

Results: Logistic regression has found the following variables, obviously correlated with the CGI-S evolution: remission status, treatment initiation since inclusion, harm avoidance (patient TCI), thymoregulator treatment at inclusion and new comorbid disease.

CART model found that the best way for a CGI-S decrease was: patient in partial remission, with no new comorbid disease, presenting a Cooperation score ≥ 25.25 (TCI) and with less than 4.5 medical visits (mean) during the last 6 months.

Conclusion: CGI-S evolution was correlated with the remission status and also the patient personality.

References:

1. Lepine JP, Caillard V, Bisserbe JC, Boyer P, et al: A randomized, placebo-controlled trial of sertraline for prophylactic treatment of highly recurrent major depressive disorder. *Am J Psychiatry* 2004; 161:836-842.

2. Frank E, Prien RF, Jarrett RB et al: Conceptualization and rationale for consensus definitions of term in major depressive disorder. Arch Gen Psychiatry 1991; 48:851-855.

NR323 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

More Rapid Onset of Sleep-Improving Effects of Mirtazapine FDT Versus Venlafaxine XR

Supported by Organon Inc.

Armin Szegedi, M.D., Department of Psychiatry, Klinik und Hochschulambulanz, Eschenallee 3, Berlin 14050, Germany; M. Philipp, Otto Benkert, R. Kohnen, C. Heinrich, Ross Baker, Ph.D., John Simmons, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the degree of improvement in sleep (at the different time assessments, based on the HAMD Factor VI score) for patients enrolled in this multicenter trial using either mirtazapine or venlafaxine.

Summary:

Objective: Restoration of normal sleep is important for all antidepressant therapy. In the present analysis, we compared the onset of sleep improvement between mirtazapine FDT and venlafaxine XR.

Methods: The multicenter trial was conducted in Germany. Subjects with a DSM-IV major depressive disorder and a 17-HAMD score ≥ 21 , were randomized to mirtazapine FDT 30-45 mg/day (n=130; 91 completed) or venlafaxine XR 75-225 mg/day (n=128; 81 completed), titrated within six days to the highest dose. The primary outcome measure was the change in the (HAMD) Factor VI score. Assessments were performed on day 5, 8, 11, 15, 22, 29, and 43 after treatment initiation. Analyses were performed using the ITT population (LOCF approach).

Results: The change from baseline in total Factor VI score was significantly superior ($p < 0.05$) for the mirtazapine-treated group compared with the venlafaxine-treated group on day 5 (-1.16 vs -0.59 points), day 8 (-1.59 vs -0.89), day 11 (-1.78 vs -1.29), and day 43 (-2.50 vs -1.84).

Conclusion: Rapid improvement in sleep function may contribute to the antidepressant effect of mirtazapine, and extends previous observations on the rapid onset of antidepressant effect with mirtazapine. Drugs similar to mirtazapine with a shorter half-life also may be beneficial for the treatment of sleep disturbances.

References:

1. Thompson C, van Willigenburg APP, Heukels AJ, Janssens CJJG, et al: Mirtazapine vs. SSRIs: A meta-analysis on onset of antidepressant activity. Poster presented at the 157th meeting of the American Psychiatric Association (APA); May 1-6, 2004; New York.
2. Behnke K, Søgaard J, Martin S et al: Mirtazapine orally disintegrating tablet versus sertraline: a prospective onset of action study. J Clin Psychopharmacology 2003; 23:358-64.

NR324 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

More Rapid Onset of Antidepressant Effect With Mirtazapine FDT Versus Venlafaxine XR

Supported by Organon Inc.

Armin Szegedi, M.D., Department of Psychiatry, Klinik und Hochschulambulanz, Eschenallee 3, Berlin 14050, Germany; M. Philipp, Otto Benkert, R. Kohnen, C. Heinrich, Monique van der Vegte-Seden, Ross Baker, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the design and results of this clinical trial using mirtazapine fast dissolving tablets and venlafaxine XR.

Summary:

Objective: Compare the onset of antidepressant effect and tolerability between the FDT formulation of mirtazapine and venlafaxine XR.

Methods: The multicenter trial was conducted in Germany. Subjects with a DSM-IV major depressive disorder and a 17-HAMD score ≥ 21 , were randomized to mirtazapine FDT 30-45 mg/day (n=130; 91 completed) or venlafaxine XR 75-225 mg/day (n=128; 81 completed), titrated to the highest dose within six days. The primary outcome measure was the average of change from baseline HAMD-17 score over days 5, 8, 11 and 15 after treatment initiation. Secondary outcomes included change in HAMD-17 score, response (HAMD-17 score decreased by $> 50\%$) and remission (HAMD-17 scores < 7) up to day 43. Analyses were performed using the ITT population (LOCF approach).

Results: Mirtazapine subjects achieved significantly greater decreases in average HAMD-17 score (-7.48, n = 127) than venlafaxine subjects (-5.94, n = 115, $P = .008$). Response rates were significantly higher ($P < .05$) for mirtazapine subjects on days 8 (19.7% vs 6.1%), 11 (31.5% vs 15.7%), and 22 (48.0% vs 33.9%), and remission was significantly higher on day 15 (17.3% vs 7%). The tolerability of the two drugs was similar.

Conclusion: Mirtazapine FDT produced a significantly more rapid onset of antidepressant action than venlafaxine XR, extending earlier findings.

References:

1. Guelfi JD, Anseau M, Timmerman L, Korsgaard S, Mirtazapine-Venlafaxine Study Group: Mirtazapine versus venlafaxine in hospitalized severely depressed patients with melancholic features. J Clin Psychopharmacol 2001; 21:425-31.
2. Thompson C, van Willigenburg APP, Heukels AJ, Janssens CJJG et al: Mirtazapine vs. SSRIs: A meta-analysis on onset of antidepressant activity. Poster presented at: the 157th meeting of the American Psychiatric Association (APA); May 1-6, 2004; New York.

NR325 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

More Rapid Onset of Effect on the Core Symptoms of Depression With Mirtazapine Than SSRIs

Supported by Organon Inc.

Michael E. Thase, M.D., Department of Psychiatry, University of Pittsburgh Medical Center, 3811 O'Hara Street, Pittsburgh, PA 152132593; Ross Baker, Ph.D., John Simmons, M.D., Arjen PP. van Willigenburg, M.S.C., Anja J. Heukels, CJJG Janssens, Albert J. Schutte, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe how mirtazapine rapidly improves the core symptoms of depression based on the Bech-6 factor score.

Summary:

Objective: Mirtazapine has a more rapid onset of antidepressant effect than SSRIs. To determine the effect of mirtazapine on the core symptoms of depression, we conducted a meta-analysis comparing the Bech-6 factor score of individual patient data from 10 SSRI-controlled studies of mirtazapine versus SSRIs.

Methods: In all trials, subjects who met either DSM III or IV criteria for major depression were randomized to treatment for six weeks with either mirtazapine (1201; 74.5% completed) or an SSRI (1200; 77.5% completed). The time to first response (50%

reduction in Bech-6 score) and time to sustained response (50% reduction on Bech 6 score maintained to endpoint) were compared using fixed and random effects models, and Kaplan-Meier survival analysis.

Results: Patients treated with mirtazapine had a significantly greater first response ($P = .008$) and sustained response ($P = .03$) on the Bech 6 score than subjects treated with SSRIs. The cumulative probability of response was significantly higher for mirtazapine versus SSRIs, and not significantly different for the cumulative probability of sustained response.

Conclusion: The results suggest that the early onset of antidepressant effect observed with mirtazapine can be at least partially explained by a direct, rapid alleviation of the core symptoms of depression by mirtazapine.

References:

1. Thompson C, van Willigenburg APP, Heukels AJ, Janssens CJG, et al: Mirtazapine vs. SSRIs: a meta-analysis on onset of antidepressant activity. Poster presented at: the 157th meeting of the American Psychiatric Association, May 1-6, 2004; New York.
2. Behnke K, Sogaard J, Martin S, et al: Mirtazapine orally disintegrating tablet versus sertraline: a prospective onset of action study. *J Clin Psychopharmacology* 2003; 23:358-64.

NR326 Tuesday, May 24, 12:00 p.m.-2:00 p.m. **More Rapid Onset of Sleep-Improving Effects With Mirtazapine FDT Versus Sertraline** *Supported by Organon Inc.*

Ross Baker, Ph.D., *Department of Medical Affairs, Organon Pharmaceuticals, 56 Livingston Avenue, Roseland, NJ 07068*, Albert J. Schutte, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the degree of improvement in sleep (at the different time assessments, based on the HAMD Factor VI score) for patients enrolled in this multicenter trial using either mirtazapine or sertraline.

Summary:

Objective: Restoration of normal sleep is integral to all antidepressant therapy. In the present analysis, we compared the onset of sleep improvement between mirtazapine and the SSRI sertraline.

Methods: Subjects with a DSM-IV major depressive episode and HAMD-17 score of at least 18 were randomized to treatment with mirtazapine FDT 30-45 mg/day ($N = 176$; 135 completed) or sertraline 50-150 mg/day ($N = 170$; 138 completed). The primary outcome measure was the change in the (HAMD) Factor VI score of sleep disturbance. Assessments were performed on day 4, 7, 10, 14, 28, 42, and 56 after initiation of treatment. Analysis was of the ITT LOCF population with ANOVA.

Results: The change from baseline in total Factor VI score was significantly superior ($p < 0.001$) for the mirtazapine-treated group compared with the sertraline-treated group on all days of assessment: day 4 (-1.3 vs -0.5), day 7 (-2.0 vs -1.0), day 10 (-2.1 vs -1.2), day 14 (-2.4 vs -1.6), day 28 (-2.6 vs -1.9), day 42 (-2.8 vs -2.2), and day 56 (-3.0 vs -2.2).

Conclusion: Rapid improvement in sleep function may contribute to the enhanced antidepressant efficacy of mirtazapine versus SSRIs. Drugs similar to mirtazapine with a shorter half-life also may have utility as sleep aids.

References:

1. Thompson C, van Willigenburg APP, Heukels AJ, Janssens CJG, et al: Mirtazapine vs. SSRIs: a meta-analysis on onset

of antidepressant activity. Poster presented at: the 157th meeting of the American Psychiatric Association (APA); May 1-6, 2004; New York.

2. Behnke K, Sogaard J, Martin S, et al: Mirtazapine orally disintegrating tablet versus sertraline: a prospective onset of action study. *J Clin Psychopharmacology* 2003; 23:358-64.

NR327 Tuesday, May 24, 12:00 p.m.-2:00 p.m. **Efficacy of Quetiapine in Improving Quality of Life in Bipolar Depression** *Supported by AstraZeneca Pharmaceuticals*

Jan Endicott, Ph.D., *Department of Psychiatry, NY State Psychiatric Institute, 1051 Riverside Drive, Unit 123, New York, NY 10032*; Krithika Rajagopalan, Ph.D., Wayne MacFadden, M.D., Margaret C. Minkwitz, Ph.D., James Gaddy

Educational Objectives:

At the conclusion of this session, the participant should recognize the efficacy of quetiapine in improving HRQOL in patients with bipolar depression.

Summary:

Introduction: Bipolar depression is associated with impaired quality of life (QOL). However, QOL has been under-investigated as a therapeutic target in bipolar disorder. This study investigated changes in QOL in patients with bipolar depression treated with quetiapine.

Methods: Quetiapine monotherapy was studied in an eight-week, double-blind, placebo-controlled trial in patients with bipolar I or II disorder. Patients were randomized to receive quetiapine 600 mg/day ($n=180$), quetiapine 300 mg/day ($n=181$), or placebo ($n=181$). QOL was evaluated using the 16-item short form of the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q SF) at baseline, Week 4, and Week 8.

Results: Baseline Q-LES-Q SF scores were low (quetiapine 600 mg/day group: 34.1; quetiapine 300 mg/day group: 36.1; placebo group: 34.2), consistent with poor HRQOL. At final assessment the improvement in Q-LES-Q SF score was significantly greater in both quetiapine treatment groups (11.7 in the 600 mg/day group and 10.8 in the 300 mg/day group) than in the placebo group (6.4, $p < 0.001$). Significant improvement was noted at the first Q-LES-Q SF assessment (Week 4) in both quetiapine treatment groups versus placebo ($p < 0.001$). Quetiapine was generally well tolerated, with low levels of extrapyramidal side effects and minimal weight gain.

Conclusions: Quetiapine monotherapy is effective in improving QOL in patients with bipolar depression.

References:

1. Cooke RG, Robb JC, Young LT, Joffe RT: Well-being and functioning in patients with bipolar disorder assessed using the MOS 20-ITEM short form (SF-20). *J Affect Disord* 1996; 39:93-97.
2. Endicott J, Nee J, Harrison W, Blumenthal R: Quality of Life Enjoyment and Satisfaction Questionnaire: a new measure. *Psychopharmacol Bull* 1993; 29:321-326.

NR328 Tuesday, May 24, 12:00 p.m.-2:00 p.m. **Efficacy of Ziprasidone in Dysphoric Mania** *Supported by Pfizer Inc.*

John M. Zajecka, M.D., *Department of Psychiatry, Rush University Medical Center, 1700 West Van Buren Street, 5th Floor, Chicago, IL 60612*; Stephen R. Murray, M.D., Tatiana S. Ramey, M.D., Francine Mandel, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss the efficacy of ziprasidone in dysphoric mania based on the reported results of a dysphoric mania patient analysis in the ziprasidone bipolar mania trials.

Summary:

Objective: To evaluate efficacy of ziprasidone 40-80 mg BID in patients with bipolar mania who also exhibited dysphoria at baseline.

Methods: Data were pooled from two similar randomized, double-blind, three-week, placebo-controlled trials and the first three weeks of a third study comparing ziprasidone and haloperidol with placebo. Dysphoria was defined as scores ≥ 2 on ≥ 2 of the SADS-C items 1-6, 16, and 20.

Results: On the SADS-C Mania Rating Scale (MRS), the primary efficacy variable, improvement with ziprasidone ($n=160$) was rapid and significantly greater than with placebo ($n=70$) at all visits, starting at Day 2 (LOCF) ($p \leq 0.01$). Haloperidol ($n=30$) was superior to placebo ($p \leq 0.01$) at Days 4 and 14. On CGI-S, ziprasidone was superior to placebo at all visits starting at Day 4 ($p \leq 0.01$); haloperidol was superior at Day 4 only ($p \leq 0.01$). On HAM-D (SADS-C extracted), significant improvement with ziprasidone versus placebo occurred at Day 7 ($p=0.008$). Ziprasidone but not haloperidol demonstrated significant improvement versus placebo ($p \leq 0.01$) in MRS Manic Syndrome (Days 2, 7, 14, endpoint) and Behavior and Ideation subscales (Day 2 on). PANSS Total and Positive, and GAF scores (endpoint).

Conclusions: In patients with dysphoric mania, ziprasidone demonstrated rapid symptom control and reduction of illness severity, with significantly improved overall functioning.

References:

1. Potkin S, Keck P, Giller E, et al: Ziprasidone in bipolar mania: efficacy across patient subgroups. Presented at the 157th annual meeting of the American Psychiatric Association. May 1-6, 2004; New York, New York.
2. Dilsaver SC, Chen YR, Shoaib AM, Swann AC: Phenomenology of mania: evidence for distinct depressed, dysphoric, and euphoric presentations. *Am J Psychiatry* 1999; 156:426-30.

NR329 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Treatment Adherence With Antipsychotics Among Bipolar and Manic Patients

Supported by AstraZeneca Pharmaceuticals

Frank D. Gianfrancesco, Ph.D., *Hecon Associates, 9833 Whetstone Drive, Montgomery Village, MD 20886*; Krithika Rajagopalan, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to (1) describe the components of antipsychotic treatment adherence and their measurement with prescription claims data; (2) compare antipsychotics with respect to treatment compliance and treatment duration; and (3) identify patient and antipsychotic-related factors associated with poor treatment compliance and shorter treatment duration.

Summary:

Objective: To assess treatment adherence to antipsychotic monotherapy in bipolar/manic disorder.

Methods: 18,158 antipsychotic monotherapy treatment episodes for bipolar and manic disorders were identified from a claims database (1999-2003) representing 50 million U.S. insured. Adherence measures included treatment compliance, captured by regularity of prescription refills, and treatment duration. Atypicals included risperidone, olanzapine, quetiapine, and ziprasidone,

conventional agents included haloperidol, perphenazine, thioridazine, and thlothixene. Multiple regression adjusted for patient characteristics.

Results: Quetiapine alone had significantly ($P < 0.05$) greater compliance than the conventional agents and had the highest compliance among the atypicals, which was significantly greater than for risperidone or olanzapine. Olanzapine and ziprasidone demonstrated significantly greater compliance than risperidone. Daily dose was negatively associated with compliance for all agents except quetiapine ($P < 0.05$ for risperidone and the conventional agents), which had a positive, but non-significant association ($P = 0.074$). Quetiapine and risperidone had significantly longer treatment duration than olanzapine, ziprasidone, and the conventional agents. All atypicals, except ziprasidone, had significantly lower odds of switching to another psychotropic compared with conventional agents; quetiapine had the lowest estimated odds ratio.

Conclusion: According to claims data, treatment adherence for quetiapine appears higher than for other agents commonly prescribed for bipolar/manic disorder, possibly due to more favorable tolerability.

References:

1. Al-Zakwani IS, Barron JJ, Bullano MF, Arcona S, Drury CJ, Cockerham TR: Analysis of health care utilization patterns and adherence in patients receiving typical and atypical antipsychotic medications. *Curr Med Res Opin* 2003; 19:619-26.
2. Keck PE Jr, McElroy SL, Strakowski SM, et al: Factors associated with pharmacologic noncompliance in patients with mania. *J Clin Psychiatry* 1996 Jul; 57:292-7

NR330 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Brain Function and Estrogen in Perimenopausal Depression

Melinda Morgan, Ph.D., *Department of Psychiatry, UCLA, 760 Westwood Plaza, Suite 37-439, Los Angeles, CA 90024*; Ian A. Cook, M.D., Andrea J. Rapkin, M.D., Andrew F. Leuchter, M.D.

Educational Objectives:

At the conclusion of the session, the participant will be informed about the change in brain function during estrogen augmentation in perimenopausal depression. In subjects who reached full remission, there was a significant decrease in right frontal QEEG cordance.

Summary:

Objective: To investigate changes in brain function during estrogen augmentation in women with perimenopausal depression.

Method: Quantitative electroencephalography (QEEG) was used to examine brain function during estrogen augmentation of antidepressant medication in 13 women with perimenopausal depression. Women between the ages of 40 and 60 with major depressive disorder (MDD) in partial remission who were taking antidepressant medication for a minimum of eight weeks and were experiencing one or more perimenopausal symptoms (hot flashes, night sweats, irregular periods, sleep disturbance) were recruited from the community. QEEG cordance, a measure that has a moderately strong association with cerebral perfusion, was obtained before and after six weeks of treatment with .625 mg. of conjugated estrogen per day. We examined the relationship between prefrontal neurophysiologic changes and remission of depressive symptoms.

Results: Women who experienced remission of depressive symptoms ($\text{Ham-D} \leq 7$) had a significant decrease in right prefrontal cordance after six weeks of estrogen treatment ($p = .008$, $t_{(8)} = -3.54$). There was no significant change in right prefrontal cordance in participants who did not remit.

Conclusion: In women with perimenopausal depression in partial remission, brain physiologic changes during estrogen augmentation were associated with full remission of depression.

References:

1. Leuchter AF, et al: Relationship between brain electrical activity and cortical perfusion in normal subjects. *Psychiatry Res* 1999; 90(2):125-140.
2. Leuchter AF, et al: Cordance: a new method for assessment of cerebral perfusion and metabolism using quantitative electroencephalography. *Neuroimage* 1994; 1(3):208-219.

NR331 Tuesday, May 24, 12:00 p.m.-2:00 p.m. **Validation of Chrono-Record Self-Reporting Software by Inpatients With Mania**

Michael Bauer, M.D., *Department of Psychiatry, Charite University Hospital, Humboldt University Schumannstr 20121, Berlin 10117, Germany*, Johanna Sasse, M.D., Natalie L. Rasgon, M.D., Tina Schlosser, M.D., Tasha Glenn, Tom Bschor, M.D., Paul Grof

Educational Objectives:

At the conclusion of this session, the participant should know more about an automated tool for self-reporting mood in bipolar disorder.

Summary:

Objective: Automation of data collection in longitudinal studies can improve data quality, decrease missing data, enhance patient compliance and lower the costs. ChronoRecord software automates daily collection of mood, sleep, medication, life events, and menstrual data. We have previously validated self-reported mood ratings on ChronoRecord with HAMD ratings using outpatients with bipolar disorder. This ongoing study validates self-reported mood ratings on ChronoRecord with clinician mood ratings on YMRS and Beech-Rafaelsen Manic Rating Scale (MRS) using inpatients with mania.

Methods: The inclusion criteria were inpatients in a hypomanic or manic episode with a DSM-IV diagnosis of bipolar disorder. The validation compared the patient self-rating of mood on the ChronoRecord software visual-analog scale with a clinical rating on YMRS and MRS taken at the same time. Pearson correlation analyses were completed.

Results: The Pearson correlation coefficient between YMRS and ChronoRecord was 0.580 ($p < .001$) for 26 ratings from 13 patients, and between MRS and ChronoRecord was 0.821 ($p < .001$) for 12 ratings.

Conclusion: Preliminary results from the inpatients with mania show a good correlation between self-reported ChronoRecord mood ratings and clinician ratings for YMRS and MRS.

References:

1. Bauer M, Grof P, Gyulai L, Rasgon N, Glenn T, Whybrow PC: Using technology to improve longitudinal studies: self-reporting in bipolar disorder. *Bipolar Disorders* 2004; 6:67-74.
2. Trendelenburg M, Sasse J, Schlosser T, Whybrow PC, Grof P, Gyulai L, Rasgon N, Glenn T, Bschor T, Bauer M: Using software to improve longitudinal studies: self-reporting with ChronoRecord in bipolar disorder. *Acta Psychiatrica Scandinavica* 2003; 423(110):39-40.

NR332 Tuesday, May 24, 12:00 p.m.-2:00 p.m. **Temporal Relation Between Sleep and Mood in Bipolar Disorder**

Michael Bauer, M.D., *Department of Psychiatry, Charite University Hospital, Humboldt University Schumannstr 20121,*

Berlin 10117, Germany; Paul Grof, Tasha Glenn, Natalie L. Rasgon, M.D., Peter C. Whybrow, M.D., Tom Bschor, M.D.

Educational Objectives:

At the conclusion of this session, the participant should know more about the relation between sleep changes and mood changes in bipolar disorder.

Summary:

Objective: Sleep disturbances are frequent warning signs of both mania and depression in bipolar disorder. This study used cross correlation analysis to characterize more precisely the relationship between sleep and mood in the prodromal period.

Methods: Self-reported mood and sleep data (mean 169 \pm 59 days) from 59 outpatients receiving standard treatment were analyzed. The cross-correlation function was used to determine the latency between a change in sleep and change in mood for time shifts of between -7 to 7 days.

Results: An inverse correlation was found between a change in sleep and change in mood in 24 of 59 patients (41%), usually with a time latency of one day. Patients with a significant cross-correlation between sleep and mood reported about two-thirds of all large sleep changes of >3 hours and three-fourths of all large mood changes (>20 on 100-unit scale).

Conclusion: In most patients with a significant correlation between sleep and mood, the mood change occurred on the day following the sleep change. Sleep changes from a previous pattern, especially those of more than three hours, appear to occur late in the prodromal period, may indicate that a large mood change is imminent, and an intervention is immediately needed.

References:

1. Bauer M, Grof P, Gyulai L, Rasgon N, Glenn T, Whybrow PC: Using technology to improve longitudinal studies: self-reporting in bipolar disorder. *Bipolar Disorders* 2004; 6:67-74.
2. Jackson A, Cavanagh J, Scott J: A systematic review of manic and depressive prodromes. *J Affect Disord* 2003; 74:209-217.

NR333 Tuesday, May 24, 12:00 p.m.-2:00 p.m. **HPA System Regulation in Treatment Monitoring and in the Long-Term Course of Depression** *Supported by GlaxoSmithKline*

Martin Hatzinger, M.D., *Department of Depression Research, Psychiatric University Hospital, Wilhelm Klein Street 27, Basel 4025, Switzerland*; Serge Brand, Katrin Baumann, Ulrich M. Hemminger, M.D., Edith Holsboer-Trachsler, M.D.

Educational Objectives:

At the conclusion of this session, the participant should learn about the neurobiological basis of the treatment course and long-term outcome of depression.

Summary:

Background: Hypothalamic-pituitary-adrenocortical (HPA) system dysregulation as reflected by the combined dexamethasone (DEX)/corticotropin releasing hormone (CRH) test is a common finding in major depression (MD). In the present study, we investigated the relationship between HPA system alteration and both treatment response during acute MD and the long-term outcome of depression.

Methods: In 20 patients with MD DEX/CRH tests and psychometric assessments (Hamilton depression rating scale) were carried out at baseline, after a six week antidepressant treatment period (trimipramine 200 mg/d), and after long-term course (follow-up after two to 10 years). After one week of treatment an additional psychometric rating was conducted to detect early treatment response. Long-term course of depression was characterized by the number of episodes until study entry.

Results: Both early treatment response and the six-week treatment outcome correlated inversely with the cortisol values during the DEX/CRH test. Additionally, the number of episodes was highly associated with the DEX/CRH test outcome.

Conclusion: We conclude that HPA system regulation in MD is associated with early treatment response during acute depression and with treatment outcome after six weeks. Furthermore, unfavorable long-term course of depression is significantly correlated with increasing HPA system dysfunction.

Funding Source: Supported by the Swiss National Foundation No. 3200-052778.97

References:

1. Holsboer F: The corticosteroid receptor hypothesis of depression. *Neuropsychopharmacology* 2000; 23:477-501.
2. Heuser I, Yassouridis A, Holsboer F: The combined dexamethasone/CRH test: a refined laboratory test for psychiatric disorders. *Journal of Psychiatric Research* 1994; 28:341-356.

NR334 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Is There a Doctor in the House? Medical Comorbidity in Patients With Affective Disorder

Supported by Pfizer Inc., GlaxoSmithKline, Forrest, Lilly, Cephalon, Novartis and Wyeth

Suhayl J. Nasr, M.D., *NASR Psychiatric Services PC, 2814 South Franklin Street, Michigan City, IN 46360-1843*; Anand Popli, M.D., Burdette J. Wendt

Educational Objectives:

At the conclusion of this session, the participant should recognize that (1) many affective disorder patients have a comorbid medical condition, and (2) bipolar patients with a comorbid medical condition are more severely ill than those without a comorbidity.

Summary:

Introduction: The comorbidity of affective disorders with other psychiatric illnesses is well established. Fewer data exist on the comorbidity of affective disorders with other medical problems.

Method: A chart review was performed on all 1,161 active patients in a rural outpatient psychiatric office. Data collected included demographic information, clinical diagnoses, MiniSCID and SCL-90, and background health questionnaires. Patients were identified as having a comorbid medical condition if they reported illnesses involving the endocrine or cardiovascular system, cancer, or any other chronic disease.

Results: Comorbid medical conditions were reported by 51% of bipolar patients and by 44% of nonbipolar patients. This difference was not significant. Bipolar patients who had a comorbid condition had significantly higher scores on the SCL-90 than those bipolar patients without a comorbid condition ($p < 0.04$ for all subscales). Unipolar patients with a comorbid condition scored significantly higher than unipolar patients without a comorbid condition ($p < 0.02$) on the somatization, obsessive-compulsive, and depression subscales.

Conclusions: Medical comorbidity is prevalent in affective disorder patients. Their psychopathology is more severe. Treatment of these patients and the training of their providers should take into account this medical comorbidity.

References:

1. Kilbourne AM, Cornelius JR, Han X, Pincus HA, Shad M, Saloum I, Conigliaro J, Haas GI: Burden of general medical conditions among individuals with bipolar disorder. *Bipolar Disord* 2004; 6:368-73.
2. Beyer J, Kuchibhatla M, Gersing K, Krishnan KR: Medical comorbidity in a bipolar outpatient clinical population. *Neuropsychopharmacology* 2004.

NR335 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Yoga Augmentation in Partial Response to Antidepressant Medications

Ian A. Cook, M.D., *Department of Psychiatry, University of California Los Angeles NPI, 760 Westwood Plaza, Room 37-426, Los Angeles, CA 90024-1759*; David Shapiro, Ph.D., Andrew F. Leuchter, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the use of yoga as a complement to antidepressant medication in managing partial response in unipolar depression.

Summary:

Objective: While patients with major depression derive great symptomatic improvement with antidepressant pharmacotherapy, many individuals experience a partial response to first-line treatment, with the persistence of residual symptoms and ongoing functional disability. Depression is often offered as a reason to participate in yoga classes, but with little systematic evidence to guide its use. Our objective was to examine yoga as a complement to pharmacotherapy for antidepressant partial responders.

Methods: Subjects were 25 adult outpatients with unipolar major depression (mean age 44.6 (s.d 14.8) yrs, 7M:18F), already receiving an antidepressant medication for >3 months but experiencing residual symptoms (initial Hamilton Depression Score (HAM-D) 13.1 (2.8)). The Iyengar yoga intervention was an eight-week course with three, 90-minute sessions/wk.

Results: 11 subjects completed the program; most dropouts occurred in the first week. Of completers, HAM-D scores decreased from 12.4 (4.1) to 4.1 (3.4), with a mean change of -8.3 (4.4) points ($p < 0.0001$); 10 of 11 subjects achieved remission (HAM-D <7).

Conclusions: Yoga may be useful as a complementary treatment for residual symptoms in partial responders to antidepressants. The proportion of subjects who left the study suggests that refinement of the yoga course is needed to improve acceptability to depressed patients.

References:

1. Complementary and Alternative Medicine Use Among Adults: United States, 2002. *Advance Data, US Dept HHS, Number 343, 2004.*
2. Jorm AF, Christensen H, Griffiths KM, Rodgers B: Effectiveness of complementary and self-help treatments for depression. *Med J Aust* 2002; 176:S84-S96.

NR336 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Medication Adherence in Bipolar Patients With Substance Use Disorders

Supported by Abbott Laboratories

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Educational Objectives:

At the conclusion of the session, the participant should be able to recognize specific adherence issues in bipolar substance abusers.

Summary:

Objective: Comorbid SUD is associated with medication non-compliance in bipolar patients (Keck, et al 97). Another study found significantly greater compliance with valproate than lithium in bipolar substance abusers (Weiss, et al 98). This study compares adherence and response to mood stabilizers in patients with and without comorbid substance use disorders (SUDs).

Method: We conducted structured interviews with 120 bipolar patients (60 with SUD and 60 without SUD) about their experience and adherence with mood stabilizers.

Results: Adherence to mood stabilizers was quite high overall: 88% of SUD and 90% of Non-SUD subjects. In the SUD group, female patients were more likely to be fully compliant with medications than male patients (50% vs. 25%, $p < .05$). Men (16% vs 5%, $p < .04$) and subjects with SUD (22% vs 5%, $p < .007$) were more likely to endorse substance-related reasons (intoxication/hung-over/did not want to mix medications with substances) for noncompliance, compared to women and subjects without SUD.

Conclusion: There was no overall difference in mood stabilizer adherence between SUD and non-SUD subjects. However, in the SUD group, men were less adherent to medications than women. Clinicians should be alert to this gender difference in adherence among patients with bipolar disorder.

References:

1. Keck PE Jr, McElroy SL, Strakowski SM, et al: Compliance with maintenance treatment in bipolar disorder. *Psychopharmacology Bulletin* 1997; 33:87-91.
2. Weiss RD, Greenfield SF, Najavits LM, et al: Medication compliance among patients with bipolar disorder and substance use disorder. *J Clin Psychiatry* 1998; 59:4, 172-174.

NR337 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Suicide-Related Events Across Affective and Anxiety Disorder Treatment Studies: A Meta-Analysis of Double-Blind Sertraline Trials

Supported by Pfizer Inc.

Gail Farfel, Ph.D., 235-10-59, Pfizer Inc., 235 East 42nd Street, New York, NY 10017; Tal Burt, M.D., Guy Cohen, Ph.D., Evan Batzar, M.A., Brian Klee, M.D.

Educational Objectives:

At the conclusion of this session, the participant should have an improved understanding of the relative safety and risks of sertraline, other antidepressants, and placebo in the treatment of affective and anxiety disorders.

Summary:

Introduction: Recent concerns have been raised regarding the potential risk of suicide-related events among patients treated with various selective serotonin (SSRI) and noradrenaline (SNRI) reuptake inhibitors. The authors analyzed all available Pfizer-sponsored, double-blind, controlled trials of sertraline for the treatment of anxiety and depressive disorders.

Method: Data were pooled from 156 double-blind trials of sertraline (N=11548), other antidepressants (N=5696), and placebo (N=5207). The incidence [\pm 95%-CI] of all suicide related events (completed suicides, suicidal ideation, and self-harm [with or without suicidal intent]) were analyzed using the Cochran-Mantel-Haenszel test. Various variables (gender, age, suicidal ideation at baseline, and diagnosis [depression; PTSD; panic, social or generalized anxiety disorder, PMDD]) were analyzed as risk factors.

Results: The incidence of all suicide-related events was 0.48% [\pm 0.13%] on sertraline, including 6 completed suicides among 11,548 subjects; 0.61% [\pm 0.20%] on active control; and 0.29% [\pm 0.15%] on placebo. The majority (50-75% of events) occurred within the first 2 weeks. Suicidal risk was unaffected by baseline variables.

Conclusions: This meta-analytic dataset did not show an overall difference in the risk of suicide-related events between patients treated with sertraline, and those treated with other antidepressants or placebo.

References:

1. Khan A, et al: Suicide rates in clinical trials of SSRIs, other antidepressants, and placebo: analysis of FDA reports. *Am J Psychiatry* 2003; 160:790-792.
2. Khan A, et al: Symptom reduction and suicide risk in patients treated with placebo in antidepressant clinical trials: an analysis of the FDA database. *Arch Gen Psychiatry* 2000; 57:311-317.

NR338 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

The Prevalence Rate of Depression and Birth Weight: A Register Study

Supported by Inger and Max Worzner Foundation

Jens K. Larsen, M.D., *Gentofte Psychiatric Center, Niels Andersenvej 65, DK-2900 Hellerud, Denmark*; Birgitte B. Bendsen, M.D., Gurli Perto, Povl Munk-Joergensen

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize low birth weight as a possible risk factor for developing affective disorder.

Summary:

Introduction: The scientific literature indicates a correlation between biological stress and the prevalence of depression. Birth complications may be regarded as stressing events affecting the Hypothalamic-Pituitary-Adrenal Axis (HPA Axis). The aim of the present study was to test the hypothesis that low birth weight is a risk factor for developing major depression.

Methods: In the Danish Psychiatric Research Register all persons diagnosed according to ICD-10 and born from Jan. 1, 1974 until Dec. 31, 2001 were identified. These individuals were screened for birth weight (bw) in the Birth Register (established Jan. 1, 1974) of the Danish National Board of Health. Mean bw was calculated for the entire population of 61496 cases, for 4543 cases with a F2 diagnosis and for 7059 cases with a F3 diagnosis. For comparison mean bw was calculated for all 1804184 persons, with no ICD-10 diagnosis, born in the same particular years.

Results: Generally bw increased slightly in all groups from 1974 and onwards. For the entire population mean bw was significantly lower in the groups of cases with a F2 diagnosis or a F3 diagnosis; mean bw being significantly lower in the F2 group than in the F3 group. In both sexes with a F3 diagnosis, compared with normal controls, mean bw was significantly lower throughout the bw interval (range 0-5000g). Comparisons were made for each bw interval of 500g from 0-5000g.

Conclusions: According to these results, low bw is presumed to be a risk factor for developing major depression.

References:

1. Gale CR, Martyn CN: Birth weight and later risk of depression in a national birth cohort. *Br J Psychiatry* 2004; 184:28-33
2. Watson S, Gallagher P, Ritchie JC, Ferrier IN, Young AH: Hypothalamic-pituitary-adrenal axis function in patients with bipolar disorder. *BR J Psychiatry* 2004; 184:496-502.

NR339 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Psychopathology Among Transsexuals Across Gender and Sex Reassignment Stage

Esther Gomez-Gil, M.D., *Department of Psychiatry, Hospital Clinic, Villarroel 170, Barcelona 08036, Spain*; Angela Vidal-Hagemeyer, M.D., Josep M. Peri-Nogues, Anna Torres, M.D., Teresa Godas-Sieso, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize if there are differential patterns of psychopathology in transsexuals according sex and sex-reassignment stage.

Summary:

Objective: To assess psychopathology on Spanish transsexuals across gender and across two stages of the sex-reassignment treatment.

Method: The Minnesota Multiphasic Personality Inventory-2 (MMPI-2) was used to assess individual patterns of psychopathology to 127 sex change applicants who had been diagnosed as transsexualism (ICD-10 and DSM-IV-TR criteria). The sample was divided in groups according gender (n=70 M-F and n=37 F-M transsexuals), and according sex reassignment stage (n=56 transsexuals requesting sex reassignment hormonal therapy (SRHT) and n=69 transsexuals requesting sex reassignment surgery (SRS)).

Results: Mean *T* scores from the MMPI-2 were within the normal range except for the Masculinity-femininity (M-f) scale. M-F transsexuals did not differ significantly in mean *T* clinical scores nor in the percentage of patients with *T*>65 from the F-M transsexual group. Compared with patients seeking for SRS, individuals seeking for SRHT trend to score higher in all scales, and score significantly higher in Hysteria and Psychopathic Deviation scales. Nevertheless, both groups neither demonstrated any significant elevations on all the clinical scales other than on scale *Mf*.

Conclusions: Results support the view that (1) transsexuals candidates to sex reassignment were notably free of psychopathology, (2) M-F did not differ from F-M in degree of psychopathology, and (3) a large number of transsexuals in the first stages of sex reassignment may experience a little more psychological distress than patients in the last stages, but the results are unlikely to reflect clinically relevant differences.

References:

1. Miach P, Berah E, Butcher J, Rouse S: Utility of the MMPI-2 in assessing gender dysphoric patients. *Journal of Personality Assessment* 2000; 75:268-279.
2. Cole C, O'Boyle M, Emory L, Moyer W: Comorbidity of gender dysphoria and other major psychiatric diagnoses. *Archives of Sexual Behavior* 1997; 26:13-26.

NR340 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

A Preliminary Estimation of Prevalence, Incidence, and Sex Ratio of Transsexualism in a Spanish Community

Esther Gomez-Gil, M.D., *Department of Psychiatry, Hospital Clinic, Villarroel 170, Barcelona 08036, Spain*; Antoni Trilla, M.D., Josep M. Peri-Nogues, Angela Vidal-Hagemeijer, M.D., Teresa Godas-Sieso, M.D., Anna Torres, M.D., Joan De Pablo, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that differential demographic data of transsexualism in a Spanish community compared with recent published data may be explained by several factors.

Summary:

Background: In the Spanish autonomous community of Catalonia, the Hospital Clinic of Barcelona is the single public hospital providing specialized psychiatric and endocrinological reference for transsexual patients. The aim of this study was to estimate the prevalence, incidence, and sex ratio of transsexualism in this Spanish region/community.

Methods: The prevalence and sex ratio were calculated on the basis of the total number of applicants who were diagnosed as gender identity disorder (ICD-10) at the Hospital Clinic, and live in Catalonia. Incidence is calculated by counting all new cases of transsexuals for the last five years, when prospective data collection was started. The results were based on the population census over 15 years of age.

Results: During the period from 1996 through 2004 a total of 201 subjects were referred to the hospital with complaints of gender dysphoria. Transsexualism was diagnosed in 182 patients (98 Catalonia-born, 161 Catalonia-living, 35 foreign-born). This means a prevalence rate of 1:21,641 males and 1:55,483 females that appear to be increasing with time. The sex ratio was 2.5 (male-to-female transsexuals: n=130; 29,76 years -SD:8.14-, female-to-male: n=52; 25,82 years -SD:6,92). The annual incidence was 0,59/100,000/year remained constant during the last five years, and was higher in men than in women.

Discussion: The relatively low prevalence recorded in Catalonia compared with recent published data from European Union countries may be due to the few relatively years of data collection and because surgical procedures costs are not covered by the public health insurance. In contrast, the high incidence, when compared with other European Union countries, may be due to the increasing demand since 2000, when a more benevolent social climate in Spain initiate (coinciding with the first approved complete public health insurance in other Spanish region, Andalusia, in 1999).

References:

1. Landén M, Walinder J, Lundström B: Prevalence, incidence and sex ratio of transsexualism. *Acta Psychiar Scand* 1996; 93:221-223.
2. Olsson SE, Möller AR: On the incidence and sex ratio of transsexualism in Sweden, 1972-2002. *Arch Sex Behavior* 2003; 32:381-386.

NR341 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Sociocultural Factors in Perinatal Depression: A Transcultural Study in Singapore

Cornelia Y.I. Chee, M.Med., *Department of Psychological Medicine, National University Hospital, 5 Lower Kent Ridge Road, Singapore 119074, Singapore*; Dominic T.S. Lee, M.D., T.P. Ng, M.D., Y.S. Chong, M.D., L.K. Tan, B.S., Calvin Fones, M.Med.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that cultural support for perinatal depression such as confinement, is a complex phenomenon that cannot necessarily be taken to be helpful to the mother, and that a negative confinement experience is a significant risk factor for perinatal depression.

Summary:

Aim: To investigate the prevalence, sociocultural, and psychosocial risk factors for perinatal depression in Singaporean women.

Method: A prospective cohort of 559 women was interviewed antenatally and at six weeks postpartum at a tertiary hospital. Women were interviewed for diagnosis of depression using a two-stage design at both time-points using a screening Edinburgh Postnatal Depression Scale (EPDS) and a diagnostic interview with the Structured Clinical Interview for DSM-IV (SCID-IV).

Results: Postnatally, a negative confinement experience was associated with depression. Other independent factors included poor emotional support, a past history of depression, unplanned pregnancy, and perceived potential conflicts with relatives over childcare antenatally and dissatisfaction, poor instrumental sup-

port postnatally. The prevalence of depression antenatally and postnatally was 12.2% and 6.8%, respectively.

Conclusions: Perinatal depression in Singaporean women is common. Contrary to expectations, a negative 'confinement' experience is a significant risk factor for postnatal depression, and is not universally welcomed by women. Depression is modulated by dissimilar sets of psychosocial factors antenatally and postnatally.

References:

1. Lee DTS, Yip ASK, Leung TYS, et al: Ethnoepidemiology of postnatal depression: prospective multivariate study of socio-cultural risk factors in a Chinese population in Hong Kong. *British Journal of Psychiatry* 2004; 184, 32-40.
2. Heh SS, Coombes L, Bartlett H: The association between depressive symptoms and social support in Taiwanese women during the month. *International Journal of Nursing Studies* 2004; 41, 573-579.

NR342 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Androgens Improve Cognitive Functioning in Transsexuals

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Educational Objectives:

At the conclusion of this session, the participant should be able to untangle sexual differences in cognitive functions, by means of an ethical paradigm, which allows understanding the direct effect of sexual hormones on brain functioning.

Summary:

Background: The association between administration of androgens for sexual reassignment treatment and performance on cognitive tasks is controversial.

Objective: To determine the effects of administered androgens on cognitive functioning in subjects to be sexually reassigned.

Method: A total of 10 transsexual female-to-male patients in sex reassignment process was assessed on cognitive tasks before and six months after treatment. Visual Paired Associates Learning I and II, Rey Complex Figure (RCF), Spatial Test of Primary Mental Abilities, Verbal Paired Associates Learning I and II, and Logical Memory were performed. Tasks were grouped under two cognitive domains: one visual index and one verbal. Z-Wilcoxon was used to compare them before and after treatment.

Results: There was a significant difference between pre and post treatment for the visual index ($Z=-2.09$, $p=0.04$). And there was no effect of time in the verbal index ($Z=-0.36$, $p=0.72$).

Conclusion: Our results support the hypothesis that androgen therapy improves visual domain functions. We did not observe an impairment of verbal functions. However, it cannot be assured the lack of a learning effect on the measures. Study limitations included lack of a comparison group and small sample.

References:

1. Slabbekoorn D, van Goozen SH, Megens J, Gooren LJ, Cohen-Kettenis PT: Activating effects of cross-sex hormones on cognitive functioning: a study of short-term and long-term hormone effects in transsexuals. *Psychoneuroendocrinology* 1999; 24(4):423-47.
2. Van Goozen SH, Cohen-Kettenis PT, Gooren LJ, Frijda NH, Van de Poll EN: Activating effects of androgens on cognitive performance: causal evidence in a group of female-to-male transsexuals. *Neuropsychologia* 1994; 32(10):1153-7.

NR343 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Social and Clinical Factors in Geriatric Depression: The Role of Race

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Educational Objectives:

At the conclusion of this session, the participant should be able to recognize differences and commonalities expressed between depressed African-American elderly, compared with depressed Caucasian-American elderly.

Summary:

Objective: Due to the acuity and prevalence of depression in the elderly, there has been an increased effort to understand differences in the expression of depression among this diverse population. Little research, however, has been conducted based on racial and cultural backgrounds in the elderly. The authors were interested in examining both the differences and commonalities expressed between depressed African-American (AA) elderly compared with depressed Caucasian-American (CA) elderly.

Methods: As part of a five-year longitudinal study of depression in the elderly at Duke University Medical Center, the authors performed an exploratory analysis on 336 subjects (35AA, and 301 CA) to evaluate demographic, medical, social, and symptomatological differences between African Americans and Caucasians. The authors then performed a multivariate analysis, controlling for age, gender, and education to evaluate the statistically significant correlates between the two groups.

Results: Differences between AA and CA elderly depressed subjects were present in the demographic background, depression symptomatology, and medical comorbidity. Elderly depressed AA were less likely to be married, less likely to be retired, socioeconomically disadvantaged; had less educational achievement, and had more people living in their household. In depressive symptoms, they experienced more lassitude and psychomotor retardation, slowed thoughts, and poorer concentration, but less suicidal ideation. Medically, they tended to rate their physical health as being poorer. This was supported by an increased incidence of diabetes, hypertension, and cancer.

Conclusion: African-American elderly depressed patients have differences in their experiences and demographic background compared with Caucasian elderly depressed patients. These factors have the potential to cause vulnerability to depression (such as more medical comorbidity) or provide some resilience from depression (such as increased social support). They may also produce differences in depressive symptomatology between the two groups. Further studies may help highlight different needs and treatment interventions, as well as provide insight into how cultural and racial factors affect the experience of depression.

References:

1. Aldwin C, Greenberger E: Cultural differences in the predictors of depression. *American Journal of Community Psychology* 1987; 15(6), 789-813.
2. Meldon S W, Emerman, C L, Schubert D S, Moffa D A, Etheart R G: Depression in geriatric ED patients: prevalence and recognition. *Annals of Emergency Medicine* 1997; 30(2), 141-145.

NR344 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Anxiety and Pulse in Acute Mania

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New Orleans, LA 70112; Jonathon E. Becker, M.S., DeAnne Winey-Ward, B.S.

Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the effect of anxiety on outcome in acute mania. Additionally, the participant should be able to discuss hemodynamic changes that occur during episodes of depression, increased anxiety, and mania.

Summary:

Little is known about the relation between anxiety and mania, although the relation between anxiety and depression has been well studied. An anxious depression has a poorer course of illness than depression alone and data suggest that anxiety adversely affects cardiovascular status.

Method: Subjects consisted of 26 patients (16F, 10M) with acute mania examined at their baseline visit in clinical trials. Subjects had been without mood stabilizers or antipsychotics from between one and seven days. Inclusion criteria included normal vital signs and absence of alcohol or substance abuse. Heart rate and blood pressure were taken at rest. We examined three PANSS/BPRS items associated with anxiety: anxiety, tension, and excitement. Scale reliability analysis demonstrated an alpha of 0.79 for this construct. We found a positive correlation ($r=.39; p<0.05$) between these anxiety measures and Young Mania Rating Scale (YMRS) scores, and a trend between YMRS and pulse ($r=.36, p=0.08$).

Conclusions: the results suggest that the anxiety subscale of the PANSS/BPRS is a valid construct that may be useful in targeting treatments in patients with mania and subsyndromal anxiety. Further work is needed to assess this relation with diagnosed anxiety disorders, with normal controls, and to examine this effect on cardiovascular tone.

References:

1. Freeman MP, Freeman SA, McElroy SL: The comorbidity of bipolar and anxiety disorders: prevalence, psychobiology, and treatment issues. *J Affect Dis* 2002; 68:1-23.
2. Von Kanel F, Mills PJ, Fainman C, Dimsdale JE: Effects of psychological stress and psychiatric disorders on blood coagulation and fibrinolysis: a biobehavioral pathway to coronary artery disease? *Psychosom Med* 2001; 63:531-544.

NR345 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Lay Preferences on the Treatment of Depression in Sao Paulo, Brazil

Erica T.P. Peluso, M.A., *Department of Psychiatry, UNIFESP, Rua Dom Paulo Pedrosa 668 AP41, Sao Paulo, SP 05687-001, Brazil*; Sergio L. Blay, D.R.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that the public in São Paulo, Brazil, prefer psychological help and nonprofessional activities instead of medical ones to treat depression.

Summary:

Objective: To evaluate community preferences on the treatment of depression.

Method: A household survey was carried out with a representative sample of 2000 residents of São Paulo city, aged 18-65. A vignette depicting a person suffering from depression was presented to 500 respondents. They were given a list of ten sources of help and a list of seventeen intervention options and asked to rate them as helpful or harmful. Next, they were asked to select a first choice of help and the intervention option they considered the most helpful.

Results: The sources of help more often rated as helpful were counselor/psychologist (95%), self-help groups (92%), and close friend (85%). Medical professionals were considered less often helpful. When asked to select the first choice of help, the public chose close family (26%). The intervention more often rated as helpful was counseling (94%), "to keep the mind busy" (94%), and to improve eating habits (94%). Medical treatments, like taking medicines and hospitalization, were considered more harmful than helpful. When asked to select the intervention considered the most helpful, the public chose counseling (32%).

Conclusion: Psychological and lay support help were more often recommended than medical ones to treat depression in São Paulo, Brazil.

References:

1. Angermeyer MC, Matschinger H, Riedel-Heller SG: What to do about mental disorder. Help-seeking recommendations of the lay public. *Acta Psychiatr Scand* 2001; 103:220-225.
2. Jorm AF: Mental health literacy. Public knowledge and beliefs about mental disorders. *Br J Psychiatry* 2000; 177:396-401.

NR346 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Gender Differences in Depressive Symptoms Among College Students

Supported by Eli Lilly and Company

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that depression is prevalent among college students and that gender differences may exist in the presentation of depression.

Summary:

Objective: Researchers have reported significant depressive symptoms among college students. The purpose of this study was to assess gender differences in depressive symptoms among college students in Bombay.

Methods: We screened 1,357 college students over the age of 18 years (mean age: 19.3 ± 1.5 years; 56% women) in Bombay, India. After obtaining written, informed consent, the Beck Depression Inventory (BDI) and the Symptom Questionnaire (SQ) were distributed to all students. Chi-square and Mann Whitney-U tests were used for data analysis.

Results: 24% of the students scored ≥ 16 on the BDI and 25% had suicidal ideation (as assessed by item #9 on the BDI). 31.6% men and 18.7% women scored ≥ 16 on the BDI (chi-square=26.1; $p<0.0001$). There was no significant gender difference in the prevalence of suicidal ideation (. Among depressed subjects (as assessed by a total BDI score ≥ 16), women had statistically significantly higher scores on SQ-Depression and SQ-Anxiety scales compared to men ($Z=-4.1$; $p<0.0001$ and $Z=-3.8$; $p<0.001$).

Conclusion: Significant depressive symptoms are noted in 24% of this urban college population in India, with depressed women having significantly greater anxiety and depressive symptoms compared to men. Our study suggests the importance of gender in the clinical presentation of depressed college students.

References:

1. Sonawalla SB, Kelly K, Neault N, Farabaugh A, Almeida D, Yeung A, Mischoulon D, Pava J, Otto M, Fava M: Predictors of suicidal ideation in a college population. 154th Annual Meet-

ing of the American Psychiatric Association. New Orleans, 2001.

2. Peden AR, Hall LA, Rayens MK, Beebe L: Negative thinking mediates the effect of self-esteem on depressive symptoms in college women. *Nursing Research* 2000; 49(4):201-207.

NR347 Tuesday, May 24, 12:00 p.m.-2:00 p.m.
The Efficacy of Escitalopram in Depressed Patients With Comorbid Anxiety

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Educational Objectives:

At the conclusion of this session, the participants will increase their knowledge about the efficacy and tolerability of escitalopram for the treatment of depressed patients with or without comorbid anxiety

Summary:

Objective: This was an open, multicenter prospective study assessing the efficacy and tolerability of escitalopram in depressed patients with or without comorbid anxiety.

Methods: Escitalopram 10-20mg/day was administered over a 12-week treatment period in patients retrospectively divided into three groups according to their level of anxiety determined by HAM-A total score at baseline.

Results: 649 out of 790 patients completed the study. At baseline, the mean MADRS total score was 31.5 (increasing as the HAM-A total score increased) and improved to 10.5 (OC) [12.4 (LOCF)] at endpoint. The mean HAM-A total score at baseline was 25.6, which improved to 9.0 (OC) [10.8 (LOCF)] at endpoint. The therapeutic effect on anxiety (assessed by HAM-A) was slightly increased, while the therapeutic effect on depressive symptoms (assessed by MADRS) was slightly reduced, when either the severity of baseline anxiety or the number of comorbid anxiety disorders were high. 251 patients (32%) had adverse events (AEs). The most frequent AEs were nausea in 67 patients (8%) and headache in 38 patients (5%); 61 patients (8%) discontinued due to AEs.

Conclusion: Escitalopram was well tolerated and efficacious in reducing symptoms of depression in patients with or without comorbid anxiety over the 12-week treatment period.

References:

1. Gorman JM: Comorbid depression and anxiety spectrum disorders. *Depress Anx* 1997; 4:160-168.
2. Keller MB, Hanks DL: Anxiety symptom relief in depression treatment outcomes. *J Clin Psychiatry* 1995; 56 Suppl 6:22-29.

NR348 Tuesday, May 24, 12:00 p.m.-2:00 p.m.
Social Inequalities in Suicidality and Response to Antidepressant Treatment

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Educational Objectives:

At the conclusion of this session, the participant should recognize that socioeconomic status will influence response to antidepressant treatment.

Summary:

Background: To examine the relationship between socioeconomic status (SES) and response to treatment for depression among older adults.

Method: Secondary analysis of pooled data from the open-label phase of two NIMH-funded clinical trials of either nortriptyline or paroxetine combined with Interpersonal Psychotherapy (total N = 248). Cox-proportional hazards regression analyses were used to examine the association between SES, indexed by census tract median household income and subject's educational attainment, and treatment response and remission according to the Hamilton Depression Rating Scale. The association between SES and suicidality or depressed mood reported at each week of treatment was examined using repeated measures generalized logit models.

Results: During a treatment period of up to 26 weeks, likelihood of treatment response among subjects in middle and high income census tracts was significantly different from that among subjects in low income tracts ($X^2=9.12$, $df=2$, $P=0.01$). Middle and high income subjects were less likely to report suicidal thoughts or attempts (adjusted ORs=0.48 [95% CI=0.27, 0.86] and 0.28 [95% CI=0.12, 0.67], respectively): No association was found between SES and remission.

Conclusions: Lower SES is associated with less favorable course of depression among older adults receiving a combination of pharmacologic and psychosocial treatment.

References:

1. Isaacs SL, Schroeder, SA: Class-the ignored determinant of the nation's health. *N Engl J Med* 2004; 351:1137-1142.
2. Reynolds CF 3rd, Frank E, Perel JM, et al: Nortriptyline and interpersonal psychotherapy as maintenance therapies for recurrent major depression, a randomized controlled trial in patients older than 59 years. *JAMA* 1999; 281:39-45.

NR349 Tuesday, May 24, 12:00 p.m.-2:00 p.m.
Numbers Needed to Treat in Interpreting Bipolar Depression Trials of Atypical Antipsychotics

John Donoghue, Pharm.D., *School of Pharmacy, John Moores University, 4 Wrenfield Grove, Liverpool L179QD, United Kingdom*

Educational Objectives:

At the conclusion of this session, the participant should recognize (1) NNTs may be used to compare the clinical value of atypical antipsychotics in the treatment of bipolar depression, (2) NNTs for response and remission indicate that quetiapine is superior to olanzapine in bipolar depression.

Summary:

Objective: Evaluate olanzapine and quetiapine as monotherapy for bipolar depression by calculating Numbers Needed to Treat (NNTs) using data from similarly designed randomized, placebo-controlled trials.

Method: Data were obtained from eight-week trials evaluating the efficacy and safety of olanzapine (9.7 mg/d) and quetiapine (600/300 mg/d) in bipolar depression. NNTs [$100 / (\text{event rate} [\%] \text{ in treatment group} - \text{event rate} [\%] \text{ in placebo group})$] were calculated for olanzapine and quetiapine versus placebo for the outcomes of response ($\geq 50\%$ improvement from baseline in MADRS score) and remission (total MADRS score ≤ 12 at endpoint).

Results: Both olanzapine and quetiapine were superior to placebo ($p < 0.05$). For response, NNT was 12 for olanzapine and 5 for both quetiapine doses. For remission, NNT was 12 for olanzapine and 4 for both quetiapine doses.

Conclusions: Quetiapine appears to be superior to olanzapine for the treatment of bipolar depression. Compared with placebo, to obtain one additional patient responding to olanzapine, 12 have to be treated; in contrast, with quetiapine, an additional patient responds for every five patients treated. Similarly, to obtain one additional patient in remission with olanzapine, 12 have to be

treated; with quetiapine, an additional patient in remission is obtained for every four patients treated.

References:

1. Calabrese J, Macfadden W, McCoy R, et al: Double-blind, placebo-controlled study of quetiapine in bipolar depression. Poster presented at the 157th Annual Meeting of the American Psychiatric Association, May 1-6, 2004; New York.
2. Tohen M, Vieta E. Calabrese J, et al: Efficacy of olanzapine and olanzapine-fluoxetine combination in the treatment of bipolar I depression. *Arch Gen Psychiatr* 2003; 60:1079-1088.

NR350 Tuesday, May 24, 12:00 p.m.-2:00 p.m. **Lithium and Lactation**

Adele C. Viguera, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street/WACC 812, Boston, MA 02114*; Jeffrey D. Newport, M.D., Juliana Mogielnicki, B.A., Amanda K. Zurick, B.A., Laura Petrillo, M.D., Lee S. Cohen, M.D., Zachary N. Stowe, M.D., John C. Ritchie, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to quantify lithium levels in infant serum and breastmilk.

Summary:

Objective: Women with bipolar disorder are at high risk for relapse during the immediate postpartum period. Resumption of lithium or other mood stabilizers prior to delivery or within 24-48 hours after delivery can significantly reduce the risk of relapse and is a current standard of care for this high risk population. Breastfeeding while taking lithium has been considered a relative contraindication in the past. The American Academy of Pediatrics guidelines are less restrictive in their current recommendation, but they do recommend caution. This study aims to quantify infant exposure to lithium through breastfeeding by measuring medication levels in breastmilk and infant serum.

Methods: We report on nine cases of the use of lithium monotherapy in nursing mothers with a diagnosis of bipolar disorder. Maternal and infant serum levels of lithium were collected at around six weeks postpartum as well as lithium concentration in breastmilk. Infant thyroid function tests and renal function tests were also collected.

Results: Maternal average dose of lithium was 900 mg a day. Lithium concentration in breastmilk was on average 55% (range 35%-67%) of maternal lithium serum level. Infant lithium serum levels ranged from <0.1 mmol/l-0.22 mmol/L. There were no adverse effects in 8/9 infants. One infant was noted to have a slightly elevated TSH which normalized once lithium was discontinued. Renal and thyroid function tests were within normal limits.

Conclusion: These data suggest a low incidence of adverse clinical effects in babies exposed to lithium through breastmilk. Close clinical monitoring of infants exposed to lithium through breastmilk is recommended.

References:

1. Burt VK, Suri R, Altshuler L, Stowe Z, Hendrick VC, Muntean E: The use of psychotropic medications during breast-feeding. *Am J Psychiatry* 2001; 158(7):1001-9.
2. Tunnessen WW, Hertz CG: Toxic effects of lithium in newborn infants: a commentary. *J Pediatr* 1972; 81(804-807).

NR351 Tuesday, May 24, 12:00 p.m.-2:00 p.m. **Premenstrual Exacerbation of Bipolar Disorder**

Adele C. Viguera, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street/WACC*

812, Boston, MA 02114; Claudio N. Soaes, M.D., Hadine Joffe, M.D., Julia Coleman, M.D., Laura Petrillo, M.D., Hannah Gottschall, B.A., Lee S. Cohen, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize a high prevalence of sub-optimally or un-treated bipolar disorder (BPD) in women in the community that can be presenting itself as premenstrual syndrome (PMS).

Summary:

Background: Despite the prevalence of PMS among women of reproductive age, little is known about the relationship between the menstrual cycle and BPD.

Methods: Subjects with bipolar disorder were screened for a research study to evaluate the potential efficacy of quetiapine (Seroquel) as a treatment for premenstrual exacerbation of mood. A telephone questionnaire was used to determine the presence of premenstrual symptoms as well as current medication treatment for BPD. Women deemed eligible at screening visit tracked their symptoms with a Daily Symptom Rating Chart (DRSP) to document premenstrual worsening of mood.

Results: A total of 188 women were screened over the phone; 20% (n=37) were determined eligible. Of the 80% determined not eligible, nearly half [49% (n=60)] were ineligible due to incompletely treated symptoms of bipolar disorder manifesting as affective dysregulation during the follicular phase. Of the 10 women who have enrolled and who have successfully tracked their symptoms for one month, 20% (n=2) demonstrate premenstrual worsening of mood symptoms (defined as $\geq 30\%$ increase in total DRSP scores from follicular phase to luteal phase). DRSP scores went from 53.2 (SD 21.6) during the follicular phase to 62.54 (SD 22.7) in the luteal phase. Of the remaining 80% (n=8), 5 opted to track for an additional month leading to an additional 20% (n=2) documenting PMS.

Conclusions: These preliminary data suggest that many women with bipolar illness may complain of premenstrual symptoms and that this may be a marker of incompletely treated underlying illness across the menstrual cycle versus a circumscribed premenstrual exacerbation.

References:

1. Blehar MC, Depaulo JR, Gershon ES, Reich T, Simpson SG, Nurnberger Jr: Women with bipolar disorder: findings from the NIMH genetics initiative sample. *Psychopharmacology Bull* 1988; 34:239-43.
2. Leibenluft E, Ashman SB, Feldman-Naim S, Yonkers KA: Lack of relationship between menstrual cycle phase and mood in a sample of women with rapid cycling bipolar disorder. *Biol Psychiatry* 1999; 46:577-80.

NR352 Tuesday, May 24, 12:00 p.m.-2:00 p.m. **Oral Contraceptive Pills to Treat Premenstrual Worsening of Depression**

Hadine Joffe, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 815, Boston, MA 02114*; Janet E. Hall, M.D., Claudio N. Soares, M.D., Hannah Gottschall, B.A., Lee S. Cohen, M.D.

Educational Objectives:

At the conclusion of this session, participants will understand the rationale for use of hormonal contraceptives to treat premenstrual worsening of depression. Participants will also become aware of preliminary data supporting the efficacy of hormonal contraceptives to treat mood symptoms that break through premenstrually despite effective use of antidepressants for treatment of depression.

Summary:

Background: Depression symptoms worsen during the premenstrual phase of the menstrual cycle in some women with depressive disorders. Although this may be a consequence of sensitivity to changing hormonal levels, little is known about the efficacy of oral-contraceptive pills (OCP) to treat premenstrual worsening of depression.

Methods: Women with premenstrual (luteal-phase) worsening of depression were randomized to double-blind treatment with the unique OCP drospirenone and ethinyl estradiol (DRSP/EE) with or without additional ethinyl estradiol during the typical placebo week of the OCP for two months. Eligible subjects were women 18-45-years-old who had regular menstrual cycles, a depressive disorder (major, minor, or dysthymia), and stable use of an antidepressant for ≥ 2 months without depression symptoms during the follicular-phase of the menstrual cycle. All subjects completed a run-in tracking month to prospectively determine that depression symptoms were present in the luteal-phase (Montgomery-Åsberg Depression Rating Scale [MADRS] >14 ; and Daily Record of Severity of Problems Scale [DRSP] increase by $\geq 50\%$ over follicular-phase) but not during the follicular-phase (MADRS ≤ 10). Changes in DRSP and MADRS scores from the premenstrual (final five days before menses) and postmenstrual (menstrual cycle days 6-10) phases of the tracking month were compared with the premenstrual (final 5 days before menses) and postmenstrual (OCP days 6-10) phases of the second OCP treatment month.

Results: With 26 subjects enrolled, interim data reveal that 89% of subjects had prospectively defined premenstrual worsening of depression. For the first 11 subjects to complete the study, premenstrual DRSP scores for all subjects together were reduced from median 54.4 (interquartile range, IQR 43.8-85.2) to 35.3 (IQR 26.4-64.6) after two months of OCP therapy ($p=0.005$), while postmenstrual DRSP scores remained stable and low (median 26.6, IQR 23-37.2, to median 28.8, IQR 24.2-53.2). Premenstrual MADRS scores were similarly reduced (median 23, IQR 19-25, to median 6, IQR 3-9, $p=0.008$) while postmenstrual MADRS scores remained stable and low (median 3, IQR 2-6, to median 5, IQR 3-13).

Conclusion: Preliminary interim data reveal that almost all women who report premenstrual worsening of depression are confirmed to have premenstrual breakthrough of depressive symptoms when prospectively assessed. For subjects who have completed the study thus far, two months of the OCP DRSP/EE appears to be associated with a decrease in premenstrual depression symptoms. Treatment assignment to continued use of estradiol or placebo will be unblinded soon to examine whether continued use of estradiol provides additional benefit.

References:

1. Yonkers KA, White K: Premenstrual exacerbation of depression: one process or two? *J Clin Psychiatry* 1992; 53:289-92.
2. Freeman EW, Kroll R, Rapkin A, et al: Evaluation of a unique oral contraceptive in the treatment of premenstrual dysphoric disorder. *J Womens Health Gend Based Med* 2001; 10:561-9.

NR353 Tuesday, May 24, 12:00 p.m.-2:00 p.m. Clinical Course of Bipolar Disorder Through Perimenopause: Chart Review

Natalie L. Rasgon, M.D., *Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, 401 Quarry Road, Room 2360, Palo Alto, CA 94305-5723*; Wendy Marsh, M.D., Amanda Templeton, M.D., Terence A. Ketter, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand that mood episodes may change during the

menopausal transition in women with bipolar disorder. The participant will be aware of the frequency, type, and severity of mood episodes during the menopausal transition of one representative cohort.

Summary:

Objective: Although data are emerging in bipolar disorder (BD) regarding mood and female reproductive phases, such as in the menstrual cycle and postpartum, information regarding the menopausal transition remains limited. We explored the clinical course of mood episodes in women with BD across the typical years of the menopausal transition.

Method: We examined mood episodes in 41 women with BD between 45 and 55 years old assessed with the Systematic Treatment Enhancement Program (STEP-BD) Affective Disorders Evaluation and followed with the STEP-BD Clinical Monitoring Form. The chart review included reproductive hormonal status, medication treatment, mood episodes by type, length, number, frequency, and whether hospitalization was required.

Results: Forty-one women with BD (13 type I, 26 type II, 2 NOS) including 10 with rapid cycling were followed for a mean of 25 months. Seventy percent experienced at least one major depressive episode, with similar rates in clinically perimenopausal (7/12), naturally post-menopausal (6/10), surgically post-menopausal (7/7), and regularly menstruating (7/10) women, while 0/2 with indeterminate menstrual status experienced at least one major depressive episode.

Conclusions: Better understanding the course of mood episodes through the menopausal transition may ultimately enhance effectiveness in managing BD in women during this time of reproductive hormonal variability.

References:

1. Burt VK, Rasgon N: Special considerations in treating bipolar disorder in women. *Bipolar Disord* 2004; 6(1):2-13.
2. Freeman MP, Smith KW, et al: The impact of reproductive events on the course of bipolar disorder in women. *J Clin Psychiatry* 2002; 63(4): 284-7.

NR354 Tuesday, May 24, 12:00 p.m.-2:00 p.m. Mixed Depression: Validating a Definition

Franco Benazzi, M.D., *Department of Psychiatry, Forlì National Health Service, Via Pozzetto 17, Cervia Ra 48010, Italy*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to diagnose mixed depression.

Summary:

Aim: testing definitions of mixed depression.

Methods: Consecutive 245 bipolar-II (BP-II) and 189 major depressive disorder (MDD) outpatients interviewed (off psychoactive drugs) with Structured Clinical Interview for DSM-IV, Hypomania Interview Guide, Family History Screen, when presenting for major depressive episode (MDE) treatment. Mixed depression defined as MDE plus concurrent hypomanic symptoms. Multivariate analyses used. Bipolar disorders family history (BP-FH) was the diagnostic validator.

Results: BP-II, versus MDD, had significantly more intra-MDE hypomanic symptoms (racing/crowded thoughts, irritable mood, psychomotor agitation, more talkativeness). MDE plus >2 hypomanic symptoms was present in 68.7% BP-II, 42.3% MDD. A "motor activation" factor and a "mental activation" factor were found among intra-MDE hypomanic symptoms. Definitions of mixed depression tested versus BP-FH: MDE plus $>1,2,3,4$ hypomanic symptoms, plus psychomotor agitation, plus racing thoughts. Most balanced combination of sensitivity and specificity

(around 65%), highest ROC area (0.83), shown by MDE plus >2 hypomanic symptoms. BP-FH versus all mixed depression definitions found MDE plus >2 hypomanic symptoms was only independent predictor. Dose-response relationship found between number of intra-MDE hypomanic symptoms and BP-FH loading.

Discussion: MDE plus >2 hypomanic symptoms most supported. Mixed depression may impact treatment (antidepressants could increase hypomanic symptoms, mood stabilisers/antipsychotics could control hypomanic symptoms during antidepressants). Some mixed depression symptoms (psychomotor agitation, irritability) are possible precursors to suicidality (FDA).

References:

1. Benazzi F: Mixed states in bipolar II disorder: should full hypomania always be required? *Psychiatry Res* 2003; 127:247-257.
2. Benazzi F: Depression with racing thoughts. *Psychiatry Res* 2003; 120:273-282.

NR355 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Clinical Trial of Sertraline in Treating Vasomotor Symptoms and Mood Disturbances

Paul Gordon, M.D., *Family & Community Medicine, University of Arizona, College of Medicine, AHSC; PO Box 24-5113, Tucson, AZ 85724-5113*; James Kerwin, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to measure the efficacy of sertraline compared with placebo in treating the vasomotor symptoms characteristic of menopause; measure the efficacy of sertraline compared to placebo in treating the mood disturbances characteristic of menopause; measure quality of life indicators related to the use of sertraline compared with placebo at the time of menopause.

Summary:

Background: Ovarian failure resulting in the cessation of menstruation marking menopause results in many vasomotor symptoms. Since the results from the Women's Health Initiative's randomized control trial, the risks of hormone replacement therapy are well known. We studied sertraline in the treatment of hot flashes.

Methods: A randomized, placebo-controlled, crossover design was used. Women between the ages of 40 and 65 who were having hot flashes were recruited. We used the same measurement tools as in the HERS(2) trial. Patients were randomized to sertraline or placebo. Patients received sertraline and placebo for four weeks each with a one week washout between their cross-over.

Results: Women in the study ranged in age from 42 to 62 (mean 52.9, SD 4.3). Eighty-six percent were white, non-Hispanic, and 11% were Hispanic. A majority (58%) were married. The primary dependent measure was self-reported number and severity of hot flashes. During the sertraline phase of the study women reported an average of six fewer hot flashes a week compared with the placebo phase (Mean 37.4 for the placebo, 31.3 for sertraline, $p = .002$). The severity of hot flashes was not significantly different in the sertraline phase compared with placebo.

Conclusions: Sertraline is effective in decreasing hot flashes in menopausal women. Future studies with longer treatment periods and varying doses are needed.

References:

1. Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the women's health initiative randomized controlled trial. [See comments.]. *JAMA* 2002; 288(3), 321-33.

2. Hlatky MA, Boothroyd D, Vittinghoff E, Sharp P, Whooley MA: Quality-of-life and depressive symptoms in postmenopausal women after receiving hormone therapy: results from the heart and estrogen/progestin replacement study (HERS) trial. *JAMA* 2002; 287(5):591-7.

NR356 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Risperidone Monotherapy in Bipolar Disorder: An Analysis of Standard and Sustained Remission Criteria

Carla M. Canuso, M.D., *Janssen Medical Affairs, L.L.C., 1125 Trenton-Harbourton Road, Titusville, NJ 08560*; Cynthia Bossie, Ph.D., Marcia F.T. Rupnow, Ph.D., Young Zhu, Ph.D., Robert M.A. Hirschfeld, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the relationship between remission and improved functioning in patients with bipolar disorder when treated with risperidone; understand the effect of different cutoff points for measures of remission.

Summary:

Background: APA guidelines state that remission, defined as the virtual resolution of symptoms and return to baseline level of functioning, is the primary goal in the treatment of acute bipolar mania.

Methods: This issue was examined with data from two three-week double-blind comparisons of risperidone and placebo in patients with acute manic or mixed bipolar episodes, followed by a nine-week open-label risperidone extension study. Remission=YMRS total score ≤ 12 or ≤ 7 . Sustained remission=remission at any time point plus all subsequent time points.

Results: In the three-week studies, more risperidone than placebo patients achieved both remission at endpoint and sustained remission (YMRS ≤ 12 or ≤ 7 ; $P < 0.001$). Among patients who remit at week-3 endpoint, 68% (YMRS ≤ 12) and 60% (YMRS ≤ 7) were newly remitted at the open-label 9-week endpoint; rates of sustained remission were 53% and 46%, respectively. Over the entire 12-week study, 62% (YMRS ≤ 12) and 53% (YMRS ≤ 7) of patients reached sustained remission. In these patients mean MADRS scores decreased significantly and mean Global Assessment Scale scores improved from -38 (poor functioning) to -80 (good functioning).

Conclusions: Risperidone was associated with a substantial rate of sustained remission with decreases in depressive symptoms and substantial improvements in functioning, consistent with the goals of the APA guidelines.

References:

1. American Psychiatric Association. Practice guideline for the treatment of patients with bipolar disorder (revision). *Am J Psychiatry* 2002; 159(4 Suppl):1-50.
2. Hirschfeld RM, Keck PE Jr, Kramer M, Karcher K, Canuso C, Eerdeken M, Grossman F: Rapid antimanic effect of risperidone monotherapy: a 3-week multicenter, double-blind, placebo-controlled trial. *Am J Psychiatry* 2004; 161:1057-65.

NR357 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Predictors of Symptom Resolution With Risperidone Augmentation in Patients With Resistant Depression

Carla M. Canuso, M.D., *Janssen Medical Affairs, L.L.C., 1125 Trenton-Harbourton Road, Titusville, NJ 08560*; Cynthia Bossie, Ph.D., Ibrahim Turkoz, M.S., Georges Gharabawi, M.D.

Educational Objectives:

At the conclusion of this presentation, the participants should be able to identify predictors of symptom resolution in patients with resistant depression undergoing treatment with antidepressants.

Summary:

Background: In an international trial, open-label risperidone augmentation was associated with symptom resolution in a large number of patients with depression resistant to standard antidepressant therapy. This analysis explored whether predictors of this response could be identified.

Methods: The study included an open-label citalopram phase to confirm nonresponse to a standard antidepressant, followed by an open-label risperidone augmentation phase to identify patients who achieved symptom resolution. Logistic regression models examined the relationship between baseline demographic/disease characteristics and symptom resolution with risperidone augmentation.

Results: Univariate models identified baseline factors associated with a greater likelihood of symptom resolution as: fewer prior antidepressants in the current episode (1-2 vs >2; $p=0.003$); longer duration of the current episode (>2 years vs 1-2 years; $p=0.032$); lower anxiety ratings via HAM-D anxiety/somatization subscale (<7 vs ≥ 7 ; $p=0.006$); and lower ratings via HAM-D insomnia scores ($p=0.049$). Age, sex, race, and severity/recurrence of major depressive disorder were some variables with no significant relationship to symptom resolution. In two multiple logistic models, fewer prior antidepressants in the current episode ($p=0.001$), longer duration of the current episode ($p=0.016$), and lower anxiety ratings ($p=0.026$) again emerged as significant factors. Further analysis will address factors associated with maintenance of response.

Conclusions: This analysis may help identify patients with resistant depression most likely to benefit from risperidone augmentation.

References:

1. Greenspan A, Kosik-Gonzalez C, Bossie C, et al: Readiness to discharge among inpatients with schizophrenia: effects of risperidone, quetiapine, and placebo. Poster presented at the XXIVth Collegium Internationale Neuro-psychopharmacologicum Congress, June 20-24, 2004, Paris, France.
2. Szadoczky SE, Rozsa S, Zambori J, Furedi J: Predictors for 2-year outcome of major depressive episode. *J Affect Disord* 2004; 15:49-57.

NR358 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Effect of Mirtazapine on Chronic Insomnia of Depressive Patients With Anxiety Symptoms: Correlation With Serum Cortisol Levels

Marco Venegas, M.D., *Bogota, Colombia*; Felipe Quiroga, M.D., Gabriela Iglesias, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the effect of mirtazapine on subjective and objective sleep parameters in patients with major depressive disorder with anxiety symptoms and chronic secondary insomnia and its possible correlation with serum cortisol levels.

Summary:

Methods: In a prospective, open-label GCP study, 23 outpatients with major depressive episode diagnosis (DSM-IV criteria), with insomnia and anxiety/agitation symptoms were treated with mirtazapine 30 mg/day, during six weeks. Assessments were carried out at baseline, weeks 1; 2; 4 and 6 using HAM-D 17 items, Hamilton Anxiety Rating Scale (HAM-A); Pittsburg Sleep Quality

Index (PSQI). Sleep polygraphic recordings (sleep latency, REM latency, and sleep efficiency) and cortisol plasmatic levels AM and PM were registered at baseline, week 1 and 6. The mean scores were compared using at student test and correlations between variables with a Pearson correlation.

Results: ITT group consist of 22 patients. Statistically significant improvement on sleep quality (PSQI score), depressive and anxiety symptoms (HAMD and HAMA scores) were observed as early as week 1 progressively improving across the trial ($p=0.05$). Statistically significant changes ($p=0.05$) on sleep polygraphic measures (sleep latency and sleep efficiency) and PM serum cortisol levels were also obtained as early as week 1 to week 6.

Conclusions: Mirtazapine had an early positive effect on mood and anxiety symptoms and also sleep quality of depressed patients. Mirtazapine early normalized cortisol plasmatic levels, increased in depressed patients.

References:

1. Schittecatte, et al: Effects of mirtazapine on sleep polygraphic variables, in major depression. *Neuropsychobiology* 2002; 46:197-201.
2. Fawcett J, Barkin R: A meta-analysis of eight randomized, double blind, controlled clinical trials of mirtazapine for the treatment of patients with major depression and symptoms of anxiety. *J Clin Psychiatry* 1998; 59:123-127.

NR359 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Peripheral Resistance to Thyroid Hormone in Depressive Patient Non Responsive to Multiple Antidepressive Treatment

Danilo Quiroz, M.D., *Mood and Anxiety Program, PsicoMedica, Salvador 149 of 1001, Santiago 7500710, Chile*; Sergio Gloger, M.D., Carlos Fardella, M.D., Paola Krall, M.D., Marcela Jimenez, M.D., Cristian Carvajal, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should know about a case in which a severe and resistant depression had a very good response and tolerance to very high doses of thyroid hormone, probably related to peripheral resistance to thyroid hormone.

Summary:

We describe a 38-year-old woman with severe mood disorder refractory to treatment, reverted with the use of high dose of T3 plus T4 without evidence of hyperthyroidism, suggestive of resistance to thyroid hormone (RTH). She underwent a study protocol receiving increasing doses of T3 (0-225 $\mu\text{g/day}$) and 100 $\mu\text{g/day}$ T4. Psychological state was assayed by HAM-D and MADRS. At final stage (225 $\mu\text{g/day}$ T3 + 100 $\mu\text{g/day}$ T4) when circulating levels of T3 and fT3 where found to be >800 ng/dL and 1409 pg/dL (normal ranges: 80-180 ng/dL and 230-420 pg/dL, respectively), we observed an evident recovery of mood (HAM-D 24 to 8; MADRS 40 to 11) accompanied by an improvement of physical symptoms of asthenia, somnolence and lethargy. No significant changes were observed in SHBG, alkaline phosphatases and isoenzymes levels neither in cardiac frequency or blood pressure. TSH level remained suppressed. Binding assays results supported the diagnosis of RTH, because patient's lymphocytes tended to have lower affinity to T3 compared with control cases. We were unable to detect mutations in TR β 1 gene. No circulating anti-T3 autoantibodies were found. These data document the existence of a peripheral RTH manifested as chronic depression reverted with the use of high dose of T3.

References:

1. Refetoff S, Weiss RE, Usala SJ: The syndromes of resistance to thyroid hormone. *Endocr Rev* 1993; 14(3):348-99.

2. Bauer M, Hellweg R, Graf KJ, Baumgartner A: Treatment of refractory depression with high-dose thyroxine. *Neuropsychopharmacology* 1998; 18(6):444-55.

NR360 Tuesday, May 24, 12:00 p.m.-2:00 p.m.
Mood Episodes Induced by Sibutramine in Patients With Bipolar Disorder

Daniilo Quiroz, M.D., *Mood and Anxiety Program, PsicoMedica, Salvador 149 of 1001, Santiago 7500710, Chile*; Isabel Acevedo, M.D., Sergio Gloger, M.D.

Educational Objectives:

At the conclusion of this session, the patient will be able to know about a possible association between sibutramine and the occurrence of mood episodes in vulnerable patients.

Summary:

Objectives: To communicate a clinical series in which the Sibutramine medication is associated as a possible inductive of a mood episode.

Method: Ten cases are described, beginning from the reconstruction of the history and their mood registrations.

Result: A series of ten cases are presented, taken from our institutional experience, where a temporary relation between the use of the anorexic sibutramine with a first affective episode or a recurrence is observed. In all patients, an affective episode is registered, (the registered episodes were maniac, depressive, or mixed), and that does not happen with the suspension of the Sibutramine, being necessary to install or improve the treatment with mood stabilizers. The cases correspond to a worsening of a mood disorder previously diagnosed (6/10), or in the first episode (4/10).

In all of these cases the final diagnosis is bipolar disorder or a bipolar spectrum disorder.

Conclusions: Although it is not possible to establish a causative relationship, this already mentioned temporary relationship permits to suggest the precaution in prescribing this medication to vulnerable patients, and to patients with a diagnosed bipolar disorder. Prospective studies are required.

References:

1. Cordeiro Q, Vallada H: Sibutramine-induced mania episode in a bipolar patient. *Int J Neuropsychopharmacol* 2002; 5(3):283-4.
2. Tafilinski T, Chojnacka J: Sibutramine-associated psychotic episode. *Am J Psychiatry* 2000; 157(12):2057-a-2058.

NR361 Tuesday, May 24, 12:00 p.m.-2:00 p.m.
The 23-Year Health Outcomes of Remitted Depression

Ruth Cronkite, Ph.D., *CHCE-152MPD, VA Palo Alto HCS, 795 Willow Road, Menlo Park, CA 94025*; Rebecca Robinson, M.S., Ralph Swindle, Ph.D., Rudolph Moos, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the value of maintaining a course of remission or partial remission over the long term.

Summary:

Objective: We examined 23-year remission status and health outcomes among depressed patients versus a matched community control cohort.

Method: In 1980, 424 patients treated for unipolar depression and 424 controls completed mailed surveys. Respectively, 81.6%

and 79.1% of surviving patients and controls were followed for 23 years.

Results: Adjusting for covariates, remitted patients (30% of patient cohort) were similar ($p > .11$) to controls on mean number of Patient Health Questionnaire physical symptoms (4.3 vs. 3.8) and anxiety symptoms (0.6 vs. 0.8), current medications (2.4 vs. 2.4), doctor visits (3.7 vs. 3.4) and family activities (4.6 vs. 5.0). Partially and nonremitted cohorts were significantly ($p < .05$) worse on these outcomes. Full and partially remitted cohorts were similar to controls on hospitalizations over the past 12 years (admissions 1.0 vs. 1.1 vs. 0.9; days hospitalized 4.5 vs. 7.5 vs. 4.8), and inability to work due to emotional problems (2% vs. 1% vs. 1%), while the nonremitted cohort used significantly more services (1.5 hospitalizations and 27.4 days hospitalized) and were more unable to work (12%).

Conclusions: Outcomes of remitted patients appear to resolve to rates comparable to controls at 23 years. The benefits of maintaining remission include the return of outcomes and utilization to levels similar to controls.

References:

1. Keller MB: Past, present, and future directions for defining optimal treatment outcome in depression: remission and beyond. *JAMA* 2003; 289(23):p.3152-60.
2. Swindle RW, Jr, Cronkite RC, Moos RH: Risk factors for sustained nonremission of depressive symptoms: A 4-year follow-up. *Journal of Nervous & Mental Disease* 1998; 186(8):p.462-469.

NR362 Tuesday, May 24, 12:00 p.m.-2:00 p.m.
Physical Symptoms Recognition in Major Depression by Psychiatrists in Puerto Rico

Jorge Tamayo, M.D., *SciTech, Eli Lilly and Company, 273 Ponce de Leon, Hato Rey, PR 00917*; Karis Roman, M.P.H., Maria Rivas, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to confirm the high incidence of somatic symptoms in depressed Latino populations, the poor level of recognition of somatic symptoms by the psychiatrists treating those patients, and the impact of painful symptoms on the effectiveness of the antidepressant treatments.

Summary:

Objective: This study was designed to evaluate the psychiatrists' level of recognition of somatic symptoms associated to a major depressive episode (MDE) and their treatment consequences.

Methodology: This non-interventional study was conducted in 25 medical offices in Puerto Rico. It had two visits separated by eight weeks. The level of recognition was determined by the correlation between psychiatrists' clinical evaluation and their patients' self-evaluations using kappa statistics. Chi-square test was used to evaluate the impact of somatic symptoms on treatment antidepressants' effectiveness.

Results: All 145 recruited patients reported the presence of at least one somatic symptom associated with their current MDE. In both visits, a fair agreement between the psychiatrists' and the patients' reports was only noted for headache, abdominal pain and upper limb pains ($0.4003 < k > 0.6594$). For other painful symptoms and painless somatic symptoms, the Kappa values obtained were nonsignificant. An inversely proportional relationship was observed between the effectiveness of the antidepressants in relieving the painful symptoms and its correlation with the improvement of depression, both of which were rated by the patients ($p < .0001$).

Conclusions: This study indicates that somatic symptoms are very common in depressed Puerto Rican patients, are significantly underreported by psychiatrists, and have a significant impact on the antidepressant effectiveness.

References:

1. Piccinelli M, Simon G: Gender and cross-cultural differences in somatic symptoms associated with emotional distress. An international study in primary care. *Psychol Med* 1997; 27:433-444.
2. Greco T, Eckert G, Kroenke K: The outcome of physical symptoms with treatment of depression. *J Gen Intern Med* 2004; 19:813-818.

NR363 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Efficacy of Duloxetine in Patients With Mild, Moderate, or Severe Depressive Symptoms

Anne C. Andorn, M.D., *Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; C. Mallinckrodt, Ph.D., J. Watkin, D.Phil., M. Wohlreich, M.D.

Educational Objectives:

At the conclusion of this presentation, the participants will learn that during acute phase treatment with duloxetine, patients within all three cohorts (mild, moderate, and severe baseline symptom severity) exhibited significant improvement in a range of treatment outcomes including the HAMD17 total score and CGI-Severity scale.

Summary:

Objective: To examine the efficacy of duloxetine in depressed outpatients with mild, moderate, or severe depressive symptoms.

Method: Data were pooled from nine double-blind, placebo-controlled studies in which patients with major depressive disorder (MDD) were randomized to duloxetine (40-120 mg/day) or placebo for 8-9 weeks. Patients were retrospectively stratified according to baseline HAMD17 total scores: mild=total score \leq 19 (duloxetine, n=551; placebo, n=422); moderate=20-24 (duloxetine, n=481; placebo, n=344); severe = \geq 25 (duloxetine, n=137; placebo, n=95).

Results: Compared with placebo, duloxetine produced significantly greater baseline-to-endpoint mean change in HAMD17 total score, Maier and retardation subscales, HAMD17 Items 1 (depressed mood) and 10 (psychic anxiety), and the CGI-S scale (LOCF analyses; $p < .01$ for each outcome) in all 3 patient cohorts. Effect sizes progressively increased with greater baseline severity of depression for the above outcomes (effect size range: mild 0.21-0.40; moderate 0.38-0.45; severe 0.41-0.51). For the severely depressed cohort, superiority of duloxetine over placebo was first observed at Week 4 for HAMD17 total score, Items 2 (guilt), 3 (suicide), 13 (somatic symptoms—general), and CGI-S. Superiority for the anxiety/somatization subscale was observed at Week 8.

Conclusion: As shown here, duloxetine demonstrated superior efficacy as compared with placebo in the treatment of MDD, regardless of the baseline severity of depressive symptoms.

References:

1. Detke MJ, et al: Duloxetine 60 mg once daily dosing versus placebo in the acute treatment of major depression. *J Psychiatr Res* 2002; 36:383-390.
2. Detke MJ, et al: Duloxetine, 60 mg once daily, for major depressive disorder: a randomized double-blind placebo-controlled trial. *J Clin Psychiatry* 2002; 63:308-315.

NR364 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Influence of Premenstrual Mood Symptoms on Age of Onset of Mood Disorders in Women

Jennifer Payne, M.D., *Johns Hopkins Department of Psychiatry, 600 North Wolfe Street, Meyer 3-181, Baltimore, MD 21287*; James Potash, M.D., Karen Swartz, M.D., John Nurnberger, M.D., Douglas Levinson, M.D., J. Raymond DePaulo, Jr., M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the influence of premenstrual mood symptoms on the course of illness in mood disorders.

Summary:

Objective: To determine if the course of illness differs in women with affective disorders who also have premenstrual mood symptoms.

Method: Data were collected by a standardized clinical interview conducted as part of ongoing genetics studies in bipolar disorder and recurrent major depression. The Chi Square statistic was used to compare means between women with and without premenstrual mood symptoms.

Results: 674 women with bipolar I disorder and 1,673 women with major depression were interviewed. Approximately 65% to 70% of the women stated that they experienced premenstrual mood symptoms. The presence of premenstrual mood symptoms appeared to result in an earlier age of onset (by two years) of depressive episodes in women with both bipolar I illness and major depression and of manic episodes in women with bipolar I disorder.

Conclusions: Women with mood disorders who also have premenstrual mood symptoms appear to have an earlier age of onset of mood episodes than women without such symptoms. Future directions include examining the correlation between age of menarche and onset of mood episodes.

This study was funded by a NARSAD Young Investigator's Award.

References:

1. Payne JL: The role of estrogen in mood disorders in women. *Int Rev Psych* 2003; 15:280-290.
2. Hsiao MC, Hsiao CC, Liu CY: Premenstrual symptoms and premenstrual exacerbation in patients with psychiatric disorders. *Psychiatry Clin Neurosci* 2004; 58:186-190.

NR365 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Olanzapine/Fluoxetine and Olanzapine Treatment for Bipolar Depression: Open-Label Continuation in Rapid-Cycling Patients

Sara A. Corya, Ph.D., *Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN 46285*; Paul E. Keck Jr., M.D., Eduard Vieta, M.D., Julie Niswander, Ph.D., Wen Xu, M.S., Mauricio Tohen, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to describe the effectiveness of OFC in bipolar depression in patients with rapid cycling.

Summary:

Objective: Olanzapine/fluoxetine combination (OFC) has demonstrated efficacy in treatment of bipolar depression. This secondary analysis of patients with a history of rapid cycling (RC) examines the efficacy of OFC and olanzapine (OLZ) during a six-month, open-label (O-L) extension.

Methods: 833 subjects with an index depressive episode enrolled in an eight-week, double-blind, randomized trial with 315

RC patients receiving OFC (n=37), OLZ (N=140), or placebo (n=138). Patients achieving remission (MADRS<=8; YMRS<=12) entered O-L treatment receiving OLZ initially and switching to OFC any time after one week as needed.

Results: Compared with placebo and OLZ, mean change in total MADRS score revealed that OFC-treated RC patients improved significantly; 34.3% (12 of 35) achieved remission. During the O-L phase, 64.7% of RC (22 of 34) patients remained free from relapse (vs. 61.9% for non-RC patients). Mean time to relapse (MADRS>=16; YMRS>=15) into any mood episode was 141 days for rapid cyclers and 177 days for non-rapid cyclers. Mania relapse occurred in 12% of RC patients.

Conclusion: As management of depression is the primary unmet need in RC patients, OFC may represent an efficacious treatment for bipolar depression in patients with a history of rapid cycling.

References:

1. Tohen M, Vieta E, Calabrese J, et al: Efficacy of olanzapine and olanzapine-fluoxetine combination in the treatment of bipolar I depression. *Arch Gen Psychiatry* 2003; 60:1079-1088.
2. Calabrese JR, Shelton MD, Bowden CL, et al: Bipolar rapid cycling: focus on depression as its hallmark. *J Clin Psychiatry* 2001; 62 Suppl 14:34-41.

NR366 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

A 24-Week, Open-Label Extension Study of Olanzapine-Fluoxetine Combination and Olanzapine Monotherapy in the Treatment of Bipolar Depression

Sara A. Corya, Ph.D., *Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN 46285*; Doug Williamson, M.D., Michael Case, M.S., Daniel Lin, Ph.D., Mauricio Tohen, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the long-term effectiveness and safety of OFC in patients with bipolar depression.

Summary:

Objective: Olanzapine-fluoxetine combination (OFC) has demonstrated efficacy in the acute treatment of bipolar depression (Tohen et al., 2003). The present analyses examined the efficacy and safety of longer-term treatment with OFC or olanzapine (OLZ) in a 6-month, open-label extension study.

Methods: 376 patients with bipolar depression who completed an acute trial entered the open-label study and received one week of olanzapine (5-20 mg/day). At all subsequent visits, patients could stay with olanzapine, or change to OFC (6/25, 12/25, or 12/50 mg/day). Three treatment groups were defined retrospectively according to the medication course taken from week 1: OLZ, OFC, or Switched.

Results: Among patients who entered in non-remission, MADRS total scores decreased significantly for all treatment groups. The majority of patients who entered the study in non-remission achieved remission (MADRS total score <=12) during the trial (OFC: 66.7%, OLZ: 64.7%, Switched: 62.5%). The overall rate of depressive relapse was 27.4% and the overall rate of mania emergence was 5.9%.

Conclusions: Olanzapine-fluoxetine combination may be efficacious in long-term management of bipolar depression and carries a low risk of mania emergence.

References:

1. Tohen M, Vieta E, Calabrese J et al: Efficacy of olanzapine and olanzapine-fluoxetine combination in the treatment of bipolar I depression. *Arch Gen Psychiatry* 2003; 60(11):1079-1088.

2. Montgomery SA, Asberg M: A new depression scale designed to be sensitive to change. *Br J Psychiatry* 1979; 134:382-389.

NR367 Tuesday, May 24, 12:00 p.m.-2:00 p.m. **Psychosocial Intervention to Enhance Treatment Attitudes**

Martha Sajatovic, M.D., *Department of Psychiatry, University Hospital Cleveland, 11100 Euclid Avenue, MS 5080, Cleveland, OH 44106*; Marilyn Davies, Ph.D., Robert Hays, M.A.

Educational Objectives:

At the conclusion of the session, the participant will better understand how psychosocial interventions may enhance treatment adherence among individuals with bipolar disorder.

Summary:

Lack of adherence with treatment plays an important role in outcome of bipolar disorder (BPD), and is associated with substantial humanitarian and financial costs. It has been reported that 20% to 55% of individuals with BPD have major lapses in treatment adherence. This study seeks to examine how a psychosocial intervention based upon a collaborative treatment model affects treatment adherence attitudes and behaviors. This is a prospective, randomized, controlled study of effects on treatment adherence attitudes and behaviors associated with the addition of a standardized psychoeducational intervention (The Life Goals Program) to the medical management (usual care) of outpatients with BPD who attend a community mental health center.

To date, 92 patients have been recruited (45 to Life Goals and 47 to usual care). Mean age of the sample was 44 years. Forty percent (N=41) of the total group were individuals of minority ethnicity. Substance abuse is very common in this community-based sample, with 85% of individuals having either current or past substance abuse. The study investigators have hypothesized that life goals will improve treatment adherence attitudes among individuals with BPD. Preliminary findings support this, as patients involved in the group intervention had significant improvement in attitudes toward medication after three months (p=.012) compared to patients in usual care. A larger sample of study patients followed over the anticipated one-year study trajectory is needed to confirm these preliminary findings.

References:

1. Colom F, Vieta E: Treatment adherence in bipolar patients. *Clinical Approaches in Bipolar Disorders* 2002; 1(2):49-56.
2. Adams J, Scott J: Predicting medication adherence in severe mental disorders. *Acta Psychiatr Scand* 2000; 101(2):119-124.

NR368 Tuesday, May 24, 12:00 p.m.-2:00 p.m. **Treatment Adherence in Rapid Cycling Bipolar Disorder**

Martha Sajatovic, M.D., *Department of Psychiatry, University Hospital Cleveland, 11100 Euclid Avenue, MS 5080, Cleveland, OH 44106*; Melvin Shelton, M.D., Omar Elhaj, M.D., Eric Youngstorm, Ph.D., Sarah Bilali, M.A., Joseph R. Calabrese, M.D., Daniel Rapport, M.D.

Educational Objectives:

At the conclusion of the presentation, participants will better understand patient-related features associated with treatment adherence in rapid cycling bipolar disorder.

Summary:

Treatment adherence has not been well-studied among individuals with rapid cycling bipolar illness, but, as in non-rapid cycling illness, is likely to be associated with negative sequelae.

This secondary analysis examines treatment adherence among individuals with rapid cycling bipolar disorder and substance abuse comorbidity participating in two clinical drug trials. Individuals who dropped out of study for non-adherence were compared with individuals who were adherent. Findings from this analysis suggest that treatment non-adherence among individuals with rapid-cycling bipolar disorder is relatively common, even in a highly structured clinical trial setting. 18% of individuals dropped out of clinical trial participation due to non-adherence. Individuals who had less education and those of minority ethnicity were more likely to be non-adherent with study medication or study protocol, as were individuals with substance abuse and legal problems at baseline. Proportion of study drop-outs due to non-adherence among individuals with bipolar disorder and comorbid substance abuse was 27% compared with 12% dropouts among individuals uncomplicated by comorbid substance abuse.

Treatment adherence in bipolar disorder appears to be affected by a variety of patient clinical characteristics as well as orientation toward treatment and treatment providers. Among individuals with rapid cycling bipolar disorder, level of education, ethnicity, comorbidity, and legal history appear to affect treatment adherence.

References:

1. Lingam R, Scott J: Treatment non-adherence in affective disorders. *Acta Psychiatr Scand* 2002; 105(3):164-172.
2. Scott J, Pope M: Self-reported adherence to treatment with mood stabilizers, plasma levels, and psychiatric hospitalization. *Am J Psychiatry* 2002; 159(11):1927-1929.

NR369 **Tuesday, May 24, 12:00 p.m.-2:00 p.m.** **Quetiapine for the Treatment of Bipolar Mania in Older Adults**

Martha Sajatovic, M.D., *Department of Psychiatry, University Hospital Cleveland, 11100 Euclid Avenue, MS 5080, Cleveland, OH 44106*; Jamie Mullen, M.D., Joseph R. Calabrese, M.D.

Educational Objectives:

At the conclusion of the presentation, participants will gain familiarity with treatments for bipolar disorder in older adults.

Summary:

There is little published information on treatments for bipolar disorder in older adult populations. We report a secondary analysis from the quetiapine monotherapy clinical trials database among bipolar manic adults age 55 and older.

Data analysis combined results from two 12-week, double-blind, randomized, placebo-controlled studies comparing effects of quetiapine and placebo for treatment of bipolar mania. An additional cohort of patients received either haloperidol or lithium and were included as internal controls.

A total of 604 patients, 97 older adults and 507 younger adults, made up the intent-to-treat (ITT) population. Mean age of the older group was 62.9 (SD 5.7) years in quetiapine-treated patients and 61.3 (5.0) in placebo-treated patients and mean age of the younger group was 36.8 (9.7) years in quetiapine-treated patients and 37.0 (10.1) in placebo-treated patients.

Both older and younger individuals had significant improvement from baseline on YMRS scores. Of note, the older adult group demonstrated a particularly rapid and sustained reduction in YMRS score compared with placebo that was apparent by Day 4 of treatment.

For the quetiapine treatment group, most common adverse effects in younger patients were dry mouth, somnolence, and insomnia, while most common adverse effects in older patients were dry mouth, somnolence, postural hypotension, insomnia, weight gain, and dizziness.

This secondary analysis suggests that quetiapine represents a potentially useful treatment option among older adults with bipolar I mania.

References:

1. Alexopoulos GS, Streim J, Carpenter D, Docherty JP: Expert Consensus Panel for Using Antipsychotic Drugs in Older Patients. Using antipsychotic agents in older patients. *J Clin Psychiatry* 2004; 65(Suppl 2):5-102.
2. Charney DS, Reynolds CF 3rd, Lewis L, et al: Depression and Bipolar Support Alliance consensus statement on the unmet needs in diagnosis and treatment of mood disorders in late life. *Arch Gen Psychiatry* 2003; 60(7):664-672.

NR370 **Tuesday, May 24, 12:00 p.m.-2:00 p.m.** **A Dimensional Approach to Personality Assessment in Atypical Depression Using the Five-Factor Model**

Kevin K. Chopra, M.D., *Department of Psychiatry, University of Toronto, CAMH Room 1153, 250 College Street, Toronto, Ontario, NC M5T 1R8, Canada*; R. Michael Bagby, Ph.D., Susan Dickens, Sidney H. Kennedy, M.D., Arun Ravindran, M.D., Robert D. Levitan, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to: (1) appreciate the complex relationship of personality and atypical depression, (2) have a greater understanding of the advantages of the Five-Factor Model in evaluating personality traits in atypical depression, and (3) learn how dimensional models of personality can provide new insights into our knowledge of depressive subtypes.

Summary:

The current study aims to help clarify what personality traits are most salient in atypical depression using the Five-Factor Model (FFM). The FFM was developed independently from the Diagnostic and Statistical Manual of Mental Disorders (DSM) and thus has the advantage of providing an independent measure of personality traits in atypical depression. Outpatients (n=160) with non-psychotic major depression were characterized as having atypical (n=26), or non-atypical depression (n=134) based on DSM-IV criteria. To limit the effect of state depression, personality was assessed after subjects received a minimum of 14 weeks of antidepressant treatment. The NEO-PI-R, which generates data based on the FFM, was the primary assessment measure. Post-treatment, relative to the non-atypical comparison group, the atypical group had significantly higher scores on the dimension of Neuroticism (p=.008), the facets of Impulsivity (p=.002) and Anger-hostility (p=.009), and a significantly lower score on the facet of Deliberation (p=.007). In sum, the FFM provides new insights into which personality traits are most salient in atypical depression.

References:

1. Costa PT, McCrae RR: The Five-Factor Model of personality and its relevance to personality disorders. *Journal of Personality Disorders* 1992; 6:343-359.
2. Posternak MA, Zimmerman M: Partial validation of the atypical features subtype of major depressive disorder. *Archives of General Psychiatry* 2002; 59:70-76.

NR371 **Tuesday, May 24, 12:00 p.m.-2:00 p.m.** **Route of Admission Was Associated With the Early Administration of Antipsychotics in Bipolar**

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701, South Korea; Woo-Young Jang, M.D., Wang-Youn Won, M.D., Tae-Suk Kim, M.D.

Educational Objectives:

At the conclusion of the presentation, the participants should be able to understand and consider what kind of associated factor is related to the early administration of antipsychotics in the treatment of bipolar disorder.

Summary:

Objectives: This study was conducted to evaluate the impact of factors on the early prescription of antipsychotics in the treatment of bipolar mania.

Methods: Admission with the DSM-IV discharge diagnosis of bipolar mania was tracked via electrical records from late 2002 to early 2004 at Kangnam St. Mary's Hospital. Sixty-three patients were identified. Regression analysis was run for the clinical variable to identify the factors affecting on early prescription of antipsychotics.

Results: The route of admission such as via outpatient clinic (OPD) or emergency room (ER) was associated with the early prescription of antipsychotics ($p=0.027$, $CI=0.032-0.809$), whereas subgroup with/without psychotic feature and severity of psychopathologies were not related to the early prescription of antipsychotics.

Conclusion: This preliminary result suggests that clinicians prescribe earlier antipsychotics to patients admitted via ER than via OPD. This may be linked to the possible clinicians' prejudice on patients and patients' behavioral disturbance based on the route of admission. More well-designed studies would be warranted to replicate this preliminary finding.

References:

1. Samellas et al: Antipsychotic drugs in mania: factors predicting use of antipsychotic medication following inpatient treatment of mania. *Int Clin Psychopharmacol* 2004; 19:291-297.
2. Keck et al: Factors associated with maintenance antipsychotic treatment of patients with bipolar disorder. *J Clin Psychiatry* 1996; 57:147-151.

NR372 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Using the LIFE to Assess Outcomes in Bipolar Disorder: Reliability and Validity

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Educational Objectives:

At the conclusion of the presentation, the participant will have an understanding of the variability in symptom course for bipolar disorder over the span of a year; they will discover how the LIFE can be used as an innovative tool for assessing symptom course in longitudinal research; and will be able to identify difficulties in training multisite centers in using the LIFE and have strategies for overcoming common pitfalls.

Summary:

Introduction: The Longitudinal Interval Follow-up Evaluation (LIFE) is a semi-structured interview and rating system for assessing the longitudinal course of psychiatric illness using a retrospective weekly rating system. Few studies have used this instrument, which offers great promise. This presentation will describe the variation in symptom profiles and course among patients with BD, evaluate LIFE validity and reliability, and discuss implementation issues.

Method: The first 160 bipolar subjects in the study have been interviewed prospectively using the LIFE, producing four weekly ratings each month over four months for depressive and manic

symptoms. To assess the validity of these LIFE ratings, depressive symptom ratings were compared against Hamilton Depression Rating Scale (HAM-D 17) scores for the same months, while manic symptom ratings were compared against concurrent ratings on the Clinician Administered Rating Scale—Mania (CARS-M).

Results & Discussion: The LIFE mania and depression ratings are highly positively correlated with other standardized measures of depression and mania. The preliminary LIFE outcome data show that, on average, bipolar patients spend up to half of the time with significant mood symptoms. The utility of the LIFE for assessing symptoms of BD will be discussed.

References:

1. Keller MB, Lavori PW, Friedman B, Nielson E, Endicott J, McDonald-Scott P, Andreasen C: The Longitudinal Interval Follow-up Evaluation: A comprehensive method for assessing outcome in prospective longitudinal studies. *Archives of General Psychiatry* 1987; 44:540-548.
2. Bauer MS, Kirk GF, Gavin C, Williford WO: Determinants of functional outcome and healthcare costs in bipolar disorder: a high intensity follow-up study. *Journal of Affective Disorders* 2001; 65:231-241.

NR373 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Effects of Lamotrigine on Mood in Patients With Generalized Seizures

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Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the effect of lamotrigine on mood in patients with generalized seizures.

Summary:

Rationale: Lamotrigine (LTG) has shown positive effects on mood in patients with partial seizures. This study examined mood effects in patients with generalized seizures.

Methods: LTG-naïve patients with inadequately controlled generalized seizures were enrolled in a randomized, double-blind trial. Patients completed three mood questionnaires, the Beck Depression Inventory (BDI), the Profile of Mood States (POMS) and the Cornell Dysthymia Rating Scale (CDRS) at baseline and end of 19 weeks of treatment. Change scores were compared with ANOVA.

Results: One hundred seventeen patients were randomized and received LTG or PBO. Groups were similar in demography and showed mild depressive symptoms at baseline: mean mood scores for the LTG and PBO groups, respectively were 18.3, 16.8 for BDI; 53.9, 57.9 for POMS; and 61.1, 60.8 for CDRS. After treatment, mean change in mood scores for the LTG and PBO groups, respectively were -8.9, -1.7, $p=0.01$ for BDI; -32, -6.5, $p=0.03$ for POMS; and -7.3, -4.1, $p=NS$ for CDRS. The most common (=5%) adverse events for LTG and PBO were dizziness, somnolence, and nausea. No serious rash was reported.

Conclusion: Lamotrigine, a broad spectrum AED, improved mood scores versus placebo in patients with generalized seizures on two of three commonly used questionnaires.

References:

1. Cramer JA, Hammer AE, Kustra RP: Improved mood states with lamotrigine in patients with epilepsy. *Epilepsy Behav* 2004; 5:702-707.
2. Kalogjera DS, Sackellares JC: Improvement in depression associated with partial epilepsy in patients treated with lamotrigine. *Epilepsy Behav* 2002; 3:510-516.

NR374 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Gender Differences in Bipolar Affective Disorder: A Comparative Study

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Educational Objectives:

Although gender differences in psychiatric disorders have been widely documented in literature, studies on gender differences in bipolar affective disorder is relatively neglected. The aim of this study is to investigate the phenomenological differences in men and women with mania. This study supports the hypothesis that women with mania phenomenologically have much more dysphoric features.

Summary:

Objective: Although gender differences in psychiatric disorders have been widely documented in literature, studies on gender differences in bipolar affective disorder are relatively neglected. The aim of this study is to investigate the phenomenological differences in men and women with mania.

Method: We performed the study in Bakirköy State Training and Research Hospital for Psychiatry and Neurology Diseases, in Istanbul, Turkey, between June 1999 and July 2000. The diagnoses of the patients were made according to DSM-IV bipolar affective disorder (mania) criteria. Sociodemographic features, clinical features, type of episode, number and length of hospitalizations were investigated in equal number of men (n=90) and women (n=90). All patients have been assessed by Structured Clinical Interview for DSM-IV-Clinical Version (SCID-I), Young Mania Rating Scale (YMRS), Hamilton Depression Rating Scale (HAM-D) and Scale for the Assessment of Positive Symptoms (SAPS).

Results: Rate of single (66.7%) and divorced patients (11.1%) in men were significantly higher. Rate of unemployment status (83.3%) were higher in women than men (56.7%). Depressive mood, irritability, destructive and aggressive behaviour were found significantly higher in women in terms of phenomenological features of mania, than adult-onset adults. Delusions were found significantly higher in men's group.

Conclusion: This study supports the hypothesis that women with mania phenomenologically have much more dysphoric features.

References:

1. Hendrick V, Altshuler LL, Gitlin MJ, Delrahim S, Hammen C: Gender and bipolar illness. *J Clin Psychiatry* 2000; 61(5):393-6.
2. Leibenluft E: Women and bipolar disorder: an update. *Bull Menninger Clin* 2000; 64(1):5-17.

NR375 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Comparison of Divalproex and Quetiapine Monotherapy for Adolescent Mania

Supported by AstraZeneca, Wilmington, Delaware

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Educational Objectives:

At the conclusion of this session, the participant should be able to (1) discuss the findings from a double-blind study comparing the efficacy of divalproex versus quetiapine monotherapy for the treatment of adolescent mania; and (2) determine the comparative tolerability of divalproex versus quetiapine for the treatment of adolescent mania.

Summary:

Objective: Determine whether quetiapine monotherapy is at least 60% as effective as divalproex for the treatment of adolescent mania.

Methods: Fifty adolescents (aged 12-18 years) with bipolar disorder, manic or mixed episode were randomized to quetiapine monotherapy or divalproex for 28 days.

Results: Twenty-five subjects were randomized to each treatment group. The mean (SD) decrease from baseline to endpoint in Young Mania Rating Scale (YMRS) score was 19.6 (2.4) in the divalproex group and 22.8 (2.4) in the divalproex group. Based on the change in YMRS score in the divalproex group, the response in the quetiapine group needed to be within 4 points. The mean (SD) group difference. In YMRS change from baseline to endpoint was 3.3 (3.4) (95% CI, -3.5, 10:1). Response rate for improvement in mania (Clinical Global Impression score ≤ 2) was significantly greater in the quetiapine group than in the divalproex group (84% vs. 56%, $p=0.03$). There were no statistically significant group differences in rates of adverse events (AEs). The most common AE in both groups was sedation quetiapine $n=15$ (60%) vs. divalproex $n=9$ (36%, $p=0.1$).

Conclusions: Quetiapine is at least as efficacious as divalproex in the treatment of adolescent patients with mania. Therefore, quetiapine may be used as monotherapy for the treatment of adolescent patients with mania.

References:

1. DelBello MP, Schwerts M, Rosenberg HL, Strakowski SM: A double-blind, randomized, placebo-controlled study of quetiapine as adjunctive treatment for adolescent mania. *J Am Acad Child Adolesc Psychiatry* 2002; 41:1216-1223.
2. Jones M, Huizar K: Quetiapine monotherapy for acute mania associated with bipolar disorder (STAMP and STAMP 2). *Biol Psychiatry* 2004; 55(8 Suppl 1):33S.

NR376 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Olanzapine/Fluoxetine Combination Versus Lamotrigine for Bipolar Depression

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Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the relative merits of olanzapine-fluoxetine combination and lamotrigine for treatment of bipolar I depression.

Summary:

Objective: Determine the efficacy of olanzapine-fluoxetine combination compared with lamotrigine for treatment of bipolar I depression.

Method: The acute phase of a randomized, double-blind study compared olanzapine-fluoxetine combination (6/25, 6/50, 12/25, or 12/50 mg/day, $N=205$) with lamotrigine (200 mg/day; $N=205$) in bipolar I depression over seven weeks. Efficacy measures included Clinical Global Impression Severity (CGI-S) (primary outcome measure), Montgomery-Asberg Depression Rating Scales (MADRS), and Young-Mania Rating Scale (YMRS). Analytical techniques included mixed-models repeated measures analysis on change from baseline and Fisher's exact test for categorical comparisons.

Results: Patients treated with OFC had greater improvement than lamotrigine-treated patients across the seven-week treatment period on CGI-Severity ($p=.002$), MADRS total score ($p=.002$) and YMRS ($p=.001$). Time to response (50% decrease in MADRS) was significantly ($p=.010$) shorter for OFC-treated pa-

tients. Serious adverse events occurred more frequently in lamotrigine-treated patients (LMG 5.4%, OFC 1.0%; $p=.012$). Adverse events occurring in $\geq 10\%$ patients and more frequently ($p<.05$) with OFC treatment were somnolence, increased appetite, dry mouth, sedation, weight gain and tremor. Weight ($p<.001$), cholesterol ($p<.001$) and triglycerides ($p=.001$) were significantly elevated with OFC treatment compared to lamotrigine.

Conclusion: Patients with bipolar depression had greater improvement in both depressive and manic symptoms on olanzapine-fluoxetine combination than lamotrigine.

References:

1. Tohen M, Vieta E, Calabrese J, Ketter T, Sachs G, Bowden C, Mitchell P, Centorrino F, Risser R, Baker R, Evans A, Beymer K, Dube S, Tollefson G, Brier A: Efficacy of olanzapine and olanzapine-fluoxetine combination in the treatment of bipolar I depression. *Arch Gen Psychiatry* 2003; 60:1079-1088.
2. Calabrese J, Bowden C, Sachs G, Ascher J, Monaghan E, Rudd G for the Lamictal 602 study group: A double-blind, placebo-controlled study of lamotrigine monotherapy in outpatients with bipolar I depression. *Journal of Clinical Psychiatry* 1999; 60:79-88.

NR377 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Olanzapine and Lithium Prophylaxis of Bipolar Disorder and Episode History

John P. Houston, M.D., *Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Terence Ketter, M.D., Richard Risser, M.S.C., David Adams, Ph.D., Adam Meyers, M.S., Doug Williamson, M.D., Mauricio Tohen, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the relative merits of olanzapine and lithium for prevention of relapse/recurrence in bipolar I disorder with respect to patient history of mood episodes.

Summary:

Objective: Prevention of recurrent manic episodes early in the course of bipolar disorder may improve overall patient prognosis. We assessed treatment differences in prevention of mood episodes in patients subgrouped by number of previous manic episodes.

Method: This was a post-hoc analysis of data from a double-blind, randomized study of relapse/recurrence in 431 initially euthymic patients with bipolar I disorder randomized to olanzapine (OLZ) ($n=217$, 5-20 mg/day) or lithium (LI) ($n=214$, serum level of 0.6 to 1.2 mEq/L). Patients were subcategorized by number of previous manic episodes: early stage: 2 ($n=48$, OLZ; $n=53$, LI), intermediate: 3-5 ($n=98$, OLZ; $n=80$, LI), and late stage: >5 ($n=71$, OLZ; $n=81$, LI), and evaluated for rates of manic/mixed and depressive episode relapse/recurrence.

Results: Rates of manic/mixed recurrences for OLZ vs. LI were: 2.1% vs. 26.4% ($p=.008$), 13.3% vs. 23.8% ($p=.073$), and 23.9% vs. 33.3% ($p=.204$), for early stage, intermediate, and late-stage groups, respectively. Rates of depressive recurrences were not significantly different by treatment for the same groups.

Conclusions: Early stage patients had a significantly lower rate of recurrence of manic episodes with OLZ vs. LI. Intermediate and advanced patients did not have significant treatment differences in rates of manic recurrence.

References:

1. Post RM: Transduction of psychosocial stress into the neurobiology of recurrent affective disorder. *American Journal of Psychiatry* 1992; 149:999-1010.

2. Tohen M, Marneros A, Greil W, Calabrese JR, Sachs GS, Yatham LN, Oerlinghausen BM, Koukopoulos A, Cassano GB, Heinz G, Licht RW, Dell'Osso L, Evans AR, Risser RR, Baker RW, Crane H, Dossenbach MR, Bowden CL: *American Journal of Psychiatry* 2004, in press.

NR378 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Comparison of Efficacy and Tolerability of Paroxetine CR Versus Venlafaxine XR

Supported by GlaxoSmithKline

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Educational Objectives:

At the end of this session, the participant should be able to compare and contrast treatment with paroxetine, controlled release and venlafaxine, extended release formulations in MDD patients.

Summary:

Objective: To examine efficacy, tolerability, safety, and norepinephrine and serotonin transporter reuptake inhibition of paroxetine CR (PAR) and venlafaxine XR (VEN) in patients with major depressive disorder (MDD).

Methods: Outpatients 18 to 65 years, with a primary diagnosis of MDD were randomized to PAR ($N=42$) forced titration to 75mg/day or VEN ($N=44$) forced titration to 375 mg/day, over eight weeks. The primary efficacy measure was change from baseline in MADRS total score at week 8. Safety was assessed through adverse event (AE) monitoring.

Results: 86 patients were randomized. There was no difference in MADRS change between the two antidepressants; PAR -15.0 (SE 10.02) vs. VEN -16.2 points (SE 9.67). The VEN group had more discontinuations due to AEs than PAR (9.1% vs. 4.8%, respectively). AEs with an incidence $>5.0\%$ for PAR and twice that of VEN included nasopharyngitis and upper respiratory tract infection. AEs meeting these criteria for VEN ($>5\%$ and twice PAR) included dry mouth, dizziness, hyperhidrosis, anorgasmia, tremor, blurred vision, diarrhea, anxiety, and increased heart rate. Norepinephrine and serotonin transporter occupancy confirmed the results of previous studies. The antidepressants inhibited SERT greater than 80%.

Conclusions: Both treatments effectively reduced MDD symptoms. Paroxetine CR appeared to be better tolerated.

References:

1. Harvey AT, Rudolph RZ, Preston S. Evidence of the dual mechanisms of action of venlafaxine. *Arch Gen Psychiatry* 2000; 57:503-509.
2. Gilmore ML, Owens MJ, Nemeroff CB. Inhibition of norepinephrine uptake in patients with major depression treated with paroxetine. *Am J Psychiatry* 2002; 159:10, 1702-1710.

NR379 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Rates of Childhood Psychopathology Among Adults With Bipolar Disorder

Aude I. Henin, Ph.D., *Department of Psychiatry, Massachusetts General Hospital, 185 Alewife Brook Parkway, Cambridge, MA 02138*; Andrew A. Nierenberg, M.D., Eric Mick, Sc.D., Yelena P. Wu, B.A., Gianna Marzilli, B.A., Cindy Hwang, B.A., Joseph Biederman, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should understand that adults with bipolar disorder report a significantly higher rate of childhood behavioral, anxiety, and elimination disorders before the onset of bipolar disorder.

Summary:

Uncontrolled, retrospective studies of bipolar adults suggest that they experience childhood psychopathology, including behavioral and mood disorders. Those with a history of childhood psychopathology have worse functional and clinical outcomes. This study examined the childhood history of 88 adults with bipolar disorder compared with a control sample of 308 nonbipolar adults. Participants were assessed using the Structured Clinical Interview for DSM-III-R/DSM-IV supplemented with modules from the Kiddie Schedule for Affective Disorders and Schizophrenia. Relative to comparison participants, bipolar adults had higher rates of separation anxiety disorder (OR=5.23, CI [1.42-19.30], $p=.01$), DSM-III-R overanxious disorder (OR=25.94, CI [11.60-58.01], $p<.001$), ADHD (OR=25.35, CI [8.03-80.01], $p<.001$), oppositional-defiant disorder (OR=9.13, CI [3.34-24.97], $p<.001$), conduct disorder (OR=3.92, CI [1.47-10.44], $p=.006$), and enuresis [OR=3.80, CI [1.78-8.10], $p=.001$). There was a trend for the bipolar patients to have received higher rates of extra help in school (OR=2.01, CI [1.00-4.05], $p=.05$). The mean age of onset for these childhood disorders preceded the age of onset of bipolar disorder. These results indicate that bipolar disorder is often preceded by extensive childhood psychopathology, most notably disruptive behavior, anxiety, and elimination disorders.

References:

1. Sachs GS, Conklin A, Lafer B, et al: Psychopathology in children of late versus early onset bipolar probands. Paper presented at the annual meeting of the American Academy of Child and Adolescent Psychiatry, San Antonio, TX, 1993.
2. Perlis RH, Miyahara S, Marangell LB, Wisniewski SR, Ostacher M, DelBello MP, Bowden CL, Sachs GS, Nierenberg AA: Long-term implications of early onset in bipolar disorder: data from the first 1000 participants in the systematic treatment enhancement program for bipolar disorder (STEP-BD). *Biol Psychiatry* 2004; 55(9):875-81.

NR380 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Effect of Subjective Anxiety and Depressive Symptoms on Objectively Rated Symptoms in Depressed Patients

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Educational Objectives:

The relationship between depression and anxiety has long been a matter of controversy. This study demonstrated the effect of subjective anxiety and depressive symptoms on objective rating in depressed patients.

Summary:

Objective: This study is designed to examine the effect of subjective anxiety and depressive symptoms on objective rating by clinicians in patients with depressive disorder.

Methods: Seventy-six outpatients with major depressive disorder based on DSM-IV criteria were recruited. Subjects completed Zung Self-Rating Depression Scale (ZD) and Zung Anxiety Scale (ZA). Also, Hamilton Rating Scale for Depression (HAM-D) and Hamilton anxiety scale (HAM-A) were applied to the patients by clinicians. Structural equation model was employed with LISREL (version 8.12a).

Results: Subjective anxiety symptoms from ZA had a significant effect on objective anxiety measured with HAM-A ($rs=0.541$, $t=6.780$) and depressive symptoms with HAM-D ($rs=0.216$, $t=-3.730$). And subjective depressive symptoms from ZD affected objective anxiety ($rs=-0.205$, $t=2.061$) and depressive symptoms rated by the clinicians ($rs=0.454$, $t=-6.282$).

Conclusions: Objective depressive symptom was affected by subjective depressive symptom but also by subjective anxiety symptom. And anxiety symptoms measured objectively are affected by subjective anxiety symptom but also by subjective depressive symptom. Thus, it is very important to measure the depressive symptom, but also anxiety symptom in evaluating depressed patients.

References:

1. Lenvine J, Cole DP, Chengappa KN, Gershon S: Anxiety disorders and major depression, together or apart. *Depress Anxiety* 2001; 14(2):94-104.
2. Fava M, Rankin MA, Wright EC, Aplert Je, Niereberg AA, Pava J, Rosenbaum JF: Anxiety disorders in major depression. *Compr Psychiatry* 2000; 41(2):97-102.

NR381 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Effect on Mood After Subthalamic Stimulation in Parkinson's Disease

Isabelle Chereau-Bodet, M.D., *Department of Psychiatry B, Chu de Clermont-Ferrand, Rue Montalembert BP69, Clermont-Ferrand 63003, France*; Franck Durif, M.D., Jean-Jacques Lemaire, M.D., Pierre-Michel Llorca, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should know that subthalamic stimulation in Parkinson's disease could induce mood disorders.

Summary:

Objectives: Several case reports of transient acute depression or manic symptoms are described in the literature after bilateral subthalamic nucleus (STN) deep brain stimulation in patients with Parkinson's disease. We have few data about their frequency or cause. Different hypothesis involve premorbid personality disorders and thymic past history.

Methods: We elaborate a one-year prospective study to evaluate mood disorder frequency and physiological mechanisms of Parkinsonian patients treated by bilateral STN stimulation. We enrolled in our sample the first 20 consecutive Parkinsonians. Evaluation consist of pre and post-operative psychiatric interview and Montgomery and Asberg Depression Rating Scale (MADRS), Mini International Neuropsychiatric Inventory (MINI), Scale Inventory Personality Disorder (SIPD), Mania Assessment Scale (Bech), Assessment of Depression (Beck) and Apathic scale.

Results: After six months, among 12 operated patients, temporary results show one case of hypomania with behavioral disorder (DSM-IV criteria disorder). This patient, without thymic history, presented a paranoid personality disorder. Using evaluating tools, we did not identified in the other 11 patients, acute depression or manic symptoms.

Conclusion: Data are still being analysed, but this case draws our attention to the effects of STN stimulation on mood and behavioural disorders and to the importance of the psychiatric follow-up.

References:

1. Kulisevsky J, Berthier ML, Gironell A, Pascual-Sedano B, Molet J, Pares P: Mania following deep brain stimulation for Parkinson's disease. *Neurology* 2002; 59(9):1421-4.
2. Bejjani BP, Damier P, Arnulf I, Thivard L, Bonnet AM, Dormont D, Cornu P, Pidoux B, Samson Y, Agid Y: Transient acute

depression induced by high-frequency deep-brain stimulation. *N England J Med* 1999, 13: 1476-1480.

mood disorders and the possible relationship of these changes to pharmacologic treatment strategies.

Summary:

Background: Recurrent major depressive episodes are associated with hippocampal volume loss. Although preclinical data support the hypothesis that antidepressants and other medications such as lithium have neuroprotective effects, there is a paucity of clinical data informing this question.

Method: Treatment naive patients with SCID-IV diagnoses of unipolar or bipolar disorder completed magnetic resonance scans and neuropsychological profiles before initiation of pharmacotherapy. Subjects were followed prospectively using a life charting technique for a minimum of two years and were then reassessed.

Results: Preliminary results suggest that long-term continuous treatment with lithium may prevent hippocampal volume loss; the effect of antidepressants remains indeterminate with a small sample size. There may be differential effects in different brain regions. In this sample, there was a 19.2% increase in volume in the left hippocampus for patients treated with lithium, versus a 0.5% and 1.7% loss of volume in patients treated with antidepressants and other pharmacological strategies respectively.

Conclusions: These findings support the notion that lithium may have neuroprotective effects that are detectable in clinical samples. The sample of patients treated with antidepressants over the long term is being increased in this study.

References:

1. Campbell S, Marriott M, Nahmias C, MacQueen GM: Lower hippocampal volume in patients suffering from depression: a meta-analysis. *American Journal of Psychiatry* 2004; 151:598-607.
2. MacQueen GM, Campbell S, McEwen BS, Macdonald K, Amano S, Joffe RJ, Nahmias C, Young LT: Course of illness, hippocampal function, and volume in major depression. *Proc Natl Acad Sci USA*. 2003; 100:1387-92.

**NR382 Tuesday, May 24, 12:00 p.m.-2:00 p.m.
History of Depressive and Anxiety Disorders as Predictors of Response in Fibromyalgia**

Ashwin A. Patkar, M.D., *Department of Psychiatry, Duke University, 4323 Ben Franklin Boulevard, Suite 700, Durham, NC 27704*; Kathleen Peindl, Ph.D., Stan Krulewicz, M.A., Paolo Mannelli, M.D., Amanda Lindsay, B.S., Prakash S. Masand, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the relationship between depressive and anxiety disorders and response to treatment in fibromyalgia.

Summary:

Objective: We investigated whether history of depressive and anxiety disorders predicted response to treatment in a double-blind, randomized, placebo-controlled trial of Paroxetine CR in fibromyalgia.

Method: 180 subjects with fibromyalgia were screened and 116 were randomized to receive paroxetine CR (dose 12.5-62.5 mg per day) or placebo for 12 weeks. Current and lifetime psychiatric diagnoses based on DSM-IV criteria were obtained using the Mini International Neuropsychiatric Interview. Patients with current depressive or anxiety disorders were excluded. Response was defined as 25% or greater reduction in Fibromyalgia Impact Questionnaire scores from randomization to end of treatment.

Results: 47.6% of randomized subjects had a lifetime diagnosis of depressive and/or anxiety disorders. While significantly more subjects in the paroxetine CR group (57%) responded compared to placebo (33%) ($p=0.016$), there was no significant difference in response between subjects with and without lifetime depression or anxiety ($\chi^2=3.13$, $p=.53$). In logistic regression, the paroxetine CR group was significantly associated with treatment response (O.R.=2.51, C.I.=1.12-5.64, $p=0.02$), however, lifetime depression or anxiety was not related to response (O.R.=1.54, C.I.=0.69-3.45, $p=0.28$).

Conclusions: Despite high comorbidity, response to paroxetine CR in fibromyalgia appears to be unrelated to history of depressive or anxiety disorders.

References:

1. Workman EA, Hubbard JR, Bradford LF: Comorbidity psychiatric disorders and predictors of pain management program success in patients with chronic pain. *Primary Care Companion Journal of Clinical Psychiatry* 2002; 4:137-140.
2. Patkar AA, Bilal LA, Masand PS: Management of fibromyalgia. *Current Psychiatry Reports* 2003; 5(3):4-11.

**NR383 Tuesday, May 24, 12:00 p.m.-2:00 p.m.
Regional Brain Volumes in Patients With Mood Disorders Before and After Long-Term Treatment With Antidepressants or Lithium**

Kathryn J. MacDonald, M.D., *Department of Psychiatry and Behavioural Neurosciences, McMaster University, 100 West 5th Street, Hamilton L8N 3K7, Canada*; Stephanie Campbell, Ph.D., Michael Marriott, Ph.D., Glenda M. MacQueen, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should have an understanding of the current state of knowledge with respect to regional changes in brain volume associated with major

**NR384 Tuesday, May 24, 12:00 p.m.-2:00 p.m.
Recovery and Recurrence of Mood Episodes in Individuals Early in the Treatment of MDD and Bipolar Disorder**

Kathryn J. MacDonald, M.D., *Department of Psychiatry and Behavioural Neurosciences, McMaster University, 100 West 5th Street, Hamilton L8N 3K7, Canada*; Michael Marriott, Ph.D., Helen Begin, R.N., Glenda M. MacQueen, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize and understand factors related to recovery and recurrence rates of episodes of illness in previously untreated subjects with mood disorders, and the possible predictive value of lifestyle and illness factors in outcome.

Summary:

Background: Mood disorders are common psychiatric illnesses with high variability in outcome and response to treatment. Little information is available on the development and progression of mood disorders from the time of initial symptoms or treatment.

Methods: The First Episode Project is a longitudinal, naturalistic study monitoring the course of illness and treatment in individuals presenting with untreated first episodes or never treated episodes of hypomania, mania and depression. Subjects have primary DSM-IV diagnoses of major depressive disorder or bipolar disorder, confirmed by SCID-IV. Extensive data on cognitive, social and physical variables are collected on each subject. Since 1999, over 100 subjects aged 16 to 50 have been enrolled in the study

and results of a survival analysis completed on these subjects are now available.

Results: This poster presents the data available on time to recovery from index episode and time to subsequent recurrence of mood episodes in subjects early in the course of illness and treatment. Analysis of variables correlating with outcome will also be reviewed.

Conclusions: Individual treatment outcomes are highly variable in mood disorders. While illness and treatment factors play a major role in recovery and recurrence, other variables such as lifestyle choices also have prognostic significance.

References:

1. Sachs GS, Rush AJ: Response, remission, and recovery in bipolar disorders: what are the realistic treatment goals? *J Clin Psychiatry* 2003; 64 Suppl 6:18-22.
2. Tohen M, Zarate CA Jr, Hennen J, Khalsa HM, Strakowski SM, Gebre-Medhin P, Salvatore P, Baldessarini RJ: The McLean-Harvard First-Episode Mania Study: prediction of recovery and first recurrence. *Am J Psychiatry* 2003; 160(12):2099-107.

NR385 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

A Prospective Study of Rapid Cycling in Bipolar Patients From the STEP-BD Project

Christopher D. Schneck, M.D., *Department of Psychiatry, University of Colorado Health Sciences Center, 4455 East 12th Avenue, Denver, CO 80220-2415*; David Miklowitz, Ph.D., Stephen Wisniewski, Ph.D., Sachiko Miyahara, M.S., Gary Sachs, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the characteristics of rapid cycling bipolar patients and the usefulness of rapid cycling as a prognostic indicator.

Summary:

Is recent rapid cycling a prognostic indicator for the course of bipolar disorder? This study hypothesized that bipolar I or II patients with current rapid cycling would have a poorer prognosis than bipolar I/II patients without current rapid cycling. We examined the first 2000 bipolar patients enrolled in the Systematic Treatment Enhancement Program for Bipolar Disorder. We compared the one-year prospective outcomes among patients who entered STEP-BD with rapid cycling ($n = 602$) within the past year versus patients who entered without rapid cycling ($n = 1,264$) or those for whom cycling status was indeterminate ($n = 134$). Rapid cycling patients were younger and had a younger age of onset of illness than non-rapid cycling patients. RC patients also had higher concurrent depression and mania symptoms scores and lower global functioning scores than non-RC patients. At one-year follow-up, the 2,000 patients could be classified as non-rapid cyclers ($n = 453$), rapid cyclers ($n = 64$), frequent cyclers (1-3 episodes during the study year, $n = 819$) and early dropouts ($n = 664$). Prospective analyses revealed continuities between prior rapid cycling and prospectively observed cycling patterns. Discussion will focus on whether rapid cycling is best viewed as a course modifier or an illness subtype.

References:

1. Schneck CD, Miklowitz DJ, Calabrese JR, et al: Phenomenology of rapid cycling bipolar disorder: data from the first 500 participants in the Systematic Treatment Enhancement Program. *Am J Psychiatry* 2004; 161:1902-1908.
2. Coryell W, Solomon D, Turvey C, et al: The long-term course of rapid cycling bipolar disorder. *Arch Gen Psychiatry* 2003; 60(9):914-20.

NR386 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Assessment of Subjective Response to Neuroleptic Medication in Schizophrenic Patients: Psychometric Properties of the Korean Version of the Drug Attitude Inventory

Bo-Hyun Yoon, M.D., *NAJU National Hospital, Sanje Sanpo, Naju Jeonnam 520-830, Korea*; Jeong-Hoon Kim, M.D., Hyeon-A Jung, M.D., Young-Hwa Sea, M.D., Chang-Hee Hong, D.Phil., Ahn Bae, M.D., Myung-Kyu Kim, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize psychometric properties of Korean version of DAI.

Summary:

Objectives: The aim of this study was to investigate the psychometric properties of the Korean version of the 10-item Drug Attitude Inventory (DAI-10), exploring its reliability and construct validity.

Methods: The subjects were 109 patients diagnosed with schizophrenia, between 19 and 65 years of both genders, who voluntarily attended the outpatient clinic of Naju National Hospital more than one year and were able to participate in the study. Maximum-likelihood methods with Varimax rotation was used to analyze the DAI score.

Results: Chronbach's alpha was 0.61. Extraction methods found three factors that explained 41.0% of the total variance. The first factor could be labeled as subjective positive response to treatment, the second as subjective negative response to treatment and the third as attitude to medication construct.

Conclusion: Although the results were preliminary, the Korean version of DAI-10 seems to maintain the original psychometric properties and it can be used easily to get a valid measurement of the patient's subjective response and attitude toward neuroleptic medication.

References:

1. Hogan TP, Awad AG: Subjective response to neuroleptics and outcome in schizophrenia: a re-examination comparing two measures. *Psychol Med* 1992; 22:347-52.
2. Cabeza IG, Amador MS, Lopez CA, Gonzalez de Chavez M: Subjective response to antipsychotics in schizophrenic patients: clinical implications and related factors. *Schizophr Res* 2000; 41:349-55.

NR387 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Characteristics of 903 Turkish Male Sexual Dysfunction Subjects: Analysis of 18 Years

Ali Bozkurt, M.D., *Department of Psychiatry, Gulhane School of Medicine, Gn. Tevfik Saglam Cd. Etilik, Ankara 06018, Turkey*; Tunay Karlidere, M.D., Mustafa Karademir, M.D., Kamil Nahit Ozmenler, M.D., Nilgun Yilmaz, M.S., Fuat Ozgen, M.D., Aydin Hamdullah, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to learn sociodemographic characteristics, symptoms, complaints, and diagnosis in a different culture.

Summary:

Objective: Sexuality is one of the most affected areas by socio-cultural background. For this reason, it is necessary to collect data in different populations. The study aims to show the sociodemographic characteristics and clinical symptomatology of sexual dysfunctions in Turkish sample.

Method: Subjects who applied to the Sexual Dysfunction Unit during September 1986-November 2004 have been included in

the study. The symptoms, complaints, diagnosis, and socio-demographic characteristics have been analyzed retrospectively.

Results: Out of 1226 cases, 903 male subjects' data has been evaluated (Table). Their diagnoses were erectile disorder due to psychological factors 63.5%, erectile disorder due to organic factors % 18.9, premature ejaculation 10.7%, orgasmic disorder 0.9%, sexual desire disorder 0.3%, other 5.7%. Their main complaints were insufficiency of erection 43.2%, no erection 29.2%, premature ejaculation 12.9%, low sexual desire 11.7%, retarded ejaculation 0.2%, other 2.9%.

Conclusion: In this study the male/female proportion is in favor of males discordant with Edinburgh study, which found almost equal application. The incidence of erectile dysfunction was higher, premature ejaculation and sexual desire disorder was lower compared with literature. These findings might be a related with cultural effects influencing the acceptance of sexual dysfunctions. Relation of different diagnosis and sociodemographic factors has been also evaluated.

References:

1. Warner P, Bancroft J and members of the Human Sexuality Group: A regional service for sexual problems: a 3-year study. *Sexual and Marital Therapy* 1987; 2:115-126.
2. Uguz S, Soyulu L, Diler RS, Evlice YE: Psychosocial factors and sexual dysfunctions: a descriptive study in Turkish males. *Psychopathology* 2004; (3):145-51.

NR388 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Adjunct Quetiapine for Bipolar Depression: Nine-Month, Open-Label, Prospective Trial

Roumen V. Milev, M.D., *Department of Psychiatry, PCCC, Mental Health Services, 752 King Street West, PO Box 603, Kingston K7L 4X3, Canada; Gaby Abraham, M.D.*

Educational Objectives:

After this presentation the participant will: (1) become aware of the longer term use of adjunct quetiapine for patients with bipolar depression, (2) be able to improve the outcome of treatment.

Summary:

Objective: Bipolar disorder is a chronic and disabling condition. While at least one third of the time patients are depressed, mood stabilizers alone do not appear to help often. Antidepressants can provoke a switch to mania or increase the cycling pattern. With increasing number of reports suggesting that atypical antipsychotics are helpful, this study investigates the long-term role of quetiapine in achieving an antidepressant response.

Method: Prospective open-label trial to assess the long-term response of patients with bipolar depression to quetiapine added to usual treatment. Inclusion criteria: Bipolar disorder type 1 or 2 (DSM-IV), age 18 or above, currently depressed (HAM-D > 18). Quetiapine was added open label and the dose increased, if tolerated, to 800 mg daily. Outcome measures were HAM-D, YMRS, CGI and AIMS at base and monthly.

Results: Nineteen patients are enrolled so far in this study, six males and 13 females. Data for 12 patients (Last Observation Carried Forward, LOCF) at nine months: HAM-D21 reduced from 27.2 to 12.7, and CGI from 4.7 to 3.0. Two patients discontinued due to side effects.

Conclusions: Quetiapine is effective and well tolerated in patients with bipolar depression when added to their usual treatment.

References:

1. Judd LL, Akiskal HS, Schettler PJ, et al: The long-term natural history of the weekly symptomatic status of bipolar I disorder. *Archives of General Psychiatry* 2002; 59(6):530-7.

2. Sajatovic M, Mullen JA, Sweitzer DE: Efficacy of quetiapine and risperidone against depressive symptoms in outpatients with psychosis. *Journal of Clinical Psychiatry* 2002; 63(12):1156-63.

NR389 Tuesday, May 24, 12:00 p.m.-2:00 p.m. **Mental Abuse, Neglect, and Temperament**

Tsuyoshi Akiyama, M.D., *Department of Psychiatry, Kanto Medical Center, 5-9 22 Higashigotanda, Tokyo 141-8625, Japan*

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that there exists a significant relationship between mental abuse or neglect and temperament.

Summary:

Introduction: This report investigates the relationship between mental abuse or neglect and temperament.

Hypothesis: There is a significant relationship between abuse or neglect and temperament.

Methods: TEMPS-A and MPT were implemented with 281 Japanese boys, age between 13 and 19, in correctional facilities. The data on experiences of mental and physical abuse or neglect were obtained independently. Regression analysis was implemented between temperament and abuse or neglect experience.

Results: There was a significant relationship between mental abuse and cyclothymic, irritable, anxious and schizoid temperament. There was a significant relationship between neglect and depressive, cyclothymic, anxious, and schizoid temperament. The significance level is indicated as ($p < 0.05$), ($p < 0.01$) and ($p < 0.001$). There was no significant relationship between hyperthymic or melancholic temperament and mental abuse or neglect. There was no significant relationship between any temperament and physical abuse.

Conclusion/Discussion: This result suggests a possibility that abuse or neglect experience may influence the formation of temperament and that there exists a difference in the influence according to the kind of abuse or neglect experience and of temperament. There is also a possibility that temperament influences the intensity of the memory of abuse or neglect experience. This issue needs a further investigation.

References:

1. Akiyama T, et al: The proposed factor structure of temperament and personality in Japan: combining traits from TEMPS-A and MPT. *J Affect Dis*, in press.
2. Sakai Y, et al: Temperament and job stress in Japanese company employees. *J Affect Dis*, in press.

NR390 Tuesday, May 24, 12:00 p.m.-2:00 p.m. **Haplotype Block Analysis Finds Association Between the Dopamine Transporter Gene and Comorbid ADHD and Bipolar Disorder But Not ADHD Without Bipolar Disorder**

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Educational Objectives:

At the conclusion of the presentation, the participant (1) will learn about the association between ADHD and bipolar disorder, (2) understand the genetic background of ADHD and bipolar disorder.

der, and (3) learn about molecular genetic findings in ADHD and bipolar disorder.

Summary:

Background: No studies to date have sought to identify genes implicated in comorbid ADHD and bipolar disorder, but markers within genes have been associated with ADHD including those in SLC6A3, DRD4, DRD5, SNAP-25 and 5HT1B.

Methods: We performed association analyses of a subgroup of ADHD patients with bipolar disorder. We genotyped 152 SNPs in six genes in 280 trios (199 families) in which probands were ascertained for DSM-III-R or DSM-IV. Fifty-four trios comprised offspring affected with comorbid bipolar disorder. Quality control metrics included analysis of SNPs for which 90% of the genotypes were available and meeting criteria for Hardy-Weinberg equilibrium and fewer than three Mendel errors. Analyses of individual SNPs and haplotypes were performed using transmission-disequilibrium test as implemented, in the software TDT-permute.

Results: No associations were detected for HTR1B, BDNF, SNAP25, DRD5. In contrast, for SLC6A3, 35 SNPs were tested and 7 SNPs were associated at the $p < 0.05$ level. Four of these SNPs were in strong linkage disequilibrium and defined a haplotype block that was overtransmitted to bipolar probands ($p = 0.00067$). We didn't find significant association between ADHD without BP and SLC6A3.

Conclusion: Ongoing work is aimed at more full definition of these haplotype blocks and replication in additional samples.

References:

1. Faraone SV, Biederman J, Mennin D, Russell R: Bipolar and antisocial disorders among relatives of ADHD children: parsing familial subtypes of illness. *American Journal of Medical Genetics (Neuropsychiatric Genetics)* 1998; 81:108-116.
2. Faraone SV, Biederman J, Mennin D, Wozniak J, Spencer T: Attention deficit/hyperactivity disorder with bipolar disorder: a familial subtype? *Journal of the American Academy of Child and Adolescent Psychiatry* 1997; 36:1378-1387.

NR391 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

How Should Remission From Depression Be Defined? The Depressed Patient's Perspective

Mark Zimmerman, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905*; Joseph McGlinchey, Ph.D., Michael Posternak, M.D., Michael Friedman, M.D., Naureen Attiullah, M.D., Daniela Boerescu, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the multiple components of remission that depressed patients consider to be important.

Summary:

Background: Experts in the treatment of depression have suggested that achieving remission should be viewed as the primary goal of treatment. However, there is some question as to how to define remission. In antidepressant efficacy trials remission is defined according to scores on symptom severity scales. Normalization of functioning is often mentioned as an important component of the definition of remission, though it is not used to identify remitted patients in treatment studies. Other constructs that seem relevant to determining whether a patient has remitted from their depressive episode include normalization of the ability to cope with stress, a sense of well-being, quality of life, and feeling like one's normal self. To better understand depressed patients' perspectives of how to conceptualize remission we conducted a sur-

vey of the factors depressed patients consider important in defining remission from depression.

Methods: Five hundred and thirty-five depressed psychiatric outpatients rated the importance of 16 factors in determining whether someone is in remission from their depression.

Results: The three factors that were the most frequently judged to be very important in determining remission were the presence of features of positive mental health such as optimism and self-confidence, a return to one's usual, normal self, and a return to usual level of functioning.

Conclusions: In contrast to how remission is defined in efficacy studies of antidepressant medications, the depressed patients in this study did not consider symptom resolution as the most important factor in determining the state of remission.

References:

1. Keller M: Past, present, and future directions for defining optimal treatment outcome in depression. *JAMA* 2003; 289:3152-3160.
2. Frank E, Prien R, Jarrett R, Keller M, Kupfer D, Lavori P, Rush A, Weissman M: Conceptualization and rationale for consensus definitions of terms in major depressive disorder. *Arch Gen Psychiatry* 1991; 48:851-855.

NR392 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Why Isn't Bupropion the Most Frequently Prescribed Antidepressant?

Mark Zimmerman, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905*; Michael Posternak, M.D., Naureen Attiullah, M.D., Michael Friedman, M.D., Robert J. Boland, M.D., Scott Baymiller, M.D., Stacie Berlowitz, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to discuss the factors used by psychiatrists to select antidepressant medication.

Summary:

Objective: Reviews of antidepressant medication efficacy suggest that all antidepressants are equally effective. Bupropion is less likely than other antidepressants to cause weight gain and sexual dysfunction, the two side effects that are of greatest concern to patients and have the greatest impact on long-term compliance. If bupropion is as effective as other antidepressants, and it does not cause the side effects that are the most frequent causes of long-term noncompliance, then why isn't it the most frequently prescribed antidepressant medication? To understand psychiatrists' decision making at the time an antidepressant is chosen we conducted the Rhode Island Factors Associated with Antidepressant Choice Survey (FAACS).

Methods: For 965 depressed patients initiated on an antidepressant, the treating psychiatrist completed a 43-item questionnaire listing factors that might have influenced the choice of medication. The questionnaire was filled out immediately after the antidepressant was prescribed to treat a depressive disorder.

Results: Bupropion was rarely prescribed when the presence of comorbid anxiety disorders or symptoms reflecting central nervous system activation influenced antidepressant selection. When the desire to avoid side effects, especially sexual dysfunction and weight gain, were the basis of selection then bupropion was significantly more often prescribed than other antidepressants.

Conclusions: Although there is little evidence that patient factors predict differential medication response, psychiatrists are strongly inclined to base antidepressant selection on clinical profiles, and avoid prescribing bupropion for depressed patients with high anxi-

ety. Possible reasons for the discrepancy between psychiatrists' prescribing habits and the results of empirical study are discussed.

References:

1. Zimmerman M, Posternak M, Friedman M, et al: Which factors influence psychiatrists' selection of an antidepressant? *Am J Psychiatry* 2004; 161:1285-1289.
2. American Psychiatric Association. Practice Guideline for the Treatment of Patients with Major Depressive Disorder (Revision). Washington, DC; 2000.

NR393 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

A Standardized Clinical Outcome Rating Scale for Depression for Use in Clinical Practice

Mark Zimmerman, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905*; Michael Posternak, M.D., Iwona Chelminski, Ph.D., Michael Friedman, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be familiar with a new measurement tool that can be easily incorporated into routine clinical practice.

Summary:

Objective: The integration of research into clinical practice in order to conduct effectiveness studies faces multiple obstacles, one of which is the burden of completing research measures of outcome. A simple, reliable, and valid measure that could be rated at every visit, incorporated into a clinician's progress note, and reflect the DSM-IV definition of a major depressive episode (including partial and full remission from the episode) would enhance the ability to conduct effectiveness research. The goal of the present study was to examine the reliability and validity of such a measure.

Methods: Three hundred and three psychiatric outpatients who were being treated for a DSM-IV major depressive episode were rated on the Standardized Clinical Outcome Rating for Depression (SCOR-D), 17-item Hamilton Rating Scale for Depression, Montgomery-Asberg Depression Rating Scale, and the Global Assessment of Functioning. We examined the correlation between the SCOR-D and the other measures, and conducted an analyses of variance to compare mean values on these measures for each rating point on the SCOR-D.

Results: The inter-rater reliability of the SCOR-D dimensional ratings and categorical determination of remission were high. The SCOR-D was highly correlated with the other scales, and there were significant differences on the other measures of depression severity between each adjacent rating level of the SCOR-D.

Conclusions: The SCOR-D is a brief standardized outcome measure linked to the DSM-IV approach towards defining remission that can be incorporated into routine clinical practice without adding undue burden to the treating clinician with some evidence of reliability and validity. This measure could make it more feasible to conduct effectiveness studies in clinical practice.

References:

1. Zimmerman M: Integrating the assessment methods of researchers in routine clinical practice: The Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project, in *Standardized Evaluation in Clinical Practice*, vol 22. Edited by First M. Washington, American Psychiatric Publishing, Inc, 2003, pp 29-74.
2. Posternak MA, Zimmerman M, Solomon DA: Integrating outcomes research into clinical practice: A pilot study. *Psychiatric Services* 2002; 53:335-336.

NR394 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Sedation, Quality of Life, and Functioning in Bipolar Patients Prescribed Risperidone, Quetiapine, or Olanzapine

Krishnan Ramaswamy, Ph.D., *Janssen Medical Affairs, L.L.C., 1125 Trenton-Harbourton Road, Titusville, NJ 08560*; Jeff Markowitz, Ph.D., Luella Engelhart, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the relationship between atypical antipsychotic treatment and sedation, quality of life, and functioning in patients with bipolar disorder.

Summary:

Background: Medication-related sedation negatively impacts quality of life (QoL) and functioning. This survey examined QoL, functioning, and self-reported sedation in patients with bipolar disorder who were treated with atypical antipsychotics.

Methods: Data were derived from the 2003 bipolar disorder survey by Consumer Health Sciences. Respondents were those receiving risperidone, quetiapine, or olanzapine monotherapy. Frequency and severity of sedation were measured by self-assessment. QoL was self-reported using the General Well-Being (GWB) scale and the Short Form-8 Health Survey (SF-8).

Results: Of the 240 patients (mean age 45.3 years; 70% female; 95% white) analyzed, 26.7% were treated with risperidone, 39.6% with quetiapine, and 33.8% with olanzapine. In unadjusted analyses, quetiapine had significantly greater sedation compared to risperidone ($P=0.0234$) and olanzapine ($P=0.0014$). These results were confirmed by multivariate analyses that controlled for demographics and proxy measures of bipolar severity. Separate correlation analyses indicated sedation was significantly and negatively correlated with GWB Total ($P=0.0065$), GWB Vitality ($P=0.0022$), and SF-8 Mental scores ($P=0.0065$). However, after adjusting for other factors, no significant correlations were found between atypical antipsychotic use and GWB or SF-8 scores.

Conclusions: Sedation associated with the use of certain atypical antipsychotics may be related to a decline in QoL and functioning in bipolar disorder.

References:

1. Ertugrul A, Meltzer HY: Antipsychotic drugs in bipolar disorder. *Int J Neuropsychopharmacol* 2003; 6(3):277-284.
2. Tandon R: Safety and tolerability: how do newer generation "atypical" antipsychotics compare? *Psychiatr Q* 2002; 73(4):297-311.

NR395 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Patient Factors Associated With Caregiver Burden in Bipolar Disorder

Polina Eidelman, B.A., *Department of Psychiatry, Massachusetts General Hospital, Bipolar Clinic and Research Program, 50 Staniford Street, Suite 580, Boston, MA 02114*; Michael Ostacher, M.D., Deborah Perlick, Ph.D., Dan Losifescu, M.D., Andrew Nierenberg, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the clinical characteristics of bipolar patients most associated with burden and depression in their caregivers.

Summary:

Objective: The factor most reported to be associated with caregiver burden in bipolar disorder is symptom severity in the patient, although no study has examine prospectively collected, longitudinal patient factors in determining caregiver burden. We hypothe-

sized that major depressive episodes and depressive symptoms in bipolar patients would be associated with caregiver burden.

Methods: Data on caregiver burden and depression were collected from 500 caregivers of 500 bipolar patients participating in the Systematic Treatment Enhancement Program for Bipolar Disorder. (STEP-BD) Patient data were prospectively collected as part of STEP-BD.

Results: Subjective and objective burden were negatively correlated with the number of days well, a matrix measure of longitudinal symptoms in STEP-BD, and were positively correlated with both major depressive episodes and depressed mood in the patient. Mania, hypomania, and mood elevation were not associated with burden. Caregiver depression was positively correlated with depressive symptomatology in the patient. Ninety of 488 patients met DSM-IV criteria for depressed mood at a visit within 30 days of the caregiver interview.

Conclusion: The severity and chronicity of bipolar depression is most correlated with burden and depression in caregivers. Depression is present in a high percentage of bipolar patients. Interventions to reduce bipolar depression and its effects on caregivers should be a priority in the treatment of bipolar disorder.

References:

1. Perlick D, Clarkin JF, Sirey J, Raue P, Greenfield S, Struening E, Rosenheck R: Burden experienced by care-givers of persons with bipolar affective disorder. *Br J Psychiatry* 1999; 175:56-62.
2. Chakrabarti S, Kulhara P, Verma SK: Extent and determinants of burden among families of patients with affective disorders. *Acta Psychiatr Scand* 1992; 86(3):247-52.

NR396 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Psychiatric and Medical Comorbidity in Bipolar Disorder

Polina Eidelman, B.A., *Department of Psychiatry, Massachusetts General Hospital, Bipolar Clinic and Research Program, 50 Staniford Street, Suite 580, Boston, MA 02114*; Dan Losifescu, M.D., Michael Ostacher, M.D., Staphanie Gironde, B.A., Andrew Nierenberg, M.D., Gary Sachs, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the relationships between medical illness and psychiatric comorbidities in a bipolar outpatient population.

Summary:

Objective: We examined the relationships between general medical illness and psychiatric comorbid conditions diagnosed in a bipolar outpatient population.

Method: In 83 outpatients meeting DSM-IV criteria for bipolar disorder, we used the Cumulative Illness Rating Scale (CIRS) to determine the presence and severity of medical comorbidity. The MINI Diagnostic interview was utilized to assess lifetime and current Axis I comorbidities for all subjects. The association between medical illness severity and comorbid Axis I psychiatric diagnosis was investigated using chi-square analyses.

Results: We found no statistically significant relationships between OCD, PTSD, GAD, alcohol abuse, drug abuse, or ADHD and medical illness severity. However, patients meeting a lifetime diagnosis for Agoraphobia (with or without panic disorder) or current Social Phobia were more severely ill medically ($p < 0.05$).

Conclusions: Our present findings suggest that the previously reported relationship between medical illness and the course of bipolar disorder cannot be explained simply by the presence of additional psychiatric comorbidity. The relationship between medical illness, agoraphobia, and social phobia in bipolar disorder

and direction of influence among these illnesses requires further exploration.

References:

1. Iosifescu DV, Eidelman P, Ostacher MJ, et al: Negative Impact of Medical Comorbidity on the Course of Bipolar Disorder. Accepted for presentation at the American Psychiatric Association 158th Annual Meeting, Atlanta, GA, 2005.
2. Iosifescu DV, Nierenberg AA, Alpert JE, Papakostas GI, Perlis RH, Sonawalla S, Fava M: Comorbid medical illness and relapse of major depressive disorder in the continuation phase of treatment. *Psychosomatics* 2004; 45:419-425.

NR397 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

What Happened to Lithium? Antidepressant Augmentation in Clinical Settings

Marcia T. Valenstein, M.D., *HSR & D, Veterans Affairs, PO Box 130170, Ann Arbor, MI 48113-0170*; John McCarthy, Ph.D., Karen Austin, M.P.H., Elizabeth Young, M.D., John Greden, M.D., Frederic Blow, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize current practice patterns in antidepressant augmentation and consider the evidence base for these practices.

Summary:

Background: Antidepressant augmentation is recommended when patients fail antidepressant monotherapy. However, little is known about antidepressant augmentation practices in clinical settings and whether these practices reflect the research evidence.

Methods: We identified 237,819 patients treated in VA mental health settings who received a diagnosis of depression and an antidepressant prescription during fiscal year (FY) 2002. Patients with schizophrenia, dementia, or bipolar I disorder were excluded. We examined the prevalence and characteristics of antidepressant augmentation during the year, defined as receiving an antidepressant and a specified augmenting agent (lithium, second-generation antipsychotics, combination antidepressants, anticonvulsants, or "other") for > 60 consecutive days in specified doses, without other clinical indications. Mixed regression models were used to examine predictors of augmentation.

Results: 22% of patients received an augmentation agent. The most commonly used agents were a second antidepressant, used by 11% of patients, and a second-generation antipsychotic medication, used by 7%. Only 0.5% of patients received lithium. Whites, younger patients, and those with a prior hospitalization were more likely to receive augmentation. African Americans were more likely to receive antipsychotic augmentation, while whites were more likely to receive lithium.

Conclusions: Antidepressant augmentation is common in clinical settings. However, patients often receive agents with relatively limited research support, such as antipsychotic medications, rather than agents with more support, such as lithium. Augmenting agents are used differentially across patient groups. Research is urgently needed on the relative effectiveness of widely-used augmenting agents. Efforts should also be made to promote treatment practices that reflect the research evidence.

References:

1. Fava M, Rush AJ, Trivedi MH, Nierenberg AA, Thase ME, Sackeim HA, Quitkin FM, Wisniewski S, Lavori PW, Rosenbaum JF, Kupfer DJ: Background and rationale for the sequenced treatment alternatives to relieve depression (STAR*D) study. *Psychiatr Clin North Am* 2003; 26:457-94.

2. Bauer M, Adli M, Baethge C, Berghofer A, Sasse J, Heinz A, Bschor T: Lithium augmentation therapy in refractory depression: clinical evidence and neurobiological mechanisms. *Can J Psychiatry* 2003; 48:44-8.

NR398 **Tuesday, May 24, 12:00 p.m.-2:00 p.m.**
Late-Onset Bipolar Disorder: Clinical and Outcome Features

A. Carlo Altamura, M.D., *Department of Psychiatry and Clinical Sciences, University of Milan, via G.B. Grassi 74, Milan 20157, Italy*; Annalisa Santini, M.D., Daniele Salvadori, M.D., Michela Russo, M.D., Emanuela Mundo, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the main clinical differences between earlier and later onset bipolar disorder.

Summary:

Objectives: The aim of this study was to investigate for the differences in the clinical characteristics between patients with late (>40 yrs) or earlier (< or = 40 yrs) onset Bipolar Disorder (BD).

Methods: 300 outpatients with DSM-IV BD I, BD II or schizoaffective disorder (bipolar type), were subdivided in two groups according to the age of onset of BD (defined as the age when first the patient fulfilled the diagnostic criteria for a mood episode). All patients had been diagnosed with the administration of the SCID-I and gave their informed consent to participate into the study. The main clinical variables were compared between the two groups (t-tests or chi-square tests).

Results: 254 patients had an onset < or = 40 yrs and 46 an onset > 40 yrs. Patients with later onset had a higher frequency of BD II diagnosis (chi-square=4.698, df=1, p=0.03) and a lower frequency of positive family history for mood disorders (chi-square=10.796, df=1, p=0.01). In addition, patients with later onset had a lower number of suicide attempts than BD patients with earlier onset (t=1.907, p=0.05). No significant differences between the two groups were found for the other clinical variables investigated.

Conclusions: These results suggest the existence of specific clinical features in patients with later onset BD. Future studies will investigate the effect of age at onset on outcome measures and response to medication.

References:

1. Schurhoff F, Bellivier F, Jouvent R, Mouren-Simeoni MC, Bouvard M, Allaire JF, Leboyer M: Early and late onset bipolar disorders: two different forms of manic-depressive illness? *J Affect Disord* 2002; 68(2-3):343-345.
2. Depp CA, Jin H, Mohamed S, Kashow J, Moore DJ, Jeste DV: Bipolar disorder in middle aged and elderly adults: is age of onset important? *J Nerv Ment Dis* 2004; 192(11):796-799.

NR399 **Tuesday, May 24, 12:00 p.m.-2:00 p.m.**
Screening for Bipolar Spectrum Disorders in UK Adolescents

Karen D. Wagner, M.D., *Division of Child and Adolescent Psychiatry, University of Texas Medical Branch, 1.302 Rebecca Sealy, 301 University Boulevard, Galveston, TX 77555-0188*; Robert Hirschfeld, M.D., Theresa Frangiosa, Maneesha Mehra, Michael L. Reed, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should understand the prevalence and detection patterns for bipolar disorder among UK adolescents.

Summary:

Objective: To determine the prevalence and diagnosis rate for bipolar spectrum disorder (BSD) among United Kingdom (UK) adolescents.

Methods: The Mood Disorder Questionnaire (MDQ) was mailed to a representative sample of n=30,960 UK adults from the National Family Opinion household panel. Each person was asked to report on their own symptoms as well as those of adolescent household members aged 12-17. Following two survey mailings, the MDQ was also administered via phone interviews among a random sample of n=1,202 non-responders.

Results: N=13,387 mail surveys (43% response) and 1,202 phone surveys. There were 1,389 adolescents in the sample. MDQ positive cases (scored using validated adolescent criteria: five or more of 13 symptoms, plus symptom co-occurrence and moderate to severe impairment) totalled 3.2% in the mail phase and 1.7% in the non-responder phone phase. After weighting and adjusting for non-response bias, the prevalence of MDQ positive cases was estimated at 2.4% of adolescents. Only 2% of cases reported a diagnosis of bipolar disorder or manic depression., while 14% reported a diagnosis of unipolar depression and 84% had neither diagnosis.

Conclusions: BSD was estimated at 2.4% of UK adolescents. This is similar to rates seen in UK adults.

References:

1. Hirschfeld RMA, Calabrese JR, Weissman MM, Reed ML, et al: Screening for bipolar disorder in the community. *Journal of Clinical Psychiatry* 2003; 64:53-59.
2. Weissman, MM, Bland RC, Canino GJ, et al: Cross-national epidemiology of major depression and bipolar disorder. *JAMA* 1996; 276:293-299.

NR400 **Tuesday, May 24, 12:00 p.m.-2:00 p.m.**
The Therapeutic Effect of Follow-Up Assessments on Placebo Response Rates

Michael A. Posternak, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Providence, RI 02905*; Mark Zimmerman, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the impact that follow-up assessments have on placebo response rates in antidepressant trials.

Summary:

Context: Placebo response rates in antidepressant trials are robust and have been increasing over time. It remains unclear how much various factors contribute to the placebo response.

Objective: To estimate the therapeutic impact that follow-up assessments have on placebo response rates.

Data Sources and Study Selections: Double-blind, placebo-controlled antidepressant trials that reported weekly changes in Hamilton Depression Rating Scale (HDRS) scores over the course of six weeks were selected.

Data Synthesis: Forty-one published studies, comprised of 3,063 subjects randomized to placebo, were included. Three types of follow-up schedules were used in these studies that conducted either 4, 5, or 6 follow-up assessments over the course of six weeks. An extra follow-up assessment at Week 3 was associated with a 1.02 further reduction in HDRS scores, while an extra visit at Week 5 was associated with a 0.67 further reduction in HDRS scores. These effects represent approximately 40% of the placebo response that occurred over these time frames. Two additional visits were associated with twice the reduction in HDRS scores as one extra visit, suggesting that the therapeutic impact of assessments is both cumulative and proportional. A comparable

therapeutic effect was found to be present in subjects receiving active medication.

References:

1. Kirsch I, Sapirstein G: Listening to Prozac but hearing placebo: a meta-analysis of antidepressant medications, in Kirsch I, ed. *How Expectancies Shape Experience*. Washington, DC: American Psychological Association; 1999 pp. 303-320.
2. Khan A, Khan SR, Walens G, Kolts R, Giller EL: Frequency of positive studies among fixed and flexible dose antidepressant clinical trials: an analysis of the food and drug administration summary basis of approval reports. *Neuropsychopharmacology* 2003; 28:552-7.

NR401 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Personality as Predictor of Response to Treatment of Adults With Major Depression

Paula Ravitz, M.D., *Department of Psychiatry, University of Toronto; CAMH, 250 College Street, Toronto, Ontario M4S 1L3, Canada*; Carolina McBride, Ph.D., R. Michael Bagby, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to: (1) appreciate the role personality plays in the response to treatment of depression, (2) understand the relation between patient characteristics and the best treatment options, and (3) recognize how personality may affect the course of treatment and its outcome.

Summary:

Objective: Dimensional personality traits are thought to confer vulnerability to depression; however, few studies have examined whether different personality traits predict response to treatment. This controlled trial examines personality dimensions as predictors of response in depression.

Method: 103 self-referred, SCID diagnosed depressed adults, with a HAMD >16, were randomly assigned to 16-20 weeks of treatment with pharmacotherapy (PHT), cognitive behavioral therapy (CBT) or interpersonal psychotherapy (IPT). The five-factor model of personality (measured by the Revised NEO Personality Inventory (NEO PI-R) was collected on each subject, as were weekly BDI-II scores. The study was conducted in the outpatient department of a university affiliated tertiary care hospital.

Results: All treatment groups showed equivalent and significant decreases in BDI-II scores; 54/85 recovered. On the NEO PI-R, the domain trait of Openness-to-Experience, $B=.322$, $p<.05$, and the facet traits of 'depression', $B=.370$, $p<.04$, 'ideas' $B=-.296$, $p<.05$, and 'trust', $B=.366$, $p<.03$, predicted response to psychotherapy. There were no specific domain traits associated with response to PHT, however, the facet trait 'excitement seeking' predicted response to PHT, $B=-.597$, $p<.04$.

Conclusions: There is strong, preliminary evidence to suggest that personality traits predict response to different treatments for depression.

References:

1. Bagby RM, Joffe RT, Parker JDA, Kalembe V, Harkness KL: Major depression and the five-factor model of personality. *J of Personality Disorders* 1995; 9:224-234.
2. Santor DA, Bagby RM, Joffe RT: Stability and change in personality and depression. *J of Personality and Social Psychology* 1997; 73: 1354-1362.

NR402 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Treatment of Major Depressive Disorder With Escitalopram Versus Venlafaxine XR

Stuart A. Montgomery, M.D., *Imperial College School of Medicine, PO Box 8751, London W13 8WH, United Kingdom*

Educational Objectives:

At the conclusion of the presentation, the participants will increase their understanding of the risk/benefit profile of escitalopram.

Summary:

Introduction: Escitalopram is a highly selective serotonin reuptake inhibitor (SRI) antidepressant. Venlafaxine is a non-selective SRI that also inhibits noradrenergic reuptake.

Methods: Two randomized, double-blind, eight-week trials compared the efficacy and tolerability of escitalopram with that of venlafaxine in major depressive disorder (MDD). The primary efficacy variable was the mean change from baseline in Montgomery Asberg Depression Rating Scale (MADRS) scores.

Results: In the study in primary care in Europe, 10-20mg/day escitalopram (N=148) was at least as effective as 75-150mg/day venlafaxine (N=145), with a better side-effect profile. Survival analysis of sustained response and sustained remission, showed escitalopram to be significantly superior to venlafaxine ($p<0.05$). In the study in depressed outpatients in specialist settings in the US, 20mg/day escitalopram (N=97) appeared to be more effective than 225mg/day venlafaxine (N=98). In the subpopulation of severely depressed patients (MADRS \geq 30, N=121), escitalopram was more effective than venlafaxine. The venlafaxine group had a higher overall incidence of treatment-emergent adverse events than the escitalopram group (85% vs. 68%), and more patients withdrew due to adverse events from the venlafaxine group than from the escitalopram group (16% vs. 4%; $p<0.01$).

Conclusion: Escitalopram has a better risk/benefit profile than venlafaxine in the treatment of MDD.

References:

1. Bielski RJ, Ventura D, Chang C-C: A double-blind comparison of escitalopram and venlafaxine extended release in the treatment of major depressive disorder. *J Clin Psych* 2004; 65:1190-1196.
2. Montgomery SA, Huusom AKT, Bothmer J: A randomised study comparing escitalopram with venlafaxine XR in primary care patients with major depressive disorder. *Neuropsychobiology* 2004; 50:57-64.

NR403 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Relapse Prevention in Patients Suffering From Social Anxiety Disorder

Stuart A. Montgomery, M.D., *Imperial College School of Medicine, PO Box 8751, London W13 8WH, United Kingdom*

Educational Objectives:

At the conclusion of the presentation, participants will increase their knowledge concerning the effectiveness of escitalopram in preventing relapse in patients with SAD.

Summary:

Introduction: Escitalopram is the most selective SSRI, whose efficacy and tolerability in the short-term treatment of SAD has been established.

Methods: This study was conducted in outpatients (18-80 years) with a primary diagnosis of generalized SAD (DSM-IV) and an LSAS score \geq 70. After 12 weeks of open-label treatment (10-20mg/day escitalopram), responders (CGI-I of 1 or 2) were randomized to 24 weeks of escitalopram (n=190) or placebo (n=181)

treatment, to assess the relapse rate. The initial dose of 10 mg/day could be doubled to a maximum of 20 mg/day, if clinically indicated, at Week 2, 4, or 8 of open treatment. Relapse was defined as an increase in LSAS score ≥ 10 or withdrawal due to lack of efficacy.

Results: Time to relapse was significantly lower for escitalopram compared to placebo (log-rank: $p < 0.001$), and significantly fewer escitalopram-treated patients relapsed (22% versus 50%, Fisher's test, $p < 0.001$). Significantly more escitalopram-treated patients completed the study (66% versus 44%, $p < 0.001$). The favorable side-effect profile of escitalopram in long-term treatment was confirmed, with only 4% of escitalopram-treated patients withdrawing due to adverse events.

Conclusion: Escitalopram 10-20 mg/day is highly effective in preventing relapse in patients with SAD and well tolerated.

References:

1. Lader M, Stender K, Burger V, Nil R: Efficacy and tolerability of escitalopram in 12- and 24-week treatment of social anxiety disorder: randomized, double-blind, placebo-controlled, fixed-dose study. *Depress Anxiety* 2004; 19:241-248.
2. Kasper S, Stein DJ, Loft H, Nil R: Escitalopram in the treatment of social anxiety disorder: a randomised, placebo-controlled, flexible-dose study. *Br J Psychiatry*, in press.

NR404 Tuesday, May 24, 12:00 p.m.-2:00 p.m. Incremental Health Benefits Cost of Bipolar Disorder Among Insured Employees

Nathan Kleinman, Ph.D., *Department of Research, HCMS Group, 1800 Carey Avenue, Suite 300, Cheyenne, WY 82001*; Richard A. Brook, M.S., Hank Gardner, M.D., Krithika Rajagopalan, Ph.D., James E. Smeeding, R.Ph.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the economic impact of BD with regard to total health benefits and absenteeism to an employer; recognize the impact of BD on pharmacy costs.

Summary:

Objective: To determine the economic impact of bipolar disorder (BD) from an employer perspective.

Methods: Medical, pharmacy, workers' compensation (WC), short- and long-term disability (STD, LTD), and sick leave (SL) costs were examined in a database consisting of 2001-2002 claims, payroll, and demographic data from more than six large U.S. based employers. Regression modeling was used to measure the cost differences between employees with BD and employees without BD while controlling for age, tenure, gender, salary, region, and other factors.

Results: Data were available for 761 employees with BD and a control group of 229,145 employees without BD. The BD group had higher costs with a 217% difference (\$6,836) summed across all measures ($P = 0.05$). The individual differences in medical and pharmacy costs were \$3,860 and \$1,866, respectively. Work absence costs had differences of \$80 (SL), \$254 (WC), \$668 (STD) and \$108 (LTD).

Conclusions: The impact of BD can be costly, not only in terms of health care costs, but also in its impact on lost productivity due to absenteeism. Employer-based interventions focusing on managing BD should be evaluated and implemented to manage potential short- and long-term economic impact.

References:

1. Practice Guideline for the treatment of patients with bipolar disorder (revision). *Am J Psychiatry* 2002; 159 (4 Suppl):1-50.

2. Narrow WE, Rae DS, Robins LN, Regier DA: Revised prevalence estimates of mental disorders in the United States: using a clinical significance criterion to reconcile 2 surveys' estimates. *Arch Gen Psychiatry* 2002; 59(2):115-123. Comment in *Arch Gen Psychiatry* 2002; 59(2):129-130.

NR405 Tuesday, May 24, 12:00 p.m.-2:00 p.m. Physical and Mental Comorbidities Among Employees With Bipolar Disorder: Analysis of Major Diagnostic Categories

Nathan Kleinman, Ph.D., *Research Department, HCMS Group, 1800 Carey Avenue, Suite 300, Cheyenne, WY 82001*; Hank Gardner, M.D., Krithika Rajagopalan, Ph.D., Richard Brook, M.S., James E. Smeeding, R.Ph.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to: (1) recognize the economic impact of BD with regard to total health and co-morbidities, and (2) understand that persons with BD might require programs to support total health management.

Summary:

Objective: To compare the costs associated with physical and mental comorbidities among employees with and without bipolar disorder (BD).

Methods: Retrospective analysis of a database comparing health care service utilization and costs for employees with BD and without BD in 2001-2002. The Agency for Health Care Research and Quality (AHRQ) 17 major diagnostic categories (MDCs) were used to define physical and mental comorbidities. T-tests and 95% confidence intervals were used to test statistical differences in these categories of costs between the cohorts.

Results: Data were available for 761 people with BD and 229,145 people without BD to explore the costs of comorbidities. All categories, with the exception of the perinatal and pregnancy categories, were associated with higher costs for the BD cohort. Differences for seven of the 17 MDCs were significant ($p < 0.05$). MDCs that were significantly different for BD persons include (additional costs for BD persons in parentheses): Mental disorders including BD (\$1,993); injury and poisoning (\$390); musculo/connective tissue (\$356); Other Conditions (\$151); Respiratory System (\$118); nervous system/sensory organs (\$114); and pregnancy childbirth puerperium (-\$171).

Conclusions: BD patients have significantly more costly comorbidities than do patients without BD, including comorbidities that are more physical than mental in nature.

NR406 Tuesday, May 24, 12:00 p.m.-2:00 p.m. Physical and Mental Comorbidities Among Employees With Bipolar Disorder: Analysis of AHRQ 261 Specific Categories

Nathan Kleinman, Ph.D., *Research Department, HCMS Group, 1800 Carey Avenue, Suite 300, Cheyenne, WY 82001*; Krithika Rajagopalan, Ph.D., Richard A. Brook, M.S., James E. Smeeding, R.Ph., Hank Gardner, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to: (1) recognize the economic impact of BD with regard to total health and comorbidities. (2) understand which types of costs are most likely to be impacted for persons with BD.

Summary:

Objective: To compare the costs associated with specific concurrent conditions among employees with bipolar disorder (BD) and without bipolar disorder.

Methods: Retrospective analysis of an employer database. Cost and utilization of services among individuals with BD and without BD were examined using the Agency for Healthcare Research and Quality 261 specific categories in 2001 and 2002. T-tests and 95% confidence intervals were used to assess cost differences between employees with and without BD.

Results: Data were available for 761 employees with BD and 229,145 employees without BD. Costs for people with BD were higher in 53% (138) of the categories, 22 of which were significantly higher ($p < 0.05$). Categories significantly more costly for BD employees include (annual difference in parentheses): affective disorders (\$1,582); intervertebral disc disorders (\$126); other mental conditions (\$119); schizophrenia and related conditions (\$110); poisoning medical/drugs (\$62); alcohol-related mental disorders (\$52); abdominal pain (\$47); substance-related mental (\$43); dissociative/personality (\$41); headache including migraine (\$39); other non-traumatic joint disorders (\$19).

Conclusions: BD patients have significantly more costly comorbidities than do patients without BD, including some that are physical and mental in nature. Caring for patients with BD requires a focus on total health management, not just on the patient's mental health.

References:

1. Practice Guideline for the Treatment of Patients With Bipolar Disorder (revision). *Am J Psychiatry* 2002; 159(4 Suppl):1-50.
2. Narrow WE, Rae DS, Robins LN, Regier DA: Revised prevalence estimates of mental disorders in the United States: using a clinical significance criterion to reconcile 2 surveys' estimates. *Arch Gen Psychiatry* 2002; 59(2):115-123. Comment in *Arch Gen Psychiatry* 2002; 59(2):129-130.

NR407 Tuesday, May 24, 12:00 p.m.-2:00 p.m. Comorbid Cannabis Use in Patients With Acute Mania: Functional Status

Catherine Reed, M.D., *Eli Lilly and Company LTD, Erl Wood Manor, Sunninghill Road, Windlesham GU20 6PH, United Kingdom*; I. Goetz, M.D., J. van Os, M.D., M. Tohen, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should understand the clinical characteristics, treatment patterns, and functional outcomes of patients presenting with acute mania and comorbid cannabis use.

Summary:

Objectives: To describe the functional status of patients with cannabis comorbidity enrolled in EMBLEM (European Mania in Bipolar Longitudinal Evaluation of Medication study).

Methods: EMBLEM is a two-year prospective, observational study on outcomes of patients experiencing a manic or mixed episode conducted in 14 European countries. Adult patients with bipolar disorder were enrolled within standard course of care as in/outpatients if they initiated/changed oral medication (excluding benzodiazepines) for treatment of acute mania. All treatment decisions are at the discretion of the treating psychiatrist. 530 psychiatrists enrolled 3653 patients between 12/2002-06/2004 using the same study methods assessing demographics, psychiatric history, clinical status, functional status, and pharmacological treatment patterns.

Results: Of 3,536 eligible patients at baseline, 12% ($n=386$) currently use cannabis. Of this comorbid group 69% were male, 58% were inpatients, 83% were rated ≥ 20 on YMRS and 63% had

delusions/hallucinations during the presenting episode. 58% had no relationship, 51% did not live independently, and 26% were unable to work.

Conclusions: With 3,536 patients, EMBLEM represents the largest naturalistic study on outcomes in bipolar disorder. Baseline information and 12-week longitudinal results both on clinical status and functional outcomes will be discussed.

References:

1. Haro JM, et al: European mania in bipolar longitudinal evaluation of medication (EMBLEM) study: study design and recruitment of a 2-year, pan-European, observational health outcomes study in bipolar disorder. *Bipolar Disorders* 2003; 5 (Suppl. 1): P82.
2. Wells KB: Treatment research at the crossroads: the scientific interface of clinical trials and effectiveness research. *American Journal of Psychiatry* 1999; 156:5-10.

NR408 Tuesday, May 24, 12:00 p.m.-2:00 p.m. The Effect of Previous Psychotic Mood Episodes on Cognitive Impairment in Euthymic Bipolar Patients: A Comparison of Psychotic, Nonpsychotic, and Healthy Patients

Emre Bora, M.D., *Department of Psychiatry, Ege University Hospital Medical School, Kazim Dirik, Bornova Izmir 35100, Turkey*; Simavi Vahip, M.D., Ali Saffet Gonul, M.D., Ayse Eryavuz, Ph.D., Melise Ogut, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate that history of psychotic mood episode has a negative impact on cognitive function of the patients with bipolar disorder.

Summary:

Objective: Cognitive dysfunction in several domains was proposed to be trait markers of the bipolar patients. The aim of this study was to evaluate the effect of psychotic features on neuropsychological measures, including sustained attention, in remitted patients.

Method: The participants of the study were 40 euthymic psychotic, 25 nonpsychotic bipolar I patients, and 30 healthy control subjects. Participants were assessed with a battery of neuropsychological tests targeting attention, executive functions, psychomotor speed, verbal learning, and memory.

Results: Euthymic psychotic bipolar patients performed worse than controls in most of the measures, after controlling for the confounding effects of education, age, and residual symptoms. Nonpsychotic patients were also impaired on tasks of attention, fluency, and psychomotor speed. Number of categories achieved was the only measure that psychotic patients performed significantly worse compared with nonpsychotic patients. Differences among patients groups were not explainable by illness severity measures. Duration of illness is related to slowness in psychomotor speed tasks. Verbal memory deficits may be related to serum lithium levels and age of onset of the disease.

Conclusion: Some aspects of executive dysfunction may be the trait marker of psychosis among bipolar patients. However, verbal fluency and sustained attention deficits may be trait markers of bipolar disorder in general.

References:

1. Murphy FC, Sahakian BJ: Neuropsychology of bipolar disorder. *Br J Psychiatry Suppl* 2001; 41:120-127.
2. Martinez-Arán A, Vieta E, Reinares M, et al: Cognitive function across manic or hypomanic, depressed and euthymic states in bipolar disorder. *Am J Psychiatry* 2004; 161:262-270.

NR409 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Metabolic Syndrome in Women With Fibromyalgia: Psychiatric and Somatic Mediators

Barbara L. Loevinger, M.D., *Womens Health Research, University of Wisconsin Medical School, 6245 S Highlands Avenue, Madison, WI 53705-1114*; Daniel Muller, M.D., Christopher Coe, Ph.D.

Educational Objectives:

After attending the poster, the participant will have learned that fibromyalgia syndrome (FMS) carries a high risk for metabolic syndrome. The importance of both psychiatric (depression, negative emotions, fatigue, dyssomnias, and childhood maltreatment) and medical (abnormalities in red blood cells, creatinine, and catecholamines, deconditioning) mediators will be understood.

Summary:

Objective: To determine the risk of metabolic syndrome in women with fibromyalgia syndrome (FMS) and to evaluate the potential contributions of associated psychiatric and medical features.

Methods: Metabolic syndrome measurements (blood pressure, waist, serum triglycerides, HDL cholesterol, and hemoglobin A1C) were taken in 115 premenopausal women with FMS and 48 matched, healthy women recruited from the community. Psychiatric diagnosis, perceived stress, fatigue, affective states, childhood trauma, muscle strength, neuroendocrine and hematologic profiles were also evaluated.

Results: Women with FMS have a significantly elevated risk of metabolic syndrome. FMS was also significantly associated with higher levels of depression, childhood maltreatment, perceived stress, negative emotion, and red cell abnormalities. Metabolic syndrome had significant relationships with depressive symptoms, fatigue, childhood maltreatment, creatinine, and catecholamine profiles.

Conclusions: The high risk of metabolic syndrome found in women with FMS suggests that, although premenopausal, these women also may be at greater risk for cardiovascular disease and insulin resistance. Prior studies have shown that chronic stress, depressive symptoms, and negative emotions, which are common but not universal in FMS, are associated with metabolic risk and cardiovascular morbidity. We are investigating the relative importance of several mediating factors, e.g., hematologic abnormalities, muscle deconditioning, catecholamines, and sleep disturbance.

References:

1. Vitaliano PP, Scanlan JM, Zhang J, Savage MV, Hirsch IB, Siegler IG: A path model of chronic stress: the metabolic syndrome, and coronary heart disease. *Psychosom Med* 2002; 64:418-435.
2. McCaffery JM, Niaura R, Todaro JF, Swan GE, Carmelli D: Depressive symptoms and metabolic risk in adult male twins enrolled in the National Heart, Lung, and Blood Institute Twin Study. *Psychosom Med* 2003; 65:490-497.

NR410 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Adjunctive Herbal Medicine With Carbamazepine for the Treatment of Bipolar Disorder: A Double-Blind, Randomized, Controlled Study

Zhang-Jin Zhang, M.D., *Department of Psychiatry, The First Hospital of Xi'an Jiaotong University, 1 Jiankang Road, Xi'an, Shannxi Province 710061, China*; Wan-Hu Kang, M.D., Qing-Rong Tan, M.D., Qiang Li, M.D., Cheng-Ge Gao, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should recognize that these results suggest that adjunctive herbal medicine with CBZ can enhance therapeutic effects in bipolar patients.

Summary:

The efficacy and safety of the herbal medicine called FEWP is evaluated as an adjunct to carbamazepine (CBZ) in patients with bipolar disorders. Bipolar patients in depressive or manic episode were randomized to CBZ+placebo (n = 90), CBZ+FEWP (n = 90), or equivalent placebo (n = 44) for 12 weeks. CBZ commenced with 300 mg/day and FEWP was given at a fixed dose of 36 g/day. Patients in CBZ monotherapy had a significantly greater improvement on CGI-S, YMRS, and MADRS at some time points compared with patients in placebo groups. CBZ-treated patients had significantly higher response rates than those in placebo. Compared with CBZ alone, CBZ plus FEWP yielded significantly better outcomes on the HAMD and MADRS at week 4 and week 8. Adjunctive FEWP also significantly reduced mean CGI-S score on depression at week 8 and increased the amplitude of the reduced mean YMRS score at week 4 versus CBZ monotherapy. Adjunctive FEWP significantly elevated the response rate of depressed patients from that in CBZ monotherapy. The incidences of adverse events in CBZ+FEWP treated patients were similar to those in CBZ alone. These results suggest that adjunctive herbal medicine with CBZ can enhance therapeutic effects in bipolar patients.

References:

1. Zhang ZJ: Therapeutic effects of herbal extracts and constituents in animal models of psychiatric disorders. *Life Sci* 2004; 75:1659-99.
2. Maclocia G: *The Practice of Chinese Medicine: The Treatment of Diseases With Acupuncture and Chinese Herbs*. Edinburgh, UK: Churchill Livingstone, 1994 p. 342.

NR411 Tuesday, May 24, 12:00 p.m.-02:00 p.m.

Clinical Characteristics of Patients With Minor Depression

Supported by National Institute of Mental Health and National Center for Complementary and Alternative Medicine

Robert H. Howland, M.D., *WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213-2593*; Andrew Nierenberg, M.D., Mark Rapaport, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to diagnose minor depression and describe the clinical characteristics of minor depression.

Summary:

Objective: Describe the baseline clinical and demographic characteristics of a group of outpatients with minor depression enrolled in an ongoing randomized clinical trial comparing St. Johns Wort, citalopram, and placebo.

Methods: Minor depression was defined as the presence of two to four DSM-IV major depression symptoms persisting for at least six months, with at least one symptom being depressed mood or diminished interest, and not meeting criteria for major depression or dysthymia. Clinical data are collected at baseline prior to randomization into the clinical trial. Assessments include the Structured Clinical Interview for DSM-IV (SCID), 17-item Hamilton Depression Rating Scale (HAM-D), Clinical Global Impressions Severity Scale (CGI), Inventory of Depressive Symptomatology-Self Report (IDS-SR), Inventory of Depressive Symptomatology-Clinician Rated (IDS-C), Quality of Life Satisfaction Questionnaire

(Q-LES-Q), Scales of Psychological Well-Being (WBS), Global Assessment of Functioning Scale (GAF), Medical Outcome Survey-Short Form (MOS), Cumulative Illness Rating Scale (CIRS), and Sexual Function Questionnaire (SFQ).

Results: To date, 50 subjects have been enrolled. Subjects have mild levels of depression symptom severity and mild to moderate levels of impaired psychosocial function.

Conclusion: Despite milder symptoms, these patients have significant functional impairment.

References:

1. Judd LL, Rapaport MH, Yonkers KA, Rush AJ, Frank E, Thase ME, Kupfer DJ, Plewes JM, Schettler PJ, Tollefson G: Randomized, placebo-controlled trial of fluoxetine for acute treatment of minor depressive disorder. *Am J Psychiatry* 2004; 161:1864-1871.
2. Rapaport MH, Judd LL, Schettler PJ, Yonkers KA, Thase ME, Kupfer DJ, Frank E, Plewes JM, Tollefson G, Rush AJ: A descriptive analysis of minor depression. *Am J Psychiatry* 2002; 159:637-643.

NR412 Tuesday, May 24, 12:00 p.m.-02:00 p.m.

A Meta-Analysis of Randomized, Controlled Trials With Paroxetine: Does Mode of Action Really Improve Clinical Outcome?

Martin Katzman, M.D., *Ontario, Canada*; Andrea Tricco, M.S.C., Diane McIntosh, M.D., Marie-Josée Filteau, M.D., Pierre J. Bleau, M.D., Pratap Chokka, M.D., Kevin D. Kjernisted, M.D., Ba Pham, M.S.C., Hiram L. Mok, M.D.

Educational Objectives:

Past research suggested that use of antidepressants affecting the brain in multiple pathways result in better remission for individuals with depression. This is most likely due to selective reporting of outcomes. We showed that both formulations of Paxil, a single-pathway agent in the range of clinical use, are as effective as the multiple pathway antidepressants.

Summary:

Introduction: Recent meta-analyses have suggested a direct correlation between mode of action and clinical outcomes. We further evaluated this using the large body of published clinical evidence on paroxetine.

Methods: MEDLINE, EMBASE, and five other databases were searched to identify randomized paroxetine trials for depressive disorders. Screenings of citations, data abstraction, and assessment of trial quality were conducted by two independent reviewers. Outcome data including remission (e.g., HAMD<8), clinical response (e.g., 50% reduction in HAMD), symptom score, and dropouts were analyzed using random-effects models.

Results: 7,475 citations were screened, 351 articles retrieved, and 62 trial reports were included. These compared paroxetine with placebo, 8 TCAs, 3 SSRIs, and 7 other anti-depressants.

Paroxetine was consistently more efficacious than placebo; remission rate difference (n=6 trials): 10%[95%CI:6;14%], clinical response (n=5): 17%[7,27%], and effect size (ES, n=9): 0.2[0.1,0.3]. Venlafaxine's response rate was significantly higher than paroxetine's (n=2): 21%[8,34%], but not with the remission rate (n=3): 12%[-5,29%], and ES (n=3): 0.1[-0.1, 0.2]. Mirtazapine's remission rate was significantly higher than paroxetine's (n=3): 9%[2, 16%], as was its ES (n=3): 0.2[0.1,0.4], but not response rate (n=3): 7%[-1,14%].

Compared with still immediate-release paroxetine, dropout rate was significantly higher with placebo 8%[4,13%] and TCA 5%[2,7%] but significantly less with paroxetine controlled-release 5%[0.1,11%].

Conclusion: There was no consistent evidence to support other meta-analyses suggesting a direct correlation between mode of action and clinical outcomes.

References:

1. Thase ME, Entsuah AR, Rudolph, RL: Remission rates during treatment with venlafaxine or selective serotonin reuptake inhibitors. *British Journal of Psychiatry* 2001; 178:234-241.
2. Golden RN, Nemeroff CB, McSorley: Efficacy and tolerability of controlled-release and immediate-release paroxetine in the treatment of depression. *Journal of Clinical Psychiatry* 2002; 63(7):577-84.

NR413 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Prevention of Late-Life Depression in Primary Care: A Matter of Multiple Risk Factors?

Robert A. Schoevers, M.D., *Program Director, Mentrum Mental Health Care, 2e Constantijn Huijgensstraat 37, Amsterdam 1054 AG, Netherlands*; Filip Smit, M.S.C., Dorly Deeg, Ph.D., Pim Cuijpers, Ph.D., Jack Dekker, Ph.D., Willem Van Tilburg, Ph.D., Aartjan Beekman, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should recognize the potential for preventative intervention to reduce the onset of late-life depression, and a model to delineate subjects at high risk in the population.

Summary:

Context: Depression is a highly prevalent disorder causing the largest amount of non-fatal burden of all diseases. Even optimal evidence-based treatment would only reduce the burden by 1/3. In older persons, depression has a predominantly chronic course. It is therefore of great interest to determine whether the onset of late-life depression can be prevented in primary care.

Objective: To explore two models to identify high-risk groups in the population, taking into account the potential costs and benefits of different types of preventative interventions.

Methods: Depression onset was assessed at three-year follow-up using GMS-AGECAT in a randomly selected cohort of 1940 non-depressed and non-demented older community-living persons in the city of Amsterdam. Of these, a comprehensive set of risk factors that can easily be identified in primary care was available.

Main outcome measures: The association of risk factors with depression incidence in terms of Absolute and Relative Risk estimates, Numbers-Needed-to-be-Treated, and Population Attributable Fraction. Models for selective prevention (persons at risk) and indicated prevention (persons with subsyndromal symptoms of depression) are represented using Classification And Regression Tree (CART) analyses indicating subgroups with higher risk due to multiple risk factors.

Results: Overall, both the indicated (45.1%) and the selective prevention model (41.6%) accounted for a substantial proportion of new cases of depression. Subsyndromal symptoms of depression were associated with a risk of almost 40% to develop depression, an NNT of 5.8, and accounted for 24.6% of new cases. Adding more risk factors yielded higher AR, lower NNT, but also lower AF values. In the selective prevention model, persons who recently lost their spouse were at highest risk (AR 37%, NNT 5.3, AF 8.2%), a risk that became even higher if they also had a chronic medical illness.

Conclusions: Considering the costs and benefits of both models in the context of the availability of evidence-based preventative interventions, indicated prevention aimed at elderly persons with depressive symptoms currently is the preferred option, but more research is needed to define the efficacy of other, low-cost commu-

nity-based interventions to reduce the onset of depression. The exclusive focus on treatment, as opposed to prevention, is not in agreement with the rapidly developing evidence in common mental disorders.

References:

1. Cuijpers P: Examining the effects of prevention programs on the incidence of new cases of mental disorders: the lack of statistical power. *Am J Psychiatry* 2003; 160(8):1385-1391.
2. Smit F, Ederveen A, Cuijpers P, Deeg D, Beekman AT: Opportunities for cost-effective prevention of late-life depression: an epidemiological approach. *Archives of General Psychiatry*, in press.

NR414 Tuesday, May 24, 12:00 p.m.-2:00 p.m.
Gender Differences in Bipolar Disorder: The Emblem Study

Cecilia Gijsbers Van Wijk, Ph.D., *SPDC c/ow, Mentrum, 2e C. Huygenstraat 39, Amsterdam 1054 AG, Holland*; Simone Knijff, D.Sc.

Educational Objectives:

At the conclusion of the presentation, the participants should be able to appreciate differences between male and female bipolar patients in clinical features, presentation, course, treatment response, medication compliance and tolerance, and health care utilization.

Summary:

Bipolar disorders occur equally in men and women, but significant gender differences in manifestation and course have been reported. Women present more often with a depressive or mixed episode, whereas men experience more manic episodes. Women are more likely to suffer from the rapid cycling subtype and from comorbid psychiatric and medical disorders than men. Gender differences in response to psychotropic drugs have not been studied systematically.

The EMBLEM study (European Mania in Bipolar Longitudinal Evaluation of Medication) is a large-scale multi-center observational study in 14 European countries evaluating the optimal pharmacotherapeutic treatment during the acute phase of a manic or mixed episode. From December 2002 - June 2004 a total of 3,653 bipolar outpatients and inpatients 18 years and older with a manic or mixed episode, who started a new oral medication (antipsychotics, anticonvulsants, or lithium) were included in the study.

Based on the EMBLEM study we compared baseline data of 1,943 women and 1,582 men. We present results on gender differences in sociodemographic characteristics, course (age at onset, nature and frequency of former episodes, rapid cycling), comorbid substance abuse, suicidal behavior, nature and severity of the current episode (CGI-BP, HAM-D, YMRS, psychotic features), and medication preference. Findings from the literature are partially replicated.

References:

1. Leibenluft E: Women with bipolar disorder: clinical and research issues. *American Journal of Psychiatry* 1996; 153:163-173.
2. Arnold LM: Gender differences in bipolar disorder. *Psychiatric Clinics of North America* 2003; 26(3), 595-620.

NR415 Tuesday, May 24, 12:00 p.m.-2:00 p.m.
Adjunctive Oxcarbazepine for Treatment-Resistant Bipolar Disorder

Supported by Novartis Pharmaceuticals Corporation

Charles R. Conway, M.D., *Department of Psychiatry, Saint Louis University, 1221 South Grand Boulevard, Saint Louis,*

MO 63104; John T. Chibnall, Ph.D., Vadim Y. Baram, M.D., Leigh Anne Nelson, Pharm.D., J. Michael McGuire, Pharm.D., Praveen F. Abraham, D.O., George T. Grossberg, M.D., Bernard J. Carroll, M.B.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the potential efficacy of adjunctive oxcarbazepine in mood maintenance for treatment-resistant patients with bipolar I disorder.

Summary:

Objective: To investigate the efficacy of adjunctive oxcarbazepine in treatment-resistant bipolar I disorder outpatients.

Methods: This was a prospective, open-label, 12-week pilot study, with 12-week extension phase. Twenty outpatients (depressed, manic, or both) participated. Patients were titrated to a maximum tolerated dose of oxcarbazepine (300-1800 mg/day). All were taking concomitant medications for bipolar disorder. Outcome measures were Hamilton Depression Scale (HAM-D₂₄), Young Mania Rating Scale (YMRS), Clinical Global Impression of Change, and Social Adjustment Scale-Self Report.

Results: An intent-to-treat analysis indicated significant and positive changes in all outcome measures at weeks 12 and 24. For baseline depressed patients (n=15), depression response rate was 46.7% at week 12 and 26.7% at week 24; remission rate was 40% at week 12 and 26.7% at week 24. None of these patients became significantly more depressed; only one became manic. For baseline hypomanic/manic patients (n=7), response rate for mania was 71.4% at weeks 12 and 24; remission rate was 71.4% at week 12 and 42.9% at week 24. None of these patients became significantly more manic; only one became depressed.

Conclusion: Oxcarbazepine may be an effective adjunctive medication in treatment-resistant bipolar I disorder patients.

References:

1. Ghaemi SN, Ko JY, Kaizow JJ: Oxcarbazepine in treatment of refractory bipolar disorder: a retrospective chart review. *Bipolar Disorders* 2002; 4:70-73.
2. Benedetti A, Lattanzi L, Pini S, et al: Oxcarbazepine as add-on treatment in patients with bipolar manic, mixed, or depressive episode. *J Affect Disord* 2004; 79:273-277.

NR416 Tuesday, May 24, 12:00 p.m.-2:00 p.m.
Prevalence and Key Comorbidities Among Patients With Bipolar Disorders in a Large Managed Care Population

Jeff J. Guo, Ph.D., *Department of Pharmacy, University of Cincinnati, 3223 Eden Avenue, Cincinnati, OH 45267*; Paul E. Keck, Jr., M.D., Raymond Jang, Ph.D., Hong Li, Ph.D., Patricia Corey-Lisle, Ph.D., Dongming Jiang, M.S.

Educational Objectives:

At the conclusion of this session, participants will be able to describe the prevalence of treated bipolar disorder and comorbidities for patients with bipolar disorders in a large U.S. managed care population.

Summary:

Objective: To identify the prevalence of treated bipolar disorder, and to categorize medical and psychiatric comorbidities among patients with bipolar disorders in a large managed care population.

Methods: Using a multi-state claims database, 123,292 patients who had at least one bipolar diagnosis indicated by ICD9 codes 296.0x, 296.1x, 296.4x, 296.5x, 296.6x, 296.7x, 296.8x, and 301.13 were selected from 1/1/1998 to 12/31/2002. Cumulative monthly prevalence rate was constructed. Spearman Pearson was used to generate the correlation matrix of comorbidities.

Results: The cumulative monthly prevalence of treated bipolar disorders increased each year from 1998 to 2002, and increased by age with a peak (mean 2.3%, 95%CI 2.13-2.46) for age 35-49. The monthly prevalence rates were 2.03% (95%CI 1.88-2.19) for female and 1.05% (95%CI 0.97-1.14) for male. Patients' last bipolar diagnoses indicated 8.2% with psychosis, 14.6% with manic, 42.5% with mixed, 30.6% with depression, and 12.3% with hypomanic. Key psychiatric comorbidities included previous major depressive disorders 44.4%, anxiety disorder 36.7%, alcohol use disorder 6.4%, substance use disorder 5.6%, and personality disorder 3.7%. Medical comorbidities included hypertension 41.0%, diabetes mellitus 16.8%, obesity 13.8%, COPD 7.4%, ischemic heart disease 8.0%, and cerebral vascular diseases 6.0%. Anxiety disorder was significantly correlated with psychiatric and medical comorbidity. Diabetes and hypertension are significantly correlated with each medical comorbidity.

Conclusions: The prevalence of treated BPD peaked for ages 35-49. BPD was more prevalent in women. Common comorbidities of BPD included anxiety disorders, hypertension, diabetes mellitus, and obesity. It suggests component of metabolic syndrome is worrisome for the treatment of BPD.

References:

1. Freeman MP, Freeman SA, McElroy SL: The comorbidity of bipolar and anxiety disorder: prevalence, psychobiology, and treatment issues. *J Affect disorders* 2002; 68(1):1-231616.
2. Unutzer J, Simon G, Pabiniak C, Bond K, Katon W: The treated prevalence of bipolar disorder in a large staff-model HMO. *Psychiatr Serv* 1998; 49(8):1072-8.

NR417 Tuesday, May 24, 12:00 p.m.-2:00 p.m. Predicting Dropout in the Treatment of Depression

Gerda van Aalst, M.D., *AAZ West, Mentrum Mental Health Organization, Frederik Hendrikstraat 47, Amsterdam 1052 HK, Netherlands*; Robert Schoevers, Ph.D., Frans de Jonghe, Ph.D., Jack Dekker, Ph.D., Jaap Peen, Psy.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize dropout predictors in depressed patients treated with pharmacotherapy.

Summary:

Objective: Antidepressant efficacy may be compromised by early discontinuation. It is hypothesized that patient dropout is due to adverse events or inefficacy. However, there is little agreement about which variables are most predictive for treatment discontinuation.

The current study assessed differences between patients who dropped out of antidepressant treatment at remission (HDRS <7) and recovery (HDRS <50%) compared with those who did not (HDRS >7; HDRS >50%).

Method: In a mega-analysis of two six-month, randomized clinical trials, 180 depressed outpatients (HDRS 14-24) were treated in two therapy modalities: pharmacotherapy or combined therapy (pharmacotherapy and psychotherapy). Fifty-seven pharmacotherapy patients dropped out of these two therapy modalities. We analyzed the dropouts (2-sides Pearson Chi-square) in the Per Protocol sample regarding demographic and clinical measures.

Results: Eighteen subjects (25%) met remission criteria and 40 subjects (70%) met recovery criteria. Patients in the HDRS >7 population had significant more somatic complaints compared with the HDRS <7 group. Patients in the HDRS >50% group showed also significant more somatic complaints compared with the HDRS <50% group.

Conclusions: Twenty-five percent dropped out of therapy due to efficacy. Somatic complaints in pharmacotherapy dropouts who

met criteria of remission or recovery are significant dropout predictors compared with pharmacotherapy dropouts who did not meet these criteria.

References:

1. De Jonghe F, Kool S, van Aalst G, Dekker J, Peen J: Combining psychotherapy and antidepressants in the treatment of depression.
2. de Jonghe F, Hendriksen M, van Aalst G, Dekker J, van den Eijnden E, Kool S, Peen J: Psychotherapy alone and combined with pharmacotherapy in the treatment of depression. *British Journal of Psychiatry* 2004; 185:37-45.

NR418 Tuesday, May 24, 12:00 p.m.-2:00 p.m. Safety and Efficacy of Zonisamide Treatment of Bipolar Depression

Tamara B. Pardo, B.A., *Department of Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139*; Claudia Baldassano, M.D., Nassir Ghaemi, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to determine the safety and efficacy of zonisamide in the treatment of acute bipolar depression.

Summary:

Objective: Only two previously published studies suggest zonisamide, a novel anticonvulsant, may have potential utility in bipolar disorder. In a recent retrospective chart review, zonisamide demonstrated some improvement in bipolar depression using the clinical global impression—severity (CGI-S). This is the first prospective study in the safety and efficacy of zonisamide in bipolar depression.

Method: An open-label, prospective, non-randomized, eight-week study conducted in bipolar outpatients (type I, type II, or NOS) with depressive symptoms. Previous treatments were continued unchanged, but no new treatments were allowed. Montgomery Asberg Rating Scale (MADRS) and the Mania Rating Scale (MRS) from the SADS-C were used. Preliminary analysis of nine patients was conducted; full data on 20 patients will be presented.

Results: Mean \pm SD age was 42.5 ± 7.5 years with four males five females (8 BPI, 1 NOS). Dose ranged from 100 to 300mg/day, mean maximum dose 144.4 ± 72.6 . Mean MADRS improved significantly from baseline (22.8 ± 5.9) to endpoint (15.8 ± 6.3) (paired t-test, $t=2.49$, $p<0.04$). Four patients (44.4%) terminated early due to adverse effects including nausea/vomiting, cognitive impairment, increased suicidal ideations, and hypomania.

Conclusion: Our study found evidence of improvement of depressive symptoms in this sample.

References:

1. Baldassano CF, Ghaemi SN, Chang A, Lyman, Lipari M: Acute treatment of bipolar depression with adjunctive zonisamide: a retrospective chart review. *Bipolar Disord* 2004; 6:432-434.
2. Kanba S, Yagi G, Kamijama K, et al: The first open study of Zonisamide, a novel anticonvulsant, shows efficacy in mania. *Prog Neuro-Psychopharmacol & Biol Psychiatry* 1994; 18:707-715.

NR419 Tuesday, May 24, 12:00 p.m.-2:00 p.m. Physical Effects of Zonisamide Treatment of Bipolar Depression on Weight and Sexual Function

Benjamin Zablotzky, B.A., *Department of Psychiatry, Cambridge Health Alliance, 1493 Cambridge Street,*

Cambridge, MA 02139; Claudia F. Baldassano, M.D., Tamara B. Pardo, A.B., S. Nassir Ghaemi, M.D., Robert T. Dunn, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the short-term effects of zonisamide on weight and sexual experience in the treatment of acute bipolar depression.

Summary:

Objective: Most agents used to treat bipolar disorder induce weight gain or sexual dysfunction. A previously published study suggests zonisamide, a novel anticonvulsant, may demonstrate efficacy in bipolar disorder. In this first prospective study in the safety and efficacy of zonisamide in bipolar depression, we examined the effects on weight and sexual dysfunction.

Method: An open label, prospective, non-randomized, eight-week study was conducted in bipolar outpatients (type I, type II, or NOS), depressed phase. Previous treatments were continued unchanged, but no new treatments were allowed. Weight and Arizona Sexual Experience Scale (ASEX) were collected. Preliminary analysis of nine patients was conducted; full data on 20 patients will be presented.

Results: Weight data were obtained in six patients (three males, three females, all BPI, mean age 43.5, mean endpoint dose 150mg). Baseline weight was 193.4 ± 7.5 . Endpoint weight was 190.9 ± 7.5 . ASEX data obtained in seven patients (three males, four females, all BPI, mean age 42.8, mean endpoint dose 150mg). Baseline ASEX was 13.9 ± 5.0 . Endpoint ASEX was 14.8 ± 3.5 .

Conclusion: A small amount of weight loss was observed in this secondary analysis. There was no evidence of sexual dysfunction. Results on the full sample will be presented.

Funding Source: Eisai Inc.

References:

1. Ghaemi SN: Practical Guides in Psychiatry: Mood Disorders. Lippincott Williams & Wilkins, Philadelphia, 2003.
2. Baldassano CF, Ghaemi SN, Chang A, Lyman A, Lipari M: Acute treatment of bipolar depression with adjunctive zonisamide: a retrospective chart review.

NR420 Tuesday, May 24, 12:00 p.m.-2:00 p.m.

Aripiprazole and Ziprasidone as Adjunctive Therapy for Bipolar Disorder

Yahya Siddiqui, M.D., *Department of Psychiatry/Forensics, Siddhartha Medical College, Techouse, Nazarabad, Tumkur 572101, India*; Narayana Murthy, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the efficacy of ziprasidone and aripiprazole in depression

Summary:

Objective: To describe the antidepressant effectiveness of aripiprazole and ziprasidone when given adjunctively in bipolar I/II disorder.

Method: In an open label study, 112 patients with DSM-IV defined bipolar I/II disorder, in any phase of the illness, openly received adjunctive Aripiprazole or ziprasidone. The primary efficacy parameters were the Hamilton Depression Rating Scale (HDRS-17), Secondary efficacy parameters included the Young Mania Rating Scale (YMRS) along with the Clinical Global Impressions Scale (CGI) and Abnormal Involuntary Movement Scale (AIMS) along with changes in weight and body mass index (BMI-kg/m²). Response was defined as a significant change from baseline to endpoint in the total mean HDRS-17 score. Patients were evaluated by psychiatrists every two weeks for four months.

Results: Fifty subjects received aripiprazole; 62 received ziprasidone adjunctive to either lithium or divalproex. Total mean HDRS-17 scores significantly decreased from baseline to endpoint in both groups ($p=0.001$), with the mean HDRS-17 total scores falling from 18(SD=3.2) to 8(SD=1.5) by 4 months in the risperidone-treated group and from 18 (SD=1.9) to 5 (SD=2.0) in the ziprasidone-treated group. The mean dosage for ziprasidone was 120 mg/day and that for aripiprazole was 12 mg/day. Both groups were well tolerated. No patients developed tardive dyskinesia nor QTc prolongation. There was no significant weight gain for the both groups.

Conclusions: This study shows the usefulness of aripiprazole and ziprasidone in bipolar disorder, as an adjunctive medication to reduce depressive symptoms. Double-blind, placebo-controlled trials need to be done to replicate the data.

References:

1. DeLeon A, Patel NC, Crismon ML: Aripiprazole: a comprehensive review of its pharmacology, clinical efficacy, and tolerability. *Clin Ther* 2004; 26(5):649-66.
2. Barbee JG, Conrad EJ, Jamhour NJ: The effectiveness of olanzapine, risperidone, quetiapine, and ziprasidone as augmentation agents in treatment-resistant major depressive disorder. *J Clin Psychiatry* 2004; 65(7):975-81.

NR421 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Functional Improvement and Quality of Life in Youth After One Year

Leo J. Bastiaens, M.D., *Family Services WPA, 33 Sunnyhill Drive, Pittsburgh, PA 15228*; Cathy Dello Stritto, R.N.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that during treatment, level of functioning and quality of life stagnate after an initial improvement, and that more intensive treatment may be needed.

Summary:

Objective: To evaluate if quality of life improves for youth treated under real world circumstances.

Methods: Eighty-nine patients (11.8+/- 3.6 y/o), who were administered a structured interview, the Columbia Impairment Scale (CIS), the Health and Life Functioning Scale (HALFS/ a quality of life scale), and the Global Assessment of Functioning Scale (GAF), were started in pharmacotherapy. Diagnoses were as follows: disruptive behavior- (n=45), depressive- (n=21), anxiety- (n=11), bipolar- (n=9), and other disorders (n=3). The CIS, HALFS, and GAF were re-administered after three months (n=59) and 1 year (n=35).

Results: Level of functioning improved after three months with 21.9% (CIS: from 25 to 18.9) and 17.8% (GAF: from 51.1 to 60.2). Quality of life improved less: 13.5% (HALFS: from 11.1 to 12.6). During the next nine months, there was hardly any further improvement: CIS from 18.9 to 18.4 (2.6%); GAF from 60.2 to 61.4 (2%); and HALFS from 12.6 to 12.9 (2.4%).

Conclusions: After an initial improvement, level of functioning and quality of life stagnate. Since residual symptoms continue to cause impairment, more intensive and innovative treatments may need to be put in place to achieve remission and wellness in these young psychiatric patients.

References:

1. Sawyer MG, Whaites L, Rey JM, Hazell PL, Graetz BW, Baghurst P: Health-related quality of life of children and adolescents with mental disorders. *J Am Acad Child Adolesc Psychiatry* 2002; 41(5): 530-537.

2. Bastiaansen D, Koot HM, Ferdinand RF, Verhulst FC: Quality of life in children with psychiatric disorders: self-parent, and clinician report. *J Am Acad Child Adolesc Psychiatry* 2004; 43(2): 221-230.

NR422 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Prevalence of Impulse Control Disorders in Adult Psychiatric Inpatients

Jon E. Grant, M.D., *Department of Psychiatry, Brown Medical School, Butler Hospital, 345 Blackstone, Providence, RI 02906*;
Marc N. Potenza, M.D., Laura B. Levine, M.D., Daniel S. Kim, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand how common impulse control disorders are among psychiatric patients and to recognize the need to screen for these disorders.

Summary:

Objective: To examine the prevalence of impulse control disorders (ICDs) in psychiatric inpatients.

Method: 204 consecutive inpatient psychiatric admissions [112 (54.9%) females; age (means±SD)=40.5 ± 13.2 (range 18-83)] were screened for ICDs using the Minnesota Impulsive Disorders Interview, a semistructured clinical interview assessing pathological gambling, trichotillomania, kleptomania, pyromania, intermittent explosive disorder, compulsive buying, and compulsive sexual behavior. Subjects screening positive for an ICD were then evaluated using structured clinical interviews.

Results: Sixty-three (30.9%) patients were diagnosed with at least one current ICD. The most common ICDs were compulsive buying (9.3%), kleptomania (7.8%), and pathological gambling (6.9%). Patients with co-occurring ICDs did not differ significantly from those without on demographic measures or number or type of non-ICD psychiatric diagnoses.

Conclusions: ICDs appear common among psychiatric inpatients. Additional, larger studies are needed to examine the prevalence of ICDs in the general population and specific psychiatric groups.

References:

1. Moeller FG, Barratt ES, Dougherty DM, Schmitz JM, Swann AC: Psychiatric aspects of impulsivity. *Am J Psychiatry* 2001; 158:1783-1793.
2. Grant JE, Potenza MN: Impulse control disorders: Clinical characteristics and pharmacological management. *Ann Clin Psychiatry* 2004; 16:27-34.

NR423 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Pediatric Experience With Aripiprazole

Devra Bastiaens, M.D., *Family Services WPA, 33 Sunnyhill Drive, Pittsburgh, PA 15228*; Leo J. Bastiaens, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that aripiprazole is well-tolerated and effective in pediatric patients

Summary:

Objective: to evaluate the effectiveness and safety of aripiprazole in a pediatric sample treated in a community mental health center.

Method: A retrospective chart review was performed in 30 consecutive patients (13.8+/- 2.6 y/o / 19 males / 28 Caucasians), started on aripiprazole. Patients were diagnosed, with the Mini

International Neuropsychiatric Interview and the Child/Adolescent Symptom Inventory-IV, as follows: bipolar- (n=12), disruptive behavior- (n=8), psychotic- (n=6), and other disorders (n=4). Initial Global Assessment of Functioning Scale (GAF) was 48.8 +/- 5.2. Medication trials prior to aripiprazole numbered 3.8 +/- 2.7. Patients were started on 5 mg of aripiprazole. Ten patients took concomitant medications.

Results: After three months, 24 patients were still on aripiprazole, with a mean daily dose of 7.6 +/- 4.0 mg. Mean GAF score increased to 55.6 +/- 7.4 and the Clinical Global Impressions Improvement (CGI) score was 2.7 +/- 1.2. Eighteen patients had a CGI of 3 or less. Thirteen patients reported side effects: somnolence and GI disturbance were most frequent, but mild and transient. One patient, with significant organicity, discontinued because of agitation.

Conclusions: Aripiprazole was well tolerated and moderately effective in a variety of chronic pediatric conditions.

References:

1. Findling RL, Blumer JL, Kauffman R, Batterson JR, Gilbert DL, Bramer S, Marcus R: Pharmacokinetic effects of aripiprazole in conduct disorder. Poster presented at the European College of Neuropsychopharmacology, Prague, Czech Republic, 2003.
2. Pigott TA, Carson WH, Saha AR, Torbeyns AF, Stock EG, Igento GG: Aripiprazole for the prevention of relapse in stabilized patients with chronic schizophrenia: a placebo-controlled 26-week study. *J Clin Psychiatry* 2003; 64: 1048-1056.

NR424 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Children With ADHD: Eight-Year, Post-Treatment Study
Supported by McNeil Consumer & Specialty Pharmaceuticals

Syed Ahsan, M.D., *PO Box 308, Pennington Gap, VA 24277*;
Saira Ahsan, M.D., Mujeeb Shad, M.D., Richard Saylor, M.S.

Educational Objectives:

At the conclusion of the study, the participant should be able to demonstrate understanding of the long-term effects of untreated ADHD on behavioral, academic, and social areas.

Summary:

Objective: To determine the rate of continuation of medication for the treatment of ADHD eight years post treatment.

Method: One hundred charts from a pediatric and a psychiatric practice, with a primary diagnosis of ADHD were selected. Questionnaires were mailed to collect the following data: medications prescribed for the treatment of ADHD, response to the treatment, current functioning in the following areas: (1) academic, (2) behavioral; (3) social.

Results: Among the respondents, 41% (11) currently received medication. 73% (8) were male, 37% (3) were female. The average age for the children on medication was 13.7 years and 12 years for those not on any medication. For those receiving medication, 90% were medicated with an FDA-approved product for the treatment of ADHD. Majority (59%) of the patients did not continue medication following the diagnosis of ADHD. These children were rated by their caregivers as poor performers compared with those on medication. Those who continued medication performed better in all three areas, that is, academics, social, and behavioral.

Conclusion: The findings from this study support the existing data that children with ADHD who receive medication perform better academically, socially, and behaviorally.

References:

1. Hectman L: ADHD predictors of long-term outcome in children with ADHD. *Pediatric Clinics of (NA)* 1999;46:1039-1052.

2. Diagnostic and statistical manual of mental disorders. Fourth Edition, text revision.
3. Wender Esther H: ADHD, is it common? Archives of Pediatric and Adolescent Medicine 2002; 156:209-210.

NR425 **Tuesday, May 24, 3:00 p.m.-5:00 p.m.**
The Clinical Dilemma of Using Medications in Substance Abusing Adolescents

Timothy E. Wilens, M.D., *Department of Child Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 725, Boston, MA 02114*; Michael C. Monuteaux, Sc.D., Lindsey E. Snyder, B.A., Hadley Moore, B.A., Martin Gignac, M.D.

Educational Objectives:

At the conclusion of this presentation, participants should be able to recognize the potential benefits associated with the pharmacological treatment of attention deficit hyperactivity disorder (ADHD) in adolescents and adults with ADHD and substance use disorders (SUD). Once informed of the poor SUD prognosis for individuals with comorbid ADHD and SUD, participants will learn that treating ADHD pharmacologically does not result in specific drug-drug related adverse events with substances of abuse, or exacerbate craving, or the SUD.

Summary:

Objective: Adolescents and adults with attention deficit/hyperactivity disorder (ADHD) and substance-use disorders (SUD) are increasingly recognized in clinical practice. The role of pharmacological treatment for ADHD in these comorbid individuals remains unclear.

Methods: A systematic review of the medical literature was conducted through PubMed, supplemented with data from scientific presentations, to evaluate the role of medication treatment of ADHD in substance abusing individuals with ADHD. Meta-analysis was used to evaluate the effects of medication therapy on ADHD and SUD outcomes in general, while specifically addressing trial design, trial duration, retention, class of medication, age group, concurrent psychotherapy, and outcome in both SUD and ADHD domains.

Results: Four studies in adolescents and five studies in adults with ADHD plus SUD were identified (two controlled and seven open studies; N=222 subjects). The standard mean difference (SMD) indicated statistically significant improvements in ADHD and SUD that were not maintained when evaluating controlled studies only. Albeit limited by power, concurrent psychotherapy, trial duration, retention rate, and age group did not influence outcome. No worsening of SUD or drug-drug interactions was observed in any of the studies. The results could not be accounted for by any single study or by publication bias.

Conclusion: Treating ADHD pharmacologically in individuals with ADHD plus SUD has a moderate impact on ADHD and SUD that is not observed in controlled trials, and does not result in worsening of SUD or adverse interactions specific to SUD. Further controlled trials evaluating the effect of novel combinations of psychotherapy and ADHD pharmacotherapy on SUD relapse in these groups are warranted.

References:

1. Levin FR, Evans SM, McDowell DM, Brooks DJ, Nunes E: Bupropion treatment for cocaine abuse and adult attention-deficit/hyperactivity disorder. *J Addict Dis* 2002; 21:1-16.
2. Riggs PD, Hall SK, Mikulich-Gilbertson SK, Lohman M and Kayser A: A randomized controlled trial of pemoline for attention-deficit/hyperactivity disorder in substance-abusing adolescents. *J Am Acad Child Adolesc Psychiatry* 2004; 43:420-429.

NR426 **Tuesday, May 24, 12:00 p.m.-5:00 p.m.**
Amphetamine Treatment of ADHD in Adults With Primary Essential Hypertension
Supported by Shire US, Inc.

Timothy E. Wilens, M.D., *Department of Child Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 725, Boston, MA 02114*; Joseph Biederman, M.D., Amy Podolski, B.A., Martin Gignac, M.D., Paul Hammerness, M.D., Craig B. Surman, M.D., Randall Zusman, M.D.

Educational Objectives:

After reviewing this poster, the participant should have preliminary evidence suggesting that patients with treated hypertension are eligible candidates for mixed amphetamine salts extended release (MAS XR) up to 60 mg/day for the treatment of adult ADHD.

Summary:

Objective: Data from controlled clinical trials indicate that stimulant and nonstimulant medications currently used for the treatment of normotensive adults with ADHD result in minor increases in blood pressure (BP) and pulse. However, no data exist on the use of stimulant medications in adult patients with controlled hypertension (HTN). We describe preliminary results from an ongoing study evaluating the safety of mixed amphetamine salts extended release (MAS XR) in adults with HTN receiving antihypertensive medication(s).

Methods: Forty adults with ADHD, treated with stable doses of antihypertensive medications and achieving a stable BP for ≥ 4 weeks ($<135/85$ mm Hg), will be entered into an eight-week, two-phase study. Subjects received MAS XR for six weeks along with their current antihypertensive agents; the MAS XR dosage was increased once weekly to a maximum of 60 mg/d. BP and pulse were assessed at baseline, during, and two weeks after treatment.

Results: To date, 17 subjects have entered the protocol. Fifty-five percent received the target dose and 80% received dosages ≥ 40 mg/day because of efficacy at lower doses or non-cardiovascular adverse effects. None of the subjects developed HTN (BP $> 140/90$ mm Hg for two consecutive weeks) during MAS XR treatment. Increases in BP/pulse were similar to those reported in controlled trials. Subjects responded positively to treatment with significant reductions in their ADHD Rating Scale—IV scores.

Conclusion: In this ongoing trial, MAS XR was not associated with clinically significant increases in systolic or diastolic blood pressure or pulse in adults with well-controlled HTN.

References:

1. Wilens T, Hammerness P, Biederman J, Kwon A, Spencer T, Biederman J, Clark S, Scott M, Podolski A, Moore H: Blood pressure changes associated with medication treatment of adults with ADHD. *J Clin Psychiatry* 2004; accepted for publication.
2. Wilens TE, Spencer TJ, Biederman J: Pharmacotherapy of ADHD in adults: a review of the literature. *J Atten Disord* 2002; 4:189-202.

NR427 **Tuesday, May 24, 3:00 p.m.-5:00 p.m.**
Mixed Amphetamine Salts XR: Cardiovascular Safety in Adolescents With ADHD
Supported by Shire US, Inc.

Timothy E. Wilens, M.D., *Department of Child Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 725, Boston, MA 02114*; Thomas J. Spencer, M.D., Joseph Biederman, M.D., Richard H. Weisler, M.D., Stephanie C. Read, M.S., Arnaud Partiot, M.D.

Educational Objectives:

After reviewing this poster, the participant should be able to discuss the cardiovascular safety profile of mixed amphetamine salts extended release (MAS XR) in adolescents with attention-deficit/hyperactivity disorder.

Summary:

Objective: To assess the short-term cardiovascular effects of mixed amphetamine salts extended release (MAS XR; Adderall XR®) 10-60 mg/d in adolescents (aged 13-17) with ADHD.

Methods: Randomized, double-blind, multicenter, parallel-group, forced-dose-escalation study. Subjects ≤ 75 kg ($n=278$) received placebo, 10, 20, 30, or 40 mg MAS XR QAM for four weeks; subjects >75 kg ($n=40$) received placebo, 50, or 60 mg MAS XR. Vital signs were assessed at baseline and weekly visits, and a 12-lead ECG was completed at screening and endpoint.

Results: At endpoint, there was a statistically significant treatment effect of MAS XR 10-40 mg for pulse (mean change \pm SD), 1.7 ± 10.6 vs 0.6 ± 9.6 bpm for placebo, $P=0.01$), but not systolic ($P=0.05$) or diastolic blood pressure ($P=0.36$). Similarly, for the MAS XR 50- or 60-mg subjects, the treatment effect for pulse was statistically significant (6.7 ± 14.2 vs -4.5 ± 9 bpm, $P=0.01$), but not for systolic ($P=0.81$) or diastolic blood pressure ($P=0.48$). MAS XR had no statistically significant treatment effects on mean ECG interval measurements at endpoint except for ECG heart rate (9.2 ± 15.1 bpm, $P=0.01$) in the 50-60-mg cohort.

Conclusion: MAS XR (up to 60 mg/d) has an acceptable cardiovascular profile in adolescents with ADHD.

References:

1. Findling RL, Short EJ, Manos MJ: Short-term cardiovascular effects of methylphenidate and Adderall. *J Am Acad Child Adolesc Psychiatry* 2001; 40:525-529.
2. Gutgesell H, Atkins D, Barst R, Buck M, Franklin W, Humes R, et al: AHA Scientific Statement: cardiovascular monitoring of children and adolescents receiving psychotropic drugs. *J Am Acad Child Adolesc Psychiatry* 1999; 38:1047-1050.

NR428 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Do Adults and Adolescents With ADHD Respond Differently to Atomoxetine?

Supported by Eli Lilly & Company, Indianapolis, IN.

Timothy E. Wilens, M.D., *Department of Child Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 725, Boston, MA 02114*; Lenard A. Adler, M.D., Haitao Gao, Ph.D., Holland Detke, Ph.D., Louise Levine, M.D.

Educational Objectives:

At the conclusion of this presentation, the attendee should be aware of the similarities and differences in adults' and adolescents' response to atomoxetine in terms of both efficacy and tolerability.

Summary:

Objective: In order to examine efficacy and safety of atomoxetine across the lifespan, we compared treatment effects in adults and adolescents with attention-deficit/hyperactivity disorder (ADHD).

Methods: Pooled data were analyzed from adults (270 atomoxetine, 266 placebo) and adolescents (107 atomoxetine, 69 placebo) enrolled in similarly designed, acute, double-blind, placebo-controlled trials. DSM-IV ADHD diagnoses were confirmed by CAAR-D for adults and K-SADS-PL for adolescents. Efficacy measures included the Conners' Adult ADHDRS-Investigator Version for adults, the ADHDRS-Parent Version for adolescents, and the CGI-Severity for all subjects.

Results: Adults were slightly less symptomatic at baseline. Overall treatment effect was lower in adults ($p=.04$; effect size=0.39 for adults; 0.70 for adolescents). A similar trend was seen for the CGI-S. No significant treatment-by-age interactions were observed for time to response. Tolerability profiles were generally similar between age groups although more adults discontinued due to adverse events. No clinically meaningful treatment-by-age interactions were observed for vital signs or weight.

Conclusions: Acute treatment with atomoxetine for ADHD was effective and well-tolerated for both adults and adolescents, with greater efficacy noted in adolescents. Methodological differences, dosing, and symptom differences among studies and age groups may account for some of these noted differences.

References:

1. Wilens TE, Biederman J, Spencer TJ: Attention deficit/hyperactivity disorder across the lifespan. *Annu Rev Med* 2002; 53:113-131.
2. Michelson D, Adler L, Spence T, et al: Atomoxetine in adults with ADHD: two randomized, placebo-controlled studies. *Biol Psychiatry* 2003; 53:112-120.

NR429 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Pregabalin's Sustained Effect on Somatic Symptoms in Patients With GAD

Supported by Pfizer Inc.

Karl Rickels, M.D., *Department of Psychiatry, University of Pennsylvania, 3535 Market Street, Suite 670, Philadelphia, PA 19104-3309*; Fran Mandel, Ph.D., Gwen Zornberg, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to improve understanding of pregabalin's rapid onset of anxiolytic efficacy and the persistence of its effect in relieving somatic symptoms of GAD, which is not due to side effects, such as sedation, which is transient.

Summary:

Objective: To examine the persistence of pregabalin's efficacy in relieving physical-somatic symptoms in randomized, controlled trials of GAD. Pregabalin has demonstrated onset of efficacy at week 1 in six of six GAD trials.

Methods: Data from all six placebo controlled trials of pregabalin in GAD (4-6 weeks in duration) were combined to analyze three pregabalin treatment groups (low-dose, 150, mid-dose, 200-450; or high-dose, 600 mg/day; total $n=1149$) compared with placebo ($n=484$). Responders to treatment were defined as having $\geq 30\%$ improvement on the HAM-A somatic factor score persisting at all visits or all except one.

Results: Significantly more patients treated with pregabalin (low-dose, 54.2%, $p=0.03$; mid-dose, 60.5%, $p<0.0001$; high-dose, 60.5% $p<0.0001$) than with placebo (41.9%) responded. Median duration of somnolence and dizziness was 9 and 16 days on pregabalin versus eight and ten days on placebo. Discontinuation rates due to adverse events for low-dose (6.2%) and mid-dose (8.3%) pregabalin treatment groups were lower than in the placebo (9.3%) and high-dose (18.0%) pregabalin groups.

Conclusion: Pregabalin demonstrated rapid onset of efficacy and a favorable safety profile in relieving physical somatic symptoms of GAD across the dosing range. The most common AEs associated with treatment were transient in most patients, while pregabalin's anxiolytic effect persisted.

References:

1. Goodman WK: Selecting pharmacotherapy for generalized anxiety disorder. *J Clin Psychiatry* 2004; 65(suppl 13):8-13.

2. Witchen HU, Kessler RC, Beesdo K, Krause P, Hoffer M, Hoyer J: Generalized anxiety and depression in primary care prevalence, recognition, and management. *J Clin Psychiatry* 2002; 63(suppl 8):24-34.

NR430 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

A Placebo-Controlled Study of Topiramate in Civilian PTSD

Supported by Ortho-McNeil Pharmaceuticals

Phebe M. Tucker, M.D., *Department of Psychiatry, University of Oklahoma Health Science, 920 SL Young Boulevard, Box 26901, Oklahoma City, OK 73104*; Richard P. Trautman, M.D., Dorothy Wyatt, R.N., Jamie Thompson, Shu-Chen Wu, Ph.D., Julie A. Capece, B.A., Norman Rosenthal, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to delineate rationale for advancing pharmacotherapeutic treatment options in civilian populations with chronic PTSD. Identify the potential role of topiramate for the treatment of civilian PTSD.

Summary:

Objective: To assess the efficacy and safety of topiramate in civilian posttraumatic stress disorder (PTSD).

Method: Outpatients (18-64 y) with a DSM-IV diagnosis of PTSD and Clinician-Administered PTSD Scale (CAPS) scores ≥ 50 received placebo or topiramate (starting dose, 25 mg/d; titrated to 400 mg/d or maximum tolerated dose). Primary efficacy, change in total CAPS, and secondary efficacy measures were assessed by ANCOVA in the intent-to-treat (ITT) population with last observation carried forward.

Results: The ITT population consisted of 38 patients with mean baseline total CAPS scores of 88.3 ± 13.8 (topiramate, $n=19$) and 91.1 ± 13.7 (placebo, $n=19$). Although total CAPS scores were decreased with topiramate (-52.7) versus placebo (-42.0), this difference was not significant ($P=0.232$). Topiramate resulted in significant reductions in reexperiencing symptoms (topiramate, 74.9%; placebo, 50.2%; $P=0.038$) and Treatment Outcome PTSD Scale (topiramate, 68%; placebo, 41.6%; $P=0.025$). Marginally significant reductions were noted in mean total Clinical Global Impression-Improvement scores (topiramate, 1.9 ± 1.2 ; placebo, 2.6 ± 1.1 ; $P=0.055$). Treatment-emergent adverse events (AEs) most frequently reported with topiramate included headache, sinusitis, and taste perversion; treatment-limiting AEs were emotional lability, nervousness, rectal bleeding, and depression aggravated.

Conclusions: These preliminary results suggest further, adequately powered studies of topiramate for the treatment of PTSD are warranted.

References:

1. Asnis GM, et al: SSRIs versus Non-SSRIs in post-traumatic stress disorder. *Drugs* 2004; 64:383-404.
2. Tucker P, et al: Understanding and treating PTSD: past, present, and future. *Bull Menninger Clin* 2000; 64:A37-51.

NR431 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Validation of a Novel, Comprehensive Computerized Assessment for Adult ADHD

Supported by Institute for the Study of Aging

Avraham Schweiger, Ph.D., *Department of Behavioral Sciences, Academic College of Tel Aviv, 6 Szold Street, Tel Aviv 64924, Israel*; Ely S. Simon, M.D., Amitai Abramovitch, B.A., Glen M. Doniger, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the construct and discriminant validity of a set of computerized cognitive tests in measuring cognitive impairment associated with attention deficit hyperactivity disorder (ADHD).

Summary:

Objective: To assess construct and discriminant validity of Mindstreams computerized cognitive tests in attention deficit/hyperactivity disorder (ADHD).

Method: 29 adults with ADHD (age: 29.1 ± 7.3 ; years of education: 13.6 ± 1.3) completed a Mindstreams[®] (Neuro Trax Corp., NY) battery, including a multi-level continuous performance (Expanded Go-NoGo) test, and the Conners' CPT-II. Construct validity was assessed by Pearson correlations between Expanded Go NoGo and Conners' CPT-II outcomes. Discriminant validity was assessed by multivariate analysis of variance comparing Mindstreams performance between ADHD participants and 71 cognitively healthy individuals (age: 26.5 ± 3.8 ; education: 13.6 ± 2.2 years), 22 of whom received only the Expanded Go-NoGo test. Area under the curve (AUC) was used as a measure of effect size.

Results: Expanded Go-NoGo and corresponding CPT-II outcomes were highly correlated (commission errors: $r=0.792$, $p<0.001$; reaction time: $r=0.723$, $p<0.001$) in ADHD participants. The Expanded Go-NoGo test exhibited excellent discriminant validity, with ADHD participants performing more poorly than controls (performance index: $F[1,48]=29.679$, $p<0.001$; $AUC=0.921$, $p<0.001$). ADHD participants also performed more poorly on Stroop (performance index; $F[1,76]=11.389$, $p=0.001$) and Staged Information Processing Speed (performance index: $F[1,76]=13.371$, $p<0.001$) tests.

Conclusions: Mindstreams tests are valid for detection of adult ADHD, showing high correspondence with the CPT-II and good discriminant validity in executive function and attention tests.

References:

1. Dwolatzky T, Whitehead V, Doniger GM, Simon ES, Schweiger A, Jaffe D, et al: Validity of a novel computerized cognitive battery for mild cognitive impairment. *BMC Genetr* 3: 4.
2. Elstein D, Doniger GM, Guedalia J, Simon ES, Antebi V, Arnon Y, et al: Computerized cognitive testing in patients with type I Gaucher disease: effects of enzyme replacement and substrate reduction. *Genet Med*, in press.

NR432 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

DAT-1 9R and DRD4 120 Alleles Do Not Predict ADHD Stimulant Response

Stephanie Hamarman, M.D., *Department of Psychiatry, New Jersey Medical School, 183 South Orange Avenue C1404, Newark, NJ 07103*; C. Ulger, Ph.D., J. Fossella, M. Brimacombe, J. Dermody, PhD

Educational Objectives:

At the conclusion of this session, the participant should be able to learn if a genetic polymorphism in the dopamine receptor DRD4 120 and dopamine transporter 1 9-repeat allele correlate with clinical treatment outcomes in children with Attention Deficit Hyperactivity Disorder.

Summary:

Objective: Genetic polymorphisms of the dopamine neurotransmitter system have been identified in ADHD. Since stimulant medications act through this system a pharmacogenetic relationship may exist. We previously have shown that ADHD children with dopamine receptor-4 (DRD4) 7-repeat polymorphism require higher doses of methylphenidate (MPH) to achieve 10-point improvement on Conners Global Index Parent (CGI-P) (30mg vs

20mg; $p=0.0002$). (J Child Adolesc Psychopharmacol, vol 15; in press). We now examine other dopamine polymorphisms.

Methods: 71 ADHD children ages 7-15, confirmed by NIMH DISC-IV-P, were enrolled in this prospective double-blind pharmacogenetic study. Subjects received increasing MPH doses based on serial CGI-P. Dopamine polymorphisms were correlated with treatment outcomes.

Results: ADHD children with dopamine transporter (DAT-1) 9-repeat ($n=24$) required similar stimulant dosing compared to children with no 9-repeats ($n=47$) for a 10-point improvement on CGI-P (24mg vs 25mg; $p=0.99$; power to detect 10mg difference > 95%). Dopamine receptor-4 (DRD4) 120 polymorphism alleles had no effect on treatment outcomes (2 allele present $n=64$: 24mg vs absent 2 allele $n=7$: 28mg; $p=0.51$; power >95%).

Conclusions: Although ADHD children with DRD4-7R allele require 1.5-times more MPH to improve ADHD symptoms, we found no influence on methylphenidate responsiveness based on DAT-1 9-repeat or DRD4 120 status.

This research was funded for Dr. Hamarman by the Elaine Schlosser Lewis Pilot Research Award for Attention Disorders, administered through the American Academy of Child and Adolescent Psychiatry.

References:

1. Hamarman S, Fossella J, Ulger C, Brimacombe M, Dermody J: DRD4 7 Repeat Allele Predicts Methylphenidate Dose Response in Children with Attention Deficit Hyperactivity Disorder: A Pharmacogenetic Study, accepted to Journal of Child and Adolescent Psychopharmacology.
2. Winsberg BG and Cornings D Association of the dopamine transporter gene DAT1 with poor methylphenidate response. JAm Acad Child Adolesc Psychiatry 38 (12); 1474-77, 1999.

NR433 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Efficacy and Safety of Ziprasidone in Youths With Axis I Diagnoses

Supported by Pfizer Inc.

Daniel A. Deutschman, M.D., Department of Psychiatry, Southwest General, 18051 Jefferson Park Road, Suite 106, Cleveland (Middleburg Heights), OH 44130; Douglas H. Deutschman, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the potential efficacy and safety of ziprasidone, as defined by symptom severity and reported adverse events, in the treatment of youths with various Axis I diagnoses.

Summary:

Objective: To assess the safety and efficacy of ziprasidone in youths with various Axis I diagnoses.

Methods: A retrospective review of a three-year, naturalistic study in youths with Axis I diagnoses tracked symptom severity using the Likert and Global Assessment of Functioning (GAF) scales. Improvement from first visit (time ziprasidone was initiated) to last visit (on ziprasidone) was determined using paired *t* tests. Adverse events (AEs) and key variables (eg, ECGs) were monitored.

Results: 109 youths with Axis I diagnoses (43% female, 92% Caucasian, mean age 16 y) received ziprasidone 80 mg/d (median) for ≥ 14 days. Of 107 problems tracked, severities of 21, grouped in seven broad categories (compliance, suicide risk, psychosis, affect, anxiety, behavior, substance abuse), were followed in ≥ 15 patients. Significant improvements ($P<0.001$) in problem severity, measured by Likert scores, occurred for all but substance abuse. The most robust responses were for compliance, suicide risk, psychosis, affect, and behavior. Individual problems also

improved, with strongest responses for medical noncompliance, delusions, self-mutilation, lack of motivation, rage attacks, and suicide. These findings were corroborated by GAF scores. Ziprasidone was well-tolerated.

Conclusion: Ziprasidone's safety and efficacy in youths with Axis I diagnoses strongly suggest a therapeutic role in this population.

References:

1. MacMillan C, Miller TP, Hsin O, Johnson F, Gonzalez-Heydrich J: Ziprasidone in pediatric patients: efficacy and tolerability. Presented at the 44th Annual New Clinical Drug Evaluation Unit Meeting; June 1-4, 2004; Phoenix, Arizona, USA.
2. Deutschman DA, Deutschman DH: High-dose ziprasidone: efficacy and tolerability in clinical practice. Presented at the 157th Annual Meeting of the American Psychiatric Association; May 1-6, 2004; New York, New York, USA.

NR434 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

The Maintenance of Effectiveness of Concerta in Children With ADHD: An Eight-Month Analysis *Supported by Janssen-Ortho Inc.*

Rosanna Prinzo, HB.Sc., Janssen-Ortho Inc., 19 Green Belt Drive, Toronto, ON M3C 1L9, Canada; Margaret M. Steele, M.D., Carin Binder, M.B.A.

Educational Objectives:

At the conclusion of this session, the participant/reader should be able to evaluate the maintenance of effectiveness of a once daily, long acting stimulant in children with ADHD after eight months of therapy.

Summary:

Objective: To determine whether or not symptomatic remission and overall improvement experienced in an eight-week, open-label effectiveness trial with once daily OROS methylphenidate (Concerta[®]) in ADHD children is maintained in an open-label, six-month follow-on study.

Methods: This was a prospective, open-label trial with DSM-IV-diagnosed ADHD children (based on KSADS and clinical interview), aged 6-12 years inclusive who completed eight months of Concerta treatment.

Results: In this open-label, follow-on study, patients ($n=54$) continued Concerta[®] for an additional six months after completing an eight-week randomized trial. Remission of ADHD symptoms was maintained in 29% of patients with continuing Concerta[®] treatment at every time point measured. Mean change in total SNAP-IV-26 item score continued to reflect statistically significant symptom improvement at every time point measured in this follow-on study, including endpoint. ($p<0.0001$).

Conclusion: These data suggest continuing treatment with once daily OROS methylphenidate (Concerta[®]) offers sustained symptom control in the longer-term treatment of children with ADHD.

References:

1. Wolraich M, Greenhill L, et al: Randomized, controlled trial of OROS methylphenidate Once-a-day in children with attention-deficit/hyperactivity disorder. Pediatrics 2001; 108:4.
2. Swanson JA, Kraemer H, et al: Clinical relevance of the primary findings of the MTA: success rates based on severity of ADHD and ODD symptoms at the end of treatment. J Am Acad Adolesc Psychiatry 2001; 40:2.

NR435 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Effectiveness of Concerta Versus Usual Care IR-MPH on Comorbid ODD Symptoms in Children With ADHD
Supported by Janssen-Ortho Inc.

Rosanna Prinzo, HB.Sc., *Janssen-Ortho Inc., 19 Green Belt Drive, Toronto, ON M3C 1L9, Canada*; Margaret M. Steele, M.D., Carin Binder, M.B.A.

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the clinical usefulness of once daily OROS[®] methylphenidate (Concerta[®]) vs. usual clinical care with IR-MPH in treating ADHD children with comorbid symptoms of oppositional defiant disorder.

Summary:

Objective: To determine the effectiveness and safety of once daily OROS methylphenidate (Concerta[®]) vs. usual clinical care with immediate-release methylphenidate (IR MPH) in treating comorbid oppositional defiant disorder (ODD) symptoms in ADHD children aged 6-12 years inclusive.

Methods: This was an eight-week prospective, parallel group, randomized, open-label trial of 143 children with DSM-IV-diagnosed ADHD (based on KSADS and clinical interview). Post hoc analyses of treatment effects on ODD symptoms were conducted.

Results: ODD symptomatic remission, defined as a mean score of ≥ 1 on each item of the last eight (items 19-26) ODD specific items of the SNAP-IV 26-item scale was statistically significant in favour of Concerta[®] vs. IR-MPH, as early as week 4 and maintained until endpoint ($p=0.004$). Mean change in ODD symptoms on SNAP-IV was statistically significant in the Concerta[®] group vs. IR-MPH group at every post-baseline visit including endpoint. ($p=0.006$). Both Concerta and IR-MPH were well tolerated with a similar side-effect profile.

Conclusion: These data suggest that the once-daily formulation of OROS[®] methylphenidate (Concerta[®]) offers better symptom control in the treatment of comorbid ODD symptoms in children with ADHD, when compared with usual clinical care with IR-MPH.

References:

1. Swanson JA, Kraemer H, et al: Clinical relevance of the primary findings of the MTA: success rates based on severity of ADHD and ODD symptoms at the end of treatment", *J Am Acad Adolesc Psychiatry* 2001; 40:2.
2. Wolraich M, Greenhill L, et al: Randomized, controlled trial of OROS methylphenidate once-a-day in children with attention-deficit/hyperactivity disorder. *Pediatrics* 2001; 108:4.

NR436 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Long-Term Effectiveness and Safety of Concerta in Children With ADHD: A Six-Month Study
Supported by Janssen-Ortho Inc.

Margaret M. Steele, M.D., *Janssen-Ortho Inc., 19 Green Belt Drive, Toronto, ON M3C 1L9, Canada*; Rosanna Prinzo, HB.Sc., Carin Binder, M.B.A.

Educational Objectives:

At the conclusion of this session, the reader should be able to evaluate the long-term effectiveness and safety of once daily OROS methylphenidate (Concerta[®]) in ADHD children aged 6-12 years.

Summary:

Objective: To determine the long-term effectiveness and safety of once daily OROS methylphenidate (Concerta[®]) in children aged 6-12.

Methods: This was a prospective, open-label trial of 109 children with DSM-IV-diagnosed ADHD (based on KSADS and clinical interview). Children who completed a previous eight-week, open-label study randomizing patients to either Concerta[®] or IR-MPH were invited to participate in an open-label extension trial. At the beginning of this six-month study, children could continue taking the medication they were randomized to in the eight-week trial or switch to the other treatment arm.

Results: N=54 patients continued on Concerta[®] treatment in this follow-on study (CON/CON group) and N=55 patients switched to Concerta[®] from IR-MPH therapy (IR-MPH/CON group). At Month 6, 52% of the CON/CON group met criteria for remission of ADHD symptoms as defined as a score of ≤ 1 on each item of the 18 item SNAP-IV. As well, 30% of the IR-MPH/CON group met remission criteria at month 6. Most frequent AEs reported were influenza-like symptoms (21%), insomnia (13%), and headache (12%).

Conclusion: These data suggest that in long-term treatment with once-daily OROS methylphenidate (Concerta[®]), symptomatic remission continues to be achievable.

References:

1. Swanson JA, Kraemer H, et al: Clinical Relevance of the Primary Findings of the MTA: Success Rates Based on Severity of ADHD and ODD Symptoms at the End of Treatment. *J Am Acad Adolesc Psychiatry* 2001; 40:2.
2. Wolraich M, Greenhill L, et al: Randomized, controlled trial of OROS methylphenidate once-a-day in children with attention-deficit/hyperactivity disorder. *Pediatrics* 2001; 108:4.

NR437 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Effectiveness of Concerta Versus Twice or Thrice Daily IR-MPH in Children With ADHD
Supported by Janssen-Ortho Inc.

Margaret M. Steele, M.D., *Janssen-Ortho Inc., 19 Green Belt Drive, Toronto, ON M3C 1L9, Canada*; Rosanna Prinzo, HB.Sc., Carin Binder, M.B.A.

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the usefulness of once daily OROS methylphenidate (Concerta[®]) vs. BID or TID dosing with IR-MPH in treating children with ADHD.

Summary:

Objective: To determine the effectiveness and safety of once daily OROS methylphenidate (Concerta[®]) vs. BID or TID dosing with immediate-release methylphenidate (IR-MPH) in treating ADHD children aged 6-12 years inclusive.

Methods: This was a prospective, parallel group, randomized, open-label trial of 143 children with DSM-IV-diagnosed ADHD (based on KSADS and clinical interview). 61% and 38% of children randomized to the IR-MPH group were prescribed IR-MPH at a TID and BID frequency, respectively. Response was analyzed based on BID vs. TID IR-MPH vs. Concerta[®].

Results: Remission of ADHD symptoms defined as a score of ≤ 1 on each item of the 18-item SNAP-IV assessment, was statistically significant in favour of Concerta[®] vs. BID or TID dosing of IR-MPH at endpoint. ($p=0.0001$, $p<0.05$ respectively). At week 8, the Concerta[®] treatment group experienced a statistically significant reduction in symptoms as noted on the IOWA Conners rating scale vs. the BID or TID IR-MPH treatment groups, respectively ($p=0.006$, $p=0.02$).

Conclusion: These data suggest that clinicians should aim for symptomatic remission as part of their standard practice. More patients on Concerta[®] achieved remission than BID or the gold standard of TID IR-MPH.

References:

1. Wolraich M, Greenhill L, et al: Randomized, controlled trial of OROS methylphenidate once-a-day in children with attention-deficit/hyperactivity disorder. *Pediatrics* 2001; 108:4.
2. Swanson JA, Kraemer H, et al: Clinical relevance of the primary findings of the MTA: success rates based on severity of ADHD and ODD symptoms at the end of treatment. *J Am Acad Adolesc Psychiatry* 2001; 40:2.

NR438 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **GAD Is Associated With Higher Health Care Costs and Lost Productivity**

Nancy Brandenburg, Ph.D., *Pfizer Inc., 235 East 42nd Street, New York, NY 10017*; Stella Chang, M.P.H., Tami L. Mark, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should gain a greater appreciation of the direct and indirect costs associated with generalized anxiety disorder.

Summary:

Objective: To understand the prevalence of comorbidities, health care utilization, costs, and worker productivity among patients with and without generalized anxiety disorder.

Methods: The 1999-2003 MarketScan claims databases of >3 million individuals (annually) were used to identify patients with diagnoses of *DSM-IV* GAD and a demographically-matched control sample. A 12-month study period was used to identify comorbidities and summarize utilization, expenditures, absence, and short-term disability (STD).

Results: The prevalence of the following conditions was significantly ($p < 0.001$) higher among the 13,836 GAD subjects than the 89,971 controls: gastrointestinal disorders (19% vs. 12%), genitourinary disorders (40% vs. 32%), cardiovascular disease (10% vs. 7%), and chronic pain (40% vs. 20%). Mean costs for GAD patients were twice as high as controls (\$6,295 vs. \$3,156, $p < 0.001$). GAD patients' mental health costs (\$2,031) accounted for only some of this difference. The largest differences in mean costs were for office visits (\$389 VAD vs. \$208 control, $p < 0.0001$) and pharmacy-dispensed drugs (\$1,557 vs. \$652, $p < 0.001$). Among the subset of patients with productivity data, GAD patients had significantly higher STD days than controls (15.63 vs. 6.69), resulting in higher mean indirect costs (\$2,253 vs. \$934).

Conclusion: GAD is associated with a significant burden of physical symptoms and serious impairment.

References:

1. Hunkeler EM, Spector WD, Fireman B, Rice DP, Weisner C: Psychiatric symptoms, impaired function, and medical care costs in an HMO setting. *Gen Hosp Psychiatry* 2003; 25:178-184.
2. Wittchen HU, Kessler RC, Beesdo K, Krause P, Hofler M, Hoyer J: Generalized anxiety and depression in primary care: prevalence, recognition, and management. *J Clin Psychiatry* 2002; 63(suppl 8):24-34.

NR439 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Quetiapine Efficacy in Bipolar Adolescents With Depressive Symptoms**

Supported by AstraZeneca Pharmaceuticals

Melissa P. DelBello, M.D., *Department of Psychiatry and Pediatrics, University of Cincinnati, College of Medicine, 231 Albert Sabin Way, P.O. Box 670559, Cincinnati, OH 45267-*

0559; Caleb M. Adler, M.D., Drew H. Barzman, M.D., Stephen M. Strakowski, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that quetiapine reduces symptoms of depression and suicidal ideation in adolescents with bipolar disorder.

Summary:

Objectives: Investigate the efficacy of quetiapine in reducing depressive symptoms and suicidal ideation in bipolar adolescents.

Methods: Three studies measured change in Children's Depression Rating Scale or CGI-I score with quetiapine monotherapy/combination therapy in 132 bipolar adolescents. Thirty individuals (70% mixed state) received quetiapine with divalproex or divalproex alone, 50 (94% mixed state) received quetiapine or divalproex, and 22 (mixed state or at familial risk for bipolar disorder [BD]) received quetiapine alone for six, four, and 12 weeks, respectively.

Results: Quetiapine (mean 423 mg/day) with divalproex reduced depressive symptoms more than divalproex alone over six weeks ($P < 0.004$), decreasing mean CDRS score from 50 to 24 ($P < 0.0001$). Quetiapine (mean 412 mg/day) for four weeks decreased mean CDRS score from 52 to 25 ($P < 0.0001$). Quetiapine (to 600 mg/day) for 12 weeks elicited a response (CGI-I score ≤ 2) in 80% of 10 adolescents with mood disorder other than BD I and in 83% of 12 adolescents with BD I at familial risk for BD. On pooling the 62 bipolar adolescents experiencing major depression, mean CDRS suicide item score decreased from 3.0 to 1.3 ($P < 0.0001$).

Conclusions: Quetiapine reduces depressive symptoms and suicidal ideation in adolescents with, or at familial risk for, BD.

References:

1. DelBello MP, Schwiers M, Rosenberg HL, Strakowski SM: A double-blind, randomized, placebo-controlled study of quetiapine as adjunctive treatment for adolescent mania. *J Am Acad Child Adolesc Psychiatry* 2002; 41:1216-1223.
2. Calabrese J, et al: Double-blind, placebo-controlled study of quetiapine in bipolar depression. Poster presented at 17th Annual U.S. Psychiatric & Mental Health Congress, November 18-21, 2004. San Diego, California.

NR440 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Disability in Panic Disorder**

Sara Martinez-Barrondo, Ph.D., *Department of Psychiatry, University of Oviedo, Julian Claveria 6-3, Oviedo 33006, Spain*; Pilar A. Saiz, Ph.D., Maria P. G-Portilla, Ph.D., Teresa Bascaran, M.D., Luiz Jimenez-Trevino, M.P.H., Manuel Bousono-Garcia, M.D., Julio B. Bobes, M.D.

Educational Objectives:

At the conclusion of this presentation, participants should be able to recognize the relationship between panic disorder and disability.

Summary:

Objective: To evaluate disability in panic disorder (PD) according to the severity of PD.

Subjects and methods: Patients: 92 PD patients (ICD-10 criteria) were included. Assessment: Bandelow Panic and Agoraphobia Scale (PAS); World Health Organization Psychiatric Disability Assessment Schedule version II of 36 items (WHODAS-II).

Results: Mean age: 35.87 years old (12.38 SD); 30.4% males; mean age of PD onset: 30.98 years (10.47 SD); years of PD evolution: 4.34 (7.91 SD). Mean PAS: 18.02 (8.84 SD). Mean WHODAS-II: A1 or concentration: 21.60 (22.31 SD); A2 or mobility: 15.54 (20.98 SD); A3 or self care: 11.96 (16.38 SD); A4 or

social participation: 13.59 (19.25 SD); A5a or household jobs: 16.92 (26.22 SD); A5b or work loss days: 40.79 (44.52); and A6 or social discrimination and family burden: 26.70 (18.35 SD). All disability domains (WHODAS-II) had inverse correlation with PD severity (PAS total score) ($p = 0.000$). The strongest correlations were observed in A1 ($r = 0.563$), and A6 ($r = 0.568$).

Conclusions: The most affected domains of disability are work loss days, social discrimination and family burden, and concentration. The greater the severity of illness is, the greater the disability is, especially concentration, and social discrimination and family burden.

References:

1. Rubin HC, Rapaport MH, Levine B, Gladsjo JK, Rabin A, Auerbach M, et al: Quality of well being in panic disorder: the assessment of psychiatric and general disability. *J Affect Disord* 2000; 57:217-221.
2. The ESEMeD/MHEDEA 2000 investigators. Disability and quality of life impact of mental disorders in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. *Acta Psychiatr Scand* 2004; 109:38-46.

NR441 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Chart Review Study of the Effects of Atomoxetine on Objective Measures of Activity and Attention

Nikolaos Fourligas, Ph.D., *McLean Hospital, 115 Mill Street, Belmont, MA 02478*; Martin H. Teicher, M.D., Thomas H. Moseley, M.D., Suzy Palmer, R.N., Nelson Handal, M.D., Jay Franklin

Educational Objectives:

At the end of this presentation, the participant should have a clear understanding of the effects of non-stimulant versus stimulant drug treatment of ADHD.

Summary:

Atomoxetine has become an important medication for children with ADHD. Efficacy data emerged from double-blind, placebo-controlled trials using rating instruments. Data are lacking on the effects of atomoxetine on instrumented objective measures of activity and attention in children, and no data are available comparing atomoxetine with stimulants on these measures. Children with ADHD were identified by chart review who had been clinically assessed off all medications, and reassessed on atomoxetine, using the McLean Motion Attention Test (M-MAT), which employs a motion analysis system to precisely track the child's pattern of movement while performing a monotonous but demanding computerized vigilance test (STAR-CPT). Twelve subjects (10M/2F; 10.0 ± 1.6 yr.) were identified who met these criteria. Eight of these subjects (6M/2F; 10.2 ± 1.6 yr.) had also been assessed on a stimulant. Atomoxetine was associated with a 56% reduction in seated activity (movement area, $p=0.0006$). Atomoxetine was also associated with a 25% reduction in CPT response variability ($p=0.014$). Atomoxetine and stimulants produced equivalent average improvement. Four subjects improved more on stimulant, three on atomoxetine, and one had a split response (better motor improvement on stimulant, better attentional enhancement on atomoxetine). Overall, therapeutic response to atomoxetine can be readily detected and quantified using instrumented objective measures. Although atomoxetine and stimulants were equally effective on average, children responded preferentially to one.

References:

1. Spencer T, et al: Results from 2 proof-of-concept, placebo-controlled studies of atomoxetine in children with attention-deficit/hyperactivity disorder. *J Clin Psychiatry* 2002; 63: 1140-7

2. Teicher MH, Ito Y, Glod CA, Barber NT: Objective measurement of hyperactivity and attentional problems in ADHD. *J Am Acad Child Adolesc Psychiatry* 1996; 35: 334-42.

NR442 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Is There a Therapeutic Window for Methylphenidate in Children With ADHD

Supported by Behavioral Diagnostic Company

Martin H. Teicher, M.D., *Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02478*; Ann M. Polcari, R.N., Mary Foley, R.N., Elizabeth Valente, M.A., Cynthia McGreenery, M.A., Gordon McKay, Ph.D., Kamal Midha, Ph.D., Susan Andersen, Ph.D.

Educational Objectives:

At the end of this presentation, participants should have a clearer understanding of the relationship between blood levels and therapeutic response to methylphenidate.

Summary:

Methylphenidate (MPH) reduces ADHD symptoms and acts predominantly by inhibiting the dopamine transporter (DAT). Volkow and colleagues reported that 10ng/ml d-MPH in plasma resulted in 75% occupancy of DAT in young adults, and that higher levels did not produce any greater degree of occupancy. This suggests that MPH might lose specificity at levels beyond the minimum plateau polar, and this could represent the peak of a therapeutic window. To test this hypothesis, blood-levels (GC-MS) and objective behavioral response to MPH were evaluated in 38 boys (9-12 years) with ADHD, combined subtype. Each child received a total daily dose of 1mg/kg MPH. Subjects were tested immediately prior to their first dose and every hour thereafter (for 12 hours) with a five-minute CPT test coupled to a motion analysis system to track their degree of hyperactivity (Telcher et al 1996). Best response occurred at a mean d-MPH level of 11.3ng/ml, producing a 68% reduction in position changes versus baseline ($p 0.0001$). Maximum plasma levels averaged 14.2ng/ml. Fidgeting at peak level was significantly better than at baseline (44% reduction; $p 0.0001$), but 77% worse than at optimal level ($p 0.0001$). Optimal plasma level for CPT accuracy was 11.0ng/ml. These findings suggest that optimal response to MPH occurs at about the minimum plasma concentration needed for maximal occupancy of DAT.

References:

1. Teicher MH, Ito Y, Glod CA, et al: Objective measurement of hyperactivity and attentional problems in ADHD. *J Am Acad Child Adolesc Psychiatry* 1996; 35(3):334-42.
2. Volkow ND, Wang GJ, Fowler JA, et al: Dopamine transporter occupancies in the human brain induced by therapeutic doses of oral methylphenidate. *Am J Psychiatry* 1998; 155(10):1325-31.

NR443 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Open-Label Trial of Aripiprazole in Tourette's Syndrome Children: Young Adults

Supported by Bristol-Myers Squibb

Drake Duane, M.D., *Institute for Developmental Behavioral Neurology, 10210 North 92nd Street Suite 300, Scottsdale, AZ 85258*; Glenn E. Heimbarger, B.S.

Educational Objectives:

At the conclusion of this session, the participant should be able (1) To illustrate an open-label multidimensional investigation of pharmacotherapy (aripiprazole) for the multiple manifestations of Tourette Syndrome, (2) to demonstrate differential effectiveness

of aripiprazole pharmacotherapy for the various symptoms of Tourette syndrome.

Summary:

Objective: To evaluate the effects of aripiprazole on tics, behavior, cognition, and mood in late-childhood to young-adulthood Tourette syndrome (TS).

Method: Ten TS patients, nine male, mean age 17-years (range 11-32) were placed on aripiprazole 2.5 mg/d eventually up to 15 mg/d (mean 9.25 mg/d) with IRB approved informed consent. Initially, concomitant medications were continued (seven on SSRI, three on other atypical neuroleptics, and three on psychostimulants). Patients were monitored for eight weeks at baseline, week 4 and 8 personally; weekly by telephone. Test comparisons baseline/week 8: Behavior-DSM-IV Rating Scale (DSM-IV), Achenbach Child Behavior Checklist (CBCL); Tics-Yale Tic Rating Scale (TRS); Cognition-Test of Variables of Attention (TOVA), 3-Letter Cancellation Test (LCT), Digit Span (DS); Mood-Children's Depression Index (CDI), CBCL, Hamilton Depression Scale (Ham D).

Results: Improved/Total: Behavior-DSM-IV 6/10 attention, 4/10 hyperactivity, 6/10 impulsivity, CBCL 6/8 attention; Tics-7/10 simple motor, 6/10 complex motor, 5/10 simple phonic, 4/10 complex phonic. Improved/Abnormal: Mood-CDI 3/5, CBCL obsessive 4/5, Ham D 0/1; Cognition-LCT 2/3, DS 3/3, TOVA 2/2. Adverse Effects: Hematology/Chemistry 0/10, 2 transient nausea, 3 > 5 percentile weight increase, 1 > 5 percentile weight decrease.

Conclusion: Aripiprazole is a safe, effective treatment for TS tics, behavior and cognition.

References:

1. Popper C, Steingard R: Disorders usually first diagnosed in infancy, childhood, or adolescence, in American Psychiatric Press Textbook of Psychiatry, 2nd Edition. Washington, DC, American Psychiatric Press, 1995; pp729-832.
2. Lombroso P, et al: Risperidone treatment of children and adolescents with chronic disorders: a preliminary report. J Am Acad Child Adolesc Psychiatry 1995; 34: 1147-1152.

NR444 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

AD(H)D, Prescribed Methamphetamine: Frequency, Cognitive, and Behavior Effects

Supported by Ovation Pharmaceuticals, Inc.

Glenn E. Heimburger, B.S., *Institute for Developmental Behavioral Neurology, 10210 North 92nd Street Suite 300, Scottsdale, AZ 85258*; Drake Duane, M.D., Tam T. Chu, B.S.

Educational Objectives:

At the conclusion of this session, the participant should be able to: (1) evaluate the frequency with which AD(H)D symptoms require the consideration of alternative stimulant (methamphetamine) pharmacotherapy, (2) determine the differential effectiveness and safety of alternative stimulant pharmacotherapy (methamphetamine) on the varied manifestations of AD(H)D.

Summary:

Objective: To determine from a referral center database, the frequency of methamphetamine (MAMph) trial/subsequent prescription and effects on cognition/behavior.

Methods: Retrospective analysis of 521 subjects (437 male, mean age 13 years) meeting DSM-IV AD(H)D criteria who underwent acute trials of psychostimulants for: frequency of MAMph trials, if so acute effects on cognition, and if subsequent sustained use for behavioral effects. Tests employed included: DSM-IV Rating Scale, Achenbach CBCL, Adult Retrospective ADHD Rating Scale; Rey Auditory Verbal Learning Test (AVLT), Letter Cancellation Test (LCT), Digit Span (DS), Conners' CPT, TOVA, Wisconsin

Card Sorting Test (WCST); Kovacs Child Depression Index, MMPI-2; Pupillometry for wakefulness.

Results: 14 of 521 AD(H)D subjects (2.7%) underwent MAMph trials (mean test dose 7.5 mg) because of incomplete response to other psychostimulants (11 male, 9 < 16 years of age). Five continued MAMph > 6 months (mean dose 20 mg/d). Acutely improved cognition: AVLT-3, LCT-10, DS-3, CPT-5, TOVA-4, WCST-5; improved wakefulness-5. Acute worsened cognition-3. Subsequent improved behavior: attention-5, hyperactivity-4, impulsivity-3; improved depression-0. In all, prior to prescribing confirmed absent family history substance abuse. No case of patient medication abuse was observed.

Conclusion: In select, otherwise refractory AD(H)D subjects, MAMph may be an effective treatment alternative for cognition/alertness.

References:

1. Wender P: Methamphetamine in child psychiatry. J Child Adolesc Psychopharmacol 1993; 3:4-6.
2. Elia J, et al: Treatment of Attention Deficit-Hyperactivity Disorder. NEJM, 1999; 34(10):780-788.

NR445 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Perceived Response to Pharmacotherapy for OCD**

Maria C. Mancebo, Ph.D., *Butler Hospital, 345 Blackstone Boulevard, Providence, RI 02906*; Jane L. Eisen, M.D., Ingrid R. Dyck, M.P.H., Anthony Pinto, Ph.D., Steven A. Rasmussen, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to: 1. demonstrate knowledge of pharmacological interventions for OCD 2. recognize impact of patient's perceived response on the course of pharmacotherapy.

Summary:

Objectives: While the efficacy of pharmacological treatments for OCD is well documented, less is known about the actual treatments received in clinical settings and the effectiveness of these treatments outside of controlled clinical trials. The primary aim of this study was to describe pharmacological interventions and perceived response to treatments among individuals with a primary diagnosis of OCD.

Method: All participants were enrolled in a naturalistic, prospective study of course in OCD and were assessed with rater-administered instruments as part of their baseline interview. The sample consisted of 179 individuals who reported at least one year of treatment for OCD. Perceived response to previous treatments was assessed using Clinical Global Impression Scale-patient version.

Results: Almost all participants (n=164, 92% of sample) reported receiving at least one trial of a serotonin reuptake inhibitor (SRI). Less than half of these participants (n=77) reported a significant response to SRIs, of which 44 (26% of sample) reported a response after multiple trials and 34 (21% of sample) after a single trial. Of the 53% (n=87) that reported no response to SRIs, 27 (16% of sample) were had multiple trials of an SRI as well as at least one trial of a neuroleptic.

Conclusion: These results suggest that a large proportion of patients do not perceive medications to have produced significant improvement in their symptoms. Clinical implications and potential impact on medication adherence are discussed.

References:

1. Greist J, Jefferson J, Kobak K, Katelnick D, Serlin R: Efficacy and tolerability of serotonin transport inhibitors in obsessive-

compulsive disorder: a meta-analysis. *Arch Gen Psychiatry* 1995; 52(1):53-60.

2. Pallanti S, Hollander E, Bienstock C, Koran L, Leckman J, Marazziti D, Pato M, Stein D, Zohar J: Treatment non-response in OCD: methodological issues and operational definitions. *Int J Neuropsychopharmacol* 2002; 5(2):181-91.

NR446 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Quality of Life in OCD

Jane L. Eisen, M.D., *Butler Hospital, Brown University, 345 Blackstone Boulevard, Providence, RI 02906*; Maria C. Mancebo, Ph.D., Anthony Pinto, Ph.D., Maria E. Pagano, Ph.D., Steven A. Rasmussen, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the impact of OCD on psychosocial functioning and quality of life.

Summary:

Background: In the past decade, tremendous progress has been made in the treatment of obsessive compulsive disorder (OCD) with pharmacotherapy and cognitive-behavioral therapy. Despite these advances, many individuals with OCD have substantial impairment in their quality of life, including their ability to function and their subjective satisfaction with their life. In this study, domains of quality of life in subjects with OCD were assessed using reliable self-report and rater-administered measures.

Method: Assessments of quality of life were obtained from 197 adult subjects as part of a larger baseline interview for a five-year prospective, naturalistic study of OCD course. Two self-reports (the Quality of Life Enjoyment and Satisfaction Questionnaire and the Social Adjustment Scale-Self Report) and a number of rater-administered measures including the Range of Impaired Functioning Tool (LIFE-RIFT) were administered.

Results: Quality of life was significantly impaired compared with published community norms with large effect sizes found for 14 of the 15 domains assessed. Correlations between all quality of life measures and the Yale Brown Obsessive Compulsive Scale total score were significant, ranging from 0.40 to 0.77. Insight as measured by the Brown Assessment of Beliefs Scale was significantly correlated with these measures as well, although more modestly ($r = 0.22$ to $r = 0.37$). Severity of OCD and depressive symptoms were significant predictors of impairment in quality of life (R -Square = .54).

Conclusions: These findings indicate that all aspects of quality of life are markedly affected in individuals with OCD and are associated with OCD and depression severity.

References:

1. Masellis M, Rector NA, Richter MA: Quality of life in OCD: differential impact of obsessions, compulsions, and depression comorbidity. *Can J Psychiatry* 2003; 48(2), 72-7.
2. Koran LM, Thienemann ML, Davenport R: Quality of life for patients with obsessive-compulsive disorder. *Am J Psychiatry* 1996; 153, 783-788.

NR447 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Regional Brain Metabolism in Panic Disorder During Cognitive-Behavioral Therapy

Jan Prasko, M.D., *Prague Psychiatric Centre, Ustavni-8, Prague 8 18103, Czechoslovakia*; Jiri Horacek, Ph.D., Richard Zalesky, Miloslav Kopecek, M.D., Tomas Novak, M.D., Beata Paskova, M.D., Lucie Skrdlantova, M.D.

Summary:

The goal of our study was to identify brain structures in patients with panic disorder that show changes in ^{18}F FDG PET during the treatment with cognitive-behavioral therapy or antidepressants. Twelve patients with panic disorder were studied with ^{18}F FDG PET scanning during resting state. After PET examination patients were randomly assigned to either cognitive-behavioral group (six patients) or antidepressants group (six patients). After three months, ^{18}F FDG PET examination was repeated. Psychopathology was assessed using rating scales HAMA, CGI, and PDSS. Data were analyzed using software for statistical parametric mapping (SPM99).

The scores of rating scales decreased in both groups. Changes of ^{18}F FDG uptake in the *pharmacotherapy group*: decreases were found in a priori hypothesized regions in the right hemisphere, in superior, middle, medial and inferior frontal gyrus, superior and middle temporal gyrus, and increases were detected in a priori hypothesized regions, mainly in the left hemisphere in medial and middle frontal gyrus, superior, middle, and transverse temporal gyrus. Changes of ^{18}F FDG uptake in the *CBT group*: decreases were found in a priori hypothesized regions of right hemisphere in inferior temporal gyrus, superior and inferior frontal gyrus, and increases were detected in a priori hypothesized region, mostly in the left hemisphere: inferior frontal gyrus, middle temporal gyrus and insula. We did not detect changes in ^{18}F FDG uptake in limbic region (hippocampus, parahippocampal gyrus and amygdala).

Supported by research grant IGA NF 7565-3.

References:

1. Baxter LR Jr, Phelps ME, Mazziotta JC, Guze BH, Schwartz JM, Selin CE: Local cerebral glucose metabolic rates in obsessive-compulsive disorder. A comparison with rates in unipolar depression and in normal controls. *Arch Gen Psychiatry* 1987; 44:211-218.
2. Pašková B, Praško JP, Horaček J, Záleský R, Kopeček M, Škrdlantová L, et al: Identification of relation between ^{18}F FDG PET uptake and severity of symptomatology in panic disorder. *Psychiatrie* 2003; 7(3):6-9.

NR448 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Multivariate Model of Risk for Same-Sex Behaviors Among Incarcerated Adolescents

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Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the prevalence of risk behaviors among incarcerated adolescents; understand the necessity of multivariate models to direct prevention efforts; understand the relative risk for same-sex sexual behaviors associated with specific factors.

Summary:

Background: Incarcerated adolescents are at particularly high risk for a spectrum of unfavorable outcomes that encompass recidivism, mental disorders, substance abuse, sexual abuse, and sexually transmitted disease including HIV. Among incarcerated males, those who have sex with same-sex partners have even greater health risks.

Objective: To investigate correlates of a history of same-sex sexual behaviors among incarcerated male adolescents to help focus primary and secondary prevention efforts.

Method: Medical, psychosocial, and forensic information was obtained from a statewide database, maintained by the state department of juvenile justice. Multivariate logistic regression models

determined relative risk [Exp (B)] for having engaged in same-sex sexual behaviors.

Results: Among the 2,294 incarcerated adolescents in the sample, 55 (2.4%) had reported to multiple sources typically engaging in same-sex sexual behaviors. Those with a history of sexual abuse were more than eight times more likely to have engaged in same-sex sexual behaviors [Exp(B)=8.55; p<.001]. No family history or educational variables increased risk, but white race was associated with elevated risk [Exp(B)=1.78; p=.056] as was history of use of antidepressant medication [Exp(B)=1.72; p=.09] and a diagnosis of ADHD [Exp(B)=1.52; p=.18].

Conclusions: Multivariate models of large data sets with appropriately large samples can help to identify strong risk factors for specific behavioral risks among incarcerated adolescents.

References:

1. Kalichman SC, Gore-Felton C, Benotsch E, Cage M, Rompa D. Trauma symptoms, sexual behaviors, and substance abuse: Correlates of childhood sexual abuse and HIV risks among men who have sex with men. *Journal of Child Sexual Abuse*. 13(1):1-15, 2004.
2. Otto-Salaj LL, Gore-Felton C, McGarvey E, Canterbury, RJ: Psychiatric functioning and substance use: Factors associated with HIV risk among incarcerated adolescents. *Child Psychiatry & Human Development* 2002; 33(2): 91-106.

NR449 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Escitalopram Treatment of Trichotillomania *Supported by Forest Laboratories, Inc.*

Kishore M. Gadde, M.D., *Duke University Medical Center, Box 3292, DUMC, Durham, NC 27710*; Marko S. Foust, M.S., H. Ryan Wagner, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to learn new information regarding efficacy of escitalopram in the treatment of trichotillomania.

Summary:

Objective: To examine the effect of escitalopram treatment on symptoms and behaviors associated with trichotillomania.

Method: Twenty patients meeting DSM-IV criteria for trichotillomania were treated with open-label escitalopram in doses ranging 10-30 mg/d for 12 weeks. Responders were prospectively defined as those meeting *both* of the following criteria: (1) CGI-Improvement score of 1 or 2 (very much improved or much improved), and (2) at least 50% decrease in symptoms as assessed by the Trichotillomania Severity Scale (TSS).

Results: Twelve subjects completed the full 12-week study treatment. Eight subjects were judged to be responders using pre-defined criteria. Responders also demonstrated improvement on other trichotillomania rating scales administered in the study as secondary outcome measures. Further, improvement of co-morbid depressive and anxiety symptoms was observed. Adverse effects were mild.

Conclusion: Escitalopram treatment for 12 weeks led to significant improvement of symptoms of trichotillomania in some patients in this preliminary study.

References:

1. Guy W: ECDEU Assessment Manual for Psychopharmacology. Publication ADM 76-338. National Institute of Mental Health, Rockville, Md, 1976:218-222.
2. Swedo SE, Leonard HL, Rapoport JL, et al: A double-blind comparison of clomipramine and desipramine in the treatment of trichotillomania (hair pulling). *N Engl J Med* 1989; 321:497-501.

NR450 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Gender and Comorbidities in Children and Adolescents with ADHD

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Educational Objectives:

At the conclusion of this session, the participant should be able to learn about gender differences in comorbidities of children and adolescents with ADHD.

Summary:

Objective: To study the gender differences in comorbidities of children and adolescents with ADHD.

Methods: The study involved 433 children and adolescents (age range 2-18) assessed by DSM-IV diagnostic criteria as having ADHD. Offord-Boyle Ontario Child Health Study Based Parent and Teacher Screening and Rating Scales were used in reviewing comorbid disorders. DuPaul ADHD Rating scale aided the diagnosis, 1.5 SD above the mean of the age and gender norms was expected.

Results: The most common comorbidity in girls (52.53%) and boys (58.98%) was oppositional defiant disorder. Other common comorbid disorders in boys were conduct disorder (15.27%), anxiety disorder (11.38%), speech disorder (10.18%), PDD (4.79%), and tick disorder (4.49%). Statistically significant differences in comorbidities in boys and girls were observed in anxiety disorders (16.16% vs. 11.38%), dysthymic disorder (8.08% vs. 3.89%), obesity (7.07% vs 1.8%), PDD (6.06% vs. 4.79%), MDD (5.05% vs. 1.8%), developmental delay (5.05% vs. 0.9%) and elimination disorders (5.05% vs. 1.5%). Boys in comparison to girls were diagnosed more with ODD (58.98% vs. 52.53%), conduct disorder (15.27% vs. 11.11%) and speech disorder (10.18% vs. 5.05%).

Conclusion: All children with ADHD should be screened for associated disorders since the treatment with different comorbidity require modifications in treatment.

References:

1. DuPaul GJ, Power TJ, Anastopoulos AD, Reid R: ADHD Rating Scale-IV: Checklists, Norms and Clinical Interpretation. Guilford Press 1998.
2. Turgay A, Ansari R, Zafar M, and the Scarborough Hospital ADHD Institute Study Group: ADHD subtypes change dramatically with age and gender. *John Hopkins University School of Medicine Advanced Studies in Medicine* 2002; 2:930-931.
3. Boyle MH, Offord DR, Racine et al: Evaluation of the revised Ontario Child Health Study Scales. *Journal of Child Psychiatry* 34:189-213.

NR451 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Executive Dysfunctions in Children With ADHD as Reported by Teachers

Atilla Turgay, M.D., *Department of Psychiatry, Scarborough Hospital, 3030 Birchmount Road, Toronto, ON M5G 2C4, Canada*; Daniella Mares, M.A., Alan McLuckie, Wendy Carter, Ph.D., Melissa Rowbotham, M.Ed., David Ng, M.D., Michael Schwartz, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the use of BRIEF Teacher Rating Scale in the evaluation of cognitive dysfunctions.

Summary:

Objective: To examine teacher reports of executive dysfunctions of children diagnosed with attention-deficit/hyperactivity disorder (ADHD).

Method: Clinical sample consisted of 167 children (ages 5-15); an ADHD inattentive group (N=60) and ADHD combined group (N=101). Executive functioning was measured using the teacher version of the Behavior Rating Inventory of Executive Function (BRIEF), which is comprised of Behavior Regulation Index (BRI), Metacognition Index (MI), and Global Executive Composite (GEC).

Results: GEC revealed that 71% of the entire sample fell within the abnormally elevated range of functioning. 65% of the inattentive group and 75% of the combined group also fell within the abnormally elevated range. T-test analysis has revealed that the difference between the inattentive and the combined groups approached significance for the BRI $t(159) = 1.97, p = .05$. Due to the presence of ODD, the combined group compared with the inattentive group showed greater dysfunction with the behavior regulations of inhibition and emotional control.

Conclusion: The majority of children with ADHD experience significant executive dysfunctions, as reported by teachers. This study also revealed that the BRIEF is highly sensitive to both the underlying impairments associated with ADHD and to the presence of behavioral difficulties consistent with the DSM-IV diagnosis of ODD.

References:

1. Gioia GA, Isquith PK, Guy SC, & Kenworthy L: Behavior Rating Inventory of Executive Function. Professional Manual. Odessa, FL: Psychological Assessment Resources, 1996.
2. Barkley RA: Attention-Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment 2nd Ed. New York: The Guilford Press, 1998.

NR452 Tuesday, May 24, 3:00 p.m.-5:00 p.m. Executive Dysfunctions in Children With ADHD as Reported by Parents

Atilla Turgay, M.D., *Department of Psychiatry, Scarborough Hospital, 3030 Birchmount Road, Toronto, ON M5G 2C4, Canada*; Daniella Mares, M.A., Alan McLuckie, Wendy Carter, Ph.D., David Ng, M.D., Michael Schwartz, Ph.D., Jeffery Landine, Ph.D.

Educational Objectives:

At the conclusion of this session, the participants should be able to describe the use of BRIEF Parent Rating Scale in the evaluation of cognitive dysfunctions.

Summary:

Objective: To examine parent reports of executive dysfunctions of children diagnosed with attention-deficit/hyperactivity disorder (ADHD).

Method: Clinical sample consisted of 180 children (ages 5-15): an ADHD inattentive group (N=65) and ADHD combined (N=109). Executive functioning was measured using the parent version of the Behavior Rating Inventory of Executive Function (BRIEF), which is comprised of Behavior Regulation Index (BRI), Metacognition Index (MI), and Global Executive Composite (GEC).

Results: GEC revealed that 62% of the entire sample fell within the abnormally elevated range of functioning. 54% of the inattentive group and 66% of the combined group also fell within the abnormally elevated range. Analysis of variance revealed that the difference between the inattentive and combined groups was significant for the BRI $F(2,171) = 6.23, p < .05$. The combined group, compared with the inattentive group, showed greater dysfunction

with the behavior regulations of inhibition and organization of materials.

Conclusion: The majority of both inattentive type and combined type experienced significant executive dysfunctions, as reported by parents. Parents are able to perceive the key underlying meta-cognitive impairments associated with ADHD, as well as being attuned to the behavior regulation dysfunctions associated with ADHD combined type.

References:

1. Gioia GA, Isquith PK, Guy SC, & Kenworthy L: Behavior Rating Inventory of Executive Function: Professional Manual. Odessa, FL: Psychological Assessment Resources, 1996.
2. Barkley RA: Attention-Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment 2nd Ed. New York: The Guilford Press, 1998.

NR453 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

A DSM-IV Based Adult ADHD Rating Scale: Validity and Reliability Data

Sennur Gunay, M.A., *Department of Psychology, Bakirkoy Hospital, Bakirkoy, Istanbul, Turkey*; Canan Savran, Ph.D., Mert Aksoy, M.D., Fulya Maner, M.D., Ilhan Yargic, Atilla Turgay, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the use of the Adult ADHD Rating Scale presented.

Summary:

Objective: To investigate the validity and reliability of a DSM-IV-based Adult ADHD Diagnostic Rating Scale (Turgay, 1994).

Methods: Turgay Adult ADHD Scale consists of 48 items (18 items corresponding to DSM-IV diagnostic criteria for ADHD and 30 items of associated symptoms) on a Likert Scale. The clinical sample consisted of 90 patients (age range: 18-55 years) diagnosed as adult ADHD (n=30), bipolar disorder (n=30), or alcohol and substance abuse (n=30). The normative comparison group (n=210) was matched for age, gender, and educational level. Derogatis Symptom Checklist (SCL) 90-R, and State Anxiety Inventory were administered to aid the clinical diagnosis of comorbid disorders.

Results: The scale was found highly sensitive to the diagnosis of ADHD in the clinical sample and was not false positive for the general adult population. Internal reliability of items, test-retest reliability, construct and criterion validity were found to be quite high. General reliability of the scale was demonstrated with internal coefficients, in which the highest reliability was calculated by Cronbach Alpha (0.9566), Spearman Brown (0.9072), and Guttman (0.9072). Test-retest correlation was very high (.953).

Conclusions: The DSM-IV-based Turgay Adult ADHD Scale was found valid, reliable, and highly sensitive in identifying adult ADHD patients.

References:

1. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorder, Fourth Ed (DSM-IV). Washington DC: APA, 1994.
2. Turgay A: Adult ADHD Rating Scale and Structured Interview Guidelines. Integrative Therapy Institute, Toronto, Canada, 1994.

NR454 **Tuesday, May 24, 3:00 p.m.-5:00 p.m.**
Obstetrical Complications in Children at High Risk for Bipolar Disorder
Supported by the Stanley Medical Research Institute

Manpreet K. Singh, M.D., *Department of Psychiatry, University of Cincinnati, 231 Albert Sabin Way, Cincinnati, OH 45267-0559*; Melissa P. DelBello, M.D., Stephen M. Strakowski, M.D., Cesar A. Soutullo, M.D., Kevin Stanford

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that (1) children at risk for bipolar disorder have higher rates of psychiatric disorders compared to controls, (2) these high risk children have higher rates of obstetrical complications and, (3) this kind of investigation may better identify inherent and environmental influences important in the development of bipolar disorder.

Summary:

Objective: Few studies have examined obstetrical complications in children at high risk for developing bipolar disorder (BPD). We hypothesize that children with a parent with BPD would be at greater risk for obstetrical complications compared with controls. Additionally, within this high-risk population, the development of later psychiatric disorders would be associated with early obstetrical complications.

Methods: The Kiddie-Schedule for Affective Disorder and Schizophrenia (K-SADS) and the Rochester Research Obstetrical Scale (ROS) were administered to children (AR) who had at least one parent with BPD (N=36) and children of healthy volunteer (HV) parents (N = 27), by raters blind to diagnostic category.

Results: Children at high risk for bipolar disorder were more likely to have affective and disruptive behavioral disorders (Fisher's exact test, $p < 0.0001$ and $p < 0.001$, respectively), and higher prenatal obstetrical complication scores (Prenatal $p = 0.00$, Delivery $p = 0.09$, Infant $p = 0.02$, Total $p = 0.02$). Prenatal obstetrical complications did not increase the risk for affective, anxiety, or disruptive behavioral disorders within the high-risk group.

Conclusion: Our data suggest that families with BPD are at greater risk for obstetrical complications compared with families without BPD. However, these complications do not appear to be associated with developing disruptive behavioral, anxiety, or affective disorders later in life.

References:

1. Kinney DK, et al: Pre- and perinatal complications and risk for bipolar disorder: a retrospective study. *J Affect Disord* 1998; 50:117-124.
2. Sameroff AJ, et al: Early development of children at risk for emotional disorder. *Monographs of the Society for Research in Child Development* 1982; 47:1-82.

NR455 **Tuesday, May 24, 3:00 p.m.-5:00 p.m.**
Clinical Evaluation of the Daily Assessment of Symptoms-Anxiety Scale
Supported by Pfizer Inc.

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Educational Objectives:

At the conclusion of this session, the participant should be able to understand (1) how symptoms of GAD are measured in a clinical trial, (2) the results from this evaluation of the DAS-A, (3) how

the DAS-A might be used in GAD trials to measure the onset of a treatment effect.

Summary:

Objective: To evaluate a new scale that measures onset of efficacy in GAD.

Method: 167 GAD patients were randomized to paroxetine 20mg/day, lorazepam 4.5mg/day, or placebo for four weeks. The DAS-A was administered during the first week of treatment and at weeks 1, 2, and 4.

Results: On the primary outcome measure, average change from baseline over the first six days of DAS-A assessments, lorazepam showed a significant improvement versus placebo, whereas paroxetine did not. Lorazepam produced a significant treatment effect on the DAS-A at 24 hours, whereas paroxetine did not. Both active drugs produced statistically significant improvement versus placebo on the DAS-A total change score (LOCF, endpoint). Both active drugs produced a statistically significant separation from placebo on the HAM-A total score change from baseline to endpoint (LOCF). The HAM-A observed cases analyses were significant on the same weeks as those of the DAS-A.

Conclusions: These data indicate that the DAS-A produces results similar to the HAM-A at weeks 1 through 4, that it can detect a treatment effect during the first week of treatment, and, on a secondary measure, as early as 24 hours after the first dose of lorazepam.

References:

1. Goodman WK: Selecting pharmacotherapy for generalized anxiety disorder. *J Clin Psychiatry* 2004; 65 Suppl 13:8-13.
2. Rickels K, Zaninelli R, McCafferty J, Bellew K, Iyengar M, Sheehan D: Paroxetine treatment of generalized anxiety disorder: a double-blind, placebo-controlled study. *Am J Psychiatry* 2003; 160(4):749-56.

NR456 **Tuesday, May 24, 3:00 p.m.- 5:00 p.m.**
Psychiatric Diagnoses and Medications in Fetal Alcohol Spectrum Disorders

Julia H. Murray, M.D., *Department of Psychiatry and Behavioral Sciences, University of Washington, 2101 E. Yesler Way #100, Seattle, WA 98122*; Heather Carmichael Olson, Ph.D., Rachel Montague, B.A., Rachel Montague, B.A.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to: (1) describe psychiatric diagnoses and psychotropic medications used for children with fetal alcohol spectrum disorders; and (2) recognize the complex issues involved in the treatment of this child population.

Summary:

Introduction: We describe psychiatric diagnoses and psychotropic medications used in community practice with a sample of children with fetal alcohol spectrum disorders (FASD) and externalizing behavior problems.

Method: Chart abstraction and review was performed for 50 school-aged children with FASD and significant externalizing problems enrolled in a therapeutic intervention. Community provider records from an approximately 1 1/2-year period were examined by a child psychiatrist. Parent telephone survey was performed.

Results: 76% of children had received psychiatric diagnoses, including: ADHD (74%), learning disorders (26%), cognitive disorders (26%), disruptive behavior disorders (21%), and anxiety disorders (18%). Twenty-one children had two or more diagnoses. Twenty-three different psychiatric conditions were found. 56% had been prescribed psychotropic medications (mean=2.23 simultane-

ous medications), ranging from stimulants to atypical antipsychotics. Children had diverse other medical conditions. Prescribing professionals included psychiatrists (42%), primary care providers (50%), or both (8%).

Conclusions: A variety of psychiatric disorders are diagnosed in children with FASD and externalizing behavior problems. In community practice, psychotropic medication use is relatively common. A full range of medications are used, and polypharmacy occurs frequently. Treatment of alcohol-affected children is complex. Involving professionals with expertise in using psychotropic medications is advisable.

This research was supported by a grant awarded to Susan Astley, Ph.D., from the Centers for Disease Control, Grant # U84-CCU020163-01.

References:

1. Coe J, Sidders J, Riley K, Waltermire J, Hagerman R: A survey of medication responses in children and adolescents with fetal alcohol syndromes. *Mental Health Aspects of Developmental Disabilities* 2001; 4(4):148-155.
2. Famy C, Streissguth A, Unis A: Mental illness in adults with fetal alcohol syndrome or fetal alcohol effects. *American Journal of Psychiatry* 1998; 155(4):552-554.

NR457 Tuesday, May 24, 3:00 p.m.- 5:00 p.m. **Psychotherapy Plus Antidepressant for Panic Disorder With or Without Agoraphobia: Cochrane Systematic Review**

Toshiaki A. Furukawa, M.D., *Department of Psychiatry, Nagoya City University Medical School, Mizuho-cho, Mizuho-ku, Nagoya 467-8601, Japan*; Norio Watanabe, M.D., Rachel Churchill, M.S.C.

Educational Objectives:

At the conclusion of the presentation, the participants should be able to recognize the currently available best evidence on the short-term and long-term merits and demerits of combining psychotherapy with antidepressants in the treatment of panic disorder with or without agoraphobia, and be able to integrate it with patients' preferences and values in their own practices.

Summary:

Objective: To conduct a systematic review and meta-analysis of evidence concerning short- and long-term merits and demerits of combined psychotherapy plus antidepressant treatment for panic disorder with or without agoraphobia in comparison with either therapy alone. Data sources: The Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Register, the Cochrane Central Register of Controlled Trials, and MEDLINE. Reference search, SciSearch and personal contact with experts. Data Extraction: The primary outcome was "response," i.e., substantial overall improvement from baseline. Secondary outcomes included global severity, panic attack frequency, phobic avoidance, general anxiety, depression, social functioning, overall dropouts, and dropouts due to side effects. Data synthesis: The identified studies involved 1,709 patients in 23 randomized comparisons. In the acute phase treatment, the combined treatment was consistently superior to either monotherapy (NNT between 7 and 10). It produced more dropouts due to side effects than psychotherapy (NNH around 26). After discontinuation of the acute phase treatment, the combined therapy was as effective as psychotherapy and more effective than antidepressant pharmacotherapy alone (NNT around 6).

Conclusions: Appropriate resources should be made available so that either combined therapy or psychotherapy alone can be offered as first-line treatment for panic disorder, depending on the patient's preferences.

References:

1. Alderson P, Green S, Higgins JPT: *Cochrane Reviewers' Handbook* in: The Cochrane Library, Issue 1. Chichester, UK: John Wiley & Sons; 2004.
2. Taylor S: *Understanding and Treating Panic Disorder*. Chichester: John Wiley & Sons, 2000.

NR458 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Adolescent Predictors of Functional Outcome in Adult ADHD: A Population Survey**

Stephen V. Faraone, Ph.D., *Department of Psychology and Behavioral Services, State University of New York, Upstate Medical University, 750 East Adams St, Syracuse, NY 13210*; Joseph Biederman, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize and appreciate the functional impairments commonly seen in ADHD adolescents and the degree to which they are predictive of adult outcomes.

Summary:

Introduction: Little is known about how the impairments of ADHD adolescents evolve over time and what their implications are for adult functioning.

Methods: We will address these issues with new data comparing 500 ADHD adults with 501 gender- and age-matched non-ADHD adults.

Results: We found several domains of impairment in adolescence to significantly predict ADHD in adulthood. ADHD adults were more likely to have negative perspectives about their teenage years and were less likely to have participated in school clubs, dating; and sports. As adolescents, the ADHD adults spent less free time with friends or family and were less likely to agree that their youth prepared them for adult life. ADHD adults were significantly more likely than controls to agree with the following statements about their youth: worse than peers; have memories that bother me today; and youth experiences had a damaging impact on adult life.

Conclusions: These results provide further evidence for a wide range of impairments associated with ADHD in adolescence. They also indicate that these impairments persist into adulthood in many cases, which further emphasizes the need to treat chronic cases through adolescence into adulthood.

References:

1. Faraone SV, Spencer T, Montano CB, Biederman J: Attention deficit hyperactivity disorder in adults: a survey of current practice in psychiatry and primary care. *Archives of Internal Medicine*, in press.
2. Faraone SV, Biederman J, Spencer T, Wilens T, Seidman LJ, Mick E, & Doyle A: Attention deficit hyperactivity disorder in adults: an overview. *Biological Psychiatry* 2000; 48: 9-20.

NR459 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Adult ADHD NOS: Is it a Valid Disorder?**

Stephen V. Faraone, Ph.D., *Department of Psychology and Behavioral Services, State University of New York, Upstate Medical University, 750 East Adams St, Syracuse, NY 13210*; Joseph Biederman, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the different manifestations of ADHD NOS and

the degree to which they should be considered valid forms of the diagnosis of ADHD.

Summary:

Background: Adults who appear to have a chronic history of childhood onset ADHD but do not meet DSM-IV criteria can be diagnosed as ADHD Not Otherwise Specified (NOS). Because little is known about the validity of ADHD NOS, clinicians may be confused as to how to proceed with such cases.

Methods: We will present new data addressing this issue from a family-genetic study of adult ADHD that recruited 247 ADHD adults and 123 non-ADHD adults recruited through advertisements along with all available first degree relatives.

Results: Of the ADHD patients, 127 with met full DSM-IV criteria (Full ADHD) and 120 met partial criteria (ADHD NOS). Among the ADHD NOS, 79 had late-onset ADHD. They met full DSM-IV criteria for ADHD except for age at onset. Forty-one met the age at onset criterion but had subthreshold symptoms. Using functional impairment, psychiatric comorbidity, neuropsychological functioning, and family history as validating criteria, we found significant evidence for the validity of late-onset ADHD but less validity for subthreshold ADHD.

Conclusion: We present receiver operating curve analyses to help clinicians determine which symptom and age at onset threshold should be used for defining ADHD NOS.

References:

1. Faraone SV: Attention deficit hyperactivity disorder in adults: Implications for theories of diagnosis. *Current Directions in Psychological Science* 2000; 9: 33-36.
2. Faraone SV, Biederman J, Spencer T, Wilens T, Seidman LJ, Mick E, Doyle A: Attention deficit hyperactivity disorder in adults: an overview. *Biological Psychiatry* 2000; 48: 9-20.

NR460 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Comparative Effect Sizes of ADHD Medications Supported by Novartis Pharmaceuticals Corporation

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Educational Objectives:

At the conclusion of this session, participants should be able to objectively compare the efficacy of various medications used in the treatment of patients with attention-deficit/hyperactivity disorder by reviewing medication effect sizes.

Summary:

Judging the relative efficacy of attention-deficit/hyperactivity disorder treatments can be difficult because of differences between trials in interventions and outcome variables. However, effect size, defined as mean drug-mean placebo improvement/pooled standard deviation, determined from placebo-controlled studies, can allow for fair comparison. In the behavioral sciences, effect sizes of 0.2 are defined as small, 0.5 as medium, and 0.8 as large. In a review of 6 methylphenidate trials in adults, effect sizes ranged from 0.7 for low doses (mean, 44 mg/d) to 1.3 for high doses (mean, 69 mg/d). A study of extended-release dexamethylphenidate in adults showed effect sizes ranging from 0.53 for 20 mg/d to 0.83 for 40 mg/d. In 2 studies of atomoxetine 60-120 mg/d in adults, effect sizes were 0.20 to 0.44. A review of pediatric studies showed effect sizes of 0.62 for nonstimulants, 0.91 for immediate-release stimulants, and 0.95 for long-acting stimulants. Post-hoc analyses of 5 studies of atomoxetine 0.5-2.0 mg/kg/d yielded effect sizes of 0.6 to 0.8 for children with moderate symp-

toms and 0.6 to 0.9 for those with severe symptoms. In a study of extended-release dexamethylphenidate 5-30 mg/d in children, the effect size was 0.79.

References:

1. Faraone SV: Understanding the effect size of ADHD medications: implications for clinical care. *Medscape Psychiatry & Mental Health* 2003; 8(2).
2. Faraone SV, Spencer T, Aleardi M, Pagano C, Biederman J: Meta-analysis of the efficacy of methylphenidate for treating adult attention-deficit/hyperactivity disorder. *J Clin Psychopharmacol* 2004; 24:24-29.

NR461 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Sleep Effects of Adjunctive Risperidone in Chronic PTSD

Daniella David, M.D., *Department of Psychiatry, Miami VAMC, 1201 N.W. 16th Street, Unit 116A12, Miami, FL 33125*; Ludmila DeFaria, M.D., Thomas Mellman, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand the changes in sleep findings associated with adjunctive treatment with Risperidone in chronic PTSD.

Summary:

Background: Sleep disturbances are core symptoms of chronic PTSD and are frequently treatment resistant. There has been increased interest recently in the sleep effects of atypical antipsychotics. Study objectives were: (1) to preliminarily evaluate the sleep effects of risperidone as adjunctive treatment in veterans with chronic PTSD, (2) to compare sensitivity to therapeutic changes between prospective sleep diaries and retrospective inquiries.

Methods: This is a pilot, open-label, 12-week, flexible-dose trial of adjunctive risperidone in male veterans with a primary diagnosis of chronic, combat-related PTSD, only partially responsive to current medications. Structured diagnostic interviews for lifetime psychiatric morbidity were administered at baseline. Ratings for PTSD, depression and anxiety, and self-report sleep measures, including the Pittsburgh Sleep Quality Inventory (PSQI) and three consecutive nights sleep logs were obtained at baseline, 6, and 12 weeks. All subjects continued to attend ongoing therapeutic activities. Baseline ratings were compared with the last set of ratings that were obtained at six or 12 weeks, by paired t-tests.

Results: Seventeen patients completed at least six weeks of the trial, and 14 subjects completed at least two sets of sleep logs. Mean age was 53.7 + 3.8 years, 35.3% were white, 41.2% were black, and 23.5% were Hispanic. Comorbidity with a depressive or anxiety disorder was common. All patients were taking antidepressant, mood stabilizing, and/or anxiolytic medications at stable doses for at least four weeks prior to study enrollment. Total CAPS score, re-experiencing and heightened arousal subscales were significantly improved at endpoint. The CAPS item of "difficulty falling or staying asleep" showed significant improvement, while the item of "recurrent distressing dreams of the event" did not. The PSQI global score decreased significantly. The nighttime awakenings frequency derived from the sleep logs also decreased significantly. There were no changes in sleep latency or sleep duration as measured by the sleep logs, however there was a significant shift from trauma-related to non-trauma dreams by endpoint.

Conclusion: Preliminary results suggest that risperidone as adjunctive treatment may benefit sleep disturbances associated with treatment resistant chronic PTSD. Prospective logs may be more sensitive to therapeutic changes in dream quality than retrospective interviews.

References:

1. David D, DeFaria L, Lapeyra O, and Mellman T: Adjunctive risperidone treatment in combat veterans with chronic PTSD. *Journal of Clinical Psychopharmacology* 2004; 24(5):556-559.
2. David D, Kutcher GS, Jackson EI, Mellman TA: Psychotic symptoms in combat-related Posttraumatic Stress Disorder. *Journal of Clinical Psychiatry* 1999; 60:29-32.

NR462 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Comparison of ADHD Symptom Subtypes: Comorbidities in Clinic and Nonreferred Adults

Joyce Sprafkin, Ph.D., *Department of Psychiatry, State University of New York, Putnam Hall, South Campus, Stony Brook, NY 11794*; Kenneth Gadow, Ph.D., Jayne Schneider, Ph.D., Edith Nolan, Ph.D.

Educational Objectives:

At the conclusion of the session, the participant should be able to (1) describe comorbid psychiatric symptoms that are associated with ADHD symptoms, and (2) discuss how the comorbidities vary with ADHD subtypes.

Summary:

Objective: Recognition of comorbid conditions is critical to good clinical care of ADHD patients. This study examines differences between ADHD subtypes in the severity of comorbid symptoms in two adult samples.

Methods: Two samples of adults, a psychiatry clinic sample (N=490) and a nonreferred sample (N=900), completed the Adult Self-Report Inventory-4 (ASRI-4), a rating scale of DSM-IV symptoms. Participants (clinic/nonreferred) were sorted into one of four groups based on their ASRI-4 scores on the ADHD category: inattentive (n=83/28), hyperactive-impulsive (n=20/18), combined (n=53/14), and nonADHD (n=334/840). A series of ANOVAs compared the four groups on ASRI-4 symptom severity ratings of oppositional defiant disorder (ODD), conduct disorder (CD), major depressive disorder (MDD), bipolar disorder (BD), generalized anxiety disorder (GAD), social phobia, antisocial personality disorder (APD), and borderline personality disorder (BPD).

Results: ASRI-4 ratings of all symptom categories were significantly higher for all three ADHD subtype groups compared with nonADHD groups. The combined group had significantly higher ratings than the Inattentive group for ODD, CD, MDD, BD, APD, and BPD.

Conclusions: Findings support (1) the presence of ADHD subtypes in adults, and (2) the importance of assessing for comorbid psychiatric disorders in adults with ADHD.

References:

1. Gadow KD, Sprafkin, J, Weiss, MD: *Adult Self-Report Inventory-4 Manual*. Stony Brook, NY, Checkmate Plus, 2004.
2. Weiss MD, Weiss JR: A guide to the treatment of adults with ADHD. *J Clin Psychiatry* 2004; 65[suppl 3]:27-37.

NR463 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Weiss Functional Impairment Rating Scale: Parent Report (WFIRS-P)

Margaret D. Weiss, M.D., *Children's and Women's Mental Health, 4500 Oak Street, Box 178, Vancouver, BC V64 3H1, Canada*; Ruth Dickson, M.D., Michael Wasdell, M.A., Melissa Bomben, M.S., Stefan Caney, B.S.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to describe the psychometric properties of the WFIRS-P and

to indicate how the WFIRS-P could facilitate diagnostic evaluations.

Summary:

Objective: To develop a valid and reliable measure of the impact of ADHD on functioning.

Method: A series of non-symptom items were developed from chart review of functional impairment secondary to ADHD. Demographics, DSM-IV diagnoses, and ratings of symptom severity were collected along with the WFIRS-P.

Results: Analysis of data from 62 patients, aged 6 to 17 years, yield the WFIRS-P mean total score of 37.54 (range 0-126. High internal consistency was found for the whole scale (Cronbach's alpha=0.93) and each of the six domains (from 0.81 to 0.93). Significant correlations ($p < .0001$) between WFIRS-P and ADHD ($r = .68$), ODD ($r = .58$), CD ($r = .58$) symptoms and other DSM-IV disorders demonstrated convergent validity. Item discriminant validity was greater than 2SE for the majority of the 52 WFIRS-P items. A clinical cut-off of "pretty much" (2) or "very much" (3) represented 1.65 SD of the sample. Higher variance and greater sensitivity to academic impairment secondary to inattention was found with the WFIRS-P over the Child Global Assessment Scale.

Conclusion: The WFIRS-P is a valid and reliable measure of functional impairment from ADHD. This instrument will enable assessment of the impact of treatment in mitigating the burden of illness associated with ADHD.

References:

1. Klassen AF, Miller A, Fine S: Health-related quality of life in children and adolescent who have a diagnosis of attention-deficit/hyperactivity disorder. *Pediatrics* 2004; 114:e541-e547.
2. Matza LS, Rentz AM, Secnik K, Swensen AR, Revicki DA, Michelson D, Spencer T, Newcorn JH, Kratochvil CJ: The link between health-related quality of life and clinical symptoms among children with attention-deficit hyperactivity disorder. *J Dev Behav Pediatr* 2004; 25:166-1741616.

NR464 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Relationship Between Symptomatic and Functional Improvement in Adult ADHD

Margaret D. Weiss, M.D., *Children's and Women's Mental Health, 4500 Oak Street, Box 178, Vancouver, BC V64 3H1, Canada*; Candice Murray, Ph.D., Melissa Bomben, M.S., Michael Wasdell, M.A.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the relationship between symptom severity and functioning in adults with ADHD, and to recognize the treatment implications for functional improvement in each of the ADHD subtypes.

Summary:

Objective: Treatment outcome studies for ADHD have focused primarily on symptom reduction. The goal of this study was to investigate the relationship between symptom reduction and functional improvement.

Methods: 96 adults diagnosed with ADHD (mean age 37.7) participated in a treatment study lasting five months. Treatment involved a manualized problem focused therapy and stimulant and/or SSRI medication. ADHD symptoms were measured using the ADHD-RS-Inv. Functioning was assessed using validated clinician and self-report scales. Correlations between change in ADHD symptoms and change in functional impairment were tested.

Results: For ADHD symptoms, significant correlations were observed with measures evaluating self reported family ($r = .40$), work

($r=.39$) and social functioning ($r=.30$). Improved symptoms were associated with improved functioning across all areas. Clinician ratings of global functioning were consistent with these results. Social functioning improved more when inattentive symptoms were reduced, than when hyperactive/impulsive symptoms were reduced.

Conclusion: Reduction in ADHD symptoms was associated with improved functioning across aspects of daily living. Our findings underline the importance of targeting inattentive symptoms of ADHD for optimal functioning. These findings suggest that improvement in symptoms overlap with but are not identical to improved functioning, and that both outcomes are essential to evaluation of treatment.

References:

1. Spencer TJ: ADHD treatment across the life cycle. *J Clin Psychiatry* 2004; 65 Suppl 3:22-26.
2. Wilens TE, Faraone SV, Biederman J: Attention-deficit/hyperactivity disorder in adults. *JAMA* 2004; 292:619-623.

NR465 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Inattention in Boys With Traumatic Brain Injury and Boys With ADD**

Joungsook Ahn, M.D., *Department of Psychiatry, Wonju College of Medicine, Yonsei University, Ilsan-dong 162, Wonju 220-701, Korea*; Saehan Park, M.D., Gwangsoo Park, B.S.C.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the difference in attentional problems between the primary ADD and the ADD following TBI.

Summary:

Objective: To study the similarity and differences of characteristics of inattention of the developmental attention-deficit disorder (ADD) and attentional problems following traumatic brain injury (TBI).

Methods: Characteristics of attention in 30 boys with TBI and 32 boys with ADD (all ages 7-12) were investigated by administering Korean version of WISC (K-WISC III) and visual and auditory TOVA. For TBI boys with persisting attentional problem, more than one year had passed since head trauma at the time of this study.

Results: No differences in K-WISC III subtests were found between two diagnostic groups. Boys with TBI show lower commission error (lower impulsivity) in visual TOVA ($U = 17.0$, $p < 0.01$) and auditory TOVA ($U = 36.5$, $p < 0.05$), and lower variability of reaction time (higher information-processing consistency) in auditory TOVA ($U = 34$, $p < 0.05$) than boys with ADD.

Conclusion: Attentional problems in TBI and ADD are different in their attention components suggestively, which warrants further study for differential diagnosis and proper treatments.

Partially funded by Wonju College of Medicine.

References:

1. Anderson V, Fenwick T, Manly T: Attentional skills following traumatic brain injury in childhood: a componential analysis. *Brain Injury* 1998; 12:937-949.
2. Konrad K, Gauggel S, Manz A, Schöll M: Inhibitory control in children with traumatic brain injury and children with attention deficit/hyperactivity disorder. *Brain Injury* 2000; 14:850-875.
3. Chan RC, Hoosain R, Lee TM, Fan YW, Fong D: Are there subtypes of attentional deficits in patients with persisting post-concussive symptoms? A cluster analytical study. *Brain Injury*. 2003; 17(2):131-148.

NR466 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Anxiety and Depressive Disorders in Asthmatic Outpatients

Alexandre M. Valenca, M.D., *Department of Psychiatry, University Feder Rio Janeiro, Rua da Cascata, 13 /501, Rio de Janeiro 20530-080, Brazil*; Antonio E. Nardi, M.D., Rodrigo Falcao, M.D., Isabella Nascimento, M.D., Fabiana L. Lopes, M.D., Rafael C. Freire, M.D., Marco A. Mezzasalma, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate the demographic, clinical, and therapeutic features of the comorbidity of anxiety/mood disorders and asthma.

Summary:

Introduction: Studies have reported a high prevalence of anxiety and depressive disorders in patients with asthma. It has been suggested that the severity of asthma may be associated with a greater risk of having an anxiety or affective disorder.

Methods: Sixty-two patients of an outpatient asthma clinic were evaluated. Psychiatric diagnoses were assessed with the Mini-International Neuropsychiatric Interview 4.4 Version (MINI).

Results: Twenty-seven patients (43.5%) met the criteria for at least one psychiatric diagnosis, which mainly included major depression (24%), generalized anxiety disorder (20.9%), and panic disorder/agoraphobia spectrum disorders (17.7%). We found no significant differences in the prevalence of anxiety disorders and depression between the groups with mild/moderate and severe asthma.

Conclusion: Our study is consistent with previous findings suggesting that asthma is associated with a significantly increased likelihood of depression and anxiety disorders. Its essential to make a careful psychiatric evaluation in asthmatic patients.

Educational grant from Severino Sombra University, Vassouras; and CNPq (grant: 304671/03-7) Laboratory of Panic and Respiration, Federal University of Rio de Janeiro, Brazil.

References:

1. Nascimento I, Nardi AE, Valença AM, Lopes FL, Mezzasalma MA, Nascentes R, Zin WA: Psychiatric disorders in asthmatic outpatients. *Psychiatry Res* 2002; 110:73-80.
2. Goodwin RD, Jacobi F, Thefeld W: Mental disorders and asthma in the community. *Arch Gen Psychiatry* 2003; 60:1125-1130.

NR467 Tuesday, May 24, 3:00 p.m. 3:00-5:00 p.m.

Morning-Versus Evening-Dosed Atomoxetine: Effects on Core ADHD Symptoms

Douglas K. Kelsey, M.D., *Department of Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Virginia Sutton, Ph.D., Donald Lewis, M.D., Kory Schuh, Ph.D., Calvin Sumner, M.D., Humberto Quintana, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the core symptom efficacy and tolerability of once-daily atomoxetine dosed in the morning or evening in children with ADHD.

Summary:

Objective: Atomoxetine, a nonstimulant medication for treating ADHD, can be dosed in the morning or evening. This study compared the efficacy and tolerability of morning and evening dosing.

Methods: In this three-arm, randomized, double-blind, placebo-controlled trial, 288 patients received once-daily atomoxetine or placebo in the morning, or evening for about six weeks. Core

symptom efficacy was measured with the ADHD Rating Scale (ADHDRS) and Clinical Global Impressions-Severity (CGI-S). Parent assessments of children's home behaviors in the evening were collected using the Conners' Global Index: Parent-Evening Scale (CGIP-E).

Results: Morning and evening dosing were superior to placebo on the ADHDRS Total score, Inattentive subscore, Hyperactive/Impulsive subscore (morning dosing only), CGI-S, and the CGIP-E Total score. Morning dosing was superior to evening dosing on the ADHDRS Total score, Hyperactive/Impulsive subscore, and CGI-S. Patients were more likely to experience an adverse event on morning dosing than evening dosing.

Conclusion: Once-daily atomoxetine, dosed either in the morning or evening, significantly decreased core ADHD symptoms relative to placebo; however morning dosing showed greater efficacy whereas evening dosing showed greater tolerability. For patients with tolerability problems, evening dosing might be an effective method for initiating patients on atomoxetine treatment during the titration period.

References:

1. Michelson D, Allen AJ, Busner J, Casat C, Dunn D, Kratochvil C, Newcorn J, Sallee FR, Sangal RB, Saylor K, West S, Kelsey D, Wernicke J, Trapp NJ, Harder D: Once-daily atomoxetine treatment for children and adolescents with attention-deficit/hyperactivity disorder: A randomized, placebo-controlled study. *Am J Psychiatry* 2002; 159:1896-1901.
2. Kelsey DK, Sumner CR, Casat CD, Coury DL, Quintana H, Saylor KE, Sutton VK, Gonzales J, Malcolm SK, Schuh KJ, Allen AJ: Once-daily atomoxetine treatment for children with attention-deficit/hyperactivity disorder, including an assessment of evening and morning behavior: A double-blind, placebo-controlled trial. *Pediatrics* 2004; 114(1):e1.

NR468 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Effect of Antipanic Drugs on Pulmonary Function in Patients With Panic Disorder**

Isabella Nascimento, M.D., *Laboratory of Panic and Respiration, Federal University of Rio De Janeiro, rProf. Hermes de Lima, 364/103, Rio de Janeiro 22765095, Brazil;* Antonio E. Nardi, M.D., Alexandre M. Valença, M.D., Laura Cassabian, M.D., Cristiane B. Garcia, M.D., Fabiana L. Lopes, M.D., Walter A. Zin, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate the lung function in asymptomatic panic disorder patients with or without agoraphobia (DSM-IV) and to investigate possible antipanic drugs effect its function.

Summary:

The aims of the present study were to evaluate the lung function in asymptomatic panic disorder patients with or without agoraphobia and to investigate possible antipanic drugs effect in the results. We selected 11 panic disorder patients who, in the last three months, have had no panic attacks or agoraphobic symptoms. Lung function evaluation was performed at the Laboratory of Lung Function of Clementino Fraga Filho University Hospital, in two different days (with antipanic drugs and in washout) and it comprised spirometric evaluation and bronchodilatation test (Salbutamol inhalation). Subjective Units of Disturbance Scale (SUDS) was administered before and after each spirometric assessment. One patient (9.1%) showed a mild obstructive airway disturbance. Before bronchodilatation test, forced expiratory volume in 1 sec (FEV1) and forced expiratory flow between the 25% and 75% of forced vital capacity (FEF25-75) were significantly higher in patients with antipanic drugs than in washout period. After Salbuta-

mol inhalation, only FEV1 were significantly higher in patients with antipanic drugs than in washout period. We also observed a significantly increase in FEV1 and FEF25-75 after Salbutamol inhalation in patients without antipanic drugs. The SUDS level measurement did not show any significant difference between panic disorder patients in both test days as well as before or after Salbutamol inhalation. These results suggest a possible antipanic-drug effect on lung function in panic disorder patients.

Supported by the Brazilian Council for Scientific and Technological Development (CNPq), Grant 304671/03-7.

References:

1. Nascimento I, Nardi AE, Valença AM, Lopes FL, Mezzasalma MA, Nascentes R, Zin WA: Psychiatric disorders in asthmatics outpatients. *Psychiatric Research* 2002; 110:73-80.
2. Perna G, Marconi C, Battaglia M, Bertani A, Panzacchi A, Bellodi L: Subclinical impairment of lung airways in patients with panic disorder. *Biological Psychiatry* 1994; 36:601-605.

NR469 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Morning-Dosed Versus Evening-Dosed Atomoxetine for Treating ADHD in Children**

Virginia Sutton, Ph.D., *Department of Neuroscience, Eli Lilly and Company, 9804 Spire Lane, Plano, TX 75025;* Douglas Kelsey, M.D., Donald Lewis, M.D., Kory Schuh, Ph.D., Calvin Sumner, M.D., Humberto Quintana, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the duration of effects of once-daily atomoxetine dosed in the morning or evening for treating ADHD in children.

Summary:

Objective: When dosed once daily in the morning, atomoxetine, a medication for treating ADHD, produces efficacy into the evening and next morning. As a nonstimulant, atomoxetine also can be dosed in the evening. This study examined the duration of effects of morning-and evening-dosed atomoxetine compared with each other and to placebo.

Methods: In this double-blind trial, 288 patients received atomoxetine in the morning, evening, or placebo for about 6 weeks. Parent assessments of children's home behaviors in the evening and early morning were collected using the Daily Parent Rating of Evening and Morning Behavior-Revised (DPREMB-R) and Conners' Global Index: Parent-Morning (CGIP-M) and Evening (CGIP-E) scales. The DPREMB-R and CGIP-M data were collected using an Interactive Voice Response System.

Results: There were no significant differences between morning and evening dosing on any of these measures. Both morning and evening dosing produced improvements over placebo on the DPREMB-R Total and Evening subscore, CGIP-M and CGIP-E Total scores, and CGIP-E Restless/Impulsive subscore. Evening dosing also produced significant improvements over placebo on the CGIP-M. Restless/Impulsive and CGIP-E Emotional Lability subscores.

Conclusion: Once-daily atomoxetine, dosed either in the morning or evening, produced symptom reductions that can be measured up to 24 hours later.

References:

1. Michelson D, Allen AJ, Busner J, Casat C, Dunn D, Kratochvil C, Newcorn J, Sallee FR, Sangal RB, Saylor K, West S, Kelsey D, Wernicke J, Trapp NJ, Harder D: Once-daily atomoxetine treatment for children and adolescents with attention-deficit/hyperactivity disorder: a randomized, placebo-controlled study. *Am J Psychiatry* 2002; 159:1896-1901.

2. Kelsey DK, Sumner CR, Casat CD, Coury DL, Quintana H, Saylor KE, Sutton VK, Gonzales J, Malcolm SK, Schuh KJ, Allen AJ: Once-daily atomoxetine treatment for children with attention-deficit/hyperactivity disorder, including an assessment of evening and morning behavior: A double-blind, placebo-controlled trial. *Pediatrics* 2004; 114(1):e1.

NR470 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
An Effect-Size Analysis of the Efficacy of Pharmacotherapy for GAD

Rosario B. Hidalgo, M.D., *Department of Psychiatry and Behavioral Sciences, Duke University, Duke South, Box 3812, Durham, NC 27710*; Larry Tupler, Ph.D., Jonathan Davidson, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to (1) Learn results from placebo controlled studies of major pharmacological compounds in GAD, (2) learn effect sizes of each treatment, (3) recognize variables which may influence effect size.

Summary:

Background: Generalized anxiety disorder (GAD) is a prevalent and impairing disorder. Different drugs have been investigated in GAD: (1) SSRI; (2) SNRI; (3) BZ (benzodiazepines); (4) AZA (azapirones); (5) AH (antihistamine); (6) PGB (pregabalin); and (7) CAM (complementary/alternative). To our knowledge, this is the first meta-analysis of the efficacy of different drug treatments for GAD.

Methods: Effect size (ES) analysis of 21 double-blind, placebo-controlled trials of medications treating DSM-III-R or DSM-IV GAD using HAM-A change in score or endpoint score as the main efficacy measure.

Results: Comparing all drugs versus placebo, the ES was 0.39. Mean ES, excluding children, were PGB: 0.50, AH: 0.45, SNRI: 0.42, BZ: 0.38, SSRI: 0.36, AZA: 0.17, and CAM: -0.31. Comparing ES of adult versus children and conventional drugs versus CAM we found statistically significant differences. No significant differences were found comparing date of publication, location of site, fixed versus flexible dosing, number of study arms, or number of outcome measures.

Conclusions: Medications varied in the magnitude of their ES, ranging from moderate to poor. Adolescents and children showed a much greater ES compared with adults. Subjects taking CAM did worse than placebo. These and other analyses will be presented in more detail.

References:

1. Davidson JR: Pharmacotherapy of generalized anxiety disorder. *Journal of Clinical Psychiatry* 2001; 62(11):46-50.
2. Cooper H, Hedges LV (Eds): *The Handbook of Research Synthesis*. New York, Russell Sage Foundation, 1994.

NR471 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Is Cigarette Smoking a Gateway Drug to Subsequent Alcohol and Illicit Drug Use Disorders? A Controlled Study of Youths With and Without ADHD

Michael C. Monuteaux, Sc.D., *Department of Pediatric Psychopharmacology, Massachusetts General Hospital, 55 Fruit Street, Warren 705, Boston, MA 02114*; Joseph Biederman, M.D.

Educational Objectives:

At the end of this presentation, the participant should understand how the gateway hypothesis extends to and is particularly salient

in an ADHD sample, and recognize the heightened public health benefits of smoking prevention in ADHD youth.

Summary:

Introduction: The goal of this study was to assess cigarette smoking as a gateway drug for subsequent alcohol and illicit drug abuse and dependence in youth with ADHD, and to test if this association is stronger in ADHD youth relative to controls.

Method: We used data from a case-control family study of female youth with and without ADHD. We studied 97 ADHD and 203 control youth of both genders, aged at least 12 years. We determined ADHD, smoking, and substance use status using structured diagnostic interviews. We tested the association between cigarette smoking and subsequent substance use outcomes using logistic regression.

Results: ADHD youth who smoked cigarettes were significantly more likely to subsequently use alcohol and illicit drugs as well as to develop abuse and dependence compared with ADHD youth who did not smoke.

Conclusions: These results extend the gateway hypothesis to an ADHD sample and provide preliminary evidence that this effect may be particularly robust in ADHD youth. This study also indicates that cigarette smoking may identify a subgroup of ADHD youth at the highest risk for addictions. If replicated, these findings have enormous public health consequences, and underscore the pressing need to prevent smoking in ADHD children.

Research for this poster supported partially by USPHS (NIMH) grant R01 MH-41314-01A2 (Biederman).

References:

1. Milberger S, Biederman J, Faraone SV, Chen L, Jones J: Attention deficit/hyperactivity disorder is associated with early initiation of cigarette smoking in children and adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry* 1997; 36(1):37-44.
2. Kandel D: *Stages and Pathways of Drug Involvement: Examining the Gateway Hypothesis*. Cambridge, England, Cambridge University Press, 2002.

NR472 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
A Randomized, Double-Blind, Placebo-Controlled Clinical Trial of Bupropion for the Prevention of Smoking in Youth With ADHD

Michael C. Monuteaux, Sc.D., *Department of Pediatric Psychopharmacology, Massachusetts General Hospital, 55 Fruit Street, Warren 705, Boston, MA 02114*; Joseph Biederman, M.D.

Educational Objectives:

At the end of this presentation, the participant should understand how efficacious pharmacological prophylaxis could be a useful component of prevention efforts targeting high-risk youth, and recognize the utility of psychiatric disorders such as ADHD in the identification of high-risk groups for research and intervention programs.

Summary:

Introduction: Smoking has become widespread in youth. One well-documented risk factor for smoking is attention-deficit/hyperactivity disorder (ADHD). Bupropion, while efficacious in the treatment of ADHD and smoking cessation, has not yet been assessed as a prophylactic agent for smoking in children with ADHD.

Method: We assessed the efficacy of bupropion for the prevention of smoking using a longitudinal, randomized, double-blind, placebo-controlled design. Subjects were youth with ADHD of either sex between 9 and 18 years of age. Subjects were assessed weekly for eight weeks, biweekly for four weeks, and monthly

thereafter for up to 6.5 years. To assess smoking, we used an assay of cotinine in urine.

Results: Seventy-three subjects were randomized, and 30 were followed for at least a year. No differences were found between the groups on demographic factors. Statistical separation between bupropion and placebo in the rate of smoking was not demonstrated. However, concurrent stimulant treatment was a significantly associated with smoking abstinence.

Discussion: While Bupropion was not associated with a reduction in smoking, not all subjects were completely through the period of risk. However, stimulant therapy may be effective in the prevention of smoking in ADHD youth. Additional research is necessary to replicate this finding.

Research for this poster was supported by 5 R01 DA12531-04 (Biederman).

References:

1. Centers for Disease Control and Prevention (CDC), Youth Tobacco Surveillance-United States, 2000. MMWR, 2001; 50:p. 1-84.
2. Whalen CK, et al: Is there a link between adolescent cigarette smoking and pharmacotherapy for ADHD? *Psychol Addict Behav* 2003; 17(4):p. 332-5.

NR473 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Anxiety and Depression Levels of Infertiles Enrolling for Artificial Reproduction**

Tunay Kardlidere, M.D., *Department of Psychiatry, Gulhane Military Medical Faculty, Gata Psikiyatri AD Gn. Dr. Tevfik Saglam Cd., Ankara 06018, Turkey*; Ali Bozkurt M.D., Kamil Nahit Ozmenler, M.D., Aytakin Ozsahin, M.D., Tanzu Kucuk, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the psychiatric vulnerability of infertile individuals.

Summary:

Objective: The stress of infertility itself and the treatments for infertility were described as emotionally stressful and depressive for the couple. This study aimed to determine cross-sectionally the anxiety and depression levels of Turkish infertile couples enrolling for artificial reproduction techniques (ART) in context of perceived social support.

Methods: Eighty-six married infertile couples who did not meet any axis-1 disorder criteria according to the Diagnostic and Statistical Manual for Mental Disorders (DSM-III-R) were evaluated by self-report questionnaire, Turkish versions of the Beck's Depression Inventory (21 items), the State and Trait Anxiety Inventory, the Perceived Social Support (Family and Friends) Scale.

Results: The females demonstrated significantly more trait stress and greater degree of social support than the males. The severity of the state anxiety and the depressive symptoms of the women were insignificantly higher than the men. Several factors such as the infertility cause, family history of infertility, age, and perceived social support, contributed to the stress.

Conclusions: Even if they have no present psychiatric morbidity, the infertile couples enrolling for ART should be evaluated for the infertility cause, family history of infertility, age, and perceived social support that may cause anxiety, and the depressive symptoms.

References:

1. Hammarberg K, Astbury J, Baker HWG: Women's experience of IVF: a follow-up study. *Human Reproduction* 2001; 16(2):374-383.

2. Wright J, Duschesne C, Sabourin S, Bissonnette F, Benoit J, Girard Y: Psychosocial distress in infertility: men and respond differently. *Fertil Steril* 1991; 55:100-108.

NR474 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Risperidone for the Treatment of ADHD in Children With Bipolar Disorder**

Eric Mick, Sc.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 725, Boston, MA 02114*; Joseph Biederman, M.D.

Educational Objectives:

At the conclusion of this presentation, participants will have an understanding of the differential diagnosis of bipolar disorder in children with ADHD and the impact of risperidone monotherapy on comorbid symptoms of mania and ADHD.

Summary:

Objective: Children and adolescents with bipolar disorder are also at high risk of having comorbid attention-deficit/hyperactivity disorder. The objective of this study to estimate improvement in ADHD symptoms in children enrolled in a clinical trial of risperidone for the treatment of pediatric bipolar disorder.

Methods: Twenty-nine subjects were assigned to treatment with risperidone for pediatric bipolar disorder in an open-label, eight-week study.

Results: Subjects were 9.9 ± 2.5 years of age and predominantly male (69%). Over the eight weeks of treatment, there were significant reductions in symptoms of bipolar disorder (change score = -17.9 ± 9.7 , $p < 0.001$) and ADHD (-16.4 ± 9.3 , $p < 0.001$). Both hyperactive/impulsive (-8.3 ± 4.9 , $p < 0.001$) and inattentive (-7.6 ± 4.8 , $p < 0.001$) symptoms were improved with risperidone. However, the mean ADHD rating scale score at endpoint was 20.4 ± 9.1 indicating residual ADHD symptomatology.

Conclusions: This study suggests that risperidone is associated with improvement of both inattentive and hyperactive/impulsive symptoms of ADHD in children with bipolar disorder. However, at endpoint subjects continued to report residual symptoms of the disorder and the majority were not rated as having experience clinical improvement. Long-term data are required to fully understand the efficacy of risperidone for ADHD symptoms and to estimate functional improvements associated with this level of ADHD improvement

References:

1. Biederman J, Mick E, Faraone SV, Johnson MA, Wozniak J, Spencer T, Pandina G: Risperidone in the treatment of affective symptoms: a Secondary analysis of a randomized clinical trial in children with disruptive behavior disorder. 2004; under review.
2. Biederman J, Mick E, Johnson MA, Wozniak J, Aleardi M, Spencer T, Faraone SV: A Prospective open-label treatment of risperidone monotherapy in children and adolescents with bipolar disorder. 2004, under review.

NR475 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Self-Cutting Among Adolescents: Frequency and Associated Risks**

Larry K. Brown, M.D., *Department of Child Psychiatry, Rhode Island Hospital, 1 Hoppin Street, Suite 204, Providence, RI 02903*; Glenn Gordon, Wendy Hadley, Ph.D., Christopher Houck, Ph.D., Nancy Beausoleil

Educational Objectives:

At the conclusion of the presentation, the participants should be able to recognize the risks associated with self-cutting in adolescents.

Summary:

Objective: Examine relationships between the frequency of self-cutting, sexual abuse, recent condom use, and psychological variables.

Methods: Assess 310 adolescents in intensive psychiatric treatment.

Results: 48% (n=140) reported self-cutting; 39% who had cut four or more times were classified as "frequent cutters." Frequent cutters were significantly more likely ($p<.01$) than less frequent cutters to be female (62% vs. 42%), non-white (26% vs. 9%), been sexually abused (63% vs. 34%), to have used condoms inconsistently (61% vs. 27%), and report less impulse control (19.7 vs. 24.7). Frequent self-cutters were more likely to have a diagnosis of PTSD (16% vs. 7%). The less frequent cutters were similar to the noncutters on all variables. Two logistic regression analyses, which controlled for age, gender, ethnicity, and level of impulse control, found that frequent self-cutting was associated with sexual abuse (OR=3.2) and that lack of condom use was associated with more frequent self-cutting (OR=2.9).

Conclusion: Self-cutting is quite prevalent among adolescents in intensive treatment. Frequency of self-cutting among adolescents is strongly associated with sexual abuse histories and current sexual risk behaviors. Less frequent cutting may be more experimental or socially determined and less associated with specific trauma or pathology.

References:

1. Brown LK, Houck CD, Hadley WH, Lescano CM: Self-cutting and sexual risk among adolescents in intensive psychiatric treatment. *Psychiatric Services*, in press.
2. Sharkley V: Self-wounding: a literature review. *Mental Health Practice* 2003; 6, 35-37.

NR476 Tuesday, May 24, 3:00 p.m.-5:00 p.m. Persistence With Methylphenidate Treatment of ADHD

Mark Olsson, M.D., *Department of Psychiatry, Columbia University, 1051 Riverside Drive, New York, NY 10032*; Steven Marcus, Ph.D., George Wan, Ph.D., Jason Kemner, M.P.H.

Educational Objectives:

At the conclusion of this session, the participant should be able to identify key patient characteristics and pharmacological formulations associated with persistence of methylphenidate therapy.

Summary:

Objective: To compare persistence with extended-release (ER-MPH) and immediate-release methylphenidate (IR-MPH) treatment among Medicaid youth with ADHD.

Method: Statewide California Medicaid claims (2000-2003) were analyzed focusing on youth, ages 6-17 years, initiating ER-MPH (n=3,444) or IR-MPH (n=8,098) treatment for ADHD. The mean medication possession ratios (MPRs) of MPH formulations were compared over the year following treatment initiation. MPR is the total days supply of MPH medication during the one-year period following MPH initiation divided by 365.

Results: During the year following treatment initiation, patients treated with ER-MPH had a significantly greater mean MPR than patients treated with IR-MPH (53.8% vs. 47.6%; $p<.0001$). After controlling for patient demographics and other covariates, patients treated with ER-MPH had a mean MPR that was 1.11 (95% CI:

1.08-1.13) times greater than patients treated with IR-MPH ($p<.0001$). Among patients treated with ER-MPH, treatment initiation with OROS® MPH (Concerta®) was associated with a significantly greater mean MPR than Metadate® CD (54.9% vs. 49.3%; $p=.0007$) or Ritalin® LA (54.9% vs. 47.5%; $p<.0001$).

Conclusions: In this population, OROS® MPH (Concerta®) is associated with greater treatment persistence than IR-MPH or other ER-MPH formulations. Clinical consideration of the MPH formulation may help extend treatment persistence among Medicaid youth with ADHD.

References:

1. Thiruchelvam D, Charach A, Schachar RJ: Moderators and mediators of long-term adherence to stimulant treatment in children with ADHD. *J Am Acad Child Adolesc Psychiatry* 2001; 40:922-928.
2. Arnold LE, Elliot M, Sachs L, et al: Effects of ethnicity on treatment attendance, stimulant response/dose, and 14-month outcome in ADHD. *J Consult Clin Psychol* 2003; 71:713-727.

NR477 Tuesday, May 24, 3:00 p.m.-5:00 p.m. Short-Term Treatment of PTSD With Venlafaxine XR Versus Placebo: A Pooled Analysis of Gender Effects

Jonathan R.T. Davidson, M.D., *Department of Psychiatry, Duke University, Trent Drive, 4th Floor, Room 4082B, PO Box 3812, Durham, NC 27710*; Teri Pearlstein, M.D., Jennifer Kacmar, M.D., Bing Yan, M.D., Ron Pedersen, M.S., Jeff Musngung

Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the efficacy and safety of venlafaxine extended release (XR), a serotonin-norepinephrine reuptake inhibitor, in the short-term and continuation treatment of patients with posttraumatic stress disorder.

Summary:

Objective: To examine response by gender to venlafaxine extended-release (XR) or placebo in patients with posttraumatic stress disorder (PTSD).

Methods: Data were pooled from two flexible-dose, randomized, double-blind studies in 659 outpatients with primary diagnosis of PTSD treated with venlafaxine XR (37.5 to 300 mg/day) or placebo. Study 1 was a placebo-controlled, 12-week study that included a sertraline arm. Study 2 was a placebo-controlled, 24-week study. Evaluation of the primary outcome measure, the CAPS-SX17, was performed using week 12 LOCF and completer analyses data using appropriate parametric and nonparametric tests (ITT population).

Results: A significant treatment effect was found for all CAPS endpoints. No significant treatment-by-gender interactions were observed. The only significant gender effect was in completers for cluster C; response was greater among women across placebo and venlafaxine XR groups ($P=0.0167$). A significant protocol effect for all CAPS endpoints and significant differences between study populations in baseline characteristics (including race, gender, and baseline cluster B and C scores) or trauma types (including a higher incidence of childhood sexual abuse in study 1) were noted.

Conclusions: Overall, there does not appear to be a significant gender effect associated with venlafaxine XR treatment of PTSD.

References:

1. Walker JL, Carey PD, Mohr N, Stein DJ, Seedat S: Gender differences in the prevalence of childhood sexual abuse and in the development of pediatric PTSD. *Arch Women Ment Health* 2004; 7:111-121.

2. Zlotnick C, Zimmerman M, Wolfsdorf BA, Mattia JI: Gender differences in patients with posttraumatic stress disorder in a general psychiatric practice. *Am J Psychiatry* 2001; 158:1923-1925.

NR478 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Efficacy of Duloxetine for Anxiety in Elderly Patients With Major Depressive Disorder

Joel Raskin, M.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Curtis Wiltse, Ph.D., Daniel Walker, Ph.D., James Russell, M.D., Olga Brawman-Mintzer, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that MDD with comorbid anxiety is common in elderly patients and that duloxetine 60mg once daily is efficacious in reducing anxiety symptoms in these patients.

Summary:

Objective: To compare the efficacy of duloxetine 60mg once daily versus placebo in treating anxiety symptoms in elderly patients (>65) with MDD.

Methods: Patients were randomized to eight weeks of treatment with duloxetine 60mg (n=207) or placebo (n=104). Anxiety measures were analyzed for the total sample and by age, <75 (n=207) and >75 (n=96). Mean change from baseline to endpoint for HAMD17 items 10 (anxiety/psychic) and 11 (anxiety/somatic) and the anxiety/somatization subscale (items 10-13, 15, 17) were analyzed.

Results: Duloxetine produced greater reduction than placebo on item 10 (mean change= -0.62 vs -0.18, p<.001) and the anxiety/somatization subscale (mean change= -1.88 vs -0.99, p=.002) but not item 11. Repeated measures analyses showed separation between duloxetine and placebo beginning at week 1 for item 10 and week 4 for the anxiety/somatization subscale. Significant reduction in item 10 scores for the <75 (mean change= -0.63 vs -0.17, p=.002) and >75 (mean change = -0.61 vs 0.00, p=.007) age groups was observed in the duloxetine group versus placebo. Duloxetine significantly reduced anxiety/somatization subscale scores for the <75 group (mean change = -1.90 vs -0.80, p=.003) but not the >75 group (mean change = -1.92 vs -1.25, p=.312).

Conclusion: Duloxetine appears to be efficacious in treating anxiety symptoms in elderly patients with MDD.

References:

1. Dunner DL, Goldstein DJ, Mallinckrodt C, Lu Y, Detke MJ: Duloxetine in treatment of anxiety symptoms associated with depression. *Depress Anxiety* 2003; 18:53-61.
2. Lenze EJ, Pollock BG, Shear MK, Mulsant BH, Bharucha A, Reynolds CF 3rd: Treatment considerations for anxiety in the elderly. *CNS Spectr* 2003; 8(12 Suppl 3):6-13.

NR479 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Health Care Utilization and Costs for Adults With Undiagnosed ADHD

Stephen Able, Ph.D., *Outcomes Research, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Joseph Johnston, M.D., Chaitanya Sarawate, M.S., Wenli Luo, M.D., Maxine Fisher, Ph.D., Michael Bullano, Pharm.D., Ralph Swindle, Ph.D.

Educational Objectives:

At the conclusion of this session, participants should recognize that patients with undiagnosed ADHD utilize more medical re-

sources and generate greater direct medical costs than do patients without ADHD.

Summary:

Objective: Identify a cohort of adults with undiagnosed ADHD and compare their health care utilization and costs with those of adults previously diagnosed with ADHD and those without ADHD.

Methods: Administrative claims were used to identify 9,246 adult members of a large health plan with diagnosed ADHD. The Adult ADHD Self-Report Scale [ASRS-v1.1] screener was then administered to 20,010 adult members without diagnosed ADHD and results used to identify 1,236 members with "undiagnosed" ADHD (ASRS positive) and 18,744 non-ADHD controls (ASRS negative). Comparisons of utilization and costs were made between these three cohorts, both before and after adjustment for differences in geography, demographics, and comorbidities.

Results: On average, adults with undiagnosed ADHD demonstrated significantly greater utilization (e.g., annualized outpatient visits 3.0 vs. 2.4, p=.0007) and higher per member annual health care costs (mean \$1,411 vs. \$1,072, p=.0003) than non-ADHD controls, but significantly less utilization and lower costs than the previously diagnosed (mean outpatient visits 5.08, p<0.0001; mean total costs \$1,982, p<0.0001). After adjustment, differences between groups were smaller, but remained statistically significant.

Conclusions: Adults with undiagnosed ADHD utilize significantly greater health care resources and generate significantly higher direct medical costs than adults without ADHD, but less than those with diagnosed ADHD.

References:

1. Kessler RC, Adler L, Ames M, Demler O, Faraone S, Hiripi E, et al: The World Health Organization Adult ADHD Self-Report Scale (ASRS): A short screening scale for use in the General Population. *Psychological Med*, in press, 2004.
2. Swensen AR, Birnbaum HG, et al: Attention-deficit/hyperactivity disorder: increased costs for patients and their families. *J Am Acad Child Adolesc Psychiatry* 2003; 42:1415-1423.

NR480 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Cognitive Effect of GJT in Children With Intellectual Disabilities

Geon-Ho Bahn, M.D., *Department of Neuropsychiatry, Kyung Univ Hospital, 1 Hoegi-Dong Dongdaemun-Gu, Seoul 130-702, South Korea*; Wonserb Kang, M.D., Kyungkyu Lee, M.D., Chang Ju Kim, M.D., Yonghee Kim, Ph.D., Jaehyung Park, Ph.D., Seokong Lee, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize Gami-jihwang-tang, Oriental herbal medicinal formulation, can be a potential candidate medicine for children with subaverage IQ.

Summary:

Objectives: As clinicians, we tried to find agents with potentially curative properties for intellectual disabilities. Among the numerous herbal formulations available, we chose Gami-jihwang-tang (GJT), which showed effects on cell proliferation in the hippocampus in rats and tendency to improve cognitive performance in healthy children. In this study, we investigated the effect of GJT on intellectual function of children with subaverage IQ.

Methods: Subjects were children with intellectual disabilities, 4 to 8-year-old children. The experimental group took GJT for 16 weeks and was followed up 16 weeks after discontinuation of GJT. The control group was assessed at the same intervals but

did not receive placebos. To measure the effects of GJT, PEP and K-ABC were taken as base, 16 weeks, and 32 weeks later.

Results: For all of the ANOVAs, the treatment by time interaction terms were not significant. However, the experimental group showed the tendency to be progressed in simultaneous processing scale on K-ABC and revealed significant improvement of fine motor coordination on PEP ($F=5.20$, $p<.05$).

Conclusion: Although GJT failed to reveal significant improvement in cognition, we remain hopeful about the compound and feel that it should be evaluated by a double-blind, placebo-controlled trial in the future.

References:

1. Youn-Jung Kim, Mi-Hyun Jang, Min-Chul Shin, Baek-Vin Lim, Joo-Ho Chung, GeonHo Bahn, Eun-Kyung Paik, Jae-Hyung Park, Ee-Hwa Kim, Chang-Ju Kim: Shenqu-wan increases cell proliferation of cultured hippocampal cell line HiB5 and dentate gyrus of young Sprague Dawley rats. *The Journal of Korean Meridian and Acupoint* 2002; 19:1:79-86.
2. Shin HT, Chung SH, Lee JS, Kim SS, Shin HD, Jang MH, Shin MC, Bahn GH, Paik EK, Park JH, Kim CJ: Protective effect of shenqi-wan against H₂O₂-induced apoptosis in hippocampal neuronal cells. *Am J Chin Med* 2003; 31(5):675-686.

NR481 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

The Mechanism of Gami-Jiwhang-Tang as a Cognitive Enhancer

Geon-Ho Bahn, M.D., *Department of Neuropsychiatry, Kyung Univ Hospital, 1 Hoegi-Dong Dongdaemun-Gu, Seoul 130-702, South Korea*; Wonserb Kang, M.D., M.D., Seokyong Lee, M.D., Whanil Chang, M.D., Chang Ju Kim, M.D., Kyungkyu Lee, M.D., Eunkyung Paik, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize Gami-jiwhang-tang may be a potent protective agent against ischemia and be a hopeful agent for children with mental retardation.

Summary:

Objective: Though Gami-jiwhang-tang (GJT), an Oriental herbal medicinal formulation, has traditionally been used to treat delayed development physical and mental in children, there is little evidence in the context of modern medicine. In the present study, we investigated the effects of GJT on apoptosis, cell proliferation in the hippocampal dentate gyrus, and short-term memory defect following transient global ischemia in gerbils.

Methods: To make ischemia, we used 3% isoflurane in 20% O₂-77% N₂. Tissue preparation for cells used terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling assay and immunohistochemistry for caspase-3 and 5-bromo-2'-deoxyuridine. To evaluate the short-term memory ability, the latency for a step-down avoidance task was determined.

Results: Our results showed that apoptotic neuronal cell death and cell proliferation in the hippocampal dentate gyrus were significantly increased following transient global ischemia in gerbils and that GJT suppressed the ischemia-induced increase in apoptosis and cell proliferation in the dentate gyrus. Also provided direct evidence that improved short-term memory associated with GJT is due to reduced apoptotic neuronal cell death.

Conclusion: GJT was found to aid in recovery from central nervous system sequelae following stroke and to be a candidate medicine for children with intellectual disabilities.

References:

1. Bahn GH, Yoon DJ, Park JK, Lee TH, Jang MH, Shin MC, Kim CJ, Paik EK, Park JH, Cho SH, Lee CY: Effect of Liuweidihu-

ang-tang on alcohol-induced decrease in new cell formation in rat dentate gyrus. *Korean J Oriental Physiology & Pathology* 2002b; 16:5:1055-1059.

2. Shin HT, Chung SH, Lee JS, Kim SS, Shin HD, Jang MH, Shin MC, Bahn GH, Paik EK, Park JH, Kim CJ: Protective effect of shenqi-wan against H₂O₂-induced apoptosis in hippocampal neuronal cells. *Am J Chin Med* 2003; 31(5):675-686.

NR482 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Do Psychostimulants Lower the Seizure Threshold?

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Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the efficacy and safety of methylphenidate for the treatment of ADHD with convulsive disorder.

Summary:

Objectives: Attention deficit is one of the most frequent symptoms of pediatric convulsive disorders. Some antiepileptic drugs can induce ADHD-like symptoms or exacerbate ADHD. Although the psychostimulants are commonly believed to have effects of lowering the seizure threshold, they have been used for treating patients with ADHD. To clarify the safety of psychostimulants in patients with ADHD and convulsive disorders, related published articles are reviewed through the internet.

Methods: The total of 65 articles have been identified by conducting a computerized PUBMED and MEDLINE journal search using the key words "ADHD," "seizure," "stimulant," and "methylphenidate." Among them, we selected 15 articles involving the efficacy and safety of methylphenidate in the management of patients with ADHD and concomitant convulsive disorders with or without EEG abnormalities.

Results: In late 1980s, only a few studies had described that methylphenidate might lower the seizure threshold. Since 1989, 12 studies report that if a seizure-free period is documented, methylphenidate seems neither to increase the seizure frequency nor to worsen the EEG findings.

Conclusions: The results of this review suggest that methylphenidate is an effective and safe agent in ADHD and concomitant convulsive disorder with or without EEG abnormalities.

References:

1. Feldman H, Crumrine P, Handen BL, Alvin R, Teodori J: Methylphenidate in children with seizures and attention-deficit disorder. *Am J Dis Child* 1989; 143(9):1081-6.
2. Hemmer SA, Pasternak JF, Zecker SG, Trommer BL: Stimulant therapy and seizure risk in children with ADHD. *Pediatr Neurol* 2001; 24:99-102.

NR483 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

The Role of Patient Experience in Antidepressant Adherence

Mark R. Vanelli, M.D., *Adheris Inc, One Van DeGraff Drive, Burlington, MA 05401*; Alex Pedan, Ph.D.

Educational Objectives:

At the conclusion of this presentation, participants should be able to recognize that patients on started on antidepressants for the first time are at a higher risk of discontinuation than patients continuing therapy; more intensive education and follow-up are indicated for such antidepressant "rookies."

Summary:

Objective: While antidepressants demonstrate a high degree of effectiveness in treating depressive and anxiety disorders in short-term clinical trials, epidemiological studies suggests that over 80% of anxiety disorder patients experience symptom breakthrough under conditions of routine care. Here we explore the role of outpatient antidepressant adherence and patient experience as possible contributors to relapse.

Methods: De-identified patient data from a national retail were evaluated for patients on paroxetine (N=5, 160), venlafaxine (N=5,275), citalopam (N=7,077). Patients were considered non-adherent if they failed to pick up a prescribed refill within a 45-day window of their refill date. Adherence was evaluated for patients new to drug and new to drug class in the preceding 180 days ("rookies") and those continuing with therapy ("veterans").

Results: At three months persistence rates (veterans vs. rookies) were as follows: venlafaxine, 58 vs. 39%, citalopam 57 vs. 40%; paroxetine .42% vs. 26%. At six months persistence further significantly decreased, venlafaxine 42% vs. 24%; citalopam .40% vs. 24%; paroxetine 28% vs. 15%.

Conclusions: As antidepressants rookies were 31% to 46% less likely to remain on therapy at a given point in time, closer follow up and better educational efforts may be indicated for patients initiating therapy.

References:

1. Yonkers KA, et al: Chronicity, relapse, and illness—course of panic disorder, social phobia, and generalized anxiety disorder: findings in men and women from 8 years of follow-up. *Depression and Anxiety* 2003; 17:173-9.
2. Bull et al: Discontinuation of use and switching of antidepressants: influence of patient-physician communication. *JAMA* 2002; 228:1403-9.

NR484 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Atomoxetine Treatment for Pediatric Patients With ADHD and Comorbid Anxiety

Calvin R. Sumner, M.D., *Department of Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center DC4135, Indianapolis, IN 46285*; Craig Donnelly, M.D., Frank Lopez, M.D., Virginia Sutton, Ph.D., Rosalie Bakken, Ph.D., Martin Paczkowski, M.P.H., Douglas Kelsey, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will be able to summarize the efficacy of atomoxetine compared to placebo for treatment of pediatric patients with attention-deficit/hyperactivity disorder and comorbid anxiety.

Summary:

Background: Research indicates 25% to 50% comorbidity of anxiety disorders with attention-deficit/hyperactivity disorder (ADHD). Atomoxetine is a nonstimulant approved for treating ADHD that is not contraindicated in the presence of anxiety disorders.

Objective: This study compared atomoxetine with placebo in treating pediatric patients with ADHD and comorbid anxiety, as measured by the ADHDRS-IV-Parent:Inv (ADHDRS) Total Score and the Pediatric Anxiety Rating Scale (PARS) Total Score.

Methods: Patients in this double-blind, acute portion of an extended, multicenter trial were randomized to approximately 12 weeks of atomoxetine treatment (n=87) or placebo (n=89). Patients met DSM-IV criteria for both ADHD and anxiety disorder (generalized anxiety, separation anxiety, or social phobia). ADHDRS and PARS total scores were analyzed using ANCOVA (LOCF). Patients who responded during a placebo lead-in period were excluded from ADHDRS and PARS (total scores) analyses.

Results: Mean ADHDRS total score improved significantly from baseline to endpoint for the atomoxetine group (n=55; -10.5, SD 10.6) relative to placebo (n=58; -1.4, SD 8.3; p<.001). Mean PARS total score also improved significantly from baseline to endpoint for the atomoxetine group (n=55; -5.5, SD 4.8) relative to placebo (n=58; -3.2, SD 5.0; p=.008).

Conclusion: Results suggest atomoxetine is efficacious in pediatric patients with ADHD and comorbid anxiety.

References:

1. Biederman J, Newcorn J, Sprich S: Comorbidity of attention-deficit/hyperactivity disorder with conduct, depressive, anxiety and other disorders. *Am J Psych* 1991; 148:564-577.
2. Bird H, Gould M, Staghezza B: Patterns of diagnostic morbidity in a community sample of children aged 9 through 16 years. *J Am Acad Child Adolesc Psychiatry* 1993;32:361-368.

NR485 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

A Comparison of the Direct Treatment Costs for Children and Adolescents With Autism in a Privately Insured Population

Julie Whitworth, Pharm.D., *Outcomes Research, Innovation Center, Humana Inc., 500 West Main Street, Louisville, KY 40202*; Mohamed Hussein, M.S.C., Scott Flanders, Ph.D., Daniel Vanderpoel, Pharm.D., Timothy Sandman, M.B.A., Reshmi Siddique, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the total costs of health care services for children and adolescents with a diagnosis of autism in a health-benefits organization population and describe the differences in utilization of health care services of autistic children and adolescents compared to other chronic pediatric diseases in a health-benefits organization population.

Summary:

Objective: To compare the direct costs of treatment in children (ages 3-17) with a diagnosis of a pervasive developmental disorder (autism), diabetes, or asthma in a privately insured population.

Methods: Retrospective claims were derived from an administrative database. Non-parametric statistics were utilized to compare the six-month prediagnosis and 12-month postdiagnosis direct health care costs for autistic children (n=470) versus diabetic children (n=522) and asthmatic children (n=550).

Results: The autistic cohort exhibited a higher proportion of male subjects (80.6%) and a lower mean age (9.4 years) than the diabetic children (49.8%, 12.6 years) or asthmatic children (52.9%, 9.9 years). Children with autism had significantly higher median total health care costs than children with diabetes (\$621.09 vs. \$355.24, P<.05) or asthma (\$621.09 vs. \$291.10, P<.05) in the six-month prediagnosis period. Additionally, autistic children had significantly higher median total health care costs than children with diabetes (\$2103.58 vs. \$1605.20, P<.05) or asthma (\$2103.58 vs. \$850.27, P<.05) in the 12-month postdiagnosis period.

Conclusion: This analysis demonstrates that autistic children incur greater health care costs than children with diabetes or asthma in both the prediagnosis and postdiagnosis periods. Overall, this comparison reflects the significant cost of illness for autism in this privately insured population.

References:

1. Birenbaum A, Guyot D, Cohen H J: Health care financing for severe developmental disabilities. St. John's University, New York. Monographs of the American Association on Mental Retardation 1990 (14) p1-150, ISSN 0895-8009.

- Jarbrink K, Knapp M: The economic impact of autism in Britain. *Autism* 2001; 5:7-22.
- Newschaffer C, Curran LK: Autism: an emerging public health problem. *Public Health Reports* 2003; 118:393-399.
- Dunn OJ: Multiple comparisons using rank sums. *Technometrics* 1964; 6:241-252.

NR486 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Escitalopram and GAD: Efficacy Across Different Subgroups and Outcomes

Dan J. Stein, M.D., *Department of Psychiatry, University of Stellenbosch, P.O. Box 19063, Tygerberg 7505, South Africa;*
 Friis Andersen, Ph.D., Wayne Goodman, M.D.

Educational Objectives:

At the conclusion of this session, the participants will increase their knowledge concerning the reduction of anxiety and depressive symptoms in GAD by implementing escitalopram treatment.

Summary:

Introduction: Generalized anxiety disorder (GAD) is frequently associated with depressive symptoms. We examined the SSRI antidepressant, escitalopram, for efficacy across different subgroups and outcomes (anxious symptoms, depressive symptoms, and quality of life).

Methods: Three randomized, placebo-controlled, eight-week, double-blind, studies of escitalopram (10 to 20mg/day) in GAD have employed a similar design, allowing for pooling of the data. The primary efficacy measure was the Hamilton Anxiety Scale (HAM-A). General linear models were used to determine the efficacy of escitalopram across different subgroups and outcomes.

Results: Escitalopram was efficacious for GAD on a range of measures of both anxiety and depression, and improved the associated impairment in quality of life. There was no significant interaction of effects on the HAM-A with demographic or clinical variables. Furthermore, escitalopram was efficacious on both primary and secondary scales in the subgroup of subjects with above-median severity of depressive symptoms at baseline (Hamilton Depression Rating Scale score >12).

Conclusions: Escitalopram reduces anxiety and depressive symptoms in GAD, and improves quality of life. It is equally efficacious in GAD patients with an above-median level of depressive symptoms. Further research is needed to determine whether these results can be extrapolated to GAD patients with comorbid major depression.

References:

- Davidson JR, Bose A, Korotzer A, Zheng H: Escitalopram in the treatment of generalized anxiety disorder: double-blind, placebo controlled, flexible-dose study. *Depress Anxiety* 2004; 19:234-240.
- Goodman WK, Bose A, Wang, Q: Treatment of generalized anxiety disorder with escitalopram: pooled results from double-blind, placebo-controlled trials. *J Affect Dis*, in press.

NR487 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
The Treatment of Anxiety Symptoms Associated With Depression

Dan J. Stein, M.D., *Department of Psychiatry, University of Stellenbosch, P.O. Box 19063, Tygerberg 7505, South Africa;*
 Henning Andersen, Ph.D., Borwin Bandelow, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant will better understand comorbid depression/anxiety symptoms associated with depression.

Summary:

Introduction: Comorbidities are common in real life, and it is important to examine comorbid depression/anxiety, since both depressive and anxious symptoms need to improve with treatment to achieve stable remission.

Objective: The effect of escitalopram in treating the symptoms of anxiety in patients with major depression (without comorbid anxiety) was investigated.

Methods: Data from five escitalopram studies that included a placebo arm were analyzed. In all studies, anxiety was assessed using the inner tension item (item 3) of the MADRS. In three of the studies, anxiety symptoms were also assessed, either continuously over time or at baseline and endpoint, by using the HAMA, the anxious mood item of the HAMA (item 1), the Psychic Anxiety subscale of the HAMA (items 1-6 and 14), the psychic anxiety item of the HAMD (item 10), and the Anxiety/Somatization subfactor of the HAMD (items 10-13, 15, and 17).

Results: In all comparisons, mean improvement for escitalopram was significantly greater than for placebo. In some comparisons, escitalopram also showed a significantly earlier onset of action or an earlier separation from placebo than citalopram.

Conclusion: Anxiety symptoms in depressed patients can effectively be treated with escitalopram and a more stable remission might therefore be achieved.

References:

- Brown C, Schulberg HC, Madonia MJ, et al: Treatment outcomes for primary care patients with major depression and lifetime anxiety disorders. *Am J Psychiatry* 1996; 153:1293-1300.
- Kessler RC, Nelson CB, McGonagle KA, et al: Comorbidity of DSM-III-R major depressive disorder in the general population: results from the US National Comorbidity Survey. *Br J Psychiatry Suppl* 1996; 17-30.

NR488 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Venlafaxine XR Treatment of PTSD: A Six-Month, Placebo-Controlled Trial

Dan J. Stein, M.D., *Department of Psychiatry, University of Stellenbosch, P.O. Box 19063, Tygerberg 7505, South Africa;*
 Jonathan Davidson, M.D., David Baldwin, M.B., Enrique Kuper, Saeed Ahemd, M.D., Jeff Musgnung

Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the efficacy and safety of venlafaxine extended release (XR), a serotonin-norepinephrine reuptake inhibitor, in the short-term and continuation treatment of patients with posttraumatic stress disorder.

Summary:

Introduction/Hypothesis: This international, double-blind trial evaluated the efficacy of venlafaxine XR for moderate to severe PTSD.

Methods: 329 adult outpatients (venlafaxine XR, n=161; placebo, n=168) were randomly assigned to treatment with flexible-dose venlafaxine XR (37.5mg to 300mg/d), or placebo for 24 weeks, starting with 37.5mg (ITT population). Patients had a primary diagnosis of DSM-IV PTSD, PTSD symptoms for six months or longer, and 17-item Clinician-Administered PTSD scale (CAPS-SX17) score of 60 or more. The primary efficacy measure was baseline-to-endpoint change in CAPS-SX17 score. Secondary as-

assessments included remission (CAPS-SX17 score of 20 or less), time to remission, PTSD symptom-free days, and changes in PTSD and depression symptoms, global illness severity, stress vulnerability, resilience, quality of life, and functioning. Appropriate parametric and nonparametric tests were performed.

Results: The mean maximum dose of venlafaxine XR was 221 mg/day. Mean CAPS-SX17 total score changes were -51.7 for venlafaxine XR and -43.9 for placebo ($P=0.006$). The venlafaxine XR group showed a significantly greater remission rate, shorter time to remission, and more symptom-free days. Venlafaxine XR patients showed greater improvement in PTSD and depression symptoms, global disease severity, vulnerability, resilience, quality of life, and functioning, with a lower discontinuation rate.

Conclusions/Discussion: Venlafaxine XR was effective and well tolerated in short-term and continuation treatment of PTSD.

References:

1. Ballenger JC, Davidson JR, Lecrubier Y, Nutt DJ, Foa EB, Kessler RC, McFarlane AC, Shalev AY: Consensus statement on posttraumatic stress disorder from the International Consensus Group on Depression and Anxiety. *J Clin Psychiatry* 2000; 61(suppl 5):60-66.
2. Ballenger JC, Davidson JR, Lecrubier Y, Nutt DJ, Marshall RD, Nemeroff CB, Shalev AY, Yehuda R: Consensus statement update on posttraumatic stress disorder from the international consensus group on depression and anxiety. *J Clin Psychiatry* 2004; 65(suppl 1):55-62.

NR489 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Crossover Study of Dexmethylphenidate Extended Release**

Raul R. Silva, M.D., *Department of Psychiatry, New York University School of Medicine, 550 First Avenue, MB21 South 6, New York, NY 10016*; Rafael Muniz, M.D., Linda Pestreich, B.S.C., James Wang, Ph.D., Frank Lopez, M.D., Matthew Brams, M.D., Ann Childress, M.D.

Educational Objectives:

At the conclusion of this session, the participant will be able to describe the efficacy and safety of once-daily dexmethylphenidate extended-release (d-MPH-ER) capsules in children with attention-deficit/hyperactivity disorder.

Summary:

Objective: To evaluate the efficacy and safety of extended-release dexmethylphenidate (d-MPH-ER), at a dose of 20 mg QD, in children with attention-deficit/hyperactivity disorder (ADHD) in a laboratory classroom setting.

Methods: This double-blind, crossover study randomized 54 children aged 6-12 years, previously stabilized on methylphenidate 20-40 mg/d. They were evaluated on a practice day and on day 7 of receiving d-MPH-ER or placebo. They were then crossed over to alternate condition and retested on day 15. The primary efficacy variable was the SKAMP-Combined score; secondary efficacy variables included SKAMP-Attention and -Depotment scores and written math test results. Safety evaluations included adverse events, vital signs, body weight, and laboratory tests.

Results: Improvements in SKAMP-Combined, -Attention, and -Depotment scores were significantly greater with d-MPH-ER than with placebo at all time points up to 12 hours postdose (P values ranged from $<.001$ to $.046$). The number of math problems attempted and answered correctly was also significantly greater with d-MPH-ER at all time points ($P<.001$ vs placebo). DMPH-ER was well tolerated, with no serious or severe adverse events.

Conclusion: At 20 mg QD, dMPH-ER safely and effectively improves classroom attention, depotment, and performance in children with ADHD.

This study was supported by Novartis Pharmaceuticals Corporation.

References:

1. Quinn D, Wigal S, Swanson J, et al: Comparative pharmacodynamics and plasma concentrations of d-threo-methylphenidate hydrochloride after single doses of d-threo-methylphenidate hydrochloride and d,l-threo-methylphenidate hydrochloride in a double-blind, placebo-controlled, crossover laboratory school study in children with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 2004; 43:1422-1429.
2. Wigal S, Swanson JM, Feifel D, et al: A double-blind, placebo-controlled trial of dexmethylphenidate hydrochloride and d,l-threo-methylphenidate hydrochloride in children with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 2004; 43:1406-1414.

NR490 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Gender Differences in Response to Pharmacotherapy for Generalized Anxiety Disorder**

John J. Worthington III, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 815, Boston, MA 02114*; Alyson Zalta, B.A., Kelly Christian, B.S., Julie Stevens, B.A., Elizabeth Hoge, M.D., Naomi M. Simon, M.D., Mark Pollack, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that gender may be an important factor in SSRI treatment response for generalized anxiety disorder.

Summary:

Introduction: Women have a higher prevalence of anxiety disorders, including generalized anxiety disorder (GAD), but few studies have examined gender differences in response to pharmacotherapy.

Methods: We examined gender as a correlate of response to six weeks of open, prospective fluoxetine in 23 men and 22 women with a primary diagnosis of GAD. The primary outcome measures were the Hamilton Anxiety Rating Scale (HAM-A) and the Clinician Global Impression—Severity Scale (CGI-S).

Results: Despite a lack of gender difference in age or baseline severity measures, women had a significantly poorer response to fluoxetine as measured by both the HAM-A and CGI-S scales. Current age did not significantly predict treatment response. However, GAD onset occurred at a significantly younger age for women (mean 15.6 years) compared with men (mean 24 years). In univariate analyses, and in multivariate analyses controlling for baseline severity, gender, and age of onset in regression models, there was a significant interactive effect of age of onset with gender ($p<0.01$ for HAMA), with poorer response for men with earlier age of onset, and poorer response for women with older age of onset.

Conclusions: These data, though limited by the relatively small sample size and open nature of this study, suggest that women with GAD, and particularly those with a later age of onset of GAD, may have a poorer response to SSRI pharmacotherapy. The etiology of this difference remains unclear. Larger placebo-controlled trials are needed to examine gender and treatment response in anxiety disorders.

References:

1. Yonkers KA, Bruce SE, Dyck IR, Keller MB: Chronicity, relapse, and illness - Course of panic disorder, social phobia, and generalized anxiety disorder: findings in men and women from 8 years of follow-up. *Depression and Anxiety* 2003; 17:173-179.
2. Kornstein SG, Schatzberg AF, Thase ME, Yonkers KA, McCullough JP, Keitner GI, Gelenberg AJ, Davis SM, Harrison WM,

Keller MB: Gender differences in treatment response to sertraline versus imipramine in chronic depression. *American Journal of Psychiatry* 2000; 157:1445-1452.

NR491 **Tuesday, May 24, 3:00 p.m.-5:00 p.m.**
Comparison of ADHD Symptom Improvement and Response Rates With OROS MPH and Atomoxetine: The FOCUS Trial

Jason E. Kemner, M.P.H., *McNeil Consumer & Specialty Pharmaceuticals, 7050 Camp Hill Road, Fort Washington, PA 19034-2299*; H. Lynn Starr, M.D., *Christa Hooper-Wood, Pharm.D., Patrick E. Ciccone, M.D.*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to (1) evaluate the relative efficacy and safety of OROS MPH versus atomoxetine in children with attention-deficit/hyperactivity disorder (ADHD), (2) compare and assess the differences in response rates and effectiveness between OROS MPH and atomoxetine in children with ADHD

Objective: To evaluate the efficacy and safety of OROS methylphenidate (MPH) and atomoxetine in children with attention-deficit/hyperactivity disorder (ADHD).

Methods: Children (N=1,323) 6 to 12 years of age with ADHD were randomized (2:1) to OROS MPH or atomoxetine in this prospective, open-label, three-week study. Initiation and titration of medication was based on each investigator's clinical judgment. Improvement was measured weekly by investigators using the ADHD Rating Scale (ADHD-RS) and Clinical Global Impression—Improvement of Illness (CGI-I) and by parents using a daily satisfaction questionnaire.

Results: ADHD-RS score improvements were significantly greater with OROS MPH than with atomoxetine at all three weekly visits ($P<.0001$). A responder analysis comparing the percentage of subjects achieving $\geq 40\%$ reduction in symptom scores revealed significantly greater response rates for the OROS MPH group than for the atomoxetine group (66% vs 54%; $P<.0001$, respectively). Response measured by subjects scoring ≤ 2 on the CGI-I scale was also greater for OROS MPH (68.6% vs 52.8%, respectively; $P<.0001$). Findings from parent diaries were consistent with investigator data. Rates of adverse effects were similar in both treatment groups.

Conclusions: Results from this direct comparison demonstrate significantly greater symptom improvement and higher responder rates in children taking OROS MPH.

References:

1. Wilens T, et al: *J Am Acad Child Adolesc Psychiatry* 2003; 42:424-433.
2. Spencer T, et al: *J Clin Psychiatry*. 2002; 63:1140-1147.

NR492 **Tuesday, May 24, 3:00 p.m.-5:00 p.m.**
ADHD Symptom Improvement and Response Rates in Girls From the FOCUS Study

Jason E. Kemner, M.P.H., *McNeil Consumer & Specialty Pharmaceuticals, 7050 Camp Hill Road, Fort Washington, PA 19034-2299*; H. Lynn Starr, M.D., *Christa Hooper-Wood, Pharm.D., Patrick E. Ciccone, M.D.*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to (1) evaluate the relative efficacy and safety of OROS MPH versus atomoxetine in girls with attention-deficit/hyperactivity disorder (ADHD), (2) compare and assess the differences in response rates and effectiveness between OROS MPH and atomoxetine in girls with ADHD.

Summary:

Objective: To compare the efficacy of OROS methylphenidate (MPH) and atomoxetine in girls (6-12 years of age) with ADHD.

Methods: A subgroup of girls (n=340) was identified from a prospective, open-label, three-week, randomized (2:1) study comparing OROS MPH and atomoxetine. Initiation and titration of medication were based on the investigators' clinical judgment. Investigators measured symptom improvement using the ADHD Rating Scale (ADHD-RS).

Results: Baseline ADHD-RS scores were similar in both groups. Investigator-evaluated ADHD-RS scores demonstrated significantly greater improvements from baseline at Week 3 with OROS MPH versus atomoxetine ($P<.02$). Inattention and hyperactivity subscale score improvements were also greater with OROS MPH versus atomoxetine ($P<.05$). Response rates (percentage of patients with $\geq 50\%$ reduction from baseline on ADHD-RS) were significantly greater for OROS MPH than for atomoxetine (55% vs 39%, respectively; $P<.01$). The odds ratio indicated that girls receiving OROS MPH were 40% more likely to be responders than those on atomoxetine (95% confidence interval, 1.08-1.82).

Conclusions: Results from this direct comparison demonstrate significantly greater symptom improvement with OROS MPH compared with atomoxetine in girls with ADHD. Greater improvements were seen in symptoms of hyperactivity and inattentiveness. Results from this subgroup analysis of girls were consistent with the overall study population results.

References:

1. Wilens T, et al: *J Am Acad Child Adolesc Psychiatry* 2003; 42:424-433.
2. Spencer T, et al: *J Clin Psychiatry* 2002; 63:1140-1147.

NR493 **Tuesday, May 24, 3:00 p.m.-5:00 p.m.**
Long-Term Efficacy of Extended Release Dexmethylphenidate in Adult ADHD

Lenard A. Adler, M.D., *Department of Psychiatry, New York University School of Medicine, 530 First Avenue HCC 5A, New York, NY 10016-6497*; James McGough, M.D., *Rafael Muniz, M.D., Linda Pestreich, B.S.C., Catherine Agoropoulou, Ph.D., Hai Jiang, Ph.D.*

Educational Objectives:

At the conclusion of this session, the participant will be able to describe the efficacy and safety of once-daily dexmethylphenidate over the course of six months in adults with attention-deficit/hyperactivity disorder (ADHD).

Summary:

Objective: To evaluate the acute and long-term efficacy and safety of dexmethylphenidate extended-release (d-MPH-ER) capsules in adults with attention-deficit/hyperactivity disorder (ADHD). Dexmethylphenidate is the pharmacologically active enantiomer of methylphenidate.

Methods: In this double-blind, fixed-dose study, 221 adults were randomized to receive d-MPH-ER 20 mg, 30 mg, 40 mg, or placebo for five weeks. Dosages were initiated at 10 mg/d for one week then increased to target level. After completing this phase, 170 patients continued into a six-month open-label, flexible-dose extension. Efficacy was assessed as the change from baseline in DSM IV ADHD Rating Scale total scores.

Results: At five weeks, mean reductions from baseline in total scores were 7.9, 13.7, 13.4, and 16.9 for placebo, d-MPH-ER 20 mg ($P=.006$), 30 mg ($P=.012$), and 40 mg ($P<.001$), respectively. At six months, mean reductions from the end of the double-blind phase were 10.2 for patients previously taking placebo and 8.4 for those previously taking d-MPH-ER. In both phases, d-MPH-

ER was well tolerated; most adverse events were mild to moderate. Vital signs showed no clinically significant changes.

Conclusion: Once-daily d-MPH-ER 20-40 mg is safe and effective for the long-term treatment of ADHD in adults.

This study was supported by Novartis Pharmaceuticals Corporation.

References:

1. Wender PH, Wolf LE, Wasserstein J: Adults with ADHD: an overview. *Ann NY Acad Sci.* 2001; 931:1-16.
2. Keating GM, Figgitt DP: Dexmethylphenidate. *Drugs* 2002; 62:1899-1904.

NR494 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Help Seeking and PTSD in a Canadian Epidemiological Sample

Michael A. Van Ameringen, M.D., *Department of Psychiatry, McMaster University, 1200 Main Street, West, Hamilton L8N 3Z5, Canada*; Catherine Mancini, M.D., Beth Pipe, B.S.N., Mark Bennett, B.A., Michael Boyle, Ph.D., Jonathan Oakman, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to: (1) assess the prevalence of help-seeking behaviours in a Canadian epidemiological PTSD sample, (2) examine the relationship between help-seeking behaviours and PTSD, (3) evaluate predictors of help-seeking in individuals with PTSD.

Summary:

Objective: Few studies have looked at specific factors that affect the help seeking behavior of individuals with PTSD. A relationship has been previously found between demographic variables and help-seeking. To examine this question further, we evaluated help-seeking behaviors of individuals who had experienced a traumatic event sufficient to induce PTSD in an epidemiological sample.

Method: An epidemiological study of PTSD in 3,006 Canadian individuals was conducted. Following the completion of the PTSD portion of the survey, respondents were asked a series of questions concerning help-seeking.

Results: Of those who experienced a major trauma, 64.6% of the lifetime PTSD (LTPTSD) group versus 24.5% of those who did not meet criteria for PTSD had sought professional help ($\chi^2=99.9$; $p<.001$). A majority of the LTPTSD individuals (80.2%) received counseling, whereas 56.5% received medication. Of individuals with LTPTSD (60.1%) consulted a psychologist; 56.2% saw their family physician; and 43.4% saw a psychiatrist. Significantly high rates of help seeking were found in those who had experienced traumas classified as "Other Injury or Shock," and "Learning About Others Traumas." Demographic variables as well as geographic region, perceived social supports, comorbidity, and PTSD symptom severity did not predict help-seeking.

Conclusion: Development of PTSD was highly associated with help-seeking behavior in an epidemiological sample. In contrast to previous findings, few significant demographic or illness variables were found to be strong predictors of help-seeking behavior.

References:

1. Koenen K, Goodwin R, Stuenkel E, Hellman F, Guardino M: Posttraumatic stress disorder and treatment seeking in a national screening sample. *Journal of Traumatic Stress* 2003; 16(1): 5-16.
2. Frise S, Steingart A, Sloan M, Cotterchio M, Kreiger N: Psychiatric disorders and use of mental health services by Ontario women. *Can J Psychiatry* 2002; 47(9): 849-856.

NR495 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

The Burden of Youth Anxiety Disorders on Families

Catherine Mancini, M.D., *Department of Psychiatry, McMaster University, 1200 Main Street West, Hamilton, Ontario, Canada*; Michael A. Van Ameringen, M.D., Mark Bennett, B.A., Beth Pipe, B.S.N.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to: (1) understand the degree of burden on families experienced by families of youth with anxiety disorders, (2) describe specific areas of disruption to families when coping with the anxiety disorder of a child.

Summary:

Objective: Anxiety disorders are prevalent conditions in childhood and adolescence, affecting approximately 10%-20% of this age group. These disorders can significantly impact on the lives of youth, resulting in impairment in social, educational, and family functioning. This study examines the degree of burden placed on families of children and adolescents with anxiety disorders.

Method: Twenty-five consecutive youth admissions to an anxiety disorders clinic were evaluated for psychiatric diagnosis using a structured interview. A family member completed a questionnaire evaluating the burden/impact of having an ill child in a variety of areas of family functioning.

Results: Overall, 60.0% of families reported moderate to extreme overall burden due to their child's illness. Forty percent of families (10/25) experienced a high degree of burden due to the stoppage of recreational activities, and 40% (10/25) reported that the disruption of normal family routines caused a moderate to extreme degree of burden. Sixty-eight (17/25) percent of respondents reported a high degree of burden on their families due to the fact that family members needed to assist their child in avoiding anxiety provoking stimuli. A quarter of families reported seeking psychological help (treatment) to cope with their child's illness. No statistically significant differences were found in the rate of those reporting a high degree of burden on the family, based on the age of child ($\chi^2=.03$; $p>.05$) or primary anxiety disorder diagnosis ($\chi^2=1.59$; $p>.05$).

Conclusion: This study suggests that a significant burden is placed on family members of youth with anxiety disorders, regardless of the age of the child or the primary diagnosis.

References:

1. Bastiaansen D, Koot HM, Ferdinand RF, Verhulst FC: Quality of life in children with psychiatric disorders: self-, parent, and clinician report. *J Am Acad Child Adolesc Psychiatry* 43(2):221-230.
2. Manassis K: Childhood anxiety disorders: lessons from the literature. *Can J Psychiatry* 2000; 45:724-730.

NR496 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Attention Spectrum Disorders: Guanfacine Produces Alterations in BOLD Contrast, as Measured by fMRI

Neil Easton, Ph.D., *Institute of Neuroscience, University of Nottingham, Queens Medical Centre, Nottingham NG24 8EP, United Kingdom*; Yasmene Shah, Ph.D., Fiona Marshall, Ph.D., Charles Marsden, D.Sc.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to describe the brain regions activated in rats treated with guanfacine—as assessed with the blood oxygenation level dependent technique (BOLD).

Summary:

Objective: To determine the functional magnetic resonance imaging (fMRI) blood oxygenation level dependent (BOLD) response in rat brain regions following administration of the alpha-2A-adrenergic agonist guanfacine, a drug of potential benefit in the treatment of attention-deficit/hyperactivity disorder (ADHD).

Methods: For basal recording of changes in signal intensity, rats were individually placed into a 2.35-T Bruker magnet for 90 minutes. Saline (n = 6) or guanfacine 0.3 mg/kg, ip, (n = 9) was then administered, and recording continued for another 90 minutes. Statistical parametric maps were used to analyze data for BOLD responses. Respiration rate, blood pressure, and blood gases were monitored.

Results: The main changes were negative BOLD responses in the caudate putamen and nucleus accumbens with positive BOLD responses in frontal brain areas. All physiologic measurements remained constant throughout each analysis.

Conclusions: Guanfacine decreases caudate activity and increase frontal cortex activity. This ability to alter neuronal activity in specific areas of the rat brain, known to be impaired in ADHD2—may explain the therapeutic properties of guanfacine.

References:

1. Taylor FB, Russo J: Comparing guanfacine and dextroamphetamine for the treatment of adult attention-deficit/hyperactivity disorder. *J Clin Psychopharmacol* 2001; 21:223-228.
2. Krause KH, Dresel SH, Krause J, la Fougere C, Ackenheil M: The dopamine transporter and neuroimaging in attention deficit hyperactivity disorder. *Neurosci Biobehav Rev* 2003; 27:605-613.

NR497 Tuesday, May 24, 3:00 p.m.-5:00 p.m. Gender Difference in Adults With ADHD and Treated With Atomoxetine

Frederick W. Reimherr, M.D., *Department of Psychiatry, University of Utah, 30 North 1900 East, Room 5R218, Salt Lake City, UT 84132*; Reid Robison, Fred W. Reimherr, M.D., Stephen V. Faraone, Ph.D., Barrie K. Marchant, M.S., Lenard A. Adler, M.D., Soni Poonam, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to explore gender differences in adults with ADHD and help physicians be better able to assess and treat women with ADHD.

Summary:

Introduction: ADHD children exhibit several gender differences, a male preponderance and less females with externalizing disorders (conduct and oppositional defiant disorder).

Objective: To examine gender differences in a very large clinical trial of ADHD adults.

Methods: Data from two identical, placebo-controlled, 11-week studies of atomoxetine in adult ADHD (535 subjects at 31 sites) were combined. Both showed positive medication-placebo differences.

Results: Thirty percent of the population was female, a proportion higher than found in pediatric samples. In contrast to a predominance of inattentive ADHD subtype in female children, these females were more frequently combined type versus the males. Females were rated as more impaired on every measure of ADHD symptoms including total CAARS-INV, total WRAADDS, and subscales of both measures. Females were rated as having more emotional symptoms on the WRAADDS emotional dimension, lifetime SCID-P psychiatric diagnoses, HAM-A, and HAM-D. Females exhibited significantly greater improvement on the WRAADDS emotional dimension versus the males. There were

no significant gender by treatment effects in the CAARS-INV or CGI-S scores.

Conclusion: Females with ADHD displayed significantly greater ADHD symptoms and emotional impairment on multiple measures. On the WRAADDS emotional dimension they responded better to treatment, than their male counterparts.

References:

1. Michelson D, Adler L, Spencer T, Reimherr FW, West S, Allen A, et al: Atomoxetine in adults with ADHD: Two randomized, placebo-controlled studies. *J Biol Psych* 2004; 53(2):112-20.
2. Wender PH: Attention-deficit hyperactivity disorder in adults. 1995 Oxford University Press; New York; 1995..
3. Barkley R: Attention-deficit hyperactivity disorder. *Sci Am* 1998; 279(3):66-71.

NR498 Tuesday, May 24, 3:00 p.m.-5:00 p.m. d-Amphetamine and Guanfacine Improve Behavioral Symptoms in a Rat Model of ADHD

Terje Sagvolden, Ph.D., *Institute of Basic Medical Sciences, University of Oslo and Centre for Advanced Study, P.O. Box 1103-Blindern, Oslo NO-0317 Os, Norway*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to explain the effects of guanfacine and d-amphetamine on behavior of the spontaneously hypertensive rat, an animal model of attention-deficit/hyperactivity disorder (ADHD).

Summary:

Objective: Attention-deficit/hyperactivity disorder (ADHD) is a cognitive/behavioral developmental disorder. The main symptoms are overactivity, impulsiveness, and inattentiveness. In two studies, we tested the behavioral effects of the indirectly acting dopamine agonist d-amphetamine and the alpha2-adrenergic agonist guanfacine on the spontaneously hypertensive rat (SHR), the best validated animal model.

Methods: Correct responding in operant chambers was rewarded according to an intermittent schedule of reinforcement, with the average interval being 3 min. Rats were tested every day and drugs were given intraperitoneally every third day. Overactivity, impulsiveness, and sustained attention were measured.

Results: Results showed normalization of SHR behavior at relatively low d-amphetamine doses (0.5-2 mg/kg); the higher d-amphetamine doses tended to disrupt behavior. SHR behavior was also virtually normalized after guanfacine administration, at 0.15-0.6 mg/kg. Some sedation occurred with higher guanfacine doses, but behavioral improvements cannot be fully explained by sedation, as improvements also occurred in sustained attention, which tends to be adversely affected by sedation.

Conclusions: Both dopaminergic and noradrenergic agonists improve ADHD-like behavior. These results may mean that ADHD is a more general monoamine dysfunction, and not solely a dopamine dysfunction.

References:

1. Sagvolden T, Johansen EB, Aase H, Russell VA: A dynamic developmental theory of attention-deficit/hyperactivity disorder (ADHD) predominantly hyperactive/impulsive and combined subtypes. *Behavioral and Brain Sciences*. In press. <http://www.bbsonline.org/Preprints/Sagvolden-05152002/>.
2. Sagvolden T: Behavioral validation of the spontaneously hypertensive rat (SHR) as an animal model of attention-deficit/hyperactivity disorder (ADHD). *Neurosci Biobehav Rev* 2000; 24:31-39.

NR499 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Dexmethylphenidate Extended Release in Children and Adolescents With ADHD

Supported by Novartis Pharmaceuticals Corporation

Laurence L. Greenhill, M.D., *Department of Child Psychiatry, New York Psychiatric Institute, 1051 Riverside Drive, New York, NY 10032*; Roberta Ball, D.O., A. J. Levine, M.D., Rafael Muniz, M.D., Linda Pestreich, B.S.C., James Wang, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss the efficacy and safety of once-daily dexmethylphenidate extended-release capsules compared with placebo in children and adolescents with attention-deficit/hyperactivity disorder.

Summary:

Objective: To evaluate once-daily extended-release dexmethylphenidate (d-MPH-ER), the pharmacologically active enantiomer of methylphenidate, in pediatric attention-deficit/hyperactivity disorder (ADHD).

Method: This multicenter, double-blind, flexible-dose study randomized 103 patients aged 6-17 years to receive d-MPH-ER 5-30 mg capsules or placebo once daily for seven weeks. Doses were titrated to optimal levels during first five weeks and maintained for final two weeks. Efficacy was evaluated weekly at school and at home using Conners' ADHD/DSM-IV Scales for teachers (CADS-T) and for parents (CADS-P) and the Clinical Global Impressions Scale-Improvement (CGI-I).

Results: Efficacy was evaluated in 97 patients, safely in 100 patients. Median change from baseline in CADS-T scores was significantly greater with d-MPH-ER than with placebo (15.0 vs. 1.0, respectively; $c2 = 11.2$, $df=1$, $P=.0008$); median change from baseline in CADS-P scores was 14.5 with d-MPH-ER, 4.0 with placebo ($c2 = 14.1$, $df=1$, $P=.0002$). At final visit, 67.3% of patients receiving d-MPH-ER and 13.3% receiving placebo were "very much improved" or "much improved" on CGI-I ($P<.001$) scale. D-MPH-ER was well tolerated, with adverse event rates similar to those reported with immediate-release d-MPH.

Conclusion: Once-daily d-MPH-ER 5-30 mg is safe and effective for children and adolescents with ADHD.

References:

1. Keating GM, Figgitt DP: Dexmethylphenidate. *Drugs* 2002; 62:1899-1904.
2. Wigal S, Swanson JM, Feifel D, et al: A double-blind, placebo-controlled trial of dexmethylphenidate hydrochloride and d,l-threo-methylphenidate hydrochloride in children with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 2004; 43:1406-1414.

NR500 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Prevalence of Specific Phobia and Comorbidity With Social Phobia Symptoms in the Social Phobia Israeli Conscripts Epidemiologic Study

Julia Iancu, M.D., *Department of Psychiatry B., Beer Yaakov Hospital, POB1, Beer Yaakov, Israel*; Jennifer Poreh, Ph.D., Pinhas Dannon, M.D., Amir Poreh, Ph.D., Moshe Kotler, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the high rate of social phobia and specific phobia and to discuss the risk factors toward these disorders.

Summary:

Background: Social phobia (SP) and specific phobia are highly prevalent disorders with high comorbidity rates. In this study, we

examined the rate of specific phobia and SP symptomatology in a non-clinical sample of Israeli young adults.

Methods: 850 young soldiers from the Israel Defense Forces participated in the study. Measures included the Liebowitz Social Anxiety Scale, a questionnaire on specific phobias and a socio-demographic questionnaire. Data on eight specific fears representing DSM-IV-TR specific phobias were analyzed to evaluate their rate, the comorbidity rate with SP symptoms and to characterize risk factors.

Results: SP symptomatology was reported by 4.5% of the sample. The prevalence of fears and phobias in our sample was 49.1% and 8.7%, respectively. Most frequent fears and phobias were from animals, being alone, heights, injury, and closed places. A significant correlation was found between the number of phobias and the LSAS score. Based on a stepwise regression analysis, the following variables contributed significantly: no friends or boyfriend/girlfriend, school absenteeism, mechanic soldier, and presence of SP (LSAS score >79).

Conclusions: Our findings corroborate findings from other Western studies regarding both the high prevalence of SP symptomatology and specific phobias, as well as the high comorbidity between these disorders.

References:

1. Curtis GC, Magee WJ, Eaton WW, Wittchen HU, Kessler RC: Specific fears and phobias. *Epidemiology and classification.* *Br J Psychiatry* 1998; 173:212-217.
2. Fredrikson M, Annas P, Fischer H, Wik G: Gender and age differences in the prevalence of specific fears and phobias. *Behav Res Ther* 1996; 34, 33-39.

NR501 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Screening for Anxiety Disorders in Depressed Patients

Mark Zimmerman, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905*; Iwona Chelminski, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to describe the performance of a screening scale for anxiety disorders in depressed patients.

Summary:

Objective: The Psychiatric Diagnostic Screening Questionnaire (PDSQ) is a brief, psychometrically strong, questionnaire designed to screen for common Axis I disorders. In the present report, we examine the ability of the PDSQ to identify anxiety disorders in psychiatric outpatients with a principal diagnosis of major depressive disorder.

Methods: Eight hundred patients presenting for treatment were evaluated with the Structured Clinical Interview for DSM-IV (SCID) after completing the PDSQ. Two hundred ninety-five patients had a principal diagnosis of major depressive disorder.

Results: The mean sensitivity and negative predictive value of the anxiety disorder subscales was 88.5% and 96.5% when all patients were considered, and 88.2% and 95.6% when only depressed patients were examined.

Conclusions: The PDSQ's anxiety disorder subscales have high sensitivity and negative predictive value, thereby indicating that the scale could function well as a screening instrument in depressed patients.

References:

1. Zimmerman M, Chelminski I: Clinician recognition of anxiety disorders in depressed outpatients. *Journal of Psychiatric Research* 2003a; 37:325-333.

2. Zimmerman M, Mattia JI: A self-report scale to help make psychiatric diagnoses: The Psychiatric Diagnostic Screening Questionnaire (PDSQ). Archives of General Psychiatry 2001b; 58:787-794.

NR502 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Use of Plasma Concentration to Guide Atomoxetine Doses in ADHD Patients

Supported by Eli Lilly and Company, Indianapolis, Ind

David W. Dunn, M.D., Riley Hospital Room 3701, 702 Barnhill Drive, Indianapolis, IN 46202-5128; Atilla Turgay, M.D., Margaret Weiss, M.D., Ruth Dickson, M.D., Peter Feldman, Ph.D., Lawrence Sher, M.D., Raun Melmed, M.D.

Educational Objectives:

At the conclusion of this presentation, the attendee should be aware of the issues regarding dose adjustment and drug responsiveness and the potential utility of using plasma concentrations to determine adequate dosing.

Summary:

Objective: To determine if patients with residual symptomatology after six weeks of atomoxetine treatment will benefit from a dose increase directed by plasma concentrations of drug.

Methods: Following approximately six weeks of open-label treatment with atomoxetine (1.2 mg/kg/day), ADHD patients aged 6-16 with suboptimal responses and peak plasma concentrations = 800 ng/mL were randomly assigned for a four-week, double-blind period either to remain at 1.2 mg/kg/day ["ATX12," n=62] or to receive 1.8 mg/kg/day (increasable to 2.4 mg/kg/day if nonresponsive after 2 weeks) ["ATX18/24," n=63].

Results: Initial period open-label response rates (ADHDRS-IV-Parent:Inv total T-score =60 at 6 weeks) for patients with plasma concentrations >800 ng/mL were significantly higher than for patients with concentrations =800 ng/mL (60.5% versus 37.3%, p=.008). Double-blind period final mean doses for the ATX 18/24 and ATX12 groups, respectively, were 2.1 and 1.1 mg/kg/day, but final mean plasma concentrations (643, 416 ng/mL) remained below 800 ng/mL. Response rates were not significantly different across treatment groups. ATX18/24 vs ATX12 improvements in ADHDRS-IV-Parent:Inv total (p=.110) and CGI-ADHD-S (p=.054) scores approached, but did not achieve, statistical significance.

Conclusions: While the results suggest that raising patient plasma concentrations above 800 ng/mL may enhance improvement, further studies are warranted.

References:

1. Michelson D, Faries D, Wernicke J, Kelsey D, Kendrick K, Sallee FR, Spencer T: Atomoxetine in the treatment of children and adolescents with attention-deficit/hyperactivity disorder: a randomized, placebo-controlled, dose-response study. Pediatrics 2001; 108:e83.
2. Michelson D, Gao H, Allen AJ, Witcher J: Plasma atomoxetine concentration and response to ADHD in children and adolescents. Presented at: The 42nd Annual Meeting of the New Clinical Drug Evaluation Unit; June 10-13, 2002; Boca Raton, FL; Conference Proceedings; Page II-3; Abstract II-3.

NR503 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Specificity of Different Forms of Childhood Abuse to GAD

Iwona Chelminski, Ph.D., Department of Psychiatry, Rhode Island Hospital, 235 Plain Street Suite 501, Providence, RI 02905; Mark Zimmerman, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to better understand the relationship between various forms of childhood abuse and GAD.

Summary:

Objective: General anxiety disorder (GAD) is one of the most prevalent anxiety disorders (Blazer, et al 1991). It is a persistent and debilitating condition and there is convincing evidence that it is strongly associated with significant social and occupational disability, poorer quality of life, and overuse of health care services (Witchen et al., 1993; Massion, et al 1993; Kessler, et al., 2002, Greenberg et al., 1999). High rates of early abuse are commonly reported among all psychiatric patients. Childhood emotional and physical abuse are important to the etiology of anxiety sensitivity and may serve as warning signs for early adult anxiety disorders (Ross, et al., 2004). Limited data exist regarding specificity of different forms of abuse to the later onset of GAD. In the present study, we examined five aspects of childhood abuse in chronic worriers.

Method: Three hundred seventy-six psychiatric outpatients were evaluated with the Structured Clinical Interview for DSM-IV and completed the Childhood Trauma Questionnaire (CTQ, Bernstein, 1995) and the Penn State Worry Questionnaire (PSWQ, Molina & Borkovec, 1994) self-report measures of pathological worry. To address the issue of specific associations between childhood abuse and GAD, we examined partial correlations between the indices of five forms of abuse and the total PSWQ score. We also compared these indices in individuals with GAD (n=45) and without (n=351).

Results: The correlation between pathological worry and emotional abuse, while controlling for the other forms of abuse, was the only statistically significant association. When the Emotional Abuse and Physical Neglect subscales were combined, the association was even stronger. All indices of abuse were higher in the GAD than non-GAD group, but the difference did not reach statistical significance.

Conclusions: Childhood emotional abuse combined with physical neglect is more strongly related to the presence of pathological worry than either physical abuse, sexual abuse, or emotional neglect.

References:

1. Ross E and Wong S: News From the 24th Annual Conference of the Anxiety Disorders Association of America. Primary Psychiatry 2004; 11:13-16.
2. Torgersen S: Childhood and family characteristics in panic and generalized anxiety disorder. American Journal of Psychiatry 1986; 143:630-632.

NR504 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
History of Trauma: Is Generalized Anxiety Disorder Independent From PTSD?

Iwona Chelminski, Ph.D., Department of Psychiatry, Rhode Island Hospital, 235 Plain Street Suite 501, Providence, RI 02905; Mark Zimmerman, M.D.

Educational Objectives:

At the conclusion of this presentation, participants will be more aware of the complexity of the relationship between history of trauma and psychopathology, especially its connection to GAD.

Summary:

Objective: Considerable evidence exists linking negative life experiences and the presence of psychopathology. In the beginning of this century Freud suggested that patients with symptoms later defined as GAD experienced an excess of early trauma

(Freud 1920). Subsequent research confirmed these findings (Borkovec, 1994; Roemer et al, 1996). Other reports have documented high incidence of GAD following traumatic events (Eitinger, 1959, 1971, David et al., 1996). It is unclear whether the association between GAD and a history of trauma is an artifact of high comorbidity with PTSD, or trauma itself is an important risk factor for GAD. In the present report, we attempt to replicate earlier findings linking GAD with past trauma in a large sample of psychiatric outpatients, and also examine the prevalence of GAD and differences on a measure of pathological worrying among the trauma and no-trauma groups after removing the PTSD patients.

Method: Seven hundred eighty-one psychiatric outpatients were evaluated with the Structured Clinical Interview for DSM-IV and completed the Penn State Worry Questionnaire (PSWQ, Molina & Borkovec, 1994), a self-report measure of pathological worry. All participants were asked about 13 types of trauma, regardless of whether they entered the PTSD module or not. To address the question of whether a history of trauma is significantly associated with generalized anxiety, we compared the prevalence of GAD among those who reported trauma (n=232) and those who did not (n=549). We also compared the total PSWQ scores between those two trauma groups.

Results: Individuals with history of trauma were 1.7 times more likely to have GAD (30% vs. 18%, $\chi^2=7.9$, $p<.01$, $OR=1.67$, 95% $CI=1.2-2.4$) than those without past trauma. PSWQ scores were significantly higher in individuals endorsing history of trauma (59 vs. 54, $t=4.3$, $p<.001$). The same results were obtained after PTSD patients were removed from the analyses.

Conclusions: Exposure to traumatic events seems to be independently associated with GAD symptoms and a pattern of pathological worrying. Further research is needed to identify which trauma characteristics or immediate responses to trauma may be more specific to subsequent PTSD or GAD.

References:

1. Roemer L, Molina S, Litz BT, Borkovec TD: Preliminary investigation of the role of previous exposure to potentially traumatizing events in generalized anxiety disorder. *Depression and Anxiety* 1996/1997; 4:134-138.
2. Hubbard J, Realmuto GM, Northwood AK, Masten AS. Comorbidity of psychiatric diagnoses with posttraumatic stress disorder in survivors of childhood trauma. *Journal of American Academy of Child and Adolescent Psychiatry* 1995; 34:1167-1173.

NR505 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Child Versus Parent Report of Functioning in Youth With Inflammatory Bowel Disease**

Eva M. Szigethy, M.D., *Department of Psychiatry, Boston Children's Hospital, 300 Longwood Avenue, Boston, MA 02115-5724*; Elyse Kenney, B.A., Johanna Carpenter, B.A., David R. DeMaso, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that adolescents with IBD have a valid view of their functioning. As a result, screening for depression in youth with IBD should be conducted determinedly using child or parent report.

Summary:

Introduction: Pediatric inflammatory bowel disease (IBD) is a chronic physical illness with high rates of associated depression and family dysfunction. Given reports of discrepancies between child and parent reports of depression in physically healthy adolescents, this study examines the validity of child, parent, and clinician

reports of depression, physical illness functioning, and family functioning, in youth with IBD.

Methods: Youth (ages 11-17) with IBD (N=40) were recruited from a gastroenterology clinic. Parent and child completed the Children's Depression Inventory (CDI), Child Health Questionnaire (CHQ), and FACES-II. Objective IBD severity was measured using standardized measures. The Children's Global Assessment Scale (CGAS), a clinician rating, measured global psychosocial functioning.

Results: Mean age was 14.18 years, with 55% female. Child and parent report correlated positively and significantly on CHQ and FACES-II scores, and correlated positively at trend level on CDI scores. There was a significant negative correlation between CGAS scores and both parent and child CDI scores. Child and parent CHQ scores showed a significant negative correlation with objective disease severity ratings.

Conclusions: These results suggest that youth with IBD have a valid view of their functioning, and argue for aggressively screening for depression in pediatric clinics using child or parent report.

This study is supported by a grant from the Klingenstein Foundation and NIMH K23 MH064604-03 grant.

References:

1. Szigethy E, Levy-Warren A, Whitton S, Bousvaros A, Gauvreau K, Leichtner AM, Beardslee WR: Depressive symptoms and inflammatory bowel disease in children and adolescents: A cross-sectional study. *J Pediatr Gastroenterol Nutr* 2004; 39:395-403.
2. Verhulst FC, van der Ende J: Agreement between parents' reports and adolescents' self-reports of problem behavior. *J Child Psychol Psychiatry* 1992; 33:1011-23.

NR506 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **The Relative Benefits of OROS® MPH Versus Se-AMPH Extended Release in Driving Safety of Teenagers with ADHD**

Daniel J. Cox, Ph.D., *Department of Behavior Medicine, University of Virginia Health System, 301 Old Ivy Way, Charlottesville, VA 22903*; R. Larry Merkel, M.D., Melissa Moore, M.D., Frances Thorndike, Ph.D., Carrie Muller, B.S., Liza Schaffner, M.D., Mudhasir Bashir, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to describe the relative effects of long-acting OROS® methylphenidate (OROS® MPH) and extended-release se-amphetamine (se-AMPH ER) on simulated driving in adolescents with ADHD.

Summary:

Objective: To compare the effects of long-acting OROS® methylphenidate (MPH) and extended-release (ER) se-amphetamine on simulated driving performance in adolescents with attention-deficit/hyperactivity disorder (ADHD). Driving collisions are the leading cause of death among 16 to 20 year olds and two to four times more common among teenagers with ADHD. The largest proportion of teenage driving fatalities occurs during the evening. MPH improves simulator and on-road driving performance; evening performance is more enhanced with OROS MPH than with immediate-release MPH (Ritalin®).

Method: Thirty-four adolescent drivers with ADHD (18 males/16 females; 16-19 years) participated in this double-blind, placebo-controlled, crossover study. Each drove a high-fidelity simulator at 5, 8, and 11 PM after treatment with OROS MPH 72 mg qd, se-AMPH ER 30 mg qd, or placebo. Subjects received each treatment for five to 10 days, with >5 days between treatment phases.

Results: Overall performance on OROS MPH was superior to placebo ($P=.005$); performance on se-AMPH was not ($P=.14$). For 8 and 11 PM evaluations, performance on OROS MPH was superior to that on se-AMPH ($P=.007$) and placebo ($P=.001$); performance on se-AMPH was no better than on placebo ($P=.44$).

Conclusion: OROS MPH improves driving performance of teenagers with ADHD and is superior to se-AMPH in this respect.

References:

1. Cox DJ, et al: J Nerv Ment Dis 2000; 188:230-234.
2. Cox DJ, et al: Acad Am Assoc Child Adolesc Psychiatry. 2004; 43:269-275.

NR507 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Short-Term Treatment of Panic Disorder: Venlafaxine XR Versus Paroxetine or Placebo

Mark H. Pollack, M.D., *Department of Psychiatry, Massachusetts General Hospital, Wang ACC-815, 15 Parkman Street, Boston, MA 02114-3117*; Tim Whitaker, M.D., Richard Mangano, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the efficacy and tolerability of venlafaxine extended release (XR), a serotonin-norepinephrine reuptake inhibitor, in the treatment of patients with PD, based on comparisons with placebo and an active comparator, paroxetine

Summary:

Introduction/Hypothesis: This study compares the short-term efficacy of venlafaxine XR with paroxetine and placebo in treating panic disorder (PD).

Methods: Outpatients aged 18 years or older (placebo, $n=157$; venlafaxine XR, 75 mg, $n=156$; venlafaxine XR 225 mg, $n=160$; paroxetine, $n=151$), with primary diagnosis of DSM-IV PD (\pm agoraphobia) for three months or more were randomly assigned to receive venlafaxine XR (75 mg/d or 225 mg/d), paroxetine 40 mg/d, or placebo for 12 weeks.

The primary outcome was the percentage of patients free of full-symptom panic attacks (four or more symptoms) at endpoint. Additionally, PAAS full- and limited-symptom panic attacks, PDSS scores, Phobia Scale fear and anxiety factors, HAM-A and CGI-S means, change in anticipatory anxiety, percentage of CGI-I responders (patients with score of 1 or 2), and remission rate (no panic attacks and CGI-S score = 1 or 2) were assessed.

Results: At endpoint, active treatment groups were superior ($P<0.05$) to placebo on all secondary measures, except limited-symptom panic attacks. The venlafaxine XR 225 mg group had a significantly higher percentage of panic-free patients ($P<0.05$) and greater PDSS score improvement ($P<0.05$) than paroxetine. Both drugs were well tolerated.

Conclusion/Discussion: Venlafaxine XR (75 mg/d and 225 mg/d) and paroxetine 40 mg/d are effective in short-term treatment of PD.

References:

1. Ballenger JC, Davidson JR, Lecrubier Y, Nutt DJ, Baldwin DS, den Boer JA, Kasper S, Shear MK: Consensus statement on panic disorder from the International Consensus Group on Depression and Anxiety. J Clin Psychiatry 1998; 59(suppl 8):47-54.
2. Practice guideline for the treatment of patients with panic disorder. Work Group on Panic Disorder. American Psychiatric Association. Am J Psychiatry 1998; 155(suppl 5):1-34.

NR508 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Analysis of the Improvement of Specific Physical and Emotional Symptoms of GAD During Treatment With Venlafaxine XR

Stephen M. Stahl, M.D., *Department of Psychiatry, Neuroscience ED Institute, 5857 Owens Avenue, Suite 102, Carlsbad, CA 92008*; Vincent Haudiquet, Saeed Ahmed, M.D., David Hackett, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to: (1) have greater awareness of physical and emotional symptoms of GAD16, (2) have more familiarity with the individual items in a common rating scale used in clinical trials for GAD16, 3. Recognize that some symptoms may take longer to respond to treatment.

Summary:

Objective: To assess improvement in specific physical and emotional symptoms during treatment with venlafaxine XR.

Method: Data were pooled from five placebo-controlled, double-blind, randomized studies in patients with GAD treated with either venlafaxine XR or placebo for eight weeks ($n = 2021$), and in two of the studies for up to six months ($n = 767$). The Hamilton Rating Scale for Anxiety (HAM-A), which comprises seven items for physical symptoms (somatic component) and seven for emotional symptoms (psychic component), was the main outcome measure. Effect sizes for change from baseline for each HAM-A item and pairwise comparisons between venlafaxine and placebo groups were calculated. Missing data accounted for with LOCF technique.

Results: Improvement in both psychic and somatic symptoms was significantly greater with venlafaxine XR treatment compared with placebo, and effect changes were greater for the psychic symptoms. Statistically significant differences from placebo were observed one week earlier for psychic symptoms compared with somatic symptoms. Overall improvement of symptoms was sustained over six months for both symptom types.

Conclusions: This is the first evaluation of venlafaxine treatment effects on individual HAM-A items at each visit. In this analysis, venlafaxine treatment was associated with sustained improvement in psychic and somatic symptoms.

References:

1. Wittchen HU, Zhao S, Kessler RC, Eaton WW: DSM-III-R generalized anxiety disorder in the National Comorbidity Survey. Arch Gen Psychiatry 1994; 51:355-64.
2. Allgulander C, Hackett D, Salinas E: Venlafaxine extended release (ER) in the treatment of generalised anxiety disorder: twenty-four-week placebo-controlled dose-ranging study. Br J Psychiatry 2001; 179:15-22.
3. Meoni P, Hackett D, Lader M: Pooled analysis of venlafaxine XR efficacy on somatic and psychic symptoms of anxiety in patients with generalized anxiety disorder. Depress Anxiety 2004; 19:127-32.

NR509 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Relapse Prevention of Panic Disorder in Adult Outpatient Responders to Venlafaxine XR

Evan Tzanis, B.A., *Wyeth Pharmaceuticals, 500 Arcola Road, Collegeville, PA 19426*; James Ferguson, M.D., Timothy Whitaker, M.D., Richard Mangano, M.D., Bo Gao, Ph.D., Michael Liebowitz, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the efficacy and tolerability of venlafaxine ex-

tended release (XR), a serotonin-norepinephrine reuptake inhibitor, in preventing relapse in patients with PD who have responded to previous treatment with venlafaxine XR.

Summary:

Introduction/Hypothesis: This study compares venlafaxine XR with placebo in preventing panic disorder (PD) relapse in outpatient responders.

Methods: Outpatients aged 18 years or older, with primary diagnosis of DSM-IV PD (\pm agoraphobia) for three months or more, score of 4 or more on the CGI-S, six or more full-symptom panic attacks less than or equal to two weeks before screening, and three or more full-symptom panic attacks two weeks before baseline participated. Responders to 12-week, open-label treatment (ie, patients with less than or equal to one full-symptom panic attack per week in the last two weeks and CGI-I score of 1 or 2) were randomly assigned to receive either double-blind venlafaxine XR or placebo (reduction to 0 mg/day by week 3 of double-blind period) for 26 additional weeks.

The primary endpoint was time to relapse, defined as two or more full-symptom PAAS panic attacks per week for two consecutive weeks or discontinuation from treatment due to loss of effectiveness. Time to relapse was analyzed using Kaplan-Meier survival analysis.

Results: 291 ITT patients underwent open-label treatment; 169 ITT patients (placebo = 80, venlafaxine XR = 89) received double-blind treatment (mean venlafaxine XR dose = 164.9 to 170.8 mg/d). Time to relapse was significantly longer with venlafaxine XR. Venlafaxine XR was well tolerated.

Conclusion/Discussion: Venlafaxine XR was safe and effective in preventing PD relapse in responders.

References:

1. Mavissakalian MR: Imipramine vs. sertraline in panic disorder: 24-week treatment completers *Ann Clin Psychiatry* 2003; 15:171-180.
2. Yonkers KA, Bruce SE, Dyck IR, Keller MB: Chronicity, relapse, and illness—course of panic disorder, social phobia, and generalized anxiety disorder: findings in men and women from 8 years of follow-up. *Depress Anxiety* 2003; 17:173-179.

NR510 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Gender Differences in Mania in Pediatric Bipolar Disorder**

Meghan E. Howe, M.S.W., *Department of Psychiatry and Behavioral Sciences, Stanford University, 401 Quarry Rd, Palo Alto, CA 94304*; Diana Simeonova, M.S., Kiki Chang, M.D.

Educational Objectives:

At the conclusion of the presentation, the participants will learn more about pediatric bipolar disorder and age of onset. Additionally, participants will learn about possible gender differences in pediatric bipolar disorder.

Summary:

Objective: Because a dearth of information exists regarding gender differences in pediatric bipolar disorder, we sought to evaluate whether the manifestation of mania in bipolar disorder differed between genders.

Methods: 60 families with at least one parent with BD (mean age = 44.3, 76.7% female) were interviewed for family history and diagnosis using the FH-RDC and SCID, respectively. Additionally, 60 offspring (68.3% male, 31.7% female) were assessed with DSM-IV criteria BD (mean age = 13.08 years) using the WASH-U-KSADS. During the interview comprehensive medication history was obtained, CGAS score assigned, and Kiddie-YMRS rated.

AAO was considered the time to nearest month of first hypomanic or manic episode.

Results: Overall, the mean AAO of the 60 offspring was 11.3 years, ± 3.6 . The AAO for girls (13.0, ± 2.9) was significantly ($p = .02$) later than the boys (10.6, ± 3.7). As captured by the KSADS, the only manic or hypomanic symptom that was significantly ($p = .04$, $t = -2.2$) different between the two groups was inappropriately laughing, joking, or grinning, with girls (3.2, $\pm .77$) scoring higher than boys (2.6, $\pm .99$). Additionally, family history ($p = .25$), total number of medication exposure prior to AAO ($p = .38$), CCAS score ($p = .58$), YMRS score ($p = .35$), psychosis ($p = .29$), and total comorbid diagnosis ($p = .49$) did not differ significantly.

Conclusions: Boys who are offspring of adults with BD may possibly be at an elevated risk for earlier AAO than girls. Mechanisms for this difference require further study, as presentations of mania appear similar between genders.

References:

1. Biederman J, Kwon A, Wozniak J, Mick E, Markowitz S, Fazio V, Faraone S: Absence of gender differences in pediatric bipolar disorder: findings from a large sample of referred youth. *J Affective Disorders*. 83:207-214, 2004.
2. Chang KD, Steiner H, Ketter TA: Psychiatric phenomenology of child and adolescent bipolar offspring. *J Am Acad Child Adolesc Psychiatry* 2000; 39:453-60.
3. Chang KD, Steiner H, Ketter TA: Studies of offspring of parents with bipolar disorder. *Am J Medical Genetics* 2003; 123C:26-35.

NR511 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Pregnancy and Childbirth in 60 Patients With Panic Disorder**

Hisanobu Kaiya, M.D., *Nagoya Mental Clinic, Imon Nagoya Building, 1-16 Tubakicho Nakamura, Nagoya 453-0015, Japan*; Chika Yokoyama, M.A., Reiko Iwasa, M.A., Douglas Eames, Gaku Yamanaka, M.D., Hidehiro Fukuhara, M.D., Natsuko Kaiya

Educational Objectives:

This study provided data to understand the problems of panic disorder during pregnancy and childbirth.

Summary:

Objective: The aim of this study is to investigate the problems of pregnancy and childbirth by patients with panic disorder.

Subjects and Method: 60 patients (mean age of childbirth = 31.92 ± 3.75 years) who met DSM-IV criteria for panic disorder and delivered a child were included in this study. They were questioned after childbirth (mean = 10.25 ± 9.9 months) about the frequencies of panic attacks and anxiety in pregnancy.

Results: 50 patients (83.3%) had medication (clonazepam/imipramine, N=25; clonazepam, N=19; other medication, N=6). Regarding frequencies of panic attack during pregnancy, 18 patients (30.0%) reported no panic attack, 23 patients (38.3%) reported 1-3 times, 12 patients (20.0%) reported 4-10 times, and six patients (10.0%) reported 10 times or more. Moreover, 27 patients (45.0%) reported severe anxiety about taking medications during pregnancy, and 16 patients (26.7%) reported severe anxiety about having a panic attack during childbirth. Fifty-four patients (90.0%) had healthy children, three patients (5.0%) had immature infants, one patient (1.7%) had a child suffering from asthma, one patient (1.7%) had a child suffering from hypertrophic pyloric stenosis, and one patient had no answer.

Conclusion: These data were collected retrospectively; however these results lead us to understand panic disorder during pregnancy.

References:

1. American Psychiatric Association: Diagnostic and Statistical manual of Mental Disorders. Fourth Edition. Washington, DC, American psychiatric Association, 1994.

NR512 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **A Randomized Trial of Escitalopram and Paroxetine in the Treatment of GAD**

Eli Maehlum, M.S.C., *H Lundbeck A/S, Ottiliavej 9, Valby-Copenhagen 2500, Denmark*; Anna K. Trap Huusom, M.S.C., David Baldwin, M.D.

Educational Objectives:

At the conclusion of this presentation, the participants will be able to evaluate the efficacy and tolerability of escitalopram in the treatment of generalized anxiety disorder

Summary:

Introduction: The efficacy and tolerability of escitalopram were compared in a 12-week, randomized, placebo-controlled, double-blind study in generalized anxiety disorder (GAD), using paroxetine as active reference.

Methods: Adult patients with GAD were randomly assigned to treatment with placebo (N=139), escitalopram 5mg/day (N=134), 10mg/day (N=136), 20mg/day (N=133), or paroxetine 20mg/day (N=140).

Results: Baseline Mean Hamilton Anxiety Scale (HAM-A) total score was 27.86% of patients completed treatment. A significantly better therapeutic effect, based on mean change from baseline in HAM-A total score at Week 12, was seen for both 10mg and 20mg escitalopram than for placebo ($p<0.05$); escitalopram 10mg was significantly ($p<0.05$) more efficacious than paroxetine.

The proportion of patients in remission (HAM-A=7) at Week 12 was significantly greater for escitalopram 5mg (44%), 10mg (48%), and 20mg (43%) than placebo (30%) ($p<0.05$), and significantly greater for escitalopram 10mg than for paroxetine 20mg (33%) ($p<0.05$).

The incidence of treatment-emergent adverse events (TEAEs) was similar across treatment groups. The TEAEs that were reported with an incidence $>10\%$ in at least one treatment group were nausea, fatigue, headache, insomnia, and anorgasmia.

Conclusion: Escitalopram was efficacious and well tolerated in the 12-week treatment of GAD. Escitalopram 10mg was significantly more effective than paroxetine 20mg.

References:

1. Davidson JR, Bose A, Korotzer A, Zheng H: Escitalopram in the treatment of generalized anxiety disorder: Double-blind, placebo controlled, flexible-dose study. *Depress Anxiety* 2004; 19:234-240.
2. Pollack MH, Zaninelli P, Goddard A, McCafferty JP, Bellew KM, Burnham DB, et al: Paroxetine in the treatment of generalised anxiety disorder: results of a placebo-controlled, flexible-dose trial. *J Clin Psychiatry* 2001; 62:350-358.

NR513 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Escitalopram for Relapse Prevention in GAD**

Ioana Florea, M.D., *H Lundbeck A/S, Ottiliavej 9, Valby-Copenhagen 2500, Denmark*; Anna K. Trap Huusom, M.S.C., Christer Allgulander, M.D.

Educational Objectives:

At the conclusion of the presentation, the participants will increase their knowledge about escitalopram in preventing relapse in patients with generalized anxiety disorder

Summary:

Introduction: Escitalopram is efficacious in the acute treatment of generalized anxiety disorder (GAD). The present study investigated the effect of escitalopram on relapse rates in patients who had responded to acute treatment with escitalopram.

Methods: 491 adult patients with a primary diagnosis of GAD (DSM-IV) and a Hamilton Anxiety (HAM-A) total score ≥ 20 , received 12-week, open-label escitalopram 20mg/day. Of these, 375 patients responded (HAM-A total score ≤ 10) and were randomly assigned to 24-76 weeks of double-blind treatment with escitalopram 20mg/day (n=187) or placebo (n=188). The primary efficacy parameter was the time to relapse, defined as either a HAM-A total score ≥ 15 , or withdrawal due to lack of efficacy.

Results: Survival analysis of time to relapse showed significant advantages for escitalopram versus placebo (log-rank: $p<0.001$). The risk of relapse was four times higher for placebo- than for escitalopram-treated patients ($p<0.001$), with significantly fewer escitalopram-treated patients relapsing (19% versus 56%). Escitalopram was well tolerated during double-blind treatment with 7% of the escitalopram-treated patients withdrawing due to adverse events, versus 8% for placebo. The overall discontinuation rate, excluding relapses, was 21% for both escitalopram and placebo.

Conclusion: Escitalopram was efficacious in preventing relapses and well tolerated in the long-term treatment of GAD.

References:

1. Davidson JR, Bose A, Korotzer A, Zheng H: Escitalopram in the treatment of generalized anxiety disorder: double-blind, placebo controlled, flexible-dose study. *Depress Anxiety* 2004; 19:234-240.
2. Goodman WK: Selecting pharmacotherapy for generalized anxiety disorder. *J Clin Psych* 2004; 65(suppl 13):8-13.

NR514 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **35 Percent CO2 Challenge Test: Increase in Anxiety in Patients With Social Anxiety Disorder**

Marco A.U. Mezzasalma, M.D., *Panic & Respiration Laboratory, IPUB - UFRJ, RUA CANING 21/701 - IPANEMA, RIO DE JANEIRO 22081-040, Brazil*; Antonio E. Nardi, M.D., Alexandre M. Valença, M.D., Fabiana L. Lopes, M.D., Isabella Nascimento, M.D., Rafael C. Freire, M.D., Walter A. Zin, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the increase in subjective anxiety in social anxiety disorder patients after the inhalation of 35% CO₂. Demonstrate the value of the 35% CO₂ challenge test in the laboratorial study of social anxiety disorder.

Summary:

Objectives: Our aim was to evaluate the response of social anxiety disorder (SAD) patients to a 35% CO₂ challenge test and compare it with the responses of panic disorder (PD) patients and patients with both diagnoses.

Methods: We randomly selected 26 PD patients, 10 SA patients, and six PD and SAD patients (DSM-IV). These patients received vital capacity inhalations of a carbogenic mixture (35% of CO₂ and 65% of O₂) and compressed atmospheric air (placebo), chosen randomly and separated by a 20-minute interval.

Results: A total of 69.2% (n=18) PD patients, 40% (n=4) SAD patients, and 50% (n=3) PD and SAD patients had a panic attack after the CO₂ inhalation. We also found that 61.5% (n=16) PD patients, 60% (n=6) SAD patients and 50% (n=3) PD and SAD patients had an increase in the Subjective Units of Disturbance Scale (SUDS) equal or greater than three after the CO₂ inhalation, and this increase was statistically significant (ANCOVA, $t = -4, 128$, 95% CI: 0,939;0,318).

Discussion: The 35% CO₂ inhalation challenge is a good tool for laboratorial investigation of PD, and this test can be a useful laboratorial model for the study of SAD.

References:

1. Valença AM, Nardi AE, Nascimento I, Zin WA, Lopes FL, Mezzasalma MA, Versiani M: Early carbon dioxide challenge test may predict clinical response in panic disorder. *Psychiatr Res* 2002; 112:269-272.
2. Papp LA, Klein DF, Martinez J, Schneier F, Cole R, Liebowitz MR, Hollander E, Fyer AJ, Jordan F, Gorman JM: Diagnostic and substance specificity of carbon-dioxide-induced panic. *Am J Psychiatry* 1993; 150:250-257.

NR515 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Risperidone Prevents Relapse of Different Subtypes of Disruptive Behavior Disorder

Magali Reyes, Ph.D., *Pharmaceutical Research and Development, Johnson & Johnson, 1125 Trenton-Harbourton Road, Titusville, NJ 08560*; Jan Buitelaar, M.D., Ilse Augustyns, Ph.D., Gahan Pandina, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should understand the methodology and reasoning behind relapse-prevention trials in children and adolescents with disruptive behavior disorders (DBDs). They should also be able to evaluate the benefit of long-term pharmacological treatment in treating different subtypes of DBDs.

Summary:

Objectives: To determine the efficacy of risperidone in preventing recurrence of symptoms of different subtypes of disruptive behavior disorder (DBD), including conduct disorder (CD), oppositional defiant disorder (ODD), and DBD not otherwise specified (DBD-NOS).

Methods: Overall, 527 patients (5-17 years) with DBDs were enrolled. Responders (n = 335, 63.5%) to 12 weeks of open risperidone treatment entered a six-month, double-blind, placebo-controlled, relapse-prevention phase. The primary efficacy parameter was time to relapse: sustained deterioration on the CGI-S scale (>=2 points) or N-CBRF conduct problem subscale (>=7 points).

Results: Fewer patients continuing risperidone treatment (median dose = 0.75 mg/day for patients < 50 kg, 1.5 mg/day for patients >=50 kg) relapsed than patients switched to placebo (27.3% with risperidone vs. 42.3% with placebo, p = 0.002). Relapse occurred in 25% of patients with ODD/DBD-NOS after 118 and 29 days with risperidone (n = 110) and placebo (n = 102), respectively. Relapse occurred in 25% of patients with CD after 119 and 92 days with risperidone (n = 62) and placebo (n = 61), respectively.

Conclusions: Long-term treatment with risperidone is beneficial in preventing relapse of disruptive behavioral symptoms for all diagnostic subtypes of DBD.

References:

1. Loeber R, Burke JD, Lahey BB, Winters A, Zera M: Oppositional defiant and conduct disorder: a review of the past 10 years, part I. *J Am Acad Child Adolesc Psychiatry* 2000; 39(12):1468-84.
2. Kutcher S, Aman M, Brooks SJ, Buitelaar J, van Daalen E, Fegert J, Findling RL, Fisman S, Greenhill LL, Huss M, Kusumakar V, Pine D, Taylor E, Tyano S: International consensus statement on attention-deficit/hyperactivity disorder (ADHD) and disruptive behavior disorders (DBDs): clinical implications and treatment practice suggestions. *Eur Neuropsychopharmacol* 2004; 14(1):11-28.

NR516 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Long-Term Safety and Tolerability of Risperidone in Children and Adolescents With DBD

Magali Reyes, Ph.D., *Pharmaceutical Research and Development, Johnson & Johnson, 1125 Trenton-Harbourton Road, Titusville, NJ 08560*; Keith Karcher, M.S.

Educational Objectives:

At the conclusion of this presentation, the participant should be aware of the safety issues surrounding atypical antipsychotic use in the pediatric population, and in particular should appreciate the tolerability of risperidone in treating disruptive behavior disorder in children and adolescents.

Summary:

Objectives: To determine the long-term safety and tolerability of risperidone in treating DBDs in children and adolescents.

Methods: This open-label, one-year extension trial followed patients (aged 6-18 years) who participated in a double-blind, six-month, relapse-prevention trial of risperidone. Researchers enrolled 232 patients, including those treated with risperidone (n=115) and placebo (n=117). Safety and tolerability were assessed using records of adverse events (AEs), clinical laboratory tests, vital signs, weight, height, and Tanner stage.

Results: 169 patients (73%) completed the extension trial. The median mode dose of risperidone was 0.75 mg for patients <50 kg and 1.5 mg for patients >=50 kg. Patients previously treated with risperidone showed no additional increase in mean weight z-scores [mean(SD) changes during treatment ranged from -0.03(0.30) to 0.00(0.18)]. Weight z-scores of patients from the placebo arm increased during the first six months of this extension trial [mean(SD) increase at Month 6: 0.14(0.32)], plateauing afterwards. None met the American Diabetes Association's diabetes criteria. 151 patients (65%) experienced AEs, most of which were mild or moderate in severity. Ten patients (4.3%) experienced extrapyramidal symptom-related AEs. No cases of tardive dyskinesia were reported.

Conclusions: Risperidone is safe and well tolerated in the long-term treatment of children and adolescents.

References:

1. Kutcher S, Aman M, Brooks SJ, Buitelaar J, van Daalen E, Fegert J, Findling RL, Fisman S, Greenhill LL, Huss M, Kusumakar V, Pine D, Taylor E, Tyano S: International consensus statement on attention-deficit/hyperactivity disorder (ADHD) and disruptive behavior disorders (DBDs): clinical implications and treatment practice suggestions. *Eur Neuropsychopharmacol* 2004; 14(1):11-28.
2. Reyes M, Buitelaar J, Augustyns I, Eerdeken M: Relapse prevention of disruptive behavior disorders in children and adolescents: a six-month trial of risperidone versus placebo. Poster presented at the 16th IACAPAP congress; Aug 22-26, 2004, Berlin, Germany.

NR517 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

OROS MPH in Adolescents With ADHD: Validity of Patient Self-Assessments

Keith McBurnett, Ph.D., *The Children's Center at Langley Porter, University of California San Francisco, 401 Parnassus Ave., Box CAS-0984, Room 140, San Francisco, CA 94143*; Glen Elliott, M.D., Linda Piffner, Ph.D., Kimberly Cooper, M.S., Joseph Lynch, M.D.

Educational Objectives:

At the conclusion of this session, the participants should be able to demonstrate that self-reported measures are a sensitive

index of treatment efficacy in adolescents prescribed OROS methylphenidate (MPH).

Summary:

Objective: To assess the validity of self-reported measures of treatment efficacy in adolescents with ADHD taking once-daily OROS® methylphenidate (MPH). In adolescent patients, self-reports appear critical because (1) teacher reports may be unavailable and (2) perceived efficacy may affect adolescents' compliance.

Methods: Adolescents (ages 13-18) with ADHD (N=220) first underwent open-label dose titration (1-4 weeks) to identify individualized doses of OROS MPH (18, 36, 54, or 72 mg once daily). Patients (N=177) were then randomized to double-blind treatment with OROS MPH or placebo for two weeks. Efficacy measures included change from baseline to endpoint on the Conners-Wells' Self-Report Scale (CASS-L) and on investigator- and parent-rated ADHD Rating Scales [ADHD-RS(I) and ADHD-RS(P)].

Results: OROS MPH at doses up to 72mg once daily significantly decreased core ADHD symptoms across all informants and scales. Ratios of effect sizes (Cohen's d, active condition divided by placebo) indicated that adolescent judgment was equally or more sensitive to drug condition than parent and investigator judgment. Receiver operating characteristic (ROC) curves for each assessment scale demonstrated similar sensitivity and specificity across informants in detecting medication status.

Conclusions: Self-reported measures provide a sensitive index of treatment efficacy in adolescents with ADHD taking once-daily OROS MPH.

References:

1. Barkley RA, et al: J Am Acad Child Adolesc Psychiatry 1990; 29:546-557.
2. Greenhill LL, et al: J Am Acad Child Adolesc Psychiatry. 2002; 41(suppl 2):26S-49S.
3. Conners CK: J Clin Psychiatry. 1998; 59(suppl 7):24-30.

NR518 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Memantine and Individual Activities of Daily Living in Moderate to Severe Alzheimer's Disease**

Howard Feldman, M.D., *Department of Neurology, University of British Columbia Hospital, S192 2211 Wesbrook Mall, Vancouver V6T 2B5, Canada*; Frederick A. Schmitt, Ph.D., P. Murali Doraiswamy, M.D., Stephen M. Graham, Ph.D., Joanne M. Bell, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to assess the efficacy of memantine on functional abilities in moderate to severe Alzheimer's disease patients based on measures of individual activities of daily living.

Summary:

Objective: Alzheimer's disease (AD) leads to functional decline, affecting activities of daily living (ADLs). Memantine is a low-moderate affinity, uncompetitive NMDA-receptor antagonist approved for moderate to severe AD in the U.S. and is available in Europe. This report analyzed the effect of memantine on ADLs.

Methods: Two double-blind, placebo-controlled U.S. trials evaluated the efficacy of memantine in moderate to severe AD. The 28-week trial evaluated memantine monotherapy; the 24-week trial evaluated memantine on donepezil-treated patients. Both used the 19-item Alzheimer's Disease Cooperative Study-Activities of Daily Living Inventory [ADCS-ADL(19)]. Total score and item analyses were performed (OC and/or LOCF).

Results: For both trials, ADCS-ADL(19) total scores demonstrated significantly less deterioration for memantine versus pla-

cebo (P<.05). Items demonstrating statistical significance in the 28-week trial were: makes conversation, clears a table, dispose of litter (P<.05). For the 24-week trial significant items were: grooming, watching television, being left alone, finding belongings (P<.05). When the 24-week trial ADLs were consolidated into four subscales, statistical significance favoring memantine was found on higher level functions and autonomy (P<.05).

Conclusions: These data suggest that memantine provides benefit in ADL performance in moderate to severe AD, and that memantine has measurable benefits on autonomy and higher level functioning.

References:

1. Tariot P, Farlow M, Grossberg G, et al: Memantine treatment in patients with moderate to severe Alzheimer disease already receiving donepezil: a randomized controlled trial. JAMA 2004; 291(3):317-324.
2. Reisberg B, Doody R, Stöfler A, et al: Memantine in moderate-to-severe Alzheimer's disease. N Engl J Med 2003; 348(14):1333-1341.

NR519 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Most Troubling Symptoms Tool: A Patient-Rated Assessment for GAD**

Gahan J. Pandina, Ph.D., *Medical Affairs Department, Janssen Medical Affairs, L.L.C., 1125 Trenton-Harbourton Road, Titusville, NJ 08560*; Carla Canuso, M.D., Marcia Rupnow, Ph.D., Ibrahim Turkoz, M.S., Amy Loeschler, B.S., Jacqueline Morein, B.S., Georges Gharabawi, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should understand preliminary data associated with the Most Troubling Symptoms scale, an innovative patient-rated tool to evaluate the symptoms associated with generalized anxiety disorder.

Summary:

Background: Most rating scales evaluating symptoms of generalized anxiety disorder (GAD) are clinician-administered severity measures. We developed a tool based upon patient-rated Most Troubling Symptoms (MTS), focusing on GAD symptoms uniquely identified by patients as most troubling.

Methods: Blinded data were evaluated from the first 75 patients participating in a large, ongoing six-week double-blind pharmacological trial in GAD. The MTS tool has 7 common GAD symptoms. Patients rate the MTS (0=absent to 10=extreme) via telephone IVRS. Baseline characteristics were summarized. The degrees of association between MTS total score (top 4 MTS) and Hamilton Scale for Anxiety (HAM-A) total score and the percent of the maximal Quality of Life, Enjoyment and Satisfaction Questionnaire (Q-LES-Q) score were examined.

Results: Seventy of 75 patients were randomized (mean age=46.3+/-11.0 years; 73% female), with 56 (80%) completers. The most common MTS were "trouble sleeping" (67%) and excessive anxiety or worry (60%). Mean baseline MTS total and HAM-A scores were 28+/-6.8 and 23.2+/-6.8, respectively. Changes in MTS total scores significantly correlated with changes in HAM-A (r=0.61; p<0.001), Q-LES-Q (r=-0.70; p<0.001).

Conclusions: Preliminary data suggest that the patient-rated MTS correlates highly with well-established instruments used in GAD, warranting further study of its sensitivity to treatment effects.

References:

1. Hamilton: The assessment of anxiety states by rating. British Journal of Medical Psychology 1959; 32:50-55.
2. Brawman-Mintzer, Knapp, Nietert: Placebo-controlled study of risperidone augmentation in treatment-resistant subjects with

DSM-IV diagnosed generalized anxiety disorder. Presented at the annual meeting of the European College of Neuropsychopharmacology, September, Berlin.

NR520 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Psychiatric Comorbidities and Patterns of Medical Care Use for Patients With GAD in an Integrated-Delivery System

Dennis A. Revicki, Ph.D., *MEDTAP International, 7101 Wisconsin Avenue, Suite 600, Bethesda, MD 20814*; Mark Hornbrook, Ph.D., Louis Matza, Ph.D., Gregory Clarke, Ph.D., Nancy Brandenburg, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should have gained a better understanding of the treatment patterns and comorbidities of generalized anxiety disorder.

Generalized anxiety disorder (GAD) is prevalent, but often not recognized and treated effectively in primary care practice. Treatment is varied, and little is known about the patterns of psychopharmacologic and other treatments in community practice settings. The primary objective of this retrospective analysis of medical care encounter and claims data was to describe the comorbidities, treatment patterns, and medical service utilization of patients with GAD. Study patients (n=3,606) were age >18 years and members of a large prepaid integrated delivery system. Patients had at least two medical care encounters during 2003 with GAD (300.02) and/or anxiety state unspecified (300.00). We excluded patients with diagnoses of schizophrenia/other psychosis, bipolar disorder, and mental retardation. The patient sample, (71% women) included 25% with a diagnosis of major depressive disorder, 12% dysthymia, 23% substance abuse disorder, 13% panic disorder, 7.4% social/other phobias, 4.8% PTSD, and 3.6% OCD. We also identified 1,541 GAD patients who began new treatment during 2003. Among these patients, the most commonly dispensed medications were SSRIs (16%), benzodiazepines (11%), and combinations of SSRIs and benzodiazepines (27%). Among the SSRIs, bupropion (25%), fluvoxamine (18%), sertraline (15%), mirtazapine (15%), and venlafaxine (10%) were the most frequently prescribed treatments. On average, patients received a course of over four months on these SSRIs. About 66% of GAD patients received at least one specialty mental health service visit during the year. Few patients were hospitalized during the year for any psychiatric reasons. Based on this retrospective analysis of administrative claims data, it is apparent that the treatment patterns for GAD are varied and that half the patients continue on medication therapy for less than five months. Interventions are needed to assist primary care physicians in recognizing and treating GAD, and to increase guideline-consistent treatment patterns to improve patient functioning and well-being.

References:

1. Culppepper L: Generalized anxiety disorder in primary care: emerging issues in management and treatment. *J Clin Psychiatry* 2002; 63 Suppl 8:35-42.
2. Wittchen HU, Hoyer J: Generalized anxiety disorder: nature and course. *J Clin Psychiatry* 2001; 62 Suppl 11:15-19; discussion 20-11.

NR521 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Tolerability of Escitalopram in the Treatment of Social Anxiety Disorder

Srihari Gopal, M.D., *Forest Laboratories, Inc., 909 Third Avenue, New York, NY 10022*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to evaluate the efficacy and tolerability of escitalopram for the acute treatment of social anxiety disorder (SAD).

Summary:

Introduction: Social anxiety disorder (SAD) is a highly prevalent, chronic disorder (lifetime incidence estimates range from 2% to 16%).

Methods: Two randomized, double-blind, placebo-controlled trials of escitalopram in the treatment of SAD have been performed. All patients were \geq 18 years old, with DSM-IV SAD, and a baseline LSAS score \geq 70. One trial was flexibly dosed (escitalopram 10-20mg/day vs. placebo, 12 weeks), and one was fixed dose (escitalopram 5, 10, or 20 mg/day, paroxetine 20 mg/day, and placebo, 24 weeks). Adverse event (AE) data were pooled across the two trials.

Results: Escitalopram significantly improved mean LSAS scores relative to placebo at endpoint in both acute treatment trials (primary efficacy outcome). Withdrawal rates due to AEs were 9% escitalopram vs. 6% placebo. Only nausea and dizziness occurred at a rate exceeding 10% in the escitalopram group and twice that of placebo. The majority of AEs in escitalopram patients were mild. The overall AE incidence in the escitalopram group vs. placebo was similar in males and females.

Conclusion: Adverse event results for escitalopram in SAD are consistent with past results in major depressive disorder and generalized anxiety disorder. Escitalopram is effective and well tolerated in the acute treatment of SAD.

References:

1. Lader M, Stender K, Burger V, Nil R: Efficacy and tolerability of escitalopram in 12- and 24-week treatment of social anxiety disorder: Randomised, double-blind, placebo-controlled, fixed-dose study. *Depress Anxiety* 2004; 19:241-248.
2. Kasper S, Stein DJ, Loft H, Nil R: Escitalopram in the treatment of social anxiety disorder: a randomised, placebo-controlled, flexible-dose study. *Br J Psychiatry*, in press.

NR522 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Adjunctive Quetiapine for Treatment-Resistant Adolescent Depression: A Case Series

Sanjeev Pathak, M.D., *Childrens Hospital Medical Center, 3333 Burnet Avenue, D3014, Cincinnati, OH 45229-3039*; Erin Johns, B.S., Robert Kowatch, M.D.

Educational Objectives:

At the conclusion of the session, participants will be able to: (1) recognize the need for novel interventions for treatment resistant depression in adolescents, (2) understand the possible utility of adjunctive quetiapine in treatment resistant adolescent depression.

Summary:

Background: Empirical evidence suggests that many adolescents with major depressive disorder (MDD) do not respond or respond only partially to commonly used interventions. There are preliminary data in adults that adjunctive second-generation antipsychotics may be useful in treatment resistant major depressive disorder (TRD).

Objective: To obtain preliminary data on safety, tolerability, and clinical usefulness of quetiapine as adjunctive therapy for adolescents (13-18 years of age) diagnosed with TRD. TRD was defined as failure to respond to an adequate dose for at least eight weeks of a selective serotonin reuptake inhibitor (SSRI).

Methods: Charts of 10 adolescents (age 13-18 years) diagnosed with TRD, who were treated with adjunctive quetiapine were evalu-

ated. Doses of preexisting antidepressants remained unchanged during the period of evaluation. Response to treatment was defined as Clinical Global Impression-Improvement (CGI-I) score of 1 (very much improved) or 2 (much improved).

Results: Seven (70%) qualified as responders with treatment with adjunctive quetiapine. The median dose was 200 mg (Mean+SD=275+190.4 mg, range=150-800 mg). Side effects included sedation (40%) and weight gain (mean + SD = 4.5 + 7.24 pounds). There was no serious adverse event.

Conclusions: This suggests that there may be a role for adjunctive quetiapine in treatment-resistant adolescent depression.

References:

1. Treatment for Adolescents With Depression Study Team (2004), Fluoxetine, Cognitive-Behavioral Therapy, and Their Combination for Adolescents With Depression: Treatment for Adolescents With Depression Study (TADS) Randomized Controlled Trial. *JAMA* 2004; 292: 807-820.
2. Rapaport M, Canuso C, Rouillon R, Leblanc J, Young A, Loescher A, Bossie C, Turkoz I, Gharabawi G: Results from the Augmentation with Risperidone in Resistant Depression Trial, in American Psychiatric Association New York, NY, 2004.

NR523 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **ADHD and Bulimia Nervosa**

Javier Correas Lauffer, M.D., *Psychiatric Department, Hospital Ramón y Cajal, Crt Colmenar Km 9, 100, Madrid 28034, Spain*; Angela Ibañez-Cuadrado, M.D., Javier Quintero-Gutierrez, M.D., Jerónimo Saiz-Ruiz, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate the relationship between attention deficit/hyperactivity disorder and bulimia nervosa

Summary:

Objective: Attention-deficit/hyperactivity disorder (ADHD) is a common psychiatric disorder in childhood. Persistence in adult age and high comorbidity with antisocial personality disorder, substance abuse, and pathological gambling has been recently established. Impulsivity is a characteristic symptom in ADHD, also present in psychiatric disorders related to ADHD. Several studies include bulimia in the impulsive spectrum. This report examines the prevalence of ADHD in an eating disorders population.

Methods: Participants were 19 bulimia nervosa patients, eleven purgative anorexia nervosa and ten restrictive anorexia nervosa. These were compared with 18 control subjects with measurement instruments of ADHD as the Wender Utah Rating Scale (WURS) and the Current and Childhood Symptoms Scale-Self Report Form. Neuropsychological assessment included the Wisconsin Card Sorting Test and the Continuous Performance Test.

Results: In the Current Symptoms Scale-Self Report Form bulimic patients showed significantly more adult ADHD score (21.79) compared with anorectic patients (10.00) and healthy controls (8.72) ($p < 0.001$). When measured retrospectively using the WURS, bulimic patients also showed more retrospective ADHD score (24.27) than restrictive anorectic patients (16.50) and healthy control group (14.83) ($p < 0.05$).

Conclusions: ADHD may be a risk factor for the development of bulimia nervosa as it has been reported for pathological gambling or substance abuse disorders.

References:

1. Biederman J, Mick E, Faraone SV: Age-dependent decline of symptoms of attention deficit hyperactivity disorder: Impact of remission definition and symptom type. *Am J Psychiatry* 2000; 157:816-818.

2. Specker SM, Carlson GA, Christenson GA, Marcotte M: Impulse control disorders and attention deficit disorder in pathological gamblers. *Ann Clin Psychiatry* 1995; 7(4):175-179.

NR524 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Differences Between ODD, ADHD, and ODD Plus ADHD Symptom Subtypes: Psychiatric Symptoms in Clinic and Nonreferred Adults**

Kenneth D. Gadow, Ph.D., *Department of Psychiatry, State University of New York, Putnam Hall, Stony Brook, NY 11794-8790*; Joyce Sprafkin, Ph.D., Jayne Schneider, Ph.D., Edith Nolan, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to (1) describe differences between adults with either ADHD or ODD symptoms, and (2) discuss how the comorbid (ADHD+ODD) condition differs from each symptom subtype presenting separately.

Summary:

Objective: Examination of childhood disruptive behavior disorders in adults is critical to understanding developmental changes in these disorders. This study, examines differences between ADHD and oppositional defiant disorder (ODD) in the severity of co-occurring psychiatric symptoms in two samples of adults.

Methods: Two samples of adults, a psychiatry clinic sample (N=490) and a nonreferred sample (N=900), completed the Adult Self-Report Inventory-4 (ASRI-4), a rating scale of DSM-IV symptoms. Participants (clinic/nonreferred) were sorted into one of four groups based on their ASRI-4 scores: ADHD only (n=139/45), ODD only (n=23/15), ADHD+ODD (n=64/15), and NONE (n=264/825). A series of ANOVAs compared the four groups on ASRI-4 symptom severity ratings of conduct disorder, major depressive disorder, bipolar disorder, generalized anxiety disorder, social phobia, antisocial personality disorder, and borderline personality disorder.

Results: In general, findings indicated that the ADHD+ODD group had the most severe ratings and the NONE group the least severe ratings, with both the ADHD only and ODD only groups intermediate. Differences between ADHD only and ODD only groups suggest that each condition represents a unique clinical entity. The pattern of group differences was generally similar for males and females but much less dramatic in the nonreferred sample.

Conclusions: Findings support (1) the distinction between ADHD and ODD symptom subtypes in adults, and (2) the notion that the comorbid condition is a unique clinical entity, which is also the case for children.

References:

1. Weiss M, Weiss J: A guide to the treatment of adults with ADHD. *J Clin Psychiatry* 2004; 65[suppl 3]:27-37.
2. Gadow KD, Sprafkin J, Weiss MD: Adult Self-Report Inventory-4 Manual. Stony Brook, NY: Checkmate Plus, 2004.

NR525 Tuesday, May 24, 3:00 p.m.-5:00 p.m. **Adjunctive Levetiracetam for Treatment-Refractory PTSD**

Gustavo D. Kinrys, M.D., *Department of Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139*; Lisa Wygant, B.A., Fernanda Nery, B.A., Maria Melo, B.A.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize levetiracetam as a potential treatment for PTSD.

Summary:

Objective: To assess the use of adjunctive levetiracetam, a novel anticonvulsant agent, in the treatment of refractory PTSD.

Method: Twenty-three patients with DSM-IV PTSD who were considered partial or non-responders to antidepressant therapy received adjunctive levetiracetam in a naturalistic fashion. The primary outcome measure was the PTSD Checklist-Civilian Version (PCL-C). Secondary outcome measures included the Hamilton Anxiety Scale (HAM-A), Clinical Global Impression of Severity (CGI-S), and Clinical Global Impression of Improvement (CGI-I) scales.

Results: Levetiracetam at a mean \pm SD dose of 1967 ± 650 mg/day for 9.7 ± 3.7 weeks was generally well tolerated. Patients were relatively ill with a mean baseline PCL-C score of 67.2 ± 9.4 , CGI-S score of 6.0 ± 0.7 , and HAM-A score of 26.8 ± 4.9 . Patients improved significantly on all measures ($p < 0.001$). Thirteen patients (56%) met responder criteria at endpoint (CGI-I = 2) and six (26%) met remission criteria (CGI-S = 2). Adverse events were generally mild, and no patients discontinued levetiracetam because of side effects.

Conclusion: These preliminary data suggest that levetiracetam may be an effective treatment in combination with antidepressant therapy for patients with PTSD who remain symptomatic after initial intervention.

References:

1. Noyer M, Gillard M, Monfagne A, et al: The novel antiepileptic drug levetiracetam (ucb L059) appears to act via a specific binding site in CNS membranes. *Eur J Pharmacol* 1995; 286:137-1462.
2. Lamberty Y, Gower AJ, Klitgaard H: The new antiepileptic drug levetiracetam normalises chloroazepoxide withdrawal-induced anxiety in mice. *Eur J Pharmacol* 2002; 439:101-106.

NR526 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

A Comparison of Direct Cost of Treatment for Autism Versus Asthma and Diabetes: Data From Medi-Cal

Scott Flanders, Ph.D., *Regional Outcomes Research, Janssen Medical Affairs, L.L.C., 740 Waterford Drive, Grayslake, IL 60030*; Luella Engelhart, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the total costs of health care services for children and adolescents with a diagnosis of an autistic spectrum disorder in a state Medicaid population; describe the differences in utilization of psychiatric and nonpsychiatric health care services of autistic children and adolescents compared with other chronic pediatric diseases (diabetes and asthma) in a state Medicaid population.

Summary:

Objective: To compare the direct costs of treatment in children and adolescents with a diagnosis of a pervasive developmental disorder (autism), diabetes, or asthma.

Methods: Medical and prescription costs from the Medi-Cal database were categorized by psychiatric and nonpsychiatric services. Pre- and postdiagnosis median health care costs for autistic children were compared with costs from randomly selected, gender-matched, cohorts of children diagnosed with diabetes or asthma.

Results: The average age of the children with autism ($n=731$) was 8.6 ± 4.0 years, compared with diabetes ($n=731$) 12.1 ± 4.3 years, and asthma ($n=731$) 6.3 ± 3.0 years. Total health care costs were significantly different among groups. Children with autism had higher annual costs (prediagnosis: \$363; post: \$1199) than children with diabetes (pre: \$171; post: \$649) or asthma (pre: \$147.90; post: \$424) (all $P < 0.0001$). Psychiatric and nonpsychiat-

ric cost categories were statistically significant. Additionally, the period prevalence for autism in this population increased 114% during the study period, compared with a 42% decrease in asthma and a 3% decrease in diabetes.

Conclusion: This study estimates that autistic children incur greater health care costs than children with diabetes or asthma. These findings reflect the significant cost of illness for autism relative to other pediatric chronic conditions in this Medicaid population.

References:

1. Birenbaum A, Guyot D, Cohen HJ: Health care financing for severe developmental disabilities. St. John's University, New York. Monographs of the American Association on Mental Retardation 1990 (14) p1-150, ISSN 0895-8009.
2. Jarbrink K, Knapp M: The economic impact of autism in Britain. *Autism* 2001; 5(1): 7-22.
3. Newschaffer C, Curran LK: Autism: an emerging public health problem. *Public Health Reports* 2003; 118: 393-399.
4. Kelsey JL, Whittemore AS, Evans AS, Thompson, WD: *Methods in Observational Epidemiology*. New York, Oxford University Press, 1996.

NR527 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Evaluation of the Daily Assessment of Symptoms: Anxiety Questionnaire in Patients With Generalized Anxiety Disorder

Robert J. Morlock, Ph.D., *Department of Outcomes, Pfizer Inc., 2800 Plymouth Road, Ann Arbor, MI 48105*; Valerie Williams, Ph.D., Douglas Feltner, M.D., Joseph Cappelleri, Ph.D., Jerri Brock, M.S., Jean Endicott, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to assess the psychometric properties of the DAS-A, identify a new tool for assessing early onset of symptom relief in patients with GAD, and identify which symptoms are likely to improve first.

Summary:

Background: Fast acting anxiety medications are important to patients and society. Measuring early onset of medication action, however, requires a sensitive and clinically responsive measure.

Objectives: Evaluation of the psychometric properties of the Daily Assessment of Symptoms-Anxiety (DAS-A) and its ability to detect reduction of anxiety symptoms during the first week of treatment.

Methods: A four-week, double-blind, randomized, placebo-controlled, parallel-group study of lorazepam and paroxetine in patients with GAD was undertaken to assess the DAS-A. Analyses in support of item reduction and subscale development were conducted, as well as exploratory factor analysis and assessments of reliability, validity, and utility.

Results: The 15-item DAS-A demonstrated separation from placebo 24 hours post-dose for lorazepam. Factor analysis showed a unidimensional factor structure best described the data. Descriptive statistics are presented for the DAS-A, including internal consistency ($\alpha = 0.86$ to 0.95), test-retest reliability (ICCs = 0.67 to 0.92), and effect size estimates (ES = -0.26 to -0.99). Items with comparatively poor reliability, responsiveness, and predictive validity were identified as candidates for removal from the DAS-A.

Conclusions: This study demonstrates the reliability and validity of the DAS-A as an instrument to assess a reduction in anxiety symptoms as soon as 24 hours post-dose.

References:

1. Hamilton M: The assessment of anxiety states by rating. *Br J Med Psychol*. 1959; 32:50-55.

2. Feltner DE, Crockatt JG, Dubovsky SJ, Cohn CK, Shrivastava RK, Targum SD, Liu-Dumaw M, Carter CM, Pande AC: A randomized, double-blind, placebo-controlled, fixed-dose, multicenter study of pregabalin in patients with generalized anxiety disorder. *J Clin Psychopharmacol* 2003; 23(3):240-9.

NR528 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Proactive/Reactive Aggression and Psychopathology in High School Students

Hans Steiner, M.D., *Department of Psychiatry, Stanford University, 401 Quarry Road, Room 1117, Stanford, CA 94305*; Kirti Saxena, M.D., Sanja Medic, B.A., Belinda Plattner, M.D., Laura Delizonna, Ph.D.

Educational Objectives:

At the end of the presentation, practitioners will recognize the distinction of two major forms of aggression in youth; practitioners will be able to apply clinical screens in high school populations to identify these two forms of aggression and identify individuals with maladaptive, psychopathological forms of them.

Summary:

Objective: To replicate the two-factor structure of aggression in a sample of high school students.

Background: Previous work has identified two major forms of aggression in school age children: emotionally "hot," charged aggression, which is called reactive, affective, defensive, and impulsive (RADI); or emotionally "cold" aggression, called proactive, instrumental, planned (PIP). We present data further supporting this subtyping.

Methods: 1,315 students, mean age 16 (SD=1), 52% boys and 48% girls who were ethnically diverse, mostly of middle SES, completed a battery of screening tests (Achenbach Youth Self Report). The subscales "aggressive behavior" provided a measure of RADI aggression, and "delinquent behavior" provided a measure of PIP.

Results: Principal components analysis produced two factors: mixed psychopathology /RADI aggression (EV=4.6; accounting for 57% of the variance; RADI loading 0.356). Delinquent behavior or PIP aggression (EV=0.91; accounting for 11% of the variance; unique loading 0.600). No other factors emerged. PIP and RADI aggression correlated Pearson's $r=0.43$, $p<0.0001$, showing some overlap, but only a modest relationship (16% of the variance).

Conclusions: Results support the existence of two related, but clinically different forms of aggression. This distinction mirrors results showing that different neuroarchitectures support RADI and PIP. Clinically, RADI aggression is closer to psychopathology and a more legitimate psychiatric treatment target.

This research was supported by a grant from the California Wellness Foundation Violence Prevention Initiative to Dr. Steiner.

References:

1. Steiner H, Saxena K, Chang K: Psychopharmacological strategies for the treatment of aggression in youth. *CNS Spectrums* 2003; 8, (4):298-308.
2. Steiner H, Petersen M, Saxena K, Ford S, Matthews Z: Divalproex sodium for the treatment of conduct disorder: A randomized controlled clinical trial. *Journal of Clinical Psychiatry* 2003; 64(10):1183-1191.

NR529 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Does the Two-Factor Model of Aggression Hold Incarcerated Delinquents?

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Laura Delizonna, Ph.D., Kirti Saxena, M.D., Sanja Medic, B.A., Belinda Plattner, M.D., Rudy Haapanen, Ph.D.

Educational Objectives:

At the end of the presentation, practitioners will recognize the distinction of two major forms of aggression in incarcerated youth with conduct disorder; practitioners will be able to apply appropriate clinical screens in juvenile justice to identify these two forms of aggression and identify individuals with maladaptive, psychopathological forms of them, leading to more realistic treatment planning.

Summary:

Objective: To replicate two factors of aggression in incarcerated youths to extend the validity of this approach to samples with high ecological salience. Two factors emerged in elementary and high school populations: emotionally "hot" aggression called reactive, affective, defensive, impulsive (RADI); and emotionally "cold" aggression referred to as proactive, instrumental, planned (PIP).

Methods: 3,522 incarcerated youths (mean age 16 (SD1), 173 girls, ethnically diverse, of mostly low SES) completed a battery of screening tests (YSR, WAI and MAYSI). The YSR subscales "aggressive behavior" provided the measure of RADI aggression; while "delinquent behavior" provided a measure of PIP.

Results: Principal components analysis produced two factors: mixed psychopathology /RADI aggression (EV=4.4; accounting for 55% of the variance; RADI loading 0.344). Delinquent behavior or PIP aggression (EV=1.31; accounting for 14% of the variance; unique loading 0.660). PIP and RADI aggression correlated (Pearson's $r=0.55$, $p<0.0001$) showing some overlap, but showed only a modest relationship (25% variance). Importantly, RADI aggression correlated strongest with trauma and psychopathology (Pearson's $r=0.59-0.035$, $p<0.01$), while PIP correlated strongest with substance abuse (Pearson's $r=0.52$, $p<0.001$).

Conclusions: Results replicated other studies, supporting the existence of two related, but clinically distinct forms of aggression in this extremely violent sample. Clinical correlates of PIP and RADI aggression are distinct and suggest different treatment needs.

This study was supported by a grant from the California Wellness Foundation Violence Prevention Initiative to Dr. Steiner and grants from the National Institute of Justice and the California Youth Authority to Drs. Steiner and Haapanen.

References:

1. Steiner H, Saxena K, Chang K: Psychopharmacological strategies for the treatment of aggression in youth. *CNS Spectrums* 2003; 8, (4):298-308.
2. Steiner H, Redlich A: Child psychiatry and juvenile justice, in Lewis M, (Editor). *Child Psychiatry*, NY, Williams & Wilkins, 2002, pp1417-1425.

NR530 Tuesday, May 24, 3:00 p.m.-5:00 p.m.
Basic, Background, and Social Emotions in Adolescents

Hans Steiner, M.D., *Department of Psychiatry, Stanford University, 401 Quarry Road, Room 1117, Stanford, CA 94305*; Sanja Medic, B.A., Belinda Plattner, M.D.

Educational Objectives:

1) At the end of the presentation, practitioners will recognize gender specific emotion patterns in adolescent boys and girls in response to stress; practitioners will be able to apply the knowledge to identifying adolescents at risk for non-normative reactions to stress.

Summary:

Objective: Neuroscientific advances identify different emotions: background, basic, and social emotions. We investigated to see if these groups are applicable to adolescents, examining alongside specific gender differences.

Methods: 169 adolescents (mean age 16 (SD1) from a local high school (90 girls, ethnically diverse, SES mode upper middle class) completed tests of trait emotions (Weinberger adjustment Inventory - WAI). Subsequently, they were exposed to a standardized stress inducing speech task, during which emotional responses were measured at 10 and 20 minutes into the task by visual analogue scales.

Results: Data were analyzed by SAS utilizing ANOVA's for dispersity and Pearson's for tests of association. Background, basic, and social emotions overlapped modestly to moderately at all data points, indicating differentiation of these groups (r 's ranging from 0.05 to 0.60). Genders reported differences in basic emotions (anxiety, sadness, and anger) and social emotions (responsibility and consideration) only when asked to report on the past 12 months. Responses during the stressful task differed only in anxiety, sadness (girls>boys), but not in anger, happiness, and interest; background emotions (pleased) or social emotions (guilt and shame).

Conclusions: Examining emotional responses in vivo shows the validity of Damasio's groupings in adolescents. Gender differences seem more pronounced during retrospective recall.

This study was supported by a grant from the Eucalyptus Foundation to Dr. Steiner.

References:

1. Steiner H, Ryst E, Berkowitz J, Gschwendt M, Carrion V, Koopman C: Boys' and girls' responses to stress: affect and heart rate during a speech task. *Journal of Adolescent Health* 2002; 30S:14-21.
2. Damasio A: Looking for Spinoza, Orlando, Florida, Harcourt, 2003.

NR531 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Topiramate for Civilian PTSD: A Pilot-Controlled Study

Supported by Ortho-McNeil Pharmaceuticals

Frederick Petty, M.D., *Department of Psychiatry, Creighton University, 3528 Dodge Street, Omaha, NE 68131*; Ronald R. Fieve, M.D., Julie A. Capece, B.A., Shu-Chen Wu, Ph.D., Norman Rosenthal, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to: understand rationale for advancing pharmacotherapeutic treatment options in civilian populations with chronic PTSD; identify the potential role of topiramate for the treatment of civilian PTSD.

Summary:

Objective: Assess efficacy of topiramate (TPM) in civilian post-traumatic stress disorder (PTSD).

Method: Double-blind, randomized, placebo-controlled (PBO) 12-week study enrolled 72 outpatients (19-64 y) with DSM-IV diagnosis of noncombat-related PTSD and Clinician-Administered PTSD Scale (CAPS) scores ≥ 50 . TPM was started at 25 mg/d and titrated to 400 mg/d or maximum tolerated dose. Primary efficacy, percent change in total CAPS, was assessed by ANCOVA in the intent-to-treat (ITT) population with the last observation carried forward. Sample size was not based on statistical considerations.

Results: ITT population (N=68; mean age, 35 y; 87% women; 74% white) showed reduced total CAPS scores with TPM vs. PBO

(39.5% vs. 29.5%) but not significantly ($P=0.31$). CAPS subscale scores for symptoms of re-experiencing (43.6% vs. 34.8%), avoidance/numbing (38.3% vs. 30.6%), and hyperarousal (36.6% vs. 21.4%) were numerically but not significantly reduced in TPM vs. PBO subjects. Six TPM subjects compared with two PBO had final CAPS score <20 ($P=0.075$). Median final TPM daily dose was 100 mg; mean treatment duration 55 days. TPM treatment-emergent adverse events included paresthesia, headache, fatigue, and insomnia.

Conclusion: In this civilian PTSD study, TPM demonstrated only a numerical trend in CAPS improvement compared with PBO. Adequately powered studies are warranted.

References:

1. Asnis GM, et al: SSRIs versus non-SSRIs in post-traumatic stress disorder. *Drugs* 2004; 64:383-404.
2. Davis LL, et al: Pharmacotherapy for post-traumatic stress disorder: a comprehensive review. *Expert Opin Pharmacother* 2001; 2:1583-95.

NR532 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Relapse Prevention Study of Tiagabine for Social Anxiety Disorder

Supported by Cephalon, Inc.

Philip T. Ninan, M.D., *Department of Psychiatry, Emory University, 1841 Clifton Road, 4th Floor, Atlanta, GA 30329*; Laslo Papp, Boadie W. Dunlop, M.D., Steven J. Garlow, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the issues in the use of tiagabine as a treatment of social anxiety disorder (SAD).

Summary:

Objective: Tiagabine, a selective GABA reuptake inhibitor, was evaluated in the first ever pilot study of patients with social anxiety disorder (SAD).

Method: After informed consent, adults with SAD were enrolled in a 12-week, open-label treatment with tiagabine (Phase I) at two sites. Responders were randomized in a double-blind manner, to tiagabine or placebo for an additional six months or until relapse (Phase II).

Results: For Phase I, 63 patients entered and 54 had an evaluation after initiating tiagabine. Thirty-six patients terminated early (12 for adverse events, one for non-compliance, four for lack of efficacy, and 19 were lost to follow up/withdrew consent). Based on the last-observation-carried-forward (LOCF) analysis, 40.7% (22 of 54) were considered responders (CGI-I of 1 or 2). The common adverse events were somnolence (22%), dizziness (19%), insomnia (11%), and nausea (11%). Of the 27 completers, 17 (70%) were responders and randomized into Phase II. Seven were lost to follow up and three met criteria for relapse (all three on placebo). Kaplan-Meier survival analysis failed to separate the tiagabine and placebo groups. Repeated measure ANOVA favoured tiagabine over placebo by -0.7 on CGI-Severity ($p=.02$), -6.3 on the self-rated Social Phobia Inventory (SPIN) ($p=.09$) and -1.7 on the Sheehan Disability Scale ($p=n.s.$).

Conclusion: This pilot study of tiagabine suggests efficacy in SAD with an acceptable profile of adverse effects.

References:

1. Lydiard RB: The role of GABA in anxiety disorders. *J Clin Psychiatry* 2003; 64(suppl 3):21-27.
2. Rosenthal M: Tiagabine for the treatment of generalized anxiety disorders: a randomized, open-labeled, clinical trial with paroxetine as a positive control. *J Clin Psychiatry* 2003; 64:1245-1249.

NR533 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

The Effect of MAS XR on Simulated Driving Safety in Young Adults With ADHD

Supported by Shire US, Inc.

Gary Kay, Ph.D., *Washington Neuropsych Institute, 4910 Massachusetts Avenue NW, Suite 100, Washington, DC 20016*; Barton Pakull, M.D., Anthony Reeves, M.A., David A. Mays, Ph.D., Garrick Fiddler, M.D.

Educational Objectives:

After reviewing this poster, the participant will be able to discuss the effects of mixed amphetamine salts extended release (MAS XR) on simulated driving safety and neurocognitive function in young adults with ADHD.

Summary:

Objective: To assess the efficacy of mixed amphetamine salts extended release (MAS XR) on simulated driving safety and neurocognitive function in young adults with attention deficit/hyperactivity disorder (ADHD).

Methods: A six-week, randomized, double-blind, placebo-controlled, single-center, crossover study. Subjects (n=15) were adults aged 19-25 years diagnosed with ADHD by DSM-IV criteria. Subjects were randomized to three weeks of active treatment and three weeks of placebo in a crossover design. The active treatment arm consisted of MAS XR 20 mg once daily (QAM) during week 1, 40 mg QAM during week 2, and 50 mg QAM during week 3. Simulated driving safety and cognitive function were assessed at a practice visit and again after each three-week treatment period.

Results: At 12 hours postdose, significant improvements in simulated driving safety occurred when subjects were receiving MAS XR compared with placebo, including fewer collisions (6 vs 15, $P<0.05$), an improved crash avoidance rating (7 vs 9, $P<0.05$), longer time to collision (2.6 vs 2.4, $P<0.05$), fewer driving out of lane occurrences (22 vs 32, $P<0.05$), and less tailgating (15 vs 20, $P<0.05$).

Conclusions: MAS XR significantly improved simulated driving safety in young adults with ADHD compared with placebo.

Supported by funding from Shire Pharmaceutical Development Inc.

References:

1. Barkley RA, Murphy KR, Kwasnik D: Motor vehicle driving competencies and risks in teens and young adults with attention deficit hyperactivity disorder. *Pediatrics* 1996; 98:1089-1095.
2. Barkley RA, Murphy KR, DuPaul GJ, Bush T: Driving in young adults with attention deficit hyperactivity disorder: knowledge, performance, adverse outcomes, and the role of executive functioning. *J Int Neuropsychol Soc* 2002; 8:655-672.

NR534 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Comparative Efficacy of Amphetamine and Atomoxetine by Symptom Severity

Supported by Shire US, Inc.

James J. McGough, M.D., *University of California Los Angeles Neuropsychiatry Institute, 300 UCLA Medical Plaza, Los Angeles, CA 90095*; Sharon B. Wigal, Ph.D., Joseph Biederman, M.D., Thomas J. Spencer, M.D., James T. McCracken, M.D., David A. Mays, Ph.D., Garrick Fiddler, M.D.

Educational Objectives:

After reviewing this poster, the participant should be able to compare the response rates of school-aged children with attention-deficit/hyperactivity disorder (ADHD) to mixed amphetamine salts extended release (MAS XR) and atomoxetine.

Summary:

Objective: To compare the efficacy of mixed amphetamine salts extended release (MAS XR; Adderall XR[®]) and a once-daily selective norepinephrine reuptake inhibitor (atomoxetine; Strattera[®]) in children with ADHD.

Methods: A multicenter, randomized, double-blind, forced-dose-escalation classroom analog study. Subjects (N=215) were randomized in a 1:1 ratio to receive once-daily MAS XR or atomoxetine. Efficacy measures included the SKAMP Teacher Rating Scale. This is a post-hoc analysis of subjects with a baseline CGI-Severity score that indicated marked or severe impairment who were "improved" or "not improved" on the SKAMP deportment and attention scores at endpoint.

Results: The markedly or severely impaired ITT sample at endpoint included 71 subjects (MAS XR, n=33 and atomoxetine, n=38). Of the 33 subjects receiving MAS XR, 82% demonstrated improvement from baseline on SKAMP deportment ($P<0.0001$) and attention ($P=0.001$) scores. In contrast, 34% of those receiving atomoxetine were noted to have improvement. Approximately 66% of those subjects who received atomoxetine did not demonstrate improvement in SKAMP deportment or attention scores at endpoint. Both agents were well tolerated, and most AEs were mild or moderate.

Conclusion: These data suggest that in ADHD subjects with at least a marked impairment, more than twice as many may respond to MAS XR compared with atomoxetine.

References:

1. McCracken JT, Biederman J, Greenhill LL, et al: Analog classroom assessment of a once-daily mixed amphetamine formulation, SLI381 (Adderall XR), in children with ADHD. *J Am Acad Child Adolesc Psychiatry* 2003; 42:673-683.
2. Michelson D, Allen AJ, Busner J, et al: Once-daily atomoxetine treatment for children and adolescents with attention deficit hyperactivity disorder: a randomized, placebo-controlled study. *AM J Psychiatry* 2002; 159:1896-1901.

NR535 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Psychosocial Aspects of Pre- and Post-Liver and Kidney Transplantation in Children

Maria Gragas Lima, M.S., *Department of Psychology Services, Santa Casa Sao Paulo, Cesario Mota Jr 112, Sao Paulo, SP 01221-900, Brazil*; Rosana T. Rodrigues, M.S., Wilze L. Bruscato, D.R.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the importance of evaluating the psychosocial aspects in children who underwent transplantation proceedings.

Summary:

This work aimed to make a descriptive comparison based on the parents' perception of the psychosocial conditions of their children before and after liver and kidney transplantation procedures. This transversal and descriptive study was developed with eight transplanted children, four of whom had gone through liver and four through kidney transplantation. The sample was composed of six male and two female subjects, aged between 3 and 13 years. Semi-structured interviews based on standardized protocols were held with the parents of the transplanted children. Data were quantified and classified into different categories. The results showed that before the procedure, 75% (N=6) of the children presented low levels of academic performance and also of leisure activities. After the procedure, the same percentage of patients presented good results in both areas. Concerning emotional adaptation, 75% (N=6) of the parents considered their children to be facing emotional difficulties in the period previous to

the surgery. After the transplant, 87.5% (N=7) of the sample was considered to be emotionally adapted. In addition, before the surgery, 50% (N=4) of the subjects paid weekly visits to the hospital. After the procedure, 75% (N=6) began to pay monthly visits. Regarding quality of life, 75% of the sample considered their children to have benefited from the procedure. Thus, the findings point out positive changes in psychosocial conditions of patients in pre and post-transplantation periods. The negative aspects must be analyzed considering the characteristics of personality, the dynamic within the family group, and the quality of support that is given to the child.

References:

1. Bravata DM, Olkin L, Barnato AE, Keeffe EB, & Owens DK: Health-related quality of life after liver transplantation: A meta-analysis. *Liver Transplantation Surgery* 1999; 5(4):318-331.
2. Holzner B, Kemmler G, Korp M, Dachs E, Kaserbacher R, Spechtenhauser B, Vogel W, Spemer-Unterweger B: Preoperative expectations and postoperative quality of life in liver transplant survivors. *Archives of Physical Medicine and Rehabilitation* 2001; 82(1):73-79.

NR536 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Parental Perception Regarding the Emotional Adjustment of Transplanted Children

Maria Gragas Lima, M.S., *Department of Psychology Services, Santa Casa Sao Paulo, Cesario Mota Jr 112, Sao Paulo, SP 01221-900, Brazil*; Rosana T. Rodrigues, M.S., Wilze L. Bruscato, D.R.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the emotional changes after a transplantation procedure in children.

Summary:

Introduction: Parents of children and adolescents with chronic illnesses usually observe changes in their children's emotional adjustment as they face the full impact of long-term treatment (McDaniel, 1994).

Objectives: Assess the parental perception about the emotional adjustment of their children before and after kidney and liver transplantation.

Methods: This was a transversal and descriptive study that analyzed parental reports regarding eight children and adolescents, four male and four female, between 3 and 17 years of age, who underwent kidney and liver transplantation over three months ago. The parents were invited to participate in semi-directed interviews, which were based on a protocol designed to investigate the child's behavior and personality traits before and after transplant. The data were analyzed and classified according to two categories: emotionally adjusted or emotionally non-adjusted.

Results and Discussion: According to the parents' report, 25% (N=2) of the sample was considered as emotionally adjusted in the period that preceded the transplant. However, in the post-transplant, the number of adjusted children increased to 87.5% (N=7).

Conclusion: Despite the fact that kidney and liver transplantations are procedures that bring great changes to the patients' lives, such procedures seem to allow for better emotional adjustment of children and adolescents, as described by their parents (Holzner, 2001).

References:

1. McDaniel SH, Hepworth J, Doherty WJ: *Terapia Familiar Médica: um Enfoque Biopsicossocial às Famílias com Problemas de Saúde*. Artes Médicas. Porto Alegre, 1994.

2. Holzner B, Kemmler G, Kopp M, Dachs E, Kaserbacher R, Spechtenhauser B, Vogel W, Spemer-Unterweger B: Preoperative expectations and postoperative quality of life in liver transplant survivors. *Archives of Physical Medicine and Rehabilitation* 2001; 82(1):73-79.

NR537 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Comparative Meta-Analysis of 5HT Reuptake Inhibitors for PTSD: Efficacy and Tolerability of Double-Blind Trials

Michael Wilson, M.D., *Department of Psychiatry, Louisiana State University Health Sciences Center, 97 East Park Place, New Orleans, LA 70124*; Michael Wilson, II, M.D., Michael Wilson, Sr., Ph.D.

Summary:

Introduction: The objective was to determine not only differences in efficacy but also tolerability of the available serotonin reuptake inhibitors (SSRIs) studied for posttraumatic stress disorder (PTSD).

Methods: The authors reviewed the available literature for all double-blind trials of SSRIs for PTSD excluding all studies that were neither double-blind nor weeks in duration. The statistics for this was done using the computer software Comprehensive Meta-Analysis.

Results: The only double trials matching our criteria were two paroxetine, two sertraline, and three fluoxetine. All medications had a superior response over placebo; however, none of the medications separated from each other in efficacy. With adverse effects paroxetine had a summed incidence that was greater than placebo, sertraline, and fluoxetine; sertraline and fluoxetine did not separate from each other in the incidence of adverse effects. The paroxetine samples also had significantly more Caucasians than non-Caucasians.

Conclusion: From this analysis it can be concluded that all three medications had equal efficacy with each other and greater than placebo for treating PTSD. However, in incidence of adverse effects, there was a significant difference with paroxetine having a much worse side effect profile.

References:

1. Stein DJ, Seedat S, van der Linden GJ, Zungu-Dirwayi N: Selective serotonin reuptake inhibitors in the treatment of post-traumatic stress disorder: a meta-analysis of randomized controlled trials. *International Clinical Psychopharmacology* 2000; 15 Suppl 2:S31-9.
2. Connor KM, Sutherland SM, Tupler LA, Malik ML, Davidson JR: Fluoxetine in post-traumatic stress disorder. Randomised, double-blind study. *British Journal of Psychiatry* 1999; 175:17-22.

NR538 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Lamotrigine Adjunctive or Monotherapy in Adolescent Bipolar Depression

Kiki Chang, M.D., *Department of Psychiatry, Stanford University, 401 Quarry Road, Stanford, CA 94305-5719*; Kirti Saxena, M.D., Meghan Howe, M.S.W.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate knowledge about the effects of lamotrigine as adjunct or monotherapy in adolescent bipolar depression. To demonstrate knowledge about the dosing of lamotrigine in adolescents.

Summary:

Objective: There have been no prospective studies of the treatment of adolescent bipolar depression to date. We wished to study the efficacy and tolerability of lamotrigine as adjunctive or monotherapy in adolescent bipolar depression.

Methods: This was an eight-week, open-label trial of lamotrigine with 20 adolescents in a depressive episode, aged 13-18 years (mean = 15.8, 7 boys/12 girls) with diagnoses of bipolar disorder I, II, or NOS. There were 19 completers in the analysis. Lamotrigine was begun at 12.5-25 mg/day and gradually increased. Subjects were assessed with the Young Mania Rating Scale (YMRS), Childhood Depression Rating Scale—Revised (CDRS-R) and Overt Aggression Scale—Modified (OAS-M) weekly for eight weeks.

Results: Mean final dose was 131.6 mg/day. Fourteen subjects were on lamotrigine monotherapy. Sixteen (84%) responded by primary criteria, the Clinician Global Impression-Change (CGI-C). Twelve (63%) responded by secondary criteria, a 50% decrease in CDRS-R. Overall bipolar symptomatology decreased in severity over eight weeks, as measured by: CDRS-R ($p < 0.0001$), YMRS ($p = 0.002$), OAS-Aggression ($p = 0.02$), and OAS-Irritability ($p = 0.001$) scales. No rash or other adverse effects was noted.

Conclusions: Adolescents with bipolar depression may respond to lamotrigine treatment, adjunctive or monotherapy, with improvement of depression, mania, aggression. Placebo-controlled studies are needed.

References:

1. Findling RL, Gracious BL, McNamara NK, Youngstrom EA, Demeter CA, Branicky LA, Calabrese JR: Rapid, continuous cycling and psychiatric co-morbidity in pediatric bipolar I disorder. *Bipolar Disord.* 2001; 3(4):202-10.
2. Chang KD, Ketter TA: Special issues in the treatment of paediatric bipolar disorder. *Expert Opin Pharmacother* 2001; 2(4):613-22.

NR539 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Ropinirole Improves Mood and Reduces Symptoms of Anxiety in RLS

Supported by GlaxoSmithKline

Philip M. Becker, M.D., *Sleep Medicine Association of Texas, 8140 Walnut Lane, Suite 100, Dallas, TX 75231*; Richard K. Bogan, M.D., Stanley W. Carson, Jackie W. Kwong, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to state the impact of overall mood and symptoms of anxiety and depression in patients with RLS before and after treatment with ropinirole.

Summary:

Objective: Restless legs syndrome (RLS) impairs sleep and may increase symptoms of depression and anxiety. The presenters studied the effect of ropinirole on total mood, depression, and anxiety in patients with RLS.

Methods: TREAT RLS US (protocol 101468/249) was a 12-week, phase-III, randomized (1:1), double-blind, placebo-controlled trial of ropinirole (0.25-4.0 mg, once daily, one to three hours before bedtime) in patients with moderate-to-severe RLS (intention-to-treat population = 380). Endpoint measures included the International Restless Legs Scale (IRLS), Hospital Anxiety and Depression Scale (HADS), and Profile of Mood State (POMS).

Results: Ropinirole significantly reduced IRLS total score at week 12 (last observation carried forward), compared with placebo; adjusted mean treatment difference (AMTD): -3.7; 95% CI: -5.4,-2.0; $p < 0.0001$. HADS anxiety score was significantly reduced at 12 weeks (AMTD: -1.2; 95% CI: -2.3,-0.1; $p = 0.0385$ versus placebo). A nonsignificant improvement in HADS depres-

sion score was observed (AMTD: 1.5; 95% CI: -3.6, 0.56; $p = 0.1590$). There was a significant reduction in POMS Total Mood Disturbance score (AMTD: -5.6; 95% CI: -11.0,-0.3; $p = 0.038$).

Conclusions: In addition to improving RLS symptoms, ropinirole significantly reduced anxiety symptoms and improved total mood scores in patients with RLS.

References:

1. Sevim S et al. *J Neurol Neurosurg Psychiatr* 2004; 75: 226-230.
2. Solem B et al. *Neuropsychobiology* 2000; 41: 181-189.

NR540 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Ropinirole Improves RLS Symptoms: A 12-Week, Placebo-Controlled Study

Supported by GlaxoSmithKline

Philip M. Becker, M.D., *Sleep Medicine Association of Texas, 8140 Walnut Lane, Suite 100, Dallas, TX 75231*; Richard K. Bogan, M.D., Stanley W. Carson, Jackie W. Kwong, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the symptoms of RLS, understand the impact RLS may have on the daily lives of patients, and discuss the efficacy and tolerability of ropinirole treatment in patients with moderate-to-severe idiopathic RLS

Summary:

Objective: The symptoms of restless legs syndrome (RLS) (Ekbom syndrome) often cause sleep disruption and decreased quality of life. Dopamine agonists improve RLS symptoms and have been recommended as first-line treatment.

Methods: TREAT RLS US (protocol 101468/249) was a 12-week, phase-III, double-blind study. Patients with moderate-to-severe idiopathic RLS were randomly assigned (1:1) to placebo or ropinirole, 0.25-4.0 mg/day, once daily one to three hours before bedtime.

Results: Demographic characteristics were similar in the ropinirole (N = 187) and placebo (N = 194) groups. After 12 weeks, the mean (\pm SD) dose of ropinirole was 2.15 ± 1.18 mg/day; 37/187 (19.8%) patients were receiving the maximum daily dose. Ropinirole significantly improved International Restless Legs Scale score as early as week 1 (observed case) (adjusted mean treatment difference [AMTD]: -4.1; 95% CI, -5.6, 2.7; $p < 0.0001$) and at week 12 (last observation carried forward), compared with placebo (AMTD: -3.7; 95% CI: -5.4,-2.0; $p < 0.0001$). Overall life impact score on the RLS Quality of Life questionnaire was significantly improved with ropinirole (AMTD: 4.5; 95% CI: 1.6, 7.5; $p = 0.0026$). Withdrawal rates due to adverse events were similar in both groups (ropinirole: 3.7%; placebo: 4.7%).

Conclusions: Ropinirole significantly improved RLS symptoms and quality of life scores. Treatment was generally well tolerated.

References:

1. Allen R et al. *Sleep Med* 2003; 4:101-19.
2. Littner MR et al. *Sleep* 2004; 27: 557-9.

NR541 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Change in Frontal EEG Predicts Response to Citalopram Treatment in MDD

Supported by Aspect Medical Systems, Inc.

Russell Poland, Ph.D., *Department of Psychiatry, Cedars-Sinai Medical Center, 8730 Alden Drive, E-123, Los Angeles, CA 90048*; Scott Greenwald, Ph.D., Philip Devlin, M.Eng., Christina Kustak, Julie Schulz, Lev Gertsik, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the efficacy of automated analysis of frontal EEG in predicting antidepressant treatment efficacy in MDD.

Summary:

Objective: Prior studies have demonstrated that a reduction from baseline in prefrontal EEG theta activity predicted response to antidepressant treatment using fluoxetine, venlafaxine, or reboxetine monotherapy in major depressive disorder (MDD). This study evaluated whether reduction in prefrontal theta activity predicted response during treatment using citalopram.

Method: Twenty-two subjects with MDD (baseline HAM-D ≥ 17) entered an eight-week open-label trial (citalopram dose: weeks 1-4: 20 mg/day, weeks 5-6: 40 mg/day [optional]; weeks 7-8: 60 mg/day [optional]). Four-channel EEGs (F7-Fpz, F8-Fpz, A1-Fpz, A2-Fpz) and HAM-D assessments were made at baseline and weeks 1, 2, and 4.

Results: Eleven subjects (50%) were treatment responders (HAM-D reduction $\geq 50\%$). Frontal relative theta power (i.e., 4-8 Hz power/ 2-20 Hz power) decreased from baseline in treatment responders at weeks 1, 2, and 4, but not in nonresponders. At two weeks, the decrease in relative theta power was significantly lower in treatment responders versus nonresponders ($p = 0.022$), predicting response with 73% accuracy (73% sensitivity, 73% specificity).

Conclusion: Reduction in prefrontal theta activity in responders to citalopram treatment is consistent with changes reported with other SSRI, SNRI, and NRI treatments. It may be possible to develop a simple-to-use clinical tool using frontal EEG as an aid in the management of antidepressant treatment.

References:

1. Cook IA, Leuchter AF, Witte EA, Stubbeman WF, Abrams M, Rosenberg S: Early changes in prefrontal activity characterize Clinical Responders to Antidepressants. *Neuropsychopharmacology* 2002; 27:130-131.
2. Cook IA, Leuchter AF, Greenwald SD, Morgan ML, Abrams MJ, Siegman B: Changes in QEEG cordance predict response to treatment resistant depression and in reboxetine monotherapy. 2003 NCDEU Meeting.

NR542 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Efficacy and Tolerability of Indiplon-IR in Elderly Patients With Chronic Insomnia: Results of a Double-Blind, Placebo-Controlled, Two-Week Trial

Supported by Neurocrine Biosciences, Inc, and Pfizer Inc.

James K. Walsh, Ph.D., *Sleep Medical Center, Saint Luke's Hospital, 232 South Woods Mill Road, Chesterfield, MO 63017*; Thomas Roth, Ph.D., Philip Jochelson, M.D., Adam Moscovitch, M.D., Robert Farber, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should have an improved understanding of the treatment of insomnia in the elderly with the investigational hypnotic indiplon.

Summary:

Objective: The efficacy and tolerability of the immediate release (IR) formulation of indiplon, a GABA_A receptor potentiator with selectivity for receptors with the alpha₁ subunit, were evaluated in elderly chronic (primary) insomnia patients.

Methods: Elderly patients, age 65-80 years (N = 358; 55% female; mean age, 71 years) who met the DSM-IV criteria for chronic primary insomnia were randomly assigned to two weeks of double-blind nightly treatment with either indiplon-IR 5 mg, 10

mg, or placebo. Patient self-assessments included time to sleep onset (TSO), total sleep time (TST), number of awakenings (NAASO), wake time after sleep onset (WASO), and sleep quality.

Results: Treatment with indiplon-IR was associated with significant improvement in TSO at week 1 with the 5 mg (34.6 ± 1.8 mins) and 10 mg dose (30.4 ± 1.6 mins), relative to placebo (47.4 ± 2.5 mins) ($p < 0.0001$). Improvement was sustained at week 2 ($p < 0.0001$). Indiplon-IR was also associated with significant and sustained improvement in most sleep maintenance and duration parameters, including TST, NAASO, WASO, and sleep quality. Both doses were safe and well tolerated.

Conclusions: In elderly patients with chronic insomnia, indiplon-IR was effective in inducing and maintaining sleep and improving sleep quality. Indiplon-IR was well tolerated.

References:

1. Foster AC et al: In vivo pharmacological characterization of indiplon, a novel pyrazolopyrimidine sedative-hypnotic. *J Pharmacol Exp Ther* 2004; 311:547-559.
2. Foley DJ et al: Incidence and remission of insomnia among elderly adults: an epidemiologic study of 6,800 persons over three years. *Sleep* 1999; 22 Suppl 2:S366-372.

NR543 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Sodium Oxybate Significantly Improves Sleep Architecture in Patients With Narcolepsy Supported by Orphan Medical, Inc.

Alan Lankford, Ph.D., *Sleep Disorders Center of Georgia, 5505 Peachtree Dunwoody Road, Suite 380, Atlanta, GA 30342*

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the improvements that occur in the nocturnal sleep of patients with narcolepsy following the nightly administration of sodium oxybate.

Summary:

Objective: A pilot study suggests the nightly administration of sodium oxybate is associated with significant improvements in sleep architecture in narcolepsy. The following eight-week study repeated this study using blinded, placebo-controlled methods in a larger patient population.

Methods: Narcolepsy patients received 4.5, 6, or 9 g of sodium oxybate or placebo in two equally divided doses taken at bedtime and 2.5 to four hours later. The effects of sodium oxybate on sleep architecture were measured by using standard nocturnal polysomnography at the end of a baseline period and after four and eight weeks of treatment; 206 patients completed the trial.

Results: Sodium oxybate treatment resulted in significant median increases in Stage 3/4 sleep, reaching a maximum of nearly 53 minutes in the 9 g dose group. Delta power significantly increased at all doses, while nocturnal awakenings significantly decreased at the 6 and 9 g doses. Improved nocturnal sleep quality coincided with decreased cataplexy and daytime sleepiness. These changes corresponded with significant improvements in investigator-rated patient disease severity.

Conclusions: Nightly sodium oxybate administration resulted in consolidation of fragmented sleep and significant increases in slow wave sleep, which coincided with improved daytime symptoms.

References:

1. Mamelak M, Black J, Montplaisir J, Ristanovic R: A pilot study on the effects of sodium oxybate on sleep architecture and daytime alertness in narcolepsy. *Sleep* 2004; 27:1327-1334.
2. US Xyrem® Multicenter Study Group: A randomized, double blind, placebo-controlled multicenter trial comparing the effects

of three doses of orally administered sodium oxybate with placebo for the treatment of narcolepsy. *Sleep* 2002; 25:42-49.

NR544 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Relationship Between Adolescent Internet Addiction and Depression, Impulsivity, and Obsessive-Compulsivity

Bong Seog Kim, M.D., *Department of Psychiatry, Sanggye Patk Hospital, Nowongu Sanggyedong, Seoul 139707, Korea*; Dae Hwan Lee, Je Wook Kang, Eun Jin Park

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the relation of Internet addiction to depression, impulsivity, and obsessive-compulsivity.

Summary:

Objective: The aims of this study were to investigate the prevalence of Internet addiction and to examine the relation of Internet addiction to depression, impulsivity, and obsessive-compulsivity in Korean high school students.

Methods: Subjects were high school students in Namyangju city (N = 1,408). The questionnaire consisted of items on demographic characteristics and Internet use patterns. The levels of Internet addiction and depressive symptoms were assessed with the Young Internet Addiction Scale and the Beck Depression Inventory (BDI), respectively. The Barratt impulsiveness scale and Maudsley obsessive-compulsive inventory were also self-rated.

Results: In this study, the prevalence of Internet addiction was 4%. The addicted group had significantly higher mean scores for depression (F = 64.76, p < 0.001), impulsivity (F = 60.00, p < 0.001), and obsessive-compulsivity (F = 32.00, p < 0.001) than the ever-use group and nonaddicted group. Among the subscales of impulsivity, the addicted group had significantly higher mean scores for nonplanning impulsivity (F = 22.25, p < 0.001), motor impulsivity (F = 96.11, p < 0.001), and cognitive impulsivity (F = 20.26, p < 0.001) than the other two groups. Among the subscales of obsessive-compulsivity, subjects with Internet addiction had significantly higher mean scores for doubting (F = 9.64, p < 0.001), checking (F = 9.39, p < 0.001), slowness (F = 34.04, p < 0.001), and cleaning (F = 27.49, p < 0.001) than the other two groups.

Conclusion: In this study, the prevalence of Internet addiction was relatively similar to that in previous domestic studies. These results suggest that Internet-addicted adolescents are more depressed, impulsive, obsessive, and compulsive than nonaddicts.

References:

1. Kalwa K, Anand AP: Internet addiction in students: a cause of concern. *Cyberpsychol Behav* 2003 Dec; 6(6):653-6.
2. Yoo HJ, Cho SC, Ha J, Yune SK, Kim SJ, Hwang I, Chung A, Sung YH, Lyoo IK: Attention deficit hyperactivity symptoms and Internet addiction. *Psychiatry Clin Neurosci* 2004 Oct; 58(5):437-94.

NR545 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Long-Term Efficacy of Tolerability of Indiplon-IR in the Treatment of Chronic Insomnia: Results of a Double-Blind, Placebo-Controlled, Three-Month Study Supported by Neurocrine Biosciences, Inc, and Pfizer Inc.

Martin B. Scharf, Ph.D., *Tristate Sleep Disorders Center, 1275 East Kemper Road, Cincinnati, OH 45246*; Jed E. Black, M.D., Adam Moscovitch, M.D., Steven Hull, M.D., Robert Farber, Ph.D., Mark Mahowald, Philip Jochelson, M.D.

Educational Objectives:

At the conclusion of this session, the participant should have an improved understanding of the long-term treatment of insomnia, and the efficacy and safety of indiplon, an investigational treatment for insomnia.

Summary:

Objective: The efficacy and tolerability of the immediate release (IR) formulation of indiplon was evaluated in a 3-month study of patients with chronic insomnia.

Methods: Patients (N = 702; 61% female; mean age, 46 years) who met the DSM-IV criteria for chronic primary insomnia were randomly assigned to three months of double-blind treatment with indiplon-IR 10 mg, 20 mg, or placebo. Subjective assessments included time to sleep onset (TSO; the primary endpoint) total sleep time (sTST), wake time after sleep onset (sWASO), sleep quality, the Insomnia Severity Index (ISI), and global improvement.

Results: Treatment with indiplon-IR resulted in significant improvement, relative to placebo, at all time-points on TSO. The TSO means at month 1 were: 10 mg (34.0 ± 1.3 mins), 20 mg (33.0 ± 1.3 mins), and placebo (48.7 ± 1.9 mins) (p < 0.0001 for both comparisons); efficacy was sustained at month 3, with means of: 10 mg (29.7 ± 1.6 mins), and 20 mg (31.6 ± 1.7 mins), placebo (41.9 ± 2.3 mins) (p < 0.001 for both comparisons). Indiplon-IR resulted in significant improvement in sTST, sWASO, sleep quality, and global improvement at all assessment time-points. Both doses of indiplon-IR were well tolerated.

Conclusions: Long-term treatment with indiplon-IR resulted in significant and sustained improvement in sleep onset and sleep maintenance parameters.

References:

1. Foster AC et al: In vivo pharmacological characterization of indiplon, a novel pyrazolopyrimidine sedative-hypnotic. *J Pharmacol Exp Ther* 2004; 311:547-559.
2. Jindal RD et al: Maintenance treatment of insomnia: what can we learn from the depression literature? *Am J Psychiatry* 2004; 161:19-24.

NR546 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

PTSD and Psychiatric Comorbidity

Chandresh Shah, M.D., *Los Angeles Veterans Affairs Clinic, University of Southern California, 351 East Temple Street, #116 A, Los Angeles, CA 90012*

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize commonly occurring psychiatric disorders among those diagnosed with posttraumatic stress disorder.

Summary:

One of the inevitable outcomes of terror and war on terror is occurrence of posttraumatic stress disorder (PTSD) in affected, vulnerable populations. It is important that observations and experiences from veterans of the Vietnam War are revisited to better prepare for understanding and addressing needs of those affected by the current war. Medical records of 293 veterans (287 male, six female) with PTSD who had been in treatment for at least 180 days were reviewed. They were 54.93 ± 8.05 years old. There were 235 (80.20%) veterans who also had a diagnosis of depressive disorder, and 174 (59.38%) had other anxiety disorders. Eighty-seven (29.69%) veterans also had a diagnosis of psychotic disorder, and 57 (19.45%) were treated for addictive disorders. The veterans with co-occurring addictive disorders were younger (50.98 ± 5.83 years; p < 0.05). It was also noted that 45.39% of the veterans had two psychiatric comorbidities, and only 6.14% had no other psychiatric comorbidity. These data show that there

is a very high prevalence (93.86%) of psychiatric comorbidity among those with PTSD during their lifetime. Depressive and anxiety disorders are prevalent among those with PTSD. Therefore, while screening and treating PTSD, attention should be paid to and emphasis be placed on psychiatric comorbidity.

References:

1. Brady KT, Killeen TK, Brewerton T, Lucerini D: Comorbidity of psychiatric disorders and posttraumatic stress disorder. *J Clin Psychiatry* 2000; 61 Suppl 7:22-32.
2. Elhai JD, Frueh BC, Davis JL, Jacobs GA, Hamner MB: Clinical presentations in combat veterans diagnosed with posttraumatic stress disorder. *J Clin Psychology* 2003; 59(3):385-397.

NR547 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Lamotrigine for Affective Instability in BPD

Supported by GlaxoSmithKline

Wendy Weinstein, M.D., *Buffalo Medical Group, 295 Essjay Road, Williamsville, NY 14221*; Katrina L. Jamison, B.S.

Educational Objectives:

This poster presentation should be able to demonstrate that lamotrigine, an anticonvulsant FDA approved for the maintenance treatment of bipolar disorder, may be useful in the long term treatment of patients have a diagnosis of borderline personality and display affective instability.

Summary:

Objective: In the United States, 0.4-1.8% of the population has a diagnosis of borderline personality disorder (BPD) with many of those patients exhibiting affective instability. (Affective instability is defined as a marked emotional reactivity to environmental events, particularly events such as separations, frustrations, or losses.) No FDA-approved medication exists for this indication. This retrospective chart review was conducted to determine if lamotrigine is efficacious in treatment-refractory patients.

Methods: All charts in this private practice for treatment-refractory BPD patients who continued to display affective instability and were treated with lamotrigine (50-200 mg/day) for a minimum of three months were reviewed. All patients had received a Clinical Global Impression (CGI) Scale score before and after lamotrigine therapy.

Results: Charts from 13 symptomatic female patients who had not responded previously to two to seven psychotropic drugs were identified. Length of lamotrigine treatment ranged from three to 15 months. Initial CGI decreased from 5-6 to 1-2 for all but one patient.

Conclusions: These findings suggest that long-term treatment with lamotrigine may be useful to treat the affective instability of patients with BPD. This response in treatment-refractory patients argues against a placebo response.

References:

1. Johnson DM, Shea MT, Yen S, Battle CL, Zlotnick C, Sanislow CA, Grillo CM, Skodol AE, Bender DS, McGlashan TH, Gundersen JG, Zanarini MC: Gender differences in borderline personality disorder: findings from the Collaborative Longitudinal Personality Disorders Study. *Compr Psychiatry* 2003; 44(4):284-92.
2. Practice Guideline for the Treatment of Patients with Borderline Personality Disorder. *Am Psychiatry* 2001; (Supp) 158(10).

NR548 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

A Double-Blind, Placebo-Controlled Evaluation of Lamotrigine for Obesity

Supported by GlaxoSmithKline

Charles H. Merideth, M.D., *Affiliated Research, 8989 Rio San Diego Drive, Suite 350, San Diego, CA 92108*

Educational Objectives:

At the conclusion of the presentation, the participant should recognize that in a double-blind, placebo-controlled study, lamotrigine demonstrated a statistically significant difference in main change in BMI and also a trend toward a decrease in body weight.

Summary:

Objective: Lamotrigine has been observed to decrease weight in patients as well as decrease appetite.

Methods: Patients were randomly assigned to 200 mg/day of lamotrigine or placebo. Eligibility included a body mass index (BMI) of 30-39.99. The primary endpoint was weight change after 26 weeks. Secondary endpoints included percent body fat and serum lipids. Analysis of covariance was carried out using change from baseline to week 26 or last observation carried forward (LOCF).

Results: Forty patients were randomly assigned. The mean change in body weight from baseline to LOCF was $-6.41 \text{ lbs} \pm 10.26$ and $-1.21 \text{ lbs} \pm 7.09$ for lamotrigine and placebo respectively. Mean baseline body weight was not statically different at baseline (207.9 lbs, lamotrigine group; 225.0 lbs, placebo group). There was a statistically significant difference ($p = .0421$) in mean change in BMI from baseline to LOCF (-1.5 ± 2.78 and -0.1 ± 1.05 , for lamotrigine and placebo, respectively). No serious adverse events were reported. The most frequently reported adverse event was mild to moderate headaches for both treatment groups. There were no significant differences in the other secondary endpoints between the two treatment groups.

Conclusions: Lamotrigine demonstrated a statistically significant difference in mean change in BMI and a trend toward a decrease in body weight.

References:

1. Aronne LJ, Segal KR: Weight gain in the treatment of mood disorders. *J Clin Psychiatry* 2003; 64 (suppl 8):22-29.
2. Nemeroff CB: Safety of available agents used to treat bipolar disorder: focus on weight gain. *J Clin Psychiatry* 2003; 64:532-539.

NR549 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Neural Network of Prediction of Rehospitalization in Psychiatric Inpatients

Robert Fusco, M.D., *UBH, 425 Market St 27th Fl, San Francisco, CA 94105*; George I. Viamontes, M.D., *Ronald H. Beach, M.D., Michael Powell, Ph.D., Brett A. Hart, Ph.D.*

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the risk factors for rehospitalization in psychiatric inpatients and understand how neural network predictive models can be created and used in clinical settings.

Summary:

A neural network was trained to predict six-month rehospitalization risk in mental health/substance abuse patients. Demographic and clinical data were collected on 2,404 inpatients. A set of 1,000 patients was selected at random and reserved for validating the network's performance. The network was trained with the remaining 1,404 cases. Eight categories of variables were selected empirically from a pool of 115 as the inputs to the neural network. The variables were selected after preliminary analysis on the basis

of differential representation in rehospitalized and nonrehospitalized populations. The variable categories included: gender, age, psychiatric diagnosis, current substance abuse, number and type of psychotropic medications, history of suicide attempts, and inpatient hospitalizations in the previous 180 days. The ability of the trained neural network to predict rehospitalizations was tested with the 1,000-patient validation set. The neural network was able to identify 65.3% of the patients in the validation set who had been rehospitalized and accrued 37.6% false positives. This translates to a sensitivity of 65.3% and a specificity of 62.4%. This predictive model can be readily implemented in a clinical setting, and its use should provide new opportunities for the proactive stabilization of patients at high risk for relapse.

References:

1. Masters Practical Neural Network Recipes in C++. T: New York, Academic Press.
2. Patterson DA, Cloud RN: The application of artificial neural networks for outcome prediction in a cohort of severely mentally ill outpatients. *J Technology in Human Services* 2000;16 (213):46-61.

NR550 WITHDRAWN

NR551 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Efficacy and Safety of Indiplon-IR in Adults With Chronic Insomnia Characterized by Prolonged Nighttime Awakenings With Difficulty Returning to Sleep

Supported by Neurocrine Biosciences, Inc, and Pfizer Inc.

Thomas Roth, Ph.D., *Sleep Center, Henry Ford Hospital, 2799 West Grand Boulevard, CFP3, Detroit, MI 48202*; Gary Zammit, Ph.D., Philip Jochelson, M.D., Martin B. Scharf, Ph.D., Michele Boyd

Educational Objectives:

At the conclusion of this session, the participant should have an improved understanding of the efficacy and safety of as needed use of the investigational hypnotic indiplon in response to prolonged nighttime awakening.

Summary:

Objective: To date no medication has been shown to effectively manage prolonged nighttime awakenings in insomnia patients. The objective of this study was to evaluate the efficacy and tolerability of immediate release (IR) indiplon using an "as needed" dosing strategy in response to prolonged nighttime awakenings.

Methods: Adults (N = 260) meeting the DSM-IV criteria for primary insomnia and reporting prolonged awakenings were randomly assigned to four weeks of double-blind treatment with indiplon-IR 10 mg, 20 mg, or placebo taken upon awakening (provided four hours of bedtime remained). The primary endpoint was latency to sleep onset post-administration (LSO-pd). Secondary endpoints included subjective assessment of post-dose total sleep time (sTST-pd), wake after sleep onset (sWASO), and next-day sleepiness.

Results: Both doses of indiplon-IR reduced LSO-pd at each week, with an LSO-pd (averaged over four weeks) that was lower with indiplon-IR 10 mg (36.5 min) and 20 mg (34.4 min), compared to placebo (45.2 min) ($p < 0.005$ for both comparisons). Indiplon-IR also significantly improved secondary sleep outcomes, with no next-day residual effects.

Conclusions: Chronic insomnia patients with middle-of-the-night awakenings showed significant and sustained improvement in sleep parameters using as-needed dosing with indiplon-IR, taken

after a prolonged awakening. Indiplon-IR was well tolerated in this dosing strategy, with no next-day residual effects.

References:

1. Sullivan SK et al: Characterization of the interaction of indiplon, a novel pyrazolopyrimidine sedative-hypnotic, with the GABAA receptor. *J Pharmacol Exp Ther* 2004; 311:537-546.
2. Verster JC et al: Residual effects of middle-of-the-night administration of zaleplon and zolpidem on driving ability, memory functions, and psychomotor performance. *J Clin Psychopharmacol* 2002; 22:576-583.

NR552 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Effects of Tiagabine on Sleep in the Elderly With Primary Insomnia

Supported by Cephalon

Thomas Roth, Ph.D., *Sleep Center, Henry Ford Hospital, 2799 West Grand Boulevard, CFP3, Detroit, MI 48202*; James K. Walsh, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the effect of tiagabine on sleep in elderly patients with primary insomnia.

Summary:

Objective: Since gamma-aminobutyric acid (GABA) plays a central role in promoting sleep, increased availability of GABA may have therapeutic benefit in insomnia. The dose relationship of tiagabine, a selective GABA reuptake inhibitor (SGRI), on sleep in elderly patients with primary insomnia was studied.

Methods: Elderly patients (N = 207; age 65-85 years) with DSM-IV-TR-defined primary insomnia were randomly assigned to receive tiagabine 2, 4, 6, or 8 mg, or placebo on two consecutive nights of polysomnography.

Results: Efficacy data were obtained from 204 patients. The mean change from baseline in minutes of slow wave sleep (SWS) was greater with tiagabine than with placebo (2 mg, +11.7 min; 4 mg, +19.9 min; 6 mg, +38.0 min; 8 mg, +46.9 min; placebo, +4.5 min), with the 4-, 6- and 8-mg doses being significant ($p < 0.05$ for each). No significant differences ($p > 0.05$) between tiagabine and placebo were observed in latency to persistent sleep or total sleep time. The tolerability profiles of the 2-mg and 4-mg doses were similar to those of placebo. At doses > 4 mg, the most common adverse events included dizziness (6 mg, 7%; 8 mg, 23%) and nausea (8 mg, 16%).

Conclusion: Tiagabine increased SWS in elderly patients with insomnia in a dose-related manner. The clinical correlates of this effect warrant further research.

References:

1. Mathias S, Wetter TC, Steiger A, Lancel M: The GABA uptake inhibitor tiagabine promotes slow wave sleep in normal elderly subjects. *Neurobiol Aging* 2001 Mar-Apr; 22(2):247-53.

NR553 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Efficacy and Tolerability of Indiplon Modified Release in Elderly Patients With Chronic Insomnia: Results of a Double-Blind, Placebo-Controlled, Two-Week Study

Supported by Neurocrine Biosciences, Inc, and Pfizer Inc.

R. Bruce Lydiard, M.D., *Department of Psychiatry, South East Health Consultants, 1 Poston Road, Suite 150, Charleston, SC 29407*; D. Alan Lankford, Ph.D., Philip Jochelson, M.D., James K. Walsh, Ph.D., David Seiden

Educational Objectives:

At the conclusion of this session the participant should have an improved understanding of the treatment of insomnia in the elderly with the investigational hypnotic indiplon.

Summary:

Objective: The modified release (MR) formulation of indiplon, a novel GABA_A receptor potentiator with selectivity for receptors with the alpha₁ subunit, was evaluated in elderly chronic insomnia patients with sleep maintenance difficulties.

Methods: Elderly patients, age 65-85 years (N = 229), who met the DSM-IV criteria for chronic primary insomnia were randomly assigned to two weeks of double-blind, parallel-group nightly treatment with either indiplon-MR 15 mg or placebo. Subjective assessments of sleep maintenance included total sleep time (sTST, primary endpoint), wake time after sleep onset (sWASO), number of awakenings after sleep onset (sNAASO), and total wake time (sTWT). Time to sleep onset (TSO), sleep quality, and patient global impression (PGI) ratings were also assessed.

Results: sTST was significantly improved with indiplon-MR treatment, relative to placebo, at week 1 (377 ± 4 mins vs. 328 ± 4 mins; p < 0.0001) and week 2 (373 ± 5 mins vs. 337 ± 5 mins; p < 0.0001). Indiplon-MR demonstrated significant improvement at both weeks 1 and 2 on all secondary endpoints of sleep onset (TSO), sleep maintenance (sWASO, sNAASO, sTWT), sleep quality, and patient global impression. Indiplon-MR was well tolerated.

Conclusions: In elderly patients with chronic sleep maintenance insomnia, indiplon-MR 15 mg was well tolerated and effective in inducing and maintaining sleep.

References:

1. Foster AC et al: In vivo pharmacological characterization of indiplon, a novel pyrazolopyrimidine sedative-hypnotic. *J Pharmacol Exp Ther* 2004; 311:547-559.
2. Basu R et al: Sedative-hypnotic use of diphenhydramine in a rural, older adult, community-based cohort: effects on cognition. *Am J Geriatr Psychiatry* 2003; 11:205-213.

NR554 Wednesday, May 25, 12:00 p.m.-2:00 p.m. Patients' Attitudes Toward Telepsychiatry

Robbie Campbell, M.D., *Department of Psychiatry, University of Western Ontario, 19 Carnforth Road, London, Ontario N6G 4R2, Canada*; Jennifer O'Gorman, R.N., Zack Cernovsky, Ph.D., Terry Shkilynyk, M.A., Michael Andrews, M.A.

Educational Objectives:

At the conclusion of this session, the participant should be aware to learn that patients may describe their telepsychiatric sessions as equally beneficial as direct meetings.

Summary:

Objective: Telepsychiatry enables psychiatrists to connect to patients in remote underserved communities, with considerable savings in travel time. The presenters assessed the opinions of psychiatric patients with respect to teleconferencing with their psychiatrists.

Method: A random survey of 84 patients from various remote sites in Ontario, Canada, was carried out following their teleconferencing sessions, using a 10-item questionnaire. The items assessed whether or not the patients feel comfortable with telepsychiatry, would use it again, are able to communicate as usual, and find it as beneficial as the direct service. The patients were also asked to rate on a 5-point scale (from 1, "poor" to 5, "excellent") the quality of televideo and sound equipment.

Results: The majority indicated that they were comfortable with telepsychiatric service (95.2%), were able to communicate as if physically present (92.9%), found the sessions as beneficial as

direct meetings (84.5%), and would use this service again (98.8%). The picture quality was rated by most patients as "good" to "excellent" (97.6%), and 95.2% gave similar ratings to the sound quality.

Conclusions: Most patients were comfortable with the telepsychiatric service and rated it as beneficial as direct meetings with their psychiatrist.

References:

1. Hilty DM, Marks SL, Urness D, Yellowlees PM, Nesbitt TS: Clinical and educational telepsychiatry applications: a review. *Can J Psychiatry* 2004; 49(1):1-3.
2. De Las Cuevas C, Artiles J, De La Fuente J, Serrano P: Telepsychiatry in the Canary Islands: user acceptance and satisfaction. *Journal of Telemedicine and Telecare* 2003; 9(4):221-4.

NR555 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

A Crossover Study of Eszopiclone Treatment of Primary Insomnia

Supported by Sepracor Inc.

Milton K. Erman, M.D., *Department of Psychiatry, Pacific Sleep Medicine Services, 10052 Mesa Ridge Court, #101, San Diego, CA 92121*; James K. Walsh, Ph.D., Thomas Wessel, M.D., Judith Caron, Ph.D., David Amato, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the differences in treatment effects of eszopiclone, with zolpidem as an active control, in patients with chronic insomnia

Summary:

Objective: Evaluate efficacy and safety of eszopiclone vs placebo in adults with primary insomnia.

Methods: Multicenter, double-blind, placebo-controlled, six-way Williams-design crossover study. Patients received two nights' treatment with placebo, eszopiclone 1, 2, 2.5, and 3 mg, or zolpidem 10 mg in a random order. Visits were separated by a three to seven day washout.

Results: By polysomnography, all active treatments reduced latency to persistent sleep (p ≤ 0.0001) and increased sleep efficiency (p ≤ 0.05), compared with placebo. Only eszopiclone 3 mg significantly reduced both wake time after sleep onset and number of awakenings, relative to placebo (p ≤ 0.05). All active treatment groups improved sleep quality and depth, relative to placebo (p < 0.05). Morning sleepiness was significantly improved with eszopiclone 2.5 and 3 mg vs placebo, but not with lower doses of eszopiclone or with zolpidem. Dizziness and somnolence were reported more with zolpidem 10 mg, compared with eszopiclone 3 mg (combined incidence 20% for zolpidem, 9.4% for eszopiclone 3 mg). Hallucinations were reported only following zolpidem 10 mg (4.7%).

Conclusions: All treatments were effective in reducing time to sleep onset; only eszopiclone 3 mg had a significant impact on polysomnography measures of sleep maintenance. In this study, eszopiclone 3 mg was effective and well tolerated for the management of chronic insomnia in adults.

References:

1. Ancoli-Israel S, Roth T: Characteristics of insomnia in the United States: results of the 1991 National Sleep Foundation Survey, I. *Sleep* 1999; 22 Suppl 2:S347-S353.
2. Krystal AD, Walsh JK, Laska E, et al: Sustained efficacy of eszopiclone over six months of nightly treatment: results of a randomized, double-blind, placebo controlled study in adults with chronic insomnia. *Sleep* 2003; 26:793-799.

NR556 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Effect of Eszopiclone on Sleep Parameters That Affect Next Day Function

Supported by Sepracor Inc.

David Amato, Ph.D., *Sepracor, Inc., 84 Waterford Drive, Marlborough, MA 01752*; W. Vaughn McCall, M.S., Kendyl Schaeffer, M.S.C., Robert Rubens, M.D.

Educational Objectives:

At the end of this session participants should be able to describe sleep endpoints that correlate with next day function and the impact of improvements in sleep on daytime function.

Summary:

Objective: This analysis assessed correlation between nighttime sleep and next day function (NDF) and calculated the percent of the treatment effect (PTE) of eszopiclone due to sleep.

Methods: Data were from a randomized, double-blind, placebo-controlled, parallel-group study of 264 elderly patients with primary insomnia who received eszopiclone 2 mg or placebo nightly for two weeks. Pearson correlation coefficients between NDF and sleep quality (SQ) and total sleep time (TST) were calculated. PTE was calculated as $100(\beta_1 - \beta_2)/\beta_1$, with β_1 and β_2 being the effects on NDF due to eszopiclone alone and due to eszopiclone with adjustment for sleep, respectively.

Results: For all nights combined, NDF correlated highly with SQ ($r > 0.6$) and modestly with TST ($r > 0.2$). For both eszopiclone and placebo with regard to daytime alertness, the PTEs for eszopiclone were 100% and 89% for subjective measures of SQ and TST, respectively. For ability to function, the PTEs for eszopiclone were 100% and 75%, respectively. For physical well-being the PTEs were 100% and 80%, respectively.

Conclusion: In this study, sleep quality and TST correlated with NDF. In addition, the effect of eszopiclone 2 mg on NDF in this elderly population was largely explained by improvements in nighttime sleep.

References:

1. Ancoli-Israel S, Roth T: Characteristics of insomnia in the United States: results from the 1991 National Sleep Foundation Survey I. *Sleep* 1999; 22 Suppl 2:S347-S353
2. Zammit GK, McNabb LJ, Caron J, Amato DA, Roth T: Efficacy and safety of eszopiclone across 6-weeks of treatment for primary insomnia. *Curr Med Res Opin* 2004; 20(12):1979-1991.

NR557 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Adjunctive Eszopiclone and Fluoxetine in MDD and Insomnia: Depression Effects

Supported by Sepracor Inc.

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the effects of adjunctive eszopiclone treatment in patients with insomnia associated with MDD during concurrent fluoxetine treatment on clinician-rated measures of depression.

Summary:

Objective: Insomnia frequently coexists with depression. This study evaluated eszopiclone and fluoxetine coadministration in depressed patients with comorbid insomnia.

Methods: Patients who met the DSM-IV criteria for new major depressive disorder (MDD) and insomnia received fluoxetine 20 mg qam plus either eszopiclone 3 mg (N = 275) or placebo (N = 270) nightly for eight weeks. Efficacy was assessed with the 17-item Hamilton Depression Rating Scale (HAMD17) and Clinical Global Impression Improvement (CGI-I) and Severity (CGI-S). Response = 50% decrease from baseline HAMD17; remission = HAMD17 ≤ 7 .

Results: Eszopiclone coadministration resulted in significantly greater changes in HAMD17 scores at week 4 (-9.9 vs -8.5 for placebo, $p = 0.02$), with progressive improvement at week 8 (-13.8 vs -11.8, $p < 0.001$). At week 8, significantly more eszopiclone patients were responders (74% vs 61%, $p < 0.009$) and remitters (54% vs 41%, $p < 0.02$). Even after removing insomnia items, significant changes in HAMD17 were found at week 8 ($p < 0.03$). HAMD17 differences were greater in patients with more severe depression (baseline HAMD17 ≥ 22). CGI-I and CGI-S scores were significantly greater with eszopiclone coadministration ($p < 0.05$). Fewer eszopiclone patients required fluoxetine dose increases (44% vs 54%, $p < 0.05$). Treatment was well tolerated; dropouts due to adverse events were comparable.

Conclusions: Eszopiclone/fluoxetine coadministration significantly augmented the antidepressant response in patients with MDD and insomnia. The sleep response occurred immediately, followed by augmentation of the antidepressant response.

References:

1. Krystal AD, et al: Sustained efficacy of eszopiclone over 6 months of nightly treatment: results of a randomized, double-blind, placebo-controlled study in adults with chronic insomnia. *Sleep* 2003; 26:793-9.
2. Breslau N, Roth T, Rosenthal L, Andreski P: Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adults. *Biol Psychiatry* 1996; 39:411-418.

NR558 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Adjunctive Eszopiclone With Fluoxetine for MDD and Insomnia: Sleep Effects

Supported by Sepracor, Inc.

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the effects of adjunctive eszopiclone treatment in patients with insomnia associated with MDD during concurrent fluoxetine treatment on measures of sleep and on daytime function.

Summary:

Objective: Insomnia and depression often coexist. This study evaluated the efficacy of eszopiclone in patients with major depressive disorder (MDD) and comorbid insomnia during concurrent fluoxetine treatment.

Methods: Patients (N = 545) met the DSM-IV criteria for MDD and insomnia, including reported sleep latency (SL) ≥ 30 min (median 74), wake time after sleep onset (WASO) ≥ 45 min (median 90), and total sleep time (TST) ≤ 390 min (median 294). All patients received fluoxetine qam and were randomly assigned to double-blind treatment with eszopiclone 3 mg or placebo qhs for eight weeks. Subjective sleep and daytime function were assessed weekly.

Results: Compared with placebo, eszopiclone was associated with significantly shorter SL and greater TST at each treatment

week ($p < 0.03$); significantly lower WASO at weeks 1, 3-5, and 7-8 ($p < 0.04$); higher ratings across the treatment period in sleep quality and depth ($p < 0.005$); and higher ratings of daytime alertness, ability to concentrate, and well-being ($p \leq 0.02$). Combined treatment was well tolerated. Unpleasant taste was more common with eszopiclone.

Conclusions: Coadministration of eszopiclone with fluoxetine was well tolerated and associated with rapid, sustained improvement in sleep and daytime symptoms in patients with MDD and insomnia. The rapid sleep improvement with adjunctive eszopiclone may be important, given the relatively slower onset of antidepressant effects with selective serotonin reuptake inhibitors.

References:

1. Krystal AD, et al: Sustained efficacy of eszopiclone over 6 months of nightly treatment: results of a randomized, double-blind, placebo-controlled study in adults with chronic insomnia. *Sleep* 2003; 26:793-9.
2. Londeborg PD, Smith WT, Glaudin V, Painter JR: Short-term cotherapy with clonazepam and fluoxetine: anxiety, sleep disturbance and core symptoms of depression. *J Affect Disord* 2000; 61:73-79.

NR559 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Polymorphisms of the Interleukin-1 Gene Complex and Suicidal Behavior

Begona Paredes, M.D., *Department of Psychiatry, University Oviedo, Julian Claveria 6-3, Oviedo 33006, Spain*; Pilar A. Saiz, Ph.D., Maria P. G-Portilla, Ph.D., Blanca Morales, M.D., Rocio Herrero, M.D., Sara Martinez, Ph.D., Julio B. Bobes, M.D.

Educational Objectives:

At the conclusion of this presentation, participants should be able to recognize and discuss the role of the interleukin-1 (IL-1) gene complex in suicidal behavior in the Spanish population.

Summary:

Objective: To investigate the role of the interleukin-1 (IL-1) gene complex in suicidal behavior.

Method: The presenters genotyped 154 suicide attempters (SA) (WHO definition for suicidal attempt) (mean age: 34.19 [11.57], 66.2% females) and 342 unrelated healthy volunteers (mean age: 38.84 [10.69], 54.4% females) from Asturias (Northern Spain) (same ethnic background). All individuals gave written informed consent. The following allelisms were analyzed: IL-1 alpha C-889T, IL-1beta C+3953T, IL-1 receptor antagonist (IL-1RA) VNTR. IL-1 gene complex genotypes were determined after polymerase chain reaction (PCR) amplification, followed by digestion with restriction enzymes and electrophoresis on an agarose gel.

Results: (SA vs healthy volunteers) C-889T IL-1alpha polymorphism—TT: 9.1%, 8.8%; TC: 40.9%, 39.5%; CC: 50.0%, 51.8% ($p = 0.937$). C+3953T IL-1beta polymorphism—TT: 7.8%, 7.3%; TC: 40.3%, 38.3%; CC: 51.9%, 54.4% ($p = 0.880$). VNTR IL-1RA polymorphism—A1A1: 56.5%, 51.8%; A1A2: 31.8%, 38.0%; A2A2: 7.1%, 7.6%; others: 4.6%, 2.6% ($p = 0.359$). The allele frequencies of the three polymorphisms were similar in both groups ($p = 0.762$; $p = 0.643$; $p = 0.490$, respectively).

Conclusions: The data suggest that genetically determined changes in the IL-1 complex are not associated with suicidal behavior in the study population. However, further studies are necessary to confirm or reject the current data.

References:

1. Yu YW, Chen TJ, Hong CJ, Chen HM, Tsai SJ: Association study of the interleukin-1 beta (C-511T) genetic polymorphism with major depressive disorder, associated symptomatology,

and antidepressant response. *Neuropsychopharmacology* 2003; 28: 1182-5.

2. Fertuzinhos SM, Oliveira JR, Nishimura AL, Pontual D, Carvalho DR, Sougey EB, et al: Analysis of IL-1alpha, IL-1beta, and IL-1RA [correction of IL-RA] polymorphisms in dysthymia. *J Mol Neurosci* 2004; 22:251-6.

NR560 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Neuropsychological Measures of DSM-IV Personality Disorders

Jose L. Besteiro, Ph.D., *Department of Psychiatry, Oviedo University, Julian Claveria 6, #3, Oviedo 33006, Spain*; Serafin Lemos, Ph.D., Jose Muniz, Ph.D., Angel Garcia-Prieto, Ph.D., Maria P. G-Portilla, Ph.D., Pilar A. Saiz, Ph.D., Julio B. Bobes, M.D.

Educational Objectives:

At the conclusion of this presentation participants should be able to recognize and discuss the relationship between the triple cluster DSM-IV classification of personality disorder categories and neuropsychological profiles.

Summary:

Objectives: To analyze whether the triple-cluster DSM-IV classification of personality disorders could be connected to neuropsychological characteristics.

Method: The MCMI-II and BFQ Scale were administered to 119 subjects (mean age: 32.6 [SD: 1.85], 47.1% males) who met the DSM-IV criteria for a personality disorder (27.7% cluster A, 58% cluster B, 14.3% cluster C). Participants were also administered the following STIM neuropsychological computerised tasks: Wisconsin Card Sorting Test (WCST), Conditional Continuous Performance Test (CPT), and Stroop Test.

Results: The cluster A individuals had fewer correct responses on the Stroop Test (mean: 79.48 [SD: 20.65]; $p = 0.024$) and CPT (54.06 [10.29]; $p = 0.047$). The cluster B individuals had a higher average reaction time to incongruent stimuli on the Stroop Test (813.52 [130.06]; $p = 0.014$) and lower sensibility (α -prime) (0.9698 [0.0254]; $p = 0.046$) on the CPT. The cluster C individuals had higher commission errors (19.73 [46.54]; $p = 0.008$) on the CPT.

Conclusions: The results provide weak evidence (scarce differences on concept formation or sustained attention) for the construct validity of the DSM-IV personality disorder clusters.

References:

1. Millon T: The MCMI provides a good assessment of DSM-III disorders: the MCMI-II will prove even better. *Journal of Personality Assessment* 1985; 49:379-391.
2. Zimmerman M: Diagnosing personality disorders: a review of issues and research methods. *Arch Gen Psychiatry* 1994; 51:225-245.

NR561 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Perceived Reasons for Loss of Housing and Continued Homelessness Among Mentally Ill

Ramin Mojtabai, M.D., *Department of Psychiatry, Beth Israel Medical Center, First Avenue At 16th Street, New York, NY 10003*

Educational Objectives:

At the conclusion of this session, the participant should be able to better understand the reasons for homelessness among the mentally ill to better address this problem.

Summary:

Objective: To examine the reasons for the most recent loss of housing and for continued homelessness as perceived by homeless mentally ill individuals.

Methods: A total of 2,974 currently homeless participants of the 1996 National Survey of Homeless Assistance Providers and Clients (NSHAPC) were asked about the reasons for their most recent loss of housing and for continued homelessness. Responses of participants with mental illness, defined broadly and narrowly, were compared to those of participants without mental illness. The broad definition of mental illness was based on a set of criteria proposed by NSHAPC investigators. The narrow definition required past psychiatric hospitalization in addition to the NSHAPC criteria.

Results: Overall 56% (N = 1,620) of the participants met the broad definition, and 22% (N = 639), the narrow definition of mental illness. Forty-four percent (N = 1,345) did not meet any of these criteria and were categorized as not mentally ill. There were few differences between the mentally ill and the not mentally ill participants on the reasons for the most recent loss of housing. Both groups attributed their continued homelessness mostly to insufficient income, unemployment, and lack of suitable housing.

Conclusions: Homeless individuals with mental illness mostly report the same reasons for loss of housing and continued homelessness as individuals without mental illness. These findings support the view that structural solutions, such as wider availability of low-cost housing and income support, would reduce the risk of homelessness in mentally ill individuals as in other vulnerable social groups.

References:

1. Draine J, Salzer MS, Culhane DP, et al: Role of social disadvantage in crime, joblessness, and homelessness among persons with serious mental illness. *Psychiatric Services* 2002; 53:565-573.
2. Cohen CI, Thompson KS: Homeless mentally ill or mentally ill homeless? *American Journal of Psychiatry* 1992; 149:816-823.

NR562 Wednesday, May 25, 12:00 p.m.-2:00 p.m. The Treatment Character Inventory Can Help in the Detection of Bipolar Disorder

Dominic Vachon, Ph.D., *Residency Program, St. Joseph Reg Medical, 837 East Cedar Street, Suite 125, South Bend, IN 46617*; Suhayl J. Nasr, M.D., Joseph Gazarkiewicz, M.A., Burdette J. Wendt

Educational Objectives:

At the conclusion of this session, the participant should be able to understand that the Temperament and Character Inventory (TCI) can be a helpful instrument in the diagnosis of bipolar disorder.

Summary:

Objective: Bipolar disorder is sometimes difficult to diagnose, particularly at the initial interview. Family history and collateral information, use of certain instruments such as the MDQ, and observation of patients over time can all help identify bipolar disorder patients. Any additional tools available to the clinician will be helpful.

Method: The Temperament and Character Inventory (TCI) was administered to 230 consecutively seen patients making their first visit to an outpatient psychiatric office in 1995. After an observation period of an average of 8.8 years, patients were given a current diagnosis, or, if they were no longer being treated, a final diagnosis by their treating psychiatrist. Other data collected included patient demographics, SCL-90, MiniSCID, and medication response.

Results: In a discriminant analysis of the TCI as a predictor for the current clinical diagnosis of a bipolar disorder, the TCI had a sensitivity of 0.71 and a specificity of 0.75. Bipolar disorder patients scored significantly higher ($p < 0.05$) on the fatigability subscale and lower on the responsibility subscale than patients with unipolar disorders. There were no significant differences on any subscale between bipolar I disorder and bipolar II disorder patients.

Conclusions: The subscales of fatigability and responsibility of the TCI can help clinicians in the earlier diagnosis of bipolar disorder.

References:

1. Engstrom C, Brandstrom S, Sigvardsson S, Cloninger R, Nylander PO: Bipolar disorder: 1. temperament and character. *J Affect Disord* 2004; 82:131-4.
2. Parker G, Parker K, Malhi G, Wilhelm K, Mitchell P: Studying personality characteristics in bipolar depressed subjects: how comparator group selection can dictate results. *Acta Psychiatrica Scandinavica* 2004; 109:376-82.

NR563 WITHDRAWN

NR564 Wednesday, May 25, 12:00 p.m.-2:00 p.m. Personality Trait Predictors of Motor Vehicle Crash-Related Stress

John C. Russotto, M.D., *Department of Psychiatry, Uniformed Services University of Health Sciences, 4301 Jones Bridge Road, Bethesda, MD 20814*; Mark W. Willis, M.E., Juliana R. Tiongson, M.P.H., Miriam R.K. Gerber, Elizabeth A. Osuch, M.D.

Educational Objectives:

At the conclusion of this session, the participant will be able to recognize the roles that neuroticism and extraversion play in acute stress symptoms following a traumatic event.

Summary:

Objective: This preliminary prospective study examined the effects of personality traits on stress in an acutely traumatized community sample. The presenters hypothesized that trait neuroticism (N) directly correlated with acute and persistent stress, and trait extraversion (E) inversely correlated with acute and persistent stress.

Methods: Twenty-one subjects were assessed within three weeks of a motor vehicle crash by using the Impact of Events Scale-Revised (IES-R) and the NEO PI-R. Thirteen subjects repeated the IES-R three months later.

Results: The 21 subjects who completed the IES-R within three weeks had a mean score of 6.09 with a standard deviation of 2.27. The 13 subjects who completed the IES-R at three months had a mean score of 5.26 with a standard deviation of 2.12. There was a significant relationship between N and acute stress ($r = 0.552$; $p = 0.005$). The other hypotheses were not supported: the relationships between N and persistent stress and between E and acute and persistent stress were not significant.

Conclusion: The hypothesis that N correlated positively with acute stress was supported. There did not appear to be a relationship between N and persistent stress, or E and stress. Larger studies are warranted.

References:

1. Cox B, MacPherson P, Enns M, McWilliams L: Neuroticism and self-criticism associated with posttraumatic stress disorder in a nationally representative sample. *Behaviour Research and Therapy* 2004; 42(1):105-114.

2. Fauerbach J, Lawrence J, Schmidt C, Munster A, Costa P: Personality predictors of injury-related posttraumatic stress disorder. *The Journal of Nervous and Mental Disease* 2000; 188(8):510-517.

NR565 Wednesday, May 25, 12:00 p.m.-2:00 p.m.
Does Comorbidity of Personality Disorder Influence Treatment of Panic Disorder?

Jan Prasko, M.D., *Prague Psychiatric Centre, Ustavni-8, Prague 8 18103, Czechoslovakia*; Petra Houbova, M.D., Tomas Novak, Katerina E. Cervena, M.D., Beata Paskova, M.D., Jana Vyskocilova, Richard Zalesky

Educational Objectives:

At the conclusion of this session, the participant should be able to discuss use of combination cognitive behavioral therapy and pharmacotherapy in patients with panic disorder with and without comorbid personality disorder.

Summary:

The treatment efficacy for personality disorder (PD) has repeatedly been reported as less successful than the therapy of patients without PD. This study compared the short-term effectiveness of combination cognitive behavioral therapy and pharmacotherapy in patients with panic disorder with and without PD. The aim was to assess six- and 12-week efficacy of a six-week therapeutic program designed for panic disorder and agoraphobia (SSRIs and CBT) in patients with panic disorder and comorbid PD (29 patients) and panic disorder without comorbid PD (31 patients). They were regularly assessed at week 0, 2, 4, 6, and 12 by an independent reviewer on the CGI (Clinical Global Improvement), PDSS (Panic Disorder Severity Scale), HAMA (Hamilton Anxiety Rating Scale), SDS (Sheehan Disability Scale), HDRS (Hamilton Depression Rating Scale), BAI (Beck Anxiety Inventory), and BDI (Beck Depression Inventory). Patients in both two groups improved on all assessment instruments. A combination of CBT and pharmacotherapy proved to be an effective treatment for patients with panic disorder with or without comorbid PD. Twelve-week treatment efficacy rated with the CGI and PDSS was significantly better in the patients with panic disorder without PD, compared with the group with panic disorder comorbid with PD. Also the scores on the depression inventories (HDRS and BDI) showed significantly higher decreases during the treatment in the group without PD.

Supported by research grant IGA NF/7580-2.

References:

1. Tyler P, Davidson K: Management of personality disorder, in *New Oxford Textbook of Psychiatry*. Gelder MG, Lopez-Ibor JJ, Andreasen A (eds) Oxford University Press 2000, 970-978.
2. Perry JC, Bond M: Empirical studies of psychotherapy for personality disorders, in *Psychotherapy for Personality Disorders, Review of Psychiatry Series*, vol. 19/3. Gunderson JG, Gabbard GO (eds). Washington DC, American Psychiatric Press, 2000, pp 1-32.

NR566 Wednesday, May 25, 12:00 p.m.-2:00 p.m.
Computer Imaging System to Treat Alopecia-Related Distress

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Educational Objectives:

At the conclusion of this session, the participant should have knowledge of how computer imaging systems and virtual reality concepts can be used to treat distress and anxiety in patients.

Summary:

Objective: Virtual reality exposure therapy has been effective for treating Vietnam veterans with PTSD and patients with anxiety and body image disorders. Chemotherapy-related alopecia (hair loss) causes clinically significant psychological distress in many women, with about 50% reporting hair loss as the most disturbing side effect. The presenters report the progress at year 2 in the development of a computer-based imaging system for use by women to reduce anxiety and distress relating to alopecia, a project funded by the National Cancer Institute.

Method: Working with a technology consultant firm and utilizing advanced graphical processing techniques, the presenters are developing the proposed "Help for Alopecia through Image Representations" (HAIR) system, which will permit cancer patients of all races and ethnicities to interactively visualize, using their own image, the process of hair loss, accessorization options (e.g., wigs, head scarves, hats, etc.), and the corresponding stages of hair regrowth. "Scripting" (i.e., rehearsing) the side effects of chemotherapy and potential patient responses is expected to significantly reduce the anxiety caused by the prospect of alopecia. The process is intended to desensitize women to alopecia, to allow them to make better informed treatment decisions, and to facilitate coping when hair loss occurs.

Results: A prototype of the system is visually portrayed. Qualitative and quantitative results from samples of patients and health care professionals on the accuracy of the images and usefulness of the system are presented.

Conclusions: Computer imaging systems inspired by virtual reality concepts can be useful in providing treatment for anxiety disorders.

References:

1. McGarvey EL, Baum LD, Pinkerton RC, Rogers LM: Psychological sequelae and intervention for treatment-induced alopecia among female cancer patients. *Cancer Practice* 2201; 9(6): 283-289.
2. Rothbaum BO, Hodges L, Alarcon R, Ready D, Shahar F, Grasp K, Pair J, Bebert P, Gotz D, Wills B, Baltzell D: Virtual reality exposure therapy for PTSD in Vietnam veterans: a case study. *Journal of Traumatic Stress* 1999, 12(2): 263-271.

NR567 Wednesday, May 25, 12:00 p.m.-2:00 p.m.
Quetiapine as an Adjunctive Treatment for Refractory PTSD

Supported by AstraZeneca Pharmaceuticals

Eileen Ahearn, M.D., *Veterans Administration Hospital, 2500 Overlook Terrace, Madison, WI 53705*; Mary Mussey, R.N., Amy C. Krohn, M.D., Catherine Johnson, Pharm.D., Dean Krahn, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand the potential utility of quetiapine as an adjunctive medication for PTSD.

Summary:

Objective: To review the efficacy of quetiapine as an adjunctive medication to a selective serotonin reuptake inhibitor (SSRI) for the treatment of posttraumatic stress disorder (PTSD) in an eight-week open-label trial.

Methods: Subjects were recruited from the Madison Veterans Affairs outpatient clinic. Subjects met the DSM-IV criteria for PTSD

as determined by the Mini International Neuropsychiatric Interview (MINI) and the Clinician-Administered PTSD Scale (CAPS). Subjects with either combat or noncombat PTSD were required to have a score of 50 or higher on the CAPS at baseline. Exclusion criteria included substance abuse in the last six months, history of bipolar disorder, schizophrenia, or other psychotic disorder. Subjects were taking a stable dose of an SSRI. No other psychotropic medications were allowed. The eight-week study was an open-label, flexible-dose trial of quetiapine for the treatment of chronic PTSD. Dosing of quetiapine was started at 25 mg/day and could be increased by 100 mg per week to a maximum of 400 mg/day. Study measures included the CAPS, the Clinical Global Impression Severity scale (CGI-S), the Sheehan Disability Scale (SDS), the 17-item Hamilton depression scale (HAM-D), and the Pittsburgh Sleep Quality Index (PSQI). Clinical response was defined as at least 30% improvement on the CAPS and a CGI-Improvement score of 1 or 2. Remission was defined as a CAPS score of < 20.

Results: Thirteen subjects participated. Based on the pre-established criteria for clinical response, eight of 12 subjects who completed the study were considered responders, and one subject achieved remission. The mean dose of quetiapine was 210 mg/day.

Conclusions: Quetiapine and similar drugs show promise for the amelioration of PTSD symptoms.

References:

1. Ahearn EP, Krohn A, Connor KM, Davidson JRT: Pharmacologic treatment of posttraumatic stress disorder: a focus on neuroleptic use. *Ann Clin Psych* 2003; 15(3):193-201.
2. Sokolski KN, Denson TF, Lee RT, Reist C. Quetiapine for treatment of refractory symptoms of combat-related Posttraumatic Stress disorder. *Milt Med* 2003; 168(6):486-469.

NR568 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Mental Health Needs Assessment of Sir Ru Run Shaw Hospital, Hangzhou, China

Mary Ann Schaepper, M.D., *Department of Psychiatry, Loma Linda University Medical Center, 11374 Mountain View Avenue, Loma Linda, CA 92354*; W. Andrew Hayton, M.D., Amy C. Hayton

Educational Objectives:

At the conclusion of this session, the participant should better appreciate the mental health needs of people in China, specifically at Sir Run Run Shaw Hospital in Hangzhou, China.

Summary:

Mental illness is a growing concern for China, with suicide and depression rates reaching record highs. A mental health needs assessment was conducted at Sir Run Run Shaw Hospital (SRRSH) in Hangzhou, China, in January through March, 2004, by a team from the Loma Linda University Department of Psychiatry. A pilot study established a protocol for measuring depression in an inpatient setting. Of the 75 patients surveyed with the Chinese Beck Depression Inventory Short Form, 45% reported some symptoms of depression and 8% showed severe depression. Although not statistically significant because of the small sample size and nonuniformity in survey administration, the results warrant a more extensive study. Medical students and nurses attended focus groups and a four-day lecture series on depression. Results indicated a lack of knowledge of diagnosis and treatment of depression. The data revealed that further research could expand depression prevalence screening to create a repeatable protocol for use in other hospitals. Collaboration with Loma Linda University to teach medical students and primary care physicians would help SRRSH contribute to suicide prevention China.

References:

1. Murray CJ, Lopez AD: *The Global Burden of Disease*. Cambridge, MA, Harvard University Press, 1996.
2. Phillips M, Yang G, Zhang Y, Wang L, Ji H, Zhou M: Risk factors for suicide in China: a national case-control psychological autopsy study. *Lancet* 2002; 360: 1728-1736.

NR569 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

The Cognitive and Emotional Difference After Traumatic Brain Injury With and Without Memory Impairment

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Educational Objectives:

At the conclusion of this session, the participant should be able to demonstrate effects of memory impairment in TBI patients.

Summary:

To examine the effect of memory impairment among traumatic brain injury (TBI) patients, the presenters investigated the level of cognitive dysfunction and the character of the discrepancy between suggested premorbid intelligence and memory ability. SCL-90-R, K-WAIS, K-MAS, K-BNT, and MMPI were completed for 161 patients age 18 years and older. The patients were divided into three groups: AD, all intelligence and memory functions are damaged; ND, intelligence and memory functions are mildly damaged; MD, intact or mildly damaged intelligence and impaired memory function. For the SCL-90-R, there was a significant difference in subscale and global index, but no difference between the ND and MD groups. The K-WAIS score was lower in the AD group than in the others, but there was no difference between the ND and MD groups. Memory ability was lower in the AD and MD groups than in the ND group. The MD group had lower cued recall and recognition subtest scores than the MD group, but not the AD group. Similar results were found with the K-BNT and MMPI. For scale scores on the MMPI, the MD group had higher scores than the other groups. In this research, the AD group experienced more severe cognitive and emotional dysfunction. The MD patients had almost the same results as the ND patients, but had more defensive attitude to psychiatric symptoms.

References:

1. Butters N, Cermark L: Some analysis of amnesic syndromes in brain damaged patients, in *The Hippocampus* (Vol. 2). Isaacson R.L, Pribram KH, eds. New York, Plenum Press 1975.
2. Reid L, Skeel, Sitzer D, Fogal T, Wells J, Johnstone B: (2004). Comparison of predicted-difference, simple-difference, and premorbid-estimation methodologies for evaluating discrepancies. *Archives of Clinical Neuropsychology* 2004; 19: 363-374.

NR570 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Risk Factors of Obstructive Sleep Apnea Syndrome

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Educational Objectives:

At the conclusion of this session, the participant should be able to demonstrate the risk factors of obstructive sleep apnea syndrome.

Summary:

Obstructive sleep apnea syndrome (OSAS) is common in the general population and affects attention, academic function, physical health, etc. But it is difficult and time consuming to perform a nocturnal polysomnogram (NPSG) for all potential OSAS patients. Identification of risk factors is important. Data for a total of 159 OSAS patients who underwent NPSG were analyzed. The patients were assigned to groups according to respiratory disturbance index (RDI) results: mild ($5 < \text{RDI} < 20$), moderate ($20.1 < \text{RDI} < 40$), and severe (> 40.1). Body mass index (BMI), lowest oxygen saturation, mean oxygen saturation, desaturation index (DI), and Epworth sleepiness scale (ESS) scores were compared. BMI, lowest oxygen saturation, mean oxygen saturation, and desaturation index were significantly different, according to severity of OSAS, but ESS was significantly different only between mild and severe OSAS patients. BMI, low oxygen saturation, mean oxygen saturation, and DI were considered as risk factors for OSAS in South Korea, but ESS was especially useful as risk factor.

References:

1. Arens R, Marcus CL: Pathophysiology of upper airway obstruction: a developmental perspective. *Sleep* 2004; 27(5):997-1019.
2. Ronald KC, Michael SA: The Epworth Sleepiness Scale may not reflect objective measures of sleepiness or sleep apnea. *Neurology* 1999; 52:125-131.

NR571 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

The Comparison of Intelligence Efficacy According to Methylphenidate Administration in ADHD Patients

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Educational Objectives:

At the conclusion of this session, the participant should be able to demonstrate intelligence efficacy change according to methylphenidate administration in attention-deficit/hyperactivity disorder patients.

Summary:

The causes of ADHD (attention-deficit/hyperactivity disorder) are various, so it is difficult to understand the characteristics of ADHD with simple intelligence rating scales. The presenters compared cognitive characteristics of an ADHD group with normal control subjects. Korea Kaufman Assessment Battery for Children (K-ABC) was used to evaluate the neuropsychological and cognitive aspects of the children. Forty ADHD patients and 40 normal control subjects matched for age and sex were tested with the K-ABC. Subscale scores were used to compare pretreatment patients and control subjects, pretreatment and posttreatment patients, and posttreatment patients and control subjects. Significant differences were observed in sequential processing, simultaneous processing, cognitive processing, and achievement between pretreatment patients and control subjects, and in gestalt closure between pretreatment and posttreatment patients. There were no significant differences between pretreatment patients and control subjects in gestalt closure and reading/decoding. Methylphenidate improved scores on the simultaneous scale, which measures improvement in executive functions such as divided attention, analy-

sis, and organization. Methylphenidate also reduced destructiveness.

References:

1. Barkley RA: Behavioral inhibition, sustained attention, and executive functions: constructing a unifying theory of ADHD. *Psychol Bull* 1997; 121(1):65-94.
2. McGee R, Williams SM, Anderson J: A comparison of 13-years-old boys with attention deficit and/or reading disorder on neuropsychological measures. *J Abnorm Child Psychol* 1989; 17(1):37-53.

NR572 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Atomoxetine for Weight Reduction in Obese Women

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Educational Objectives:

At the conclusion of this session, the participant should be able to discuss new information regarding the efficacy and safety of atomoxetine in the treatment of obesity.

Summary:

Objective: Based on the physiological understanding that adrenergic agents are capable of promoting weight loss, the presenters evaluated the short-term efficacy and safety of atomoxetine in the treatment of obesity.

Method: Thirty subjects were assigned to receive atomoxetine or placebo (1:1 ratio) in a randomized, double-blind fashion for 12 weeks in addition to the recommendation of a slightly hypocaloric diet. Atomoxetine was started at 25 mg/day with gradual dose increase to 100 mg/day over one week.

Results: Last-observation-carried-forward analysis of the available data for subjects who had at least one postrandomization assessment demonstrated that the atomoxetine (N = 12) group lost more body weight over the 12-week period than the placebo (N = 14) group (mean [SE], 3.6 [1.0] kg [3.7% loss] vs a weight gain of 0.2 [0.4] kg [0.2% gain]; F = 3.9, df = 4, 96, p < 0.0001). Three subjects in the atomoxetine group and none in the placebo group lost $\geq 5\%$ weight. Atomoxetine was tolerated well with minimal side effects.

Conclusion: Atomoxetine demonstrated modest short-term weight loss that was superior to placebo in this preliminary study of obese women.

References:

1. Hoebel BG, Leibowitz SF: Brain monoamines in the regulation of self-stimulation, feeding and body weight, in *The Psychobiology of Human Eating Disorders*. Weiner H, Hofer MA, Stunkard AJ, eds. New York, NY, New York Academy of Sciences, 1989, pp 307-20.
2. Schwartz MW, Baskin DG, Kaiyala, et al: Model for the regulation of energy balance and adiposity by the central nervous system. *Am J Clin Nutr* 1999; 69:584-96.

NR573 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Judgement of Continuing Hospitalization in the Treatment of Chronic Mentally-Ill Patients in

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Educational Objectives:

At the conclusion of this session, the participant should be able to recognize issues in continuing hospitalization in the treatment of chronic mentally ill patients in Korea.

Summary:

Objective: This study was conducted to develop effective management of discharge from the hospital and to avoid the abuse of human rights in mentally ill patients. The procedures and the problems of judging the need for continuing hospitalization of chronic mentally ill patients were reviewed according to the Mental Health Act of Korea.

Methods: The mentally ill patients who submitted the request for continuing hospitalization with the certificate of the charge doctor and the agreement of the caregiver were reviewed by the Cheonbuk Mental Health Judgement Board from January 2000 to December 2003.

Results: The total number of mentally ill patients who requested continuing hospitalization was 10,411. The diagnostic distributions were 80.7% for schizophrenic patients, 4.6% for alcoholic patients, and 14.7% for others, including patients with organic mental disorder. As for the caretakers, the rate of majors was 29.8%, parents 26.9%, sibling 26.1%, spouse 6.3%, offspring 5.9%, and others 5.0%; 79.3% of the patients were receiving Medicaid, and 20.7% were insured. A total of 1,136 patients were rejected for continuing hospitalization, a rate of 11.0%. The rejection rates of the schizophrenic and alcoholic patients were 9.55% and 34.9%, respectively.

Conclusions: New policies for decreasing long-term hospitalization of chronic mentally ill patients are required. The social support systems for psychiatric rehabilitation and readjustment are presently insufficient for the already discharged mentally ill in Korea.

References:

1. American Medical Association: Report of the Council on Scientific Affairs. Evidence-Based Principles of Discharge and Discharge Criteria (CSA Report 4-A-96), Chicago, AMA, 1996.
2. Kaplan HI, Sadock BJ: Ethics in psychiatry, in Synopsis of Psychiatry, 9th ed. Baltimore, Williams & Wilkins, 2003, pp 1365-1374.

NR574 Wednesday, May 25, 12:00 p.m.-2:00 p.m. Short-Term Treatment of Binge-Eating Disorder With Antidepressants: A Systematic Review

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Summary:

Objective: The study's aim was to evaluate antidepressant interventions for patients with binge-eating disorder (BED) that have been tested in randomized controlled trials and compared with placebo.

Method: The presenters searched the following electronic databases from 1994 to November 2004: MEDLINE, EMBASE, PsycINFO, LILACS, The Cochrane Collaboration Controlled Trials Register, and The Cochrane Depression, Anxiety, and Neurosis Group Database of Trials, and hand-searched *The International Journal of Eating Disorders* from January 1994 until November 2004. Data extraction was made by two reviewers. Relative risk and standardized mean difference were used to analyze dichotomous and continuous data.

Results: A total of 3,247 articles was identified using the search strategy. Titles were scanned to exclude articles not in accordance with the objectives of this review; 1,808 abstracts were evaluated in detail, and six studies fulfilled the inclusion criteria for this review.

Meta-analysis indicated that antidepressants were superior to placebo in terms of remission (RR = 0.73, 95% CI = 0.61, 0.88) and reduction in number of binge-eating episodes (SMD = -0.55, 95% CI = -0.88, -0.21). Most studies included a small number of patients and were of very short duration.

Conclusions: Antidepressants were effective in the treatment of BED, compared with placebo. However, more studies including more patients are warranted.

References:

1. American Psychiatric Association/APA: Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition). Porto Alegre, Brazil, Artes Medicas, 1995.
2. Carter WP, Hudson JL, Lalonde JK, Pinduck L, McElroy SL, Pope Jr HG: Pharmacologic treatment of binge eating disorder. *International Journal of Eating Disorders*: 2003; 34(S1)S74-S88.

NR575 Wednesday, May 25, 12:00 p.m.-2:00 p.m. Self-Injurious Behavior in Eating Disorders: A Behavior That Matters: An MMPI-2 Study

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Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the psychopathological characteristics of eating disordered women who self-injure.

Summary:

Prevalence of self-injurious behavior (SIB) is almost 50% in eating disorders. Personality particularities are probably a key to understanding this phenomenon. Only one study (Herpertz et al. 1995) carried out an evaluation of personality with self-injurious subjects. The presenters explored whether personality MMPI-2 profiles were different in eating disordered subjects who injured themselves and those who did not. The sample consisted of 197 women with a DSM-IV current diagnosis of anorexia nervosa (N = 117) and bulimia nervosa (N = 80); 36% (N = 42) of the patients with anorexia nervosa (AN) and 31% (N = 25) with bulimia nervosa (BN) were self-injurers. The most frequent type of SIB was self-cutting by far. MMPI-2 profiles of anorexic and bulimic subjects were in accordance with the literature. Among those subjects, considering MMPI-2 subscales, two subgroups were statistically different: AN and BN subjects without self-injurious behavior presented a very similar MMPI-2 profile, which was slightly disturbed (anxiety, low self-esteem, and social awkwardness). Subjects with self-injurious behavior presented a MMPI-2 profile that was very disturbed: subjects appeared depressed, anxious, emotionally unstable, and hypersensitive, had anger problems, and presented a marginal adjustment. Whatever the type of eating disorder, two distinct MMPI-2 profiles emerged depending on whether subjects self-injured or not. Self-injurer subjects with AN and BN presented a common pathological MMPI-2 profile.

References:

1. Herpertz S: Self-injurious behaviour — psychopathological and nosological characteristics in subtypes of self-injurers. *Acta Psy Scandinavica* 1995; 91:57-69.
2. Paul T, et al: Self-injurious behaviour in women with eating disorders. *Am J Psychiatry* 2002; 159:408-411.

NR576 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Predictors of Obstructive Sleep Apnea in 1,000 Psychiatric Patients

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Educational Objectives:

At the conclusion of this session, participants will be able to use a simple clinical score for the prediction of obstructive sleep apnea and to understand the importance of weight management for the reduction of risk created by this condition.

Summary:

Objective: Obstructive sleep apnea (OSA) is estimated to occur in 2% of women and 4% of men in the middle-aged U.S. population. Limited data have suggested that a diagnosis of schizophrenia, obesity, and chronic neuroleptic use are risk factors for OSA in selected groups of psychiatric patients. In this study, the presenters used a validated clinical score to estimate the prevalence of OSA in a large sample of unselected psychiatric patients.

Methods: A structured screening instrument for OSA that is being used at a 230-bed psychiatric hospital was used to assess the presence of severe daytime somnolence (SOMN), loud snoring (SNOR), interrupted breathing during sleep (APN), a body mass index (BMI) of 25 or greater, and arterial hypertension (HTN). The presence of any two of these criteria (except for BMI \geq 25 + HTN) is known to have a positive predictive value of 75% for the detection of OSA by polysomnography.

Results: Usable data were identified for 908 of 1,000 psychiatric patients consecutively admitted in 2002. We found SOMN in 6.5%, SNOR in 26%, APN in 10.5%, and HTN in 22%; 39% had normal weight (BMI < 25), 26% were overweight (BMI, 25-29.9), and 35% were obese (BMI, 30 or greater). Twenty-one percent screened positive on admission, corresponding to an adjusted OSA prevalence of 15%. Positive screens correlated with age 35-50 ($p = 0.002$) and BMI \geq 30 ($p < 0.001$) and were found in 8% of normal weight, 13% of overweight, and 45% of obese patients. Gender, psychiatric diagnosis, and type of psychotropic medication were not correlated with a positive screen.

Conclusions: The estimated prevalence of OSA in psychiatric patients is 15%, which is at least threefold greater than in the general population. The excess appears to be related to the large number of obese psychiatric patients, a high-risk subpopulation with an estimated prevalence of OSA of 34%.

References:

1. Williams AJ, Yu G, Santiago S, Stein M: Screening for sleep apnea using pulse oximetry and a clinical score. *Chest* 1991, 100:631-35.
2. Winkelman JW: Schizophrenia, obesity and obstructive sleep apnea. *J Clin Psychiatry* 2001, 62:8-11.

NR577 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Perspectives of Forensic Psychiatry

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Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the treatment of mentally ill offenders understand the use of register based research as a tool to calibrate the future mental health system to meet the challenges to come.

Summary:

Objective: In Denmark the number of forensic psychiatric patients increased exponentially from 1980 to 1999. Parallel to this, psychiatric care has been reorganized with closure of 50% of the psychiatric beds. The aims of this study were to investigate whether the increase in the prevalence of forensic psychiatric patients in Denmark continues, to analyze the use of inpatient facilities in the period 1994-2003, and to determine whether forensic and nonforensic patients with schizophrenia are treated differently.

Methods: From the Danish Psychiatric Central Research Register the presenters gained information about admissions and outpatient contact of all patients in Denmark with a legal sanction to psychiatric treatment or placement in a psychiatric ward in the period 1994-2003 and of nonforensic patients for comparison.

Results: The number of forensic patients increased from 541 to 1,421. The use of psychiatric beds for this group increased from 5.06% to 7.07% of the total use. Average time spend in hospital by each forensic patient decreased in the period, and the total use of psychiatric inpatient facilities did not increase proportional to the increasing prevalence.

Conclusion: The results raise the question of whether forensic patients receive sufficient treatment to ensure their mental well-being and the safety of the surrounding community.

References:

1. Kramp P, Gabrielsen G: Crimes committed by mentally ill persons in the years 1977-1999: development, number and causes. *Ugeskr Laeger* 2002; 165:2553-6.
2. Wallace C, Mullen PE, Burgess P: Criminal offending in schizophrenia over a 25-year period marked by deinstitutionalization and increasing prevalence of comorbid substance use Disorders. *Am J Psychiatry* 2004; 161:716-727.

NR578 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Mental Health of Irish Psychiatrists

Supported by Trinity College Dublin

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Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the pressures facing psychiatrists and the need for support services for psychiatrists' mental health.

Summary:

Objective: To test the hypothesis that psychiatrists have no excess mental health problems other than what is expected by chance.

Method: A total of 450 anonymous, self-administered postal questionnaires were sent to all psychiatrists working in the Republic of Ireland.

Results: A total of 235 psychiatrists replied. A total of 33.6% of the respondents scored positively on the GHQ-28. About a third (30.2%) of the respondents felt constantly under strain, and 5.5% had suicidal ideas.

Conclusions: These findings suggested that a third of the psychiatrists working in Ireland have a possible psychiatric disorder. This has serious implications for the well-being of this group of service providers. Special attention is needed, and it is necessary to set up a specialized service for psychiatrists in Ireland. These services should accept self-referral and provide easy access with strict confidentiality. Additionally, preventative measures to reduce stress and enhance mental health need to be developed.

References:

1. Caplan RP: Stress, anxiety and depression in hospital consultants, general practitioners and senior health service managers. *BMJ* 1994; 309:1261-1263.
2. Weich S, Sloggett A, Lewis G: Social roles and gender difference in the prevalence of the common mental disorders. *British Journal of Psychiatry* 1998; 173: 489-493.

NR579 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Characteristics of Alcohol-Dependent Patients With Comorbid Cluster-B-PD

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Educational Objectives:

At the conclusion of this session, the participant should be aware that alcohol dependent patients with comorbid cluster B PD show characteristic patterns of substance use and more severe psychopathology compared to alcoholics without comorbid cluster B PD. These characteristics must be allowed for in treatment planning.

Summary:

Objective: Comorbidity of cluster B personality disorders (PD) and substance abuse disorders is high and is associated with worse long-term prognosis. For the development of specific treatment approaches, a detailed analysis of comorbid patients concerning severity and patterns of substance use, psychopathology, and demographics is necessary.

Method: In a descriptive design the presenters collected data from inpatients treated for alcohol dependency, of whom about 20% show a comorbid cluster B PD (in particular antisocial, borderline). In addition to structured clinical interviews and sociodemographics, data were collected concerning patterns and severity of substance use (IDTSA, AEQ, OCDS, AASE, DrINC, ADS), treatment motivation (URICA), ADHD, quality of life, interpersonal problems (IIP), and psychopathology (BDI, SCL90-R, STAXI). Starting in November 2004, 40 patients, of whom nine had at least one cluster B PD, were recruited. By May 2005, more than 200 patients (about 50 comorbid) are expected to be enrolled.

Results: Analysis of the first data shows for the comorbid patients more severe psychopathology, more ADHD, more severe substance use, less substance use in social situations and in a positive mood, more substance use in a negative mood and in order to regulate affect, and lower quality of life.

Conclusions: Treatment planning for this group must allow for severe problems as well as for specific drinking situations.

References:

1. Skodol AE, Oldham JM, Gallaher PE: Axis II comorbidity of substance use disorders among patients referred for treatment of personality disorders. *Am J Psychiatry* 1999; 156:733-738.
2. Zanarini MC, Frankenburg FR, Hennen J, Bradford Reich D, Silk KR: Axis I comorbidity in patients with borderline personality disorder: 6-year follow-up and prediction of time to remission. *Am J Psychiatry* 2004; 161:2108-2114.

NR580 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Court-Ordered Psychotropic Medications in Public Hospitals of Illinois: Four Years of Data

Jagannathan Srinivasaraghavan, M.D., *Department of Psychiatry, Southern Illinois University, Choate Mental Health Center, 1000 North Main, Anna, IL 62906*; Sarah Andrew, Ph.D., Angela McClelland

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the Illinois statute concerning overturning of the right to refuse medications and the judicial outcome of such petitions from the Illinois public hospitals.

Summary:

Objective: In the state of Illinois even committed patients have a right to refuse psychotropic medications. Other than in an emergency, the Illinois Statute 2-107.1 requires judicial determination to force psychotropic medications on nonconsenting inpatients. In 2003 the statute was amended to disallow jury trial. The objective of this study was to compare data concerning court-ordered psychotropic medications from all 10 state hospitals (one hospital closed in 2002) serving both civil and forensic patients.

Method: Data were collected on the number of patients treated, number of petitions, rate of petitions, number of petitions granted and denied, and percentage of denial in each hospital in each of the four years (2002-2003).

Results: The number of petitions from a hospital in a year ranged from 0 to 131. The rate of petitions ranged from 0 to 163 petitions per thousand patients treated. The percentage of denial of petitions ranged from 0 to 56%.

Conclusion: Considering that the public hospitals in Illinois serve mainly severely mentally ill patients, the enormous variation in the outcome of court decisions casts doubt on the effectiveness and thoroughness of the judicial process.

References:

1. Srinivasaraghavan J: Is there value in allowing judicial determination of right to refuse psychotropic medications by psychiatric inpatients? Proceedings of the 15th World Congress on Medical Law, August 1-5, 2004 pp 35-42. Sydney, Australia, pp 35-42.
2. Srinivasaraghavan J, Andrew S, Watkins N, Mahalik A: Variations in court ordered medications in Illinois, USA. XII World Congress of Psychiatry Abstracts Volume 2. August 24-29, 2002, Yokohama, Japan, p 187.

NR581 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Study Investigating Psychomotor and Cognitive Residual Effects of Zolpidem

Supported by Sanofi-Aventis

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Educational Objectives:

To aid the participants' understanding of the residual psychomotor and cognitive effects of a new formulation of the hypnotic drug zolpidem.

Summary:

Objective: To assess the residual psychomotor and cognitive effects and safety of a new zolpidem modified-release (MR) formulation eight hours after a single dose.

Methods: A randomized, double-blind, placebo- and reference-controlled, three-period crossover study in 18 healthy volunteers (22-38 years old, 10 male) comparing zolpidem MR 12.5 mg or flurazepam 30 mg to placebo. Cognitive and psychomotor tests were performed eight hours postdose: Critical Flicker Fusion (CFF), Choice Reaction Time (CRT), Compensatory Tracking Task (CTT), Immediate and Delayed Word Recall (WR_i , WR_d), and Digit Symbol Substitution Test (DSST). Subjective sleep quality was evaluated with the Leeds Sleep Evaluation Questionnaire. Clinical laboratory parameters, vital signs, and adverse event recording evaluated safety.

Results: Pairwise comparisons between zolpidem MR and placebo demonstrated no significant difference in performance in CFF, CRT, WR_i, WR_d, and DSST eight hours postdose. Flurazepam significantly impaired performance on all tests except DSST, compared to placebo.

Conclusion: This study demonstrated that unlike flurazepam (positive control), zolpidem MR 12.5 mg has no residual effects on CNS integrative capacity, sensorimotor or psychomotor performance, or immediate and delayed memory recall except for CTT time reaction, compared to placebo. Zolpidem MR was well tolerated and exhibited a comparable safety profile to placebo.

NR582 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Efficacy and Safety of a Modified Release Formulation of Zolpidem in Adults

Supported by Sanofi-Aventis

Christina Soubrane, M.D., *Department of Clinical Development, Sanofi-Aventis, 1 Avenue Pierre Brossolette, Chilly Mazarin 91385, France*; James K. Walsh, Ph.D., Thomas Roth, Ph.D.

Educational Objectives:

The research data presented will aid participants' understanding of the effects of a new formulation of the hypnotic drug zolpidem on the sleep of patients with insomnia.

Summary:

Objective: Zolpidem decreases sleep onset latency and increases sleep duration. A new zolpidem modified-release (MR) formulation has been developed with pharmacokinetic and pharmacodynamic characteristics appropriate to provide additional improvements in sleep maintenance without inducing next-day residual effects.

Methods: A placebo-controlled, three-week polysomnography (PSG) study was conducted in 212 adult patients with primary insomnia (DSM-IV criteria) using zolpidem MR 12.5 mg. Hypnotic efficacy was assessed on mean PSG sleep parameters on nights 1/2 and 15/16. Daily subjective estimates from sleep questionnaires were obtained throughout the three-week treatment period.

Results: The results showed that zolpidem MR improved sleep maintenance by significantly reducing PSG wake time after sleep onset (WASO) during the first six hours of the night, in comparison to placebo, at nights 1/2 and 15/16. In addition, the known hypnotic properties of zolpidem were confirmed with zolpidem MR 12.5 mg, which significantly decreased PSG latency to persistent sleep and increased PSG sleep efficiency, in comparison with placebo. Zolpidem MR 12.5 mg was well tolerated. No evidence of next-day residual effects was observed as measured objectively by psychometric tests and subjectively using questionnaires.

Conclusion: A modified-release formulation of zolpidem is effective and well tolerated in patients with primary insomnia and sleep maintenance difficulties.

NR583 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Zolpidem Modified-Release Formulation Has a Greater Pharmacologic Activity

Supported by Sanofi-Aventis

David J. Greenblatt, M.D., *Division of Clinical Pharmacology, Tufts University, 136 Harrison Avenue, Boston, MA 02111-1854*; Gary Zammit, Ph.D., Karen M. Rice, J.S. Harmatz, Eric Legangneux

Summary:

Objective: To demonstrate prolonged pharmacologic activity of a zolpidem modified-release (MR) formulation (12.5 mg) using relative electroencephalogram (EEG) beta frequency band

(EBFB) and establishing the relationship of this activity to plasma drug concentrations.

Methods: A double-blind, placebo-controlled, three-way crossover study of 81 subjects (age 29.5 ± 7 years, 46 male) comparing zolpidem MR (12.5 mg) to standard zolpidem (10 mg) and placebo (minimum washout periods: seven days). After a single morning dose, EEG records and blood samples were obtained at one-hour intervals for 10 hours and at 20-minute intervals for three to six hours postdose. Digit Symbol Substitution Test and visual analogue scales (VAS) for sedation were also performed concomitantly.

Results: A total of 72 subjects completed the study. Zolpidem MR, compared to standard zolpidem, demonstrated longer duration of action through duration of the relative EBFB power change: quarter-value duration, half-value duration, and three-quarter-value duration of Emax of EBFB. The effect was significantly greater at three to six hours postdose.

Conclusion: Zolpidem MR demonstrated a longer duration of action (through three variables assessing the duration of the relative EBFB power change), compared to standard zolpidem, significantly greater at three to six hours postdose. VAS for sedation also differentiated the two formulations.

References:

1. Greenblatt D et al: Clin Pharmacol Ther 1989; 45:356-365.
2. Greenblatt D et al: Clin Pharmacol Ther 1998; 64:553-561.

NR584 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Study of Residual Psychomotor and Cognitive Effects of Single, Oral Doses of Zolpidem

Supported by Sanofi-Aventis

Ian Hindmarch, Ph.D., *H.P.R.U., Surrey University, Egerton Road, Guildford, Surrey GU2 5XP, United Kingdom*; Neil Stanley, Ph.D., Eric Legangneux, I. Zobouyan

Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the residual psychomotor and cognitive effects of a new formulation of the hypnotic drug zolpidem in healthy elderly subjects.

Summary:

Objective: To assess residual psychomotor and cognitive effects and safety of a new zolpidem modified-release (MR) formulation eight hours after a single nocturnal dose in healthy elderly subjects.

Methods: A randomized, double-blind, placebo- and reference-controlled, four-way crossover study in 24 subjects (65-78 years old, 10 male) comparing zolpidem MR 6.25 mg and 12.5 mg or flurazepam 30 mg to placebo. Tests included Critical Flicker Fusion (CFF), Choice Reaction Time (CRT), Compensatory Tracking Task (CTT), Immediate and Delayed Word Recall (WR_i, WR_d), Digit Symbol Substitution Test (DSST), and the Leeds Sleep Evaluation Questionnaire (LSEQ). Hematology, biochemistry, vital sign monitoring, and adverse event recording evaluated safety.

Results: Neither zolpidem MR doses demonstrated a significant difference in performance vs placebo for CFF, CRT, total reaction time, CTT, WR_i, WR_d, and DSST, eight hours postdose. Flurazepam significantly impaired performance with respect to placebo in all tests. LSEQ assessment showed no negative effects.

Conclusion: In contrast to flurazepam, a single dose of zolpidem MR 6.25 mg or 12.5 mg had no residual effects on CNS integrative capacity, sensorimotor or psychomotor performance, or immediate and delayed memory recall, compared to placebo in elderly subjects. Zolpidem MR was well tolerated with no serious adverse safety events observed.

NR585 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Zolpidem Modified-Release Formulation Improves Sleep Maintenance Compared With Standard Zolpidem in a Pharmacodynamics Model Assessing the Return to Sleep Following Nocturnal Awakening Supported by Sanofi-Aventis

Ian Hindmarch, Ph.D., *H.P.R.U., Surrey University, Egerton Road, Guildford, Surrey GU2 5XP, United Kingdom*; Neil Stanley, Ph.D., Eric Legangneux, S. Eneqbo

Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the pharmacodynamic effects of a new formulation of the hypnotic drug zolpidem in maintaining sleep in healthy subjects.

Summary:

Objective: To assess persistence of efficacy of a zolpidem modified-release (MR) formulation (12.5 mg) to induce sleep after awakening three, four, and five hours after a single nocturnal dose.

Methods: A double-blind, placebo-controlled, nine-way cross-over study of 54 healthy subjects (age 27.9 ± 7 years, 28 male) comparing zolpidem MR to standard zolpidem and placebo. Polysomnography recordings were performed for eight hours post-dose. Subjects were awakened three, four, and five hours post-dose and exposed to a noise model that prolongs latency to persistent sleep (LPS). Primary end point: LPS following awakening at all time points. Digit Symbol Substitution Test (DSST) and Leeds Analog Rating Scales (LARS) were performed at all time points.

Results: Zolpidem MR demonstrated a significant reduction in LPS vs standard zolpidem at four and five hours postdose. Both formulations significantly reduced LPS, compared to placebo, at each time point. DSST and the "drowsy" LARS item followed a similar pattern. Total sleep time, wake time after sleep onset, and shift of sleep stages indicated that zolpidem treatment groups slept better.

Conclusion: Zolpidem MR exhibited significantly better pharmacologic activity at four and five hours postdose, compared to standard zolpidem and placebo, without compromising psychomotor performance or sleep architecture.

References:

1. Stone B et al: *J Sleep Res* 2000; 9(suppl 1):183.

NR586 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Efficacy and Safety of 6.25 mg of Zolpidem Modified-Release Formulation in Elderly Patients With Primary Insomnia

Supported by Sanofi-Aventis

Timothy A. Roehrs, Ph.D., *Department of Sleep Disorders, Henry Ford Hospital, 2799 West Grand Boulevard, CFP-3, Detroit, MI 48202*; Christina Soubrane, M.D., James K. Walsh, Ph.D., Thomas Roth, Ph.D.

Educational Objectives:

The research data presented will aid participants' understanding of the effects of a specific dose of the new formulation of the hypnotic drug zolpidem on the sleep of elderly patients with insomnia.

Summary:

Objective: To investigate the efficacy and safety of a dose of a new zolpidem modified-release (MR) formulation in elderly patients with primary insomnia.

Methods: A placebo-controlled, three-week polysomnography (PSG) study was conducted in 205 elderly patients (mean age,

70.2) with primary insomnia (DSM-IV criteria) using zolpidem MR 6.25 mg. Hypnotic efficacy was assessed on mean PSG sleep parameters on nights 1/2 and 15/16. Daily subjective estimates were obtained from sleep questionnaires throughout the three-week treatment period.

Results: Sleep maintenance was significantly improved with zolpidem MR 6.25 mg as shown by the reduction of PSG wake time after sleep onset (WASO) during the first six hours of the night at nights 1/2 and 15/16, in comparison with placebo. Sleep induction and sleep duration were also improved with zolpidem MR 6.25 mg, which significantly decreased PSG latency to persistent sleep and increased PSG sleep efficiency, in comparison with placebo. Zolpidem MR 6.25 mg was well tolerated. No evidence of next-day residual effects was observed as measured objectively by psychometric tests and subjectively using questionnaires.

Conclusion: Zolpidem MR (6.25 mg) improved sleep maintenance, sleep induction, and sleep duration and was well tolerated in elderly patients with primary insomnia.

NR587 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

The Burden of Social Phobia in a Brazilian Community and Its Relationship With Socioeconomic Circumstances: The Bambui Study

Claudia M.R. Vorcaro, M.S.C., *Psiquiatria, Consultorio, Avenida Brasil 248/214, Belo Horizonte, MG 30140001, Brazil*; Fabio L. Rocha, M.D., Elizabeth Uchoa, Ph.D., Maria Fernan Lima-Costa, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the importance of Social Phobia in developing countries.

Summary:

Objective: Social phobia in an environment of poverty and major social inequalities, as observed in most developing countries, has received little attention. This population-based study was carried out in a poor community in Brazil (15,000 inhabitants) with the aim of determining the prevalence of social phobia and its associated factors.

Method: The Composite International Diagnostic Interview was applied in a random sample of 1,037 residents age ≥ 18 years.

Results: The one-month, one-year, and lifetime prevalences of social phobia were 7.9%, 9.1%, and 11.8%, respectively. One-month social phobia was independently associated with age (45-64 years), marital status (divorced/separated), worse socioeconomic indicators (family income and education), number of months worked, worse health status, and use of health services and medications.

Conclusions: There is an important burden of social phobia in the study community, due to its high prevalence (similar or superior to those observed in most developed countries) and due to its association with worse health status and use of health services and medications. The strong association between social phobia and socioeconomic circumstance, even in a small and poor community, certainly reflects the major social inequalities in Brazil.

Supported by Financiadora de Estudos e Projetos (Brazil), Brazilian Higher Education Coordinating Office (CAPES), Brazilian Research Council (CNPq).

References:

1. Furmark T: Social phobia: overview of community surveys. *Acta Psychiatr Scand* 2002; 105: 84-93.
2. Lima-Costa MFF, Uchoa E, Guerra HL, Firmo JO, Vidigal PG, Barreto SM: The Bambui health and ageing study (BHAS): methodological approach and preliminary results of a popula-

NR588 **Wednesday, May 25, 12:00 p.m.-2:00 p.m.**

An Open-Label, Outpatient, Pilot Study of Sertraline in the Treatment of Bulimia Nervosa

Pauline Powers, M.D., *Department of Psychiatry, University of South Florida, 3515 East Fletcher Ave, Tampa, FL 33613-4706*; Yvonne Bannon, M.S.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the major symptoms of bulimia nervosa and assess changes in symptoms with treatment.

Summary:

Objective: The primary aim was to determine if sertraline is efficacious and safe in reducing episodes of binge-eating and purging in individuals with bulimia nervosa (BN). The secondary aim was to determine the effect of sertraline on various associated symptoms.

Methods: In this single-site, open-label, outpatient, flexible-dose study, sertraline 100-200 mg was given daily to subjects with DSM-IV BN. Nineteen subjects enrolled; 17 returned for at least one assessment after receiving the drug. Twelve patients completed the 10-week study. Patients completed diaries recording binge and purge episodes. At baseline and week 10, patients completed the EDI-2, BDI, MADRS, BAI, and YBC-EDS.

Results: Of the 12 patients who completed the study, six had no episodes of binge-eating or purging by vomiting at week 10. Statistically significant decreases in binge-eating ($p < 0.0001$) and purging ($p = 0.006$) were realized in a last-observation-carried-forward analysis. There were also statistically significant reductions in scores on the EDI-2 binge and drive for thinness subscales ($p = 0.003$, $p = 0.010$), MADRS ($p < 0.0001$), BDI ($p = 0.001$), BAI ($p = 0.003$), and YBC-EDS preoccupations and rituals ($p = 0.002$, $p = 0.005$).

Conclusions: There were statistically significant reductions in binge-eating, purging, and factors hypothesized to underlie disturbed eating behavior.

References:

1. Crow S, Brown E: Investigational drugs for eating disorders. *Expert Opin Investig Drugs* 2003; 12:491-499.
2. Bacaltchuk L, Hay P: Antidepressants versus placebo for people with bulimia nervosa. *Cochrane Database Syst Rev* 2001; 4:CD003391.

NR589 **WITHDRAWN**

NR590 **Wednesday, May 25, 12:00 p.m.-2:00 p.m.**

Community Risk in Psychosis: Predictors and Management

Supported by the Wellcome Trust and NHS Research and Development

Elizabeth M. Walsh, M.D., *Forensic Mental Health, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, United Kingdom*; Charles Scott, M.D., Paul Moran, M.D., Peter Tyrer, M.D., Frances Creed, M.D., Robin Murray, M.D., Tom Fahy, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate an understanding of the challenges faced by patients receiving community care in terms of their own violent

behaviour and victimization to self, to recognize risk factors for such behaviors and interventions which have addressed these problems to date, and to understand that to address stigma in severe mental illness it is important to address not only relative risk but also absolute risk to society and the risk society itself poses to this group. Participants will understand the importance of multifaceted management of illness to help alleviate suffering by both these patients and society.

Summary:

Objective: Deinstitutionalization has resulted in multiple challenges for people with psychosis, including the risk of committing violent acts and being the victim of such acts. Interventions are needed to address these problems. The aims of this study were (1) to establish the prevalence of and risk factors for violence/victimization in psychosis, (2) to determine whether increasing the intensity of community care reduces these behaviors.

Method: A total of 708 patients with psychosis were recruited and interviewed. Patients were randomly assigned to receive either intensive community care (ICM) or standard care (SCM) and followed for two years. The prevalence of violence and victimization were estimated, and baseline variables examined as possible risk factors for these outcomes.

Results: Twenty-two percent committed assault, and 20% were the victims of assault during follow-up. Eighty patients (23%) in the ICM group committed assault, compared to 78 (22%) in the SCM group ($p = 0.86$, $OR = 1.08$, 95% CI 0.78-1.44), whereas 54 (20%) in the ICM group and 67 (27%) in the SCM group were the victims of assault ($p = 0.04$, $OR = 1.48$, 95% CI 1.02-2.22). Risk factors for assault included illegal drug use, personality disorder, younger age, previous history of assault and violent convictions, being a victim of violence, and receipt of special education. Risk factors for violent victimization included illegal drug use, less family contact, personality disorder, history of violent convictions, and early age at onset of illness.

Conclusions: Violence and violent victimization are prevalent in those with psychosis. Intensive community care reduced violent victimization but not violence.

References:

1. Hiday VA, Swartz MS, Swanson JW, et al: Impact of outpatient commitment on victimization of people with severe mental illness. *Am J Psychiatry* 2002; 159: 1403-1411.
2. Silver E. Mental disorder and violent victimization: the mediating role of involvement in conflicted social relationships. *Criminology* 2002; 40: 191-211.

NR591 **Wednesday, May 25, 12:00 p.m.-2:00 p.m.**

Emergent and Worsening Suicide Ideation in Pediatric Paroxetine Depression Trials

Supported by GlaxoSmithKline

Regan Fong, Ph.D., *Department of Neurosciences Medicines Development Center, GlaxoSmithKline, 2301 Renaissance Boulevard, King of Prussia, PA 19406*; David Carpenter, R.Ph., Alan Lipschitz, M.D., Stan Krulewicz, M.A., Desiree Schaefer, B.A., John Davies, M.S.C.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the analysis of worsening and emergent suicide ideation that was conducted in the three pediatric paroxetine depression trials.

Summary:

Objective: To describe suicide-item analyses in pediatric paroxetine depression trials.

Methods: Analyses of worsening and emergent ideation were conducted in three randomized, double-blind, placebo-controlled pediatric paroxetine depression trials (paroxetine N = 378, placebo N = 285). Worsening ideation was defined as an increase above baseline of ≥ 1 point on the HAM-D "suicide" item 3 or ≥ 2 points on the CDRS-R "suicidal ideation" item 13 or MADRS "suicidal thoughts" item 10. Emergent ideation was defined by these rating scale increases: HAM-D item 3 from 0 at baseline to ≥ 1 or from 1 at baseline to ≥ 2 ; CDRS-R item 13 from 1 or 2 at baseline to ≥ 3 ; MADRS item 10 from 0 or 1 at baseline to ≥ 2 . The proportion of patients meeting criteria for emergent and worsening suicidal ideation was compared between treatment groups with logistic regression.

Results: There were no statistically significant differences in the proportion of patients meeting criteria for emergent (23.7% paroxetine vs. 23.3% placebo, $p = 1.000$) or worsening (15.0% paroxetine vs. 14.3% placebo, $p = 0.824$) ideation.

Conclusions: In contrast to the signal from more suicidality adverse event reports with paroxetine in these clinical trials, suicide-item analyses failed to reveal a risk difference between paroxetine and placebo.

References:

1. Hammad TA: Review and Evaluation of Clinical Data. Center for Drug Evaluation and Research, FDA. Available at: <http://www.fda.gov/ohrms/dockets/ac/04/briefing/2004-4065b1-10-TAB08-Hammads-Review.pdf>. Accessed September 30, 2004.
2. Paroxetine pediatric clinical study reports available at: <http://www.gsk.com/media/paroxetine.htm>.

NR592 Wednesday, May 25, 12:00 p.m.-2:00 p.m. Effectiveness of a Qigong-Based Stress Management Program in Pregnant Women

Tae Kyoo Choi, M.D., *Department of Psychiatry, Pochon Cha University, Yatapdong 351 Bundang, Sunghamsi Kyounggido, Korea*; Sang Hyuk Lee, M.D., Mujinhaeng Kim, M.D., Eun Hee Lee, M.D., Shin Young Suh, M.D., Ki Whan Yook, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that a qigong-based stress management program can be effective and safe for pregnant women.

Summary:

Objectives: The aim of this study was to examine the effectiveness of a qigong-based stress management program in pregnant women.

Method: An eight-week controlled clinical trial compared 52 pregnant women receiving qigong-based stress management program to 40 pregnant women receiving pregnancy health education program. Edinburgh Postnatal Depression Scale (EPDS), Beck Depression Inventory (BDI), Spielberger State-Trait Anxiety Inventory (STAI-1), Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Rating Scale (HAM-A) were used to measure anxiety and depressive level.

Result: Qigong-based stress management group showed significant improvement, compared to the education control group in HAM-D ($t=4.6$, $df=56$, $p=0.000$), BDI ($t=5.2$ $df=54$, $p=.000$), EPDS ($t=5.9$, $df=34.5$, $p=.000$ STAI-1 ($t=3.5$, $df 44.4$, $p=.001$); qigong-based stress management group also showed significant improvement at eight weeks termination on measures of anxiety and depression level, compared to pretreatment.

Conclusion: This study showed that qigong-based stress management program can be effective and safe for pregnant women.

References:

1. Astin JA et al: The efficacy of mindfulness meditation plus qigong movement therapy in the treatment of fibromyalgia: a randomised controlled trial. *J Rheumatol* 2003; 30:2257-2262.
2. Margaret GS, Jean E: Controlled clinical trial of interpersonal psychotherapy versus parenting education program for depressed pregnant women. *Am J Psychiatry* 2003; 160(3):555-562.

NR593 Wednesday, May 25, 12:00 p.m.-2:00 p.m. Comparison of Practice Patterns Among Psychiatrists in New Delhi, India, and Baltimore, Maryland (U.S.)

Ajay D. Wasan, M.D., *Department of Psychiatry and Anesthesiology, Brigham and Womens' Hospital, 75 Francis St., Boston, MA 02115*; Geetha Jayaram, M.D., Karin Neufeld, M.D.

Educational Objectives:

At the conclusion of the presentation the participant should be able to recognize the complexities faced by Indian psychiatrists and how the American cultural context influences the care of Indian patients in the USA.

Summary:

Little is known about the practice patterns of psychiatrists in India, such as daily practice routines or treatment approaches to major disorders. And less is known about the treatment of Indian patients in the USA. As a descriptive study of these issues, and to contrast the practice of psychiatry in two countries, the presenter used triangulated, qualitative methods (ethnographic interviews, observation of treatment in India, and treatment of Indian patients) to design and validate a survey distributed to a sample of 34 psychiatrists in New Delhi and 34 in Baltimore who treat Indian patients. Delhi psychiatrists saw more patients daily (24.3 vs. 11, $p < 0.001$) and spent less time on new evaluations (33.3 vs. 69 minutes, $p < 0.001$). Both groups had similar approaches in treating major disorders and prescribed similar medication doses. But Delhi psychiatrists were less likely to combine medication treatment with psychotherapy ($p < 0.05$). They were more likely ($p < 0.001$) to advise families to secretly administer medications to their ill family member in scenarios of treatment refusal, such as in acute schizophrenia or major depression. These differences in the handling of "delicate," ethical treatment issues highlights the salience of cultural context in the practice of psychiatry and in the treatment approach to Indian patients.

References:

1. Patel V, Chisholm D, Rabe-Hasketh S, Dias-Saxena F, et al: Efficacy and cost-effectiveness of drug and psychological treatments for common mental disorders in general health care in Goa, India: a randomized controlled trial. *Lancet* 2003, 361: 33-39.
2. Ratel S, Gaw AC: Suicide among immigrants from the Indian continent: a review. *Psychiatric Services* 47: 1996, 517-521.

NR594 Wednesday, May 25, 12:00 p.m.-2:00 p.m. Resource Utilization and Costs of Treatment for Children and Adolescents Newly Diagnosed With Gilles De La Tourette's Disorder

Chris Kozma, Ph.D., *University of South Carolina, 112 Fox Hollow Circle, West Columbia, SC 29170*; Scott Flanders, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the utilization and costs of health care services for children and adolescents with Gilles de la Tourette's disorder assessed in a Medicaid population.

Summary:

Objective: To estimate resource use and costs of health care for children and adolescents with Gilles de la Tourette's disorder (Tourette's) in a Medicaid population.

Methods: Retrospective, 18-month claims analyses comparing resource utilization and costs of child and adolescent patients before and after the first claim with a Tourette's diagnosis (ICD-9 307.23). Health resource utilization and costs were categorized by provider, facility, and prescription claims. Statistical comparisons were performed using paired t tests.

Results: The average Tourette's patient was 12.7±3.5 years old. Males and Caucasians comprised 79.6% and 63.6% of the sample (N = 44), respectively. Childhood hyperkinetic syndrome was the most common comorbidity. Total provider and facility costs increased from \$529.70 ± 961.90 (prediagnosis) to \$1275.15 ± 3143.16 (six months postdiagnosis) but were not statistically different (p = 0.09). Mental health costs increased 321% (six months postdiagnosis) (p = 0.04). Prediagnosis, 59.1% of patients used prescription medications (mean cost \$216.43 ± 478.93); this increased to 72.7% one year postdiagnosis (mean costs \$355.75 ± 649.73, p = 0.045). Antipsychotics, antidepressants and anticonvulsants accounted for the majority of medications.

Conclusions: Analyses of medical and pharmacy claims showed children diagnosed with Tourette's to have increased prescription medication use and significantly greater mental health services use six months postdiagnosis. These results highlight a change in intensity of treatment after diagnosis within this pediatric Medicaid population.

References:

1. Leckman JF: Tourette's syndrome. *Lancet* 2002; 360:1577-1586.
2. Jankovic J: Tourette's syndrome. *N Engl J Med* 2001; 345:1184-1192.

NR595 Wednesday, May 25, 12:00 p.m.-2:00 p.m. A Scale to Assess Intrusiveness in the Clinical Setting

David I. Mayerhoff, M.D., *Department of Psychiatry, Greystone Park Psychiatric Hospital/UMDNJ, 5 Marie Terrace, West Orange, NJ 07052*; Steven Schleifer, M.D., Jeffrey Nurenberg, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant will better appreciate the importance of patients' intrusive behavior and perception of such behavior as a potentially independent construct, distinct but related to violence. Participants will be provided with a new tool to assess intrusiveness and its relation to other clinical phenomena.

Summary:

Objective: Patient violence in hospital settings is of increasing concern. Related and less well-studied are patient intrusiveness and incursions into personal space, which may undermine the therapeutic environment and be a prelude to violence.

Method: In an attempt to quantify intrusiveness in a state hospital setting, a novel one-item Likert-type scale was used to assess the extent to which patients were perceived as intrusive "in-your-face." With minimal explanation, staff assigned scores (1-5) for

each patient. The Intrusiveness Scale (IS) was administered on two units.

Results: Staff from multiple disciplines found IS to have face validity, and an entire unit could be scored within 10 minutes. Patients scored along the full range. Correlations among staff varied, some quite high (Pearson $r > 0.8$). Raters showed moderate correlations for repeat ratings. IS had low correlation with other psychiatric measures (e.g., IS and BPRS: $r = -0.02$, n.s.), suggesting that it measures a distinct clinical dimension. One unit showed progressive decreases in mean patient ratings over three months, with IS lower at the fourth vs first assessment (paired $t = 2.27$, $df = 12$, $p < 0.05$).

Conclusions: The preliminary findings demonstrate potential usefulness for this easily administered instrument, showing promise for assessing patient risk. Variability in perceived individual and unit-wide intrusiveness may provide an indicator of staff needs. Further data including applications as a predictor of aggression are presented.

References:

1. Ng B, Kumar S, Ranclaud M, Robinson E: Ward crowding and incidents of violence on an acute psychiatric inpatient unit. *Psychiatric Services* 2001; 52:521-5.
2. Fagan-Pryor EC, Haber LC, Dunlap D, Nall JL, Stanley G, Wolpert R: Patients' views of causes of aggression by patients and effective interventions. *Psychiatric Services* 2003; 54:549-53.

NR596 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

An Epidemiology Study of Personality Disorder Among Senior High School Students in Beijing

Yueqin Huang, Ph.D., *Institute of Mental Health, Peking University, 51 Hua Yuan Bei Road, Beijing 100083, China*

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the prevalence of personality disorder among adolescents in Beijing, China and its related factors, family risk factors that influence the development of personality disorder and the effective of health education during adolescence.

Summary:

Objective: To describe personality disorders (PD) among senior high school students in Beijing, to explore genetic and environmental risk factors of PD, and to establish an intervention model of mental health education for adolescents.

Method: In a cross-sectional study, case-control study, cohort study, and community intervention trial, 10,002 senior high school students selected by stratified-cluster sampling were examined with the PDQ-4, EMBU, GIQ, and IPDE, and were followed up for three years. Single and multivariate analysis methods were applied for data processing.

Results: The prevalence of personality dysfunction was 8.3% at the first grade, and those with personality dysfunction and PD constituted 5.8% and 1.83% at the third grade. The self-recovering rate of personality dysfunction was 71.0%. Risk factors of PD included poor parental relationship, parental rejection, and overprotection. PDQ-4 scores of the intervention group were significantly lower than those of the nonintervention group. The incidence rates of cluster C, paranoid, narcissistic, and borderline PD were statistically decreased by the intervention.

Conclusions: The prevalence of PD in Beijing is low. There is a self-recovery tendency for personality dysfunction. Family environmental risk factors play an important role in PD occurrence. Mental health education can contribute to promotion of mental health for adolescents.

References:

1. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Washington DC, American Psychiatric Association 1994, pp 629-674.
2. Hyler SE, Rieder RO: Personality Diagnostic Questionnaire-4th version. New York, NY, New York State Psychiatric Institute, 1996.

NR597 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Effectiveness of Paroxetine CR on Depressive, Anxiety, and Irritability Symptoms in a Community Sample of Adult Hispanic Women With Major Depression or Generalized Anxiety Disorder

Supported by GlaxoSmithKlin

Rosemary I. Nourse, R.N., *Department Psychiatry, Lehigh Center for Clinical Research, 401 N. 17th Street, Suite 106, Allentown, PA 18104*; Paul Gross, M.D., Tom Wasser, Ph.D., Stan Krulewicz, M.A.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the need for improved mental health care for female Hispanics, their higher incidence of depression and anxiety, barriers faced in attempting to obtain quality care, life stressors confronting Hispanic women, women, and use of paroxetine. Paroxetine CR to alleviate depressive and anxiety symptoms, enabling positive life changes to occur.

Summary:

Objective: Previous research reports higher rates of depression in Hispanic women than Caucasian or African-American women, with Hispanics receiving lower quality mental health care. This study examined paroxetine CR treatment efficacy in Hispanic women with depression or anxiety.

Method: At a naturalistic research center, 38 women of Hispanic heritage age 18-75 with a DSM-IV diagnosis of MDD or GAD were assigned paroxetine CR 12.5-50mg/day in this seven-and-a-half month, open-label trial examining efficacy and safety with weekly, biweekly, and monthly evaluations with standard depression and anxiety rating scales. Primary outcome measures were 17-item Hamilton Depression Rating Scale, Hamilton Anxiety Rating Scale, and Clinical Global Impression Improvement and Severity scales.

Results: Data collected on 28 patients were compared by paired t-test from initial observation versus last follow-up assessment. Significance was seen with HAMD from 23.04 to 5.75 ($p < 0.001$), HAMA from 20.11 to 5.43 ($p < 0.001$), CGI-S from 4.39 to 1.86 ($p < 0.001$) and CGI-I from 4.00 to 1.56 ($p < 0.001$) Repeated measures ANOVA for 50%, 75%, and 90% symptom reduction occurred at 8, 18, 48 days, respectively.

Conclusion: Among Hispanic women, paroxetine CR was an effective treatment for anxiety and depressive symptoms.

References:

1. Lopez S: The Mental Health Needs of Hispanics in the United States. Presented at the National Congress for Hispanic Mental Health, March 2000. Retrieved from www.mentalhealth.org/cmhs/SpecialPopulations/HispmHCongress2000/appendice1.
2. The Health of Minority Women. Office on Women's Health, US Department of Health and Human Services, 2003. Retrieved from <http://www.4woman.gov/owh/minority/minority.pdf>.

NR598 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Risk Factors for Suicide Attempts Among Korean Adolescents

Supported by the Asan Institute for Life Science Hun-Soo Kim, M.D., *Department of Psychiatry, Asan Medical Center, University of Ulsan College of Medicine, 388-1 Poongnap-2dong Songpa-gu, Seoul 138-736, South Korea*; Hyun Sil Kim, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the rate, relevant variables, and risk factors for suicide attempt among Korean adolescent and contribute to developing culture-sensitive strategy for suicide prevention.

Summary:

This study examined the rate and relevant variables of suicide attempt and also identified risk factors for suicide attempt among Korean adolescents. The results showed that the rate of suicide attempt was 11.3%, and delinquent adolescents reported a higher rate of suicide attempt than did student adolescents. Adolescent suicide attempters showed higher levels of dysfunctional family dynamics and maladaptive personality. In addition, adolescent suicide attempters expressed a significantly lower level of life satisfaction and fewer effective coping strategies, compared with the nonattempt adolescents. Logistic regression analysis revealed that five predictive risk factors were statistically significant: psychosomatic symptoms, parent-child relationship, coping strategy, parental child-rearing pattern, and depression in this order at a p value of < 0.05 .

References:

1. Beautrais AL: Risk factors for suicide and attempted suicide among young people. *Australian and New Zealand Journal of Psychiatry* 2000; 34: 420-436.
2. Fergusson DM, Woodward LJ, Horwood LJ: Risk factors and life processes associated with the onset of suicidal behavior during adolescence and early adulthood. *Psychological Medicine* 2000; 30:23-39.

NR599 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Incestuous Experience Among Korean Adolescents

Supported by the Asan Institute for Life Science

Hun-Soo Kim, M.D., *Department of Psychiatry, Asan Medical Center, University of Ulsan College of Medicine, 388-1 Poongnap-2dong Songpa-gu, Seoul 138-736, South Korea*; Hyun Sil Kim, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the incidence, family dynamics, and psychological characteristics of adolescent incest victims, and contribute to developing a preventive intervention for incest victims.

Summary:

The aim of this study was to identify the incidence of incest among Korean adolescents and to determine the family problems and perceived family dynamics associated with incest and the psychological consequences to adolescent incest victims in South Korea. A cross-sectional study using anonymous, self-reporting questionnaires was performed. Statistical methods used for this study were percentage, chi-square, and t-test. A total of 1,838 adolescents selected by a proportional stratified random sampling method participated in this study. The results showed an incidence of incest of 3.7%. In families in which incest occurred, there was a higher level of family problems, such as family members with

psychotic disorders, depression, criminal acts, and alcoholism. The perceived family dynamics in families having adolescent victims of incest were more dysfunctional and unhealthy, and the psychological characteristics of these incest victims showed more maladaptive and problematic patterns than those of the nonvictimized adolescents.

References:

1. Berliner L, Elliott DM: Sexual abuse of children, in *The APSAC Handbook on Child Maltreatment*, 2nd ed. Myers JEB, Berliner L, Briere J, Hendrix CT, Reid T, Jenny C, eds. Newbury Park, CA, Sage Publications, 2002, pp 55-78.
2. Haj-Yahia MM, Tamish S: The rate of child sexual abuse and its psychological consequences as revealed by a study among Palestinian university students. *Child Abuse & Neglect* 2001; 25: 1303-1327.

NR600 Wednesday, May 25, 12:00 p.m.-2:00 p.m. **Psychiatric Disorders in a Dutch Health Area: A Repeated Cross-Sectional Survey**

Cees A. Th. Rijnders, M.D., *Department of Psychiatry, GGzMB, Postbox 770, Tilburg 4941AN, Netherlands*; Paul P.G. Hodiament, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate an understanding of the secular trends, emerging from this unique material, on the prevalence and distribution of psychiatric disorders and its implications for mental health policy and care.

Summary:

Objective: A century of psychiatric epidemiology has shown a wide variation in prevalence rates, but a consistent relationship between psychiatric disorder and sociodemographic variables. In this repeated cross-sectional survey, the prevalence of psychiatric disorders and their distribution in the general population of the same area was assessed in 1983 and 1997, using basically the same clinical, semistructured interview.

Methods: With an interval of 14 years, two two-phase studies of psychiatric prevalence were carried out among the inhabitants of a Dutch Health Area (Nijmegen). In phase 1, a random sample of persons answered the GHQ-30. In phase 2, the respondents were interviewed using the full PSE-9 in 1983 and the SCAN/PSE-10 in 1997. After conversion of PSE-10 data into PSE-9 terms, the relationship between PSE "caseness" and the GHQ score was expressed in a logistic regression model, yielding a point-prevalence of PSE cases and a distribution of these cases over a number of sociodemographic variables.

Results: The prevalence of PSE cases was estimated at 7.8% ($\pm 2.3\%$) in 1983 and at 11.9% ($\pm 2.7\%$) in 1997. This increase was mainly due to a rise in the rates of depression and anxiety disorders. In 1997, higher case rates were found in the age category of 50-54 years (as against the age category of 55-59 years in 1983), among women (whereas prevalence did not differ significantly in men and women in 1983), and (as in 1983) among divorced persons, the lower educational and occupational levels, the unemployed, the chronically ill, and those unable to work. The striking effect of urbanization on the prevalence of psychiatric disorders in 1983 was confirmed in 1997. However, the aim to ensure identical measuring instruments and designs in 1983 and 1997 could not completely be achieved.

Conclusions: In the course of time, psychiatric prevalence increased in all sociodemographic categories, despite the improved socioeconomic conditions in the survey population as a whole. The increasing complexity of life apparently takes its toll, even of the socially best equipped.

The Prevention Foundation and the Ministry of Health, Welfare, and Sport provided the resources for the data collection of the Nijmegen Health Area 2 Project.

References:

1. Hodiament PPG, Peer N, Syben N: Epidemiological aspects of psychiatric disorder in a Dutch health area. *Psychol. Med* 1987; 17: 495-505.
2. Hodiament PPG, Rijnders CATH, Mulder J, Furer JW: Psychiatric disorders in a Dutch health area: a repeated cross-sectional survey. *Journal of Affective Disorders* 2005; 84: 77-83.

NR601 Wednesday, May 25, 12:00 p.m.-2:00 p.m. **The Incidence of Axis I Disorders in A Clinical Sample of Obese Patients**

Irem Yalug, M.D., *Department of Psychiatry, Kocaeli University Medical Faculty, Gardenya 5/5B Daire: 40 Atasehir, Istanbul, Turkey*; Ali Evren Tufan, M.D., Ayten Erdogan, M.D., Mine Ozmen, M.D., Volkan Yumuk, M.D.

Educational Objectives:

At the conclusion of this session the participant should be able to recognize the importance of psychiatric examination in obese patients.

Summary:

Objective: The relationship between obesity and psychological health remains unclear. Obese individuals who present themselves for weight treatment are more frequently found to have associated psychopathology. This study was designed to clarify the incidence of axis I disorders in an obese population undergoing treatment in a tertiary care unit.

Methods: This is a cross-sectional study that evaluated the 169 patients being followed for treatment of obesity in Istanbul University Cerrahpasa Medical Faculty Department of Endocrinology for comorbid psychopathology by means of structured interviews (SCID I). Patients with BMI > 25.0 are defined as obese and those with BMI between 25.0 and 29.9 are defined as stage I, the remainder being stage II. Data were analyzed with descriptive statistics and chi-square tests. P is set at 0.05.

Results: The ratio of psychopathology, which was 33.3% in BMI stage I group and 44.2% in BMI stage II group, did not differ significantly between groups. It consisted mainly of anxiety disorders and depression.

Conclusion: Our findings clearly indicate that there is a high comorbidity of psychiatric disorders in obese patients, especially for depressive and anxiety disorders. These findings support the importance of a psychiatric examination in addition to the medical in obese patients.

References:

1. Brownell KD, Wadden TA: Obesity, in Kaplan and Sadock's *Comprehensive Textbook of Psychiatry*. Edited by BJ Sadock, VA Sadock, Philadelphia, Lippincott Williams and Wilkins, 2000; pp 1787-1797.
2. Lee L, Shapiro CM: Psychological manifestations of obesity. *J Psychosom Res* 2003; 55:477-479.

NR602 Wednesday, May 25, 12:00 p.m.-2:00 p.m. **Prevalence of Metabolic X-Syndrome in Taiwan Among Patients With Chronic Schizophrenia**

Tsuo-Hung Lan, M.D., *Department of Psychiatry, Yu-Li Hospital, DOH, 448 Chung-Hwa Road, Yu-Li, Hualien 981, Taiwan*; Hsien-Jane Chiu, M.D., Tzong-Ming Hwu, M.D., Fang-Yeh Chu, M.D., Hsiao-Ru Sun, M.D., Jiann-Jyh Chen, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to realize that schizophrenic patients constitute a high-risk population for metabolic X syndrome.

Summary:

Objective: To assess the prevalence of syndrome X among schizophrenic patients in Taiwan.

Methods: This is a multicenter, investigator-initiated, naturalistic study project. A total of 250 inpatients (132 M, 118 F) meeting DSM-IV criteria for schizophrenia or schizoaffective disorder from two Taiwan-based psychiatric hospitals were enrolled. All subjects were evaluated for syndrome X using laboratory and clinical assessments after a consent form was completed.

Results: A total of 29.8% of the schizophrenic patients met the criteria for the syndrome X, 24.3% met the criteria of overweight, and another 29.6% fulfilled the obesity level; 58.5% of the sample showed higher than 1.7 HOMA scale, suggesting the insulin resistance trait.

Conclusions: This study indicates that schizophrenic patients indeed have a higher prevalence of syndrome X in Taiwan.

References:

1. Chrousos GP: The role of stress and the hypothalamic-pituitary-adrenal axis in the pathogenesis of the metabolic syndrome: neuro-endocrine and target tissue-related causes. *International Journal of Obesity and Related Metabolic Disorders* 2000; 24(Suppl 2):S50-5.
2. Lopez-Candales A: Metabolic syndrome x: a Comprehensive review of the pathophysiology and recommended therapy. *Journal of Medicine* 2001; 32(5): 283-300.

NR603 Wednesday, May 25, 12:00 p.m.-2:00 p.m. Serum Cholesterol and Leptin Levels in Suicide Attempters

Kang J. Lee, Ph.D., *Department of Psychiatry, Inje University, Ilsan Paik Hospital, 2240, Daewha-dong, Ilsan-gu, Gyeonggi-do, Goyang-si 411-706, South Korea*; Jung S. Choo, M.D., Hyun Kim, Ph.D., Young C. Chung, Ph.D., Jae S. Park, Ph.D.

Educational Objectives:

At the conclusion of presentation, the participant should be able to recognize the clinical applicability of low serum cholesterol and leptin levels as an indicator of suicide risk and to discuss the association between serum cholesterol, leptin levels, and the severity of suicide attempt.

Summary:

Objective: Cholesterol-lowering treatment may increase the risk of death due to suicide or impulsive-aggressive behavior. The aim of this study was to examine the association between serum lipid level and violence of suicidal attempt.

Method: In this study, serum total cholesterol and leptin levels were compared in 25 suicide attempters and 24 healthy control subjects. The study consisted of 25 patients with suicide attempts who had been admitted to the emergency room of the Ilsan Paik hospital between March and August 2004. A semistructured interview was carried out in order to establish DSM-IV diagnosis. Violence of suicide attempt was evaluated by the Risk-Rescue Rating (RRR). To determine serum lipid level, venous blood samples were obtained at 08:00 a.m. after NPO during eight hours.

Results: Serum cholesterol levels were decreased in 16 patients and in one control subject. The leptin levels were decreased in 15 patients and in one control subject. The mean cholesterol and leptin levels of the patients were significantly lower than that of the control subjects ($p < 0.05$). RRR score was negatively correlated with serum cholesterol and leptin levels.

Conclusion: Suicide attempters have a decrease in serum cholesterol and leptin levels, compared to control subjects, and a negative correlation between serum lipid level (serum cholesterol and leptin) and violence of suicide attempt.

References:

1. Kim YK, Lee HJ, Kim JY, Yoon DK, Choi SH, Lee MS: Low serum cholesterol is correlated to suicidality in a Korean sample. *Acta Psychiatr Scand* 2002; 105(2):141-148.
2. Kunugi H, Takei N, Aoki H, Nanko S: Low serum cholesterol in suicide attempters. *Biol Psychiatry* 1997; 41(2):196-200.

NR604 Wednesday, May 25, 12:00 p.m.-2:00 p.m. Course of PTSD and Depression in Battle-Injured Soldiers

Thomas A. Grieger, M.D., *Department of Psychiatry, Uniform Services University Health System, 4301 Jones Bridge Road, Bethesda, MD 20814*; Stephen Cozza, M.D., Charles Engel, M.D., Charles Hoge, M.D., Patricia Martinez, R.N., Harold Wain, Ph.D., Robert J. Ursano, M.D.

Educational Objectives:

At the end of this presentation, participants should be able to discuss the variable courses of posttraumatic stress disorder (PTSD) and depression in battle injured soldiers and describe the limitations of early screening in predicting PTSD or depression six months later among battle injured soldiers.

Summary:

Objective: Much is known of the long-term consequences of exposure to combat and injury during combat, but little is known of the early course of posttraumatic stress disorder (PTSD) and depression in battle injured soldiers.

Methods: Injured soldiers requiring extended hospitalization ($N = 444$) were screened for PTSD and depression during hospitalization and six months later using the PCL-17 and PHQ-9.

Results: Twenty-two soldiers (5%) met the criteria for PTSD during initial evaluation; 10 (45%) of this group no longer met the criteria at follow-up. At follow-up 61 soldiers (14%) met the criteria for PTSD; 49 (80%) of this group had not met the criteria during initial evaluation. Twenty-one soldiers (4.7%) met the criteria for depression during initial evaluation; 13 (62%) of this group no longer met the criteria at follow-up. At follow-up 42 soldiers (10%) met the criteria for depression; 36 (86%) of this group had not met the criteria during initial evaluation.

Conclusions: These findings indicate variable courses of development and remission of PTSD and depression in battle injured soldiers. Of those who met the criteria for either condition during initial evaluation, approximately half had remission six months later. The large percentage who met the criteria at follow-up, but not at initial evaluation, demonstrates significant limitations of early screening.

References:

1. Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, Koffman RL: Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *N Engl J Med* 2004; 351(1):13-22.
2. Helzer JE, Robins LN, McEvoy L: Post-traumatic stress disorder in the general population: findings of the Epidemiologic Catchment Area survey. *N Engl J Med* 1987; 317(26):1630-4.

NR605 Wednesday, May 25, 12:00 p.m.-2:00 p.m. Relationship of Spiritual Values and Worship Frequency to Psychiatric Disorders in Canada

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Saskatoon S7N 0W8, Canada; Rudy Bowen, M.D., Ronald Griffin, Ph.D.

Educational Objectives:

At the conclusion of this session participants should be able to:
1) understand the association of worship frequency and importance of spiritual values with select DSM-IV psychiatric disorders;
2) appreciate that nuances in the definitions of religion/spirituality and factors such as the person and their motives, type of stress; may affect the outcome of research.

Summary:

Objective: The subject of religion/spirituality has only recently been included in determining risk and protective factors for psychiatric disorders. Even more recently, attempts have been made to separate positive and negative effects of the broad topic of religion and spirituality. This study examined the relationship of worship frequency and the importance of spiritual values to prevalence of DSM-IV psychiatric and substance use disorders.

Methods: Data were obtained from 37,000 respondents over the age of 15 from the Canadian Community Health Survey Cycle 1.2, Mental Health and Well-Being, collected in 2002. Odds ratios for one-year and lifetime rates of psychiatric disorders were determined, with worship frequency and spiritual values as predictors, controlling for demographic features.

Results: Higher worship frequency was associated with lower rates of psychiatric disorders. In contrast, higher spiritual values were associated with higher odds of some disorders (mood, social anxiety, and agoraphobia) and lower rates of others (panic and addictive).

Conclusions: This study confirmed the association of higher worship frequency with lower depression and expanded it to other psychiatric disorders. The relationship of spiritual values to mood, anxiety, and addictive disorders is complex.

References:

1. Kendler KS, Liu XQ, Gardner CO, McCullough ME, Larson D, Prescott CA: Dimensions of religiosity and their relationship to lifetime psychiatric and substance use disorders. *Am J Psychiatry* 2003; 160:496-503.
2. Pargament KI: The bitter and the sweet: an evaluation of the costs and benefits of religiousness. *Psychological Inquiry* 2002; 13:168-181.

NR606 Wednesday, May 25, 12:00 p.m.-2:00 p.m. Caregiver Stigma About Mental Illness in Bipolar Disorder

Jodi M. Gonzalez, Ph.D., *Department of Psychiatry, UT Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78229*; Deborah Perlick, Ph.D., Melissa Hernandez, B.S., Richard Kaczynski, Ph.D., Charles Bowden, M.D., Michael Ostacher, M.D., Robert A. Rosenheck, M.D.

Educational Objectives:

At the conclusion of this session, participants should be able to identify caregiver, patient, and illness factors associated with stigma perceptions in caregivers of bipolar disorder individuals.

Summary:

Objective: Little is known about the correlates of mental illness stigma among caregivers of individuals with bipolar disorder.

Methods: In a cross-sectional design, 500 caregivers of MINI-diagnosed bipolar disorder patients were investigated, using a structured interview to evaluate perceived stigma and related constructs. Psychiatrists rated patient clinical status over the previous year by calculating the number of days well, a measure based on DSM-IV criteria for mood episodes. Patients were classified as well if they were judged not to be in a mood episode for at least

three-quarters of the previous year and as not well if they were in a mood episode more than one-quarter of the year. We examined associations separately by patient clinical status using multivariate models.

Results: In the well group, greater perceived mental illness stigma was associated with the caregiver being a child, having a college education, fewer weekly social network interactions, and female bipolar disorder patients. In the not well group, greater stigma was associated with caregivers of Latino ethnicity, fewer weekly social network interactions, less perceived social support, taking psychotropic medications, and any previous hospitalization of the bipolar disorder in patient.

Conclusions: Mental illness stigma is prevalent among caregivers in bipolar disorder, and its correlates differ depending on prior year clinical status.

Support by NIMH STEP-BD N01MH80001 and NIMH FES R01MH65015

References:

1. Struening EL, Perlick DA, Link BG, Hellman F, Herman D, Sirey JA: Stigma as a barrier to recovery: the extent to which caregivers believe most people devalue consumers and their families. *Psychiatr Serv* 2001; 52: 1633-1638.
2. Tsang HW, Tam PK, Chan F, Cheung WM, Chang WM: Sources of burdens on families of individuals with mental illness. *Int J Rehabil Res* 2003; 26: 123-130.

NR607 Wednesday, May 25, 12:00 p.m.-2:00 p.m. Factors Affecting the Need and Use of Child Mental Health Service in South Korea

Yunmi Shin, M.D., *Department of Psychiatry, Ajou University School of Medicine, San 5 Wonchon-Dong, Paldal-Gu, Suwon, AK 442-721, South Korea*; Sunmi Cho, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to demonstrate that an understanding of factors related to child mental health referral and service utilization is valuable for designing new intervention programs.

Summary:

Objective: Population-based studies have consistently found that only a minority of children with mental health problems attend specialist mental health services. This study examined patterns of mental health service use and factors associated with help seeking behavior.

Method: In a community sample of 3,798 children age 7-13 years registered in South Korea, perceptions of need, preference of service, and psychiatric disturbance were measured. To take into account the overlapping correlations, multivariate analysis of association between family and child variables and outcome variables was performed with stepwise logistic regression analysis.

Results: Parents of 396 (10.4%) children reported that their child needed mental health services. Parents of 90 (2.4%) children reported that their child used mental health services. The most potent factors associated with service need and utilization were the children's total problem, male gender, and socioeconomic factors. The preferred source for help with the child's problems was the spouse, friends, relatives.

Conclusions: This community-based study distinguished between various factors that are associated with referral to specialist child mental health services. Key predictors of service use were parental perception that children had emotional and behavioral problems, male gender, and socioeconomic conditions.

References:

1. Sourander Ar: Have there been changes in children's psychiatric symptoms and mental health service use? A 10 year comparison from Finland. *J Am Acad Child Adolesc Psychiatry* 2004; 43: 1134-1145.
2. Wu P, et al: Factors associated with use of mental health services for depression by children and adolescents *Psychiatric Services* 2001; 52:189-195.

NR608 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

The Reliability and Validity of Korean Version of WHOQOL-BREF in Cancer Patients

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Educational Objectives:

At the conclusion of this session, the participant should understand that quality of life is an appropriate measurement of outcome for many diseases, including cancer.

Summary:

Objective: This study was designed to investigate the reliability and validity of the Korean version of the WHOQOL-BREF in cancer patients.

Methods: One hundred cancer patients (50 patients with stomach cancer and 50 patients with breast cancer) were recruited with informed consent. Age and gender matched hospital staff served as control subjects. The 100-item Korean version of WHOQOL instrument was used with all subjects. The scores of the WHOQOL-BREF, a short version (26 questions) of the WHOQOL-100, which includes four domains (physical, psychological, social, and environmental domains), were compared with those of the WHOQOL-100.

Results: Adequate internal consistency with Cronbach's alpha was demonstrated in physical (0.794), psychological (0.781), and environmental domains (0.830), but not in the social domain (0.554). The scores on the WHOQOL-BREF were significantly correlated with those on the WHOQOL in all domains.

Conclusions: The Korean version of the WHOQOL-BREF is a reliable and useful instrument for evaluating quality of life in cancer patients.

References:

1. The WHOQOL Group: The World Health Organization Quality of Life Assessment (WHOQOL): development and general psychometric properties. *Soc Sci Med* 1998; 46(12):1569-1585.
2. The WHOQOL Group: Development of the World Health Organization WHOQOL-BREF Quality of Life Assessment. *Psychological Medicine* 1998; 28:551-558.

NR609 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Development and Validation of a Korean Version of the Levels of Emotional Awareness Scale

Jungjae Lee, M.Med., *Department of Psychiatry, National Bugok Hospital, 70 Bugok-ri Bugok-myeon, Changnyeong-gun, Gyeongsangnam 635-893, Korea*; Sang-Heon Kim, M.D., Hyo-Deog Rim, M.D., Yang-Hyun Lee, M.D., Sung-Hoon Jeong, M.D., Dohoon Kwon, M.D., Sungnam Cho, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that a Korean version of a levels of emotional

awareness scale is independent of depressed mood and has high reliability and validity in Korean culture.

Summary:

Objective: The purpose of this study was to develop a Korean version of the Levels of Emotional Awareness Scale (LEAS-K) and to examine its validity and reliability.

Method: LEAS was translated into Korean with the help of English and Korean language experts. The subjects were 476 Korean medical students (322 males and 154 females). The internal consistency was evaluated with the Cronbach's alpha coefficient, and 40 protocols were independently scored by two raters to confirm interrater reliability. In addition, to evaluate concurrent validity the following were rated in the Korean version: the 20-item Toronto Alexithymia Scale (TAS-20K), the Openness to Experience Inventory (OE), the Marlowe-Crowne Scale (MCS), the Bending short form of the Taylor Manifest Anxiety Scale (TMAS), the Emotional Expressivity Scale (EES), and the Beck Depression Inventory (BDI).

Results: The internal consistency measured by Cronbach's alpha was 0.81 and interrater reliability was high at $r(40) = 0.99$. Correlation coefficients were insignificant with TMAS, EES, and BDI. LEAS-K correlated significantly with TAS-20K ($r[476] = -0.10$, $p < 0.05$), OE ($r[476] = 0.10$, $p < 0.05$) and MCS ($r[476] = 0.10$, $p < 0.05$).

Conclusions: LEAS-K was demonstrated to be independent from depressive mood, has high reliability and validity, and can be applied to assessment and treatment of psychosomatic patients in Korean culture.

References:

1. Lane RD, Schwartz GE: Levels of emotional awareness: a cognitive-developmental theory and its application to psychopathology. *Am J Psychiatry* 1987; 144:133-43.
2. Lane RD, Quinlan DM, Schwartz GE, Walker PA, Zeitlin SB: The Levels of Emotional Awareness Scale: a cognitive-developmental measure of emotion. *J Pers Assess* 1990; 55:124-34.

NR610 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Fetal Alcohol Syndrome and Related Mother-Pattern Drinking

Supported by the French Society on Alcoholism (SFA)

Ingrid de Chazeron, *Department of Psychiatry B, Chu Clermont-Fd, Rue Montalembert BP69, Clermont-Ferrand 63003, France*; Didier Boussiron, M.D., Vincent Sapin, Pharm.D., Françoise Vendittelli, M.D., Raymund Schwan, M.D., Didier Lemery, M.D., Pierre-Michel Llorca, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to estimate fetal alcohol syndrome (FAS) prevalence in France and to evaluate and identify the different alcohol consumption behaviors that could lead to FAS.

Summary:

Objectives: Children alcohol-exposed during pregnancy are at risk to develop many pathologies. One of the most serious is fetal alcohol syndrome (FAS). The main aim of this work was to study FAS prevalence and to relate it to maternal drinking patterns during pregnancy.

Method: All maternity hospitals located in central France were contacted during one month. GammaGT, ASAT, ALAT, and CDT were assayed in maternal cord blood. Each delivered woman filled out AUDIT questionnaires, and newborns' data were documented.

Results: A total of 1,131 births were registered. The prevalence of FAS was 1.8%. One pattern of concern was represented by a woman who has an AUDIT score for borderline to hazardous

alcohol use and declares regular alcohol consumption. She has no positive aminotransferase but lightly positive GammaGT. Another pattern is represented by a woman who has binge alcohol drinking (but cannot be considered a hazardous drinker according to the AUDIT score); strongly positive ASAT and GammaGT might underlie chronic alcoholism. They both have normal CDT values.

Conclusion: FAS prevalence is consistent with others findings. This study suggests that there is no simple consumption pattern that induces FAS: the amount of alcohol consumed on each occasion and its frequency will be predictive of infant outcome. Laboratory tests and self-questionnaires may together provide better accuracy for consumption history.

References:

1. Dehaene P, Crepin G, Delahousse G, Querleu D, Walbaum R, Titran M, Samaille-Villette C: Epidemiological aspects of the foetal alcoholism syndrome: 45 cases. *Nouv Presse Med* 1981; 10:2639-43.
2. Neumann T, Spies C: Use of biomarkers for alcohol use disorders in clinical practice. *Addiction* 2003; 98 Suppl 2:81-91.

NR611 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

A French Study of Alcohol and Tobacco Use in Pregnant Women

Supported by the French Society on Alcoholism (SFA)

Ingrid de Chazeron, *Department of Psychiatry B, Chu Clermont-Fd, Rue Montalembert BP69, Clermont-Ferrand 63003, France*; Didier Boussiron, M.D., Laurent Malet, M.D., Raymund Schwan, M.D., Didier Lemery, M.D., Pierre-Michel Llorca, M.D.

Educational Objectives:

At the conclusion of this session, the participants should be able to realize that many women still consume alcohol and tobacco during pregnancy although abstinence is recommended. Moreover many women request help to stop smoking.

Summary:

Objectives: Harmful effects of alcohol and tobacco during pregnancy result in fetal damage sometimes identified only after the child goes to school. The aim of this work was to evaluate the prevalence of alcohol and tobacco parturient consumption using self-questionnaires.

Method: Seventeen maternity hospitals located in central France were contacted during one month. Each delivered woman filled out AUDIT, Fagerström questionnaires, and alimentary habits questions.

Results: A total of 1,050 mother-infant dyads were included. After pregnancy diagnosis, 47.4% continued alcohol use, 11.3% declared consumption two to four times/month, 2.5% two or more times/week, 0.3% of AUDIT scores indicated hazardous or harmful alcohol use, and 7% reported binge drinking. A total of 21.8% smoked vs 37.9% prior to pregnancy; 68.6% of cessations are during the first trimester. Fagerström results revealed that 7.1% have at least a high degree of dependence. At the time of evaluation, 39.6% would like to stop smoking and 42.5% to reduce; 67.9% wish to stop with medical support.

Conclusion: Despite WHO's recommendations, alcohol use during pregnancy is more extensive than supposed. Tobacco prevalence is stable among parturients, but their smoking behavior seems to be complex. Their requests for help to stop smoking suggest the need for specific prevention programs.

References:

1. Blanchon B, Parmentier M, Colau JC, Dautzenberg B, Blum-Boisgard C: Smoking and pregnancy survey among women

enrolled in an independent worker insurance program. *J Gynecol Obstet Biol Reprod* 2004 33:21-9.

2. Goransson M, Magnusson A, Bergman H, Rydberg U, Heilig M. Fetus at risk: prevalence of alcohol consumption during pregnancy estimated with a simple screening method in Swedish antenatal clinics. *Addiction* 2003 98(11):1513-20.

NR612 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Tri-Ethnic Differences in Symptom Remission During the Long-Term Treatment of Patients With Schizophrenia

Supported by Eli Lilly and Company

Rodrigo A. Munoz, M.D., *Department of Psychiatry, University of California at San Diego, 3130 Fifth Avenue, San Diego, CA 92103*; Baojin Zhu, Ph.D., Haya Ascher-Svanum, Ph.D., Douglas Faries, Ph.D., Concepcion Barrio, Ph.D., Richard Hough, Ph.D., Ann-Marie Yamada, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that during the long-term treatment of schizophrenia patients, ethnic differences appear to differentially impact the likelihood of achieving depressive or psychotic symptom remission.

Summary:

Objective: Achieving symptomatic remission is an important goal in the treatment of schizophrenia, which may be influenced by ethnic differences in illness phenomenology. This study assessed differences between three ethnic groups—Euro Americans, African Americans, and Latinos—in remission of depressive symptoms, remission of psychotic symptoms, or remission of both depressive and psychotic symptoms.

Method: Data were drawn from a large (N = 2,327) multicenter naturalistic three-year prospective study of patients with schizophrenia. Four types of symptom remission were identified at enrollment and at 12-month intervals thereafter: remission of psychotic symptoms (using the Remission in Schizophrenia Working Group expert consensus criteria), remission of depressive symptoms (score of 9 on the Montgomery-Asberg Depression Rating Scale), remission of both psychotic and depressive symptoms, and nonremitted status. Using a Generalized Estimating Equation (GEE) model, adjusted for clinical and sociodemographic characteristics, the ethnic groups were compared on the proportion of patients achieving each type of remission across the three-year study.

Results: Latinos (N = 222) were more likely to experience remission of psychotic and depressive symptoms than Euro American (N = 1,099) or African American (N = 817) patients (p < .01). African American patients were least likely to experience remission of psychotic symptoms (p < .001). Latino patients were more likely to experience remission of depressive symptoms, compared to Euro American (p = .03), with no other significant group differences.

Conclusions: In the long-term treatment of schizophrenia patients, ethnic differences appear to differentially impact the likelihood of achieving depressive and/or psychotic symptom remission.

References:

1. Barrio C: Culture and schizophrenia: a cross-ethnic growth curve analysis. *J Nerv Ment Dis* 2001; 189(10):676-84.
2. Barrio C, Yamada AM, Atuel H, Hough RL, Yee S, Berthot B, Russo PA. A tri-ethnic examination of symptom expression on the positive and negative syndrome scale in schizophrenia spectrum disorders. *Schizophr Res* 2003; 60(2-3):259-69.

NR613 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Polysomnography and Outpatient Study to Determine the Efficacy of Ramelteon in Adults With Chronic Insomnia

Supported by Takeda Pharmaceuticals

Gary Zammit, Ph.D., *Sleep Disorders Center, CliniLabs-St. Luke's/Roosevelt Hospital, 1090 Amsterdam Ave., New York, NY 10025*; Thomas Roth, Ph.D., Milton Erman, M.D., Stephen Sainati, M.D., Sherry Weigand, M.D., Jeff Zhang, M.S.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that ramelteon, a novel selective melatonin MT1/MT2 receptor agonist under development for the treatment of insomnia, has significant sleep-promoting effects in patients with chronic insomnia, with no rebound insomnia or withdrawal effects.

Summary:

Objective: To evaluate the efficacy of ramelteon, a novel selective MT1/MT2 receptor agonist, in patients with chronic insomnia.

Methods: In this 35-night double-blind study, 405 adults (mean age, 39.3 years) with insomnia took ramelteon 8 or 16 mg or placebo every night. Patients were evaluated in the sleep laboratory on nights 1-2, 15-16, 29-30, and 36-37 with polysomnography (PSG) and a Post-sleep Questionnaire (PSQ) and at home all other nights by means of a sleep diary. Placebo was given on nights 36-37 to evaluate possible rebound insomnia and withdrawal effects.

Results: A statistically significant reduction in mean latency to persistent sleep was observed with ramelteon 8 and 16 mg vs. placebo, as measured by PSG: nights 1-2 (32.2 and 28.9 vs. 47.9 minutes; $p < 0.001$), nights 15-16 (32.6 and 27.9 vs. 45.5 minutes; $p < 0.001$), and nights 29-30 (31.5 and 29.5 vs. 42.5 minutes, $p = 0.003$). Ramelteon resulted in statistically significant improvements in total sleep time and sleep efficiency on nights 1-2. Subjective results were supportive of PSG data. No rebound insomnia or withdrawal effects were observed. Adverse event rates were similar for all treatment groups.

Conclusion: Ramelteon 8 and 16 mg significantly reduced latency to persistent sleep in patients with chronic insomnia, with no rebound insomnia or withdrawal effects.

References:

1. Roth T, Walsh J: Phase II study of the selective ML-1 receptor agonist TAK-375 in a first night effect model of transient insomnia. *Sleep* 2003; 26:A294.
2. Erman M, Seiden D, Zammit G: Phase II study of the selective ML-1 receptor agonist TAK-375 in subjects with primary chronic insomnia. *Sleep* 2003; 26:A298.

NR614 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Post-Deployment Distress in Medical Personnel Following Combat Deployment

Tonya T. Kolkow, M.D., *Mental Health Services, Naval Medical Center San Diego, 34800 Bob Wilson Drive, San Diego, CA 92134-5000*; Thomas Grieger, M.D., Jennifer Morse, M.D., James Spira, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to discuss the occurrence of depressive and posttraumatic symptoms in military medical personnel who have served in combat deployments, compared to medical personnel who have not deployed.

Summary:

Objective: Rates of posttraumatic stress disorder (PTSD) in combat troops returning from war are 15-20%. Less is known about the effects of war on medical personnel who are assigned within the combat theater.

Methods: Staff at one hospital sending personnel to the combat theater were provided a voluntary anonymous survey that included demographic information and questions about recent deployments and current symptoms of PTSD and depression (using PCL-17 and PHQ-9).

Results: One-hundred-eighty-eight responses were collected. Fifty-six (30%) reported a recent combat support deployment. Eight respondents (4%) met the full criteria for PTSD, 13 (7%) met partial criteria for PTSD, and five respondents (3%) met the criteria for depression. Of those who had deployed, 11% met the criteria for PTSD, compared to 2% who met the criteria among those who did not deploy (Fisher's Exact Test $p = 0.009$). After controlling for gender, age, race, and educational level, those with a combat support deployment were 6.61 times more likely to have PTSD than those who did not deploy (95% CI = 1.09-40.20, $p = 0.04$). There was no association between deployment and presence of depression.

Conclusions: These findings demonstrate that deployed medical personnel exposed to wounded or concerned for their own injury have rates of PTSD similar to those of returning combat soldiers.

References:

1. Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, Koffman RL: Combat duty in Iraq and Afghanistan, mental health problems, and Barriers to Care. *N Engl J Med* 2004; 351:13-22.
2. Slusarcick AL, Ursano RJ, Fullerton CS, Dinneen MP: Stress and coping in male and female health care providers during the Persian Gulf War: the USNS Comfort hospital ship. *Military Medicine* 1999; 164:166-173

NR615 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

National and International Research in the Aftermath of Disasters

Sandro Galea, M.D., *Center for Urban Epidemiologic Studies, New York Academy of Medicine, 1216 Fifth Avenue, New York, NY 10029*; Dean Kilpatrick, Ph.D., Sasha Rudenstine, B.A., Kenneth Ruggiero, Ph.D., Connie Best, Ph.D., Heidi Resnick, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the limitations of post-disaster research and understand how post-disaster mentoring programs can assist researchers in maximizing the quality of research conducted in the aftermath of a disaster.

Summary:

The Disaster Research Education and Mentoring Center (DREM), funded in June 2004 by the National Institutes of Health, works to improve post-disaster research and to facilitate cross study comparison (www.disasterresearch.org). Since DREM inception we have worked with researchers in Madrid after the March 11 train bombings and in Florida following the 2004 hurricanes. A population-based survey of Madrid, using the same survey instrument used in New York City after the September 11 attacks within a comparable time frame, showed that the prevalence of posttraumatic stress disorder (PTSD) one month after the March 11 attacks in Madrid was 1.6%, approximately four times lower than the 7.5% prevalence of PTSD that had been reported in NYC. A second study in Madrid showed that, in a comparable

timeframe, the prevalence of PTSD in (1) a suburb of Madrid where most of the victims lived was 12.3%, (2) among those injured 44.1%, and (3) among police officers who assisted in the attacks 1.3%. These two studies suggest different prevalences of psychopathology among groups differently exposed to disasters. DREM Center collaborations will explore the nature of resilience across cultures and disasters and have the potential to immeasurably advance our understanding of the burden of disasters.

References:

1. Galea S, Ahern J, Resnick H, Kilpatrick D, Bucuvalas M, Gold J, Vlahov D: Psychological sequelae of the September 11 terrorist attacks in New York City. *N Engl J Med* 2002; 346(13):982-7.
2. Galea S, Vlahov D, Resnick H, Kilpatrick D, Bucuvalas M, Morgan M, Gold J: An investigation of the psychological effects of the September 11, 2001, attacks of New York City: developing and implementing research in the acute postdisaster period. *CNS Spectrums* 2002; 7(8): 385-396.

NR616 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Teaching ECT to Medical Students: Results From Viewing Videotape and Live Demonstration

Ronald Warnell, M.D., *Department of Psychiatry, Loma Linda University, PO Box 2340, Redlands, CA 92373*; Anthony Duk, M.D., George Christison, M.D., Mark Haviland, Ph.D.

Educational Objectives:

At the conclusion of this presentation, participants will be able to (1) design an ECT instructional block for medical students and (2) select a teaching method that may produce both knowledge and attitude gains.

Summary:

Objective: To determine the effects of instructional method (live demonstration versus videotape) on medical students' knowledge of and attitudes toward electroconvulsive therapy (ECT).

Method: Medical students (N = 122 in their junior-year psychiatry clerkship) were randomly assigned to either a live ECT demonstration or a 30-minute videotape containing instructional material and a demonstration. At the beginning and the end of the clerkship, knowledge of (20 true-false questions) and attitudes toward (three Likert-type items) ECT were assessed. To evaluate pre- and post-survey differences, we used repeated-measures analysis of variance (ANOVA), one for knowledge and three separate analyses for attitudes ($\alpha = .05$).

Results: Group differences (live versus video) in both the initial and re-administered test were small. In the knowledge ANOVA, the clerkship effect was statistically significant (i.e., post-scores were higher than pre-test scores). The group effect (live versus video), however, was not significant. In the attitudes ANOVAs, the clerkship effect was statistically significant in all three instances, and the group effect was not.

Conclusions: There were statistically significant increases in ECT knowledge and attitudes over the course of the psychiatry clerkship with both instructional groups, with no difference between the two instructional methods.

References:

1. The Practice of Electroconvulsive Therapy: Recommendations for Treatment, Training, and Privileging, 2nd Edition, Washington, DC, American Psychiatric Association, 2001.
2. Duffet R, Lelliott P: Junior doctors training in the theory and the practice of electroconvulsive therapy. *J ECT* 1998; 14(2):127-30.

NR617 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Prevalence and Construct Validity of Personality Disorder Not Otherwise Specified

Supported by the Center of Psychotherapy De Viersprong, The Netherlands

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Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the size and quality of the problem of personality disorder not otherwise specified and gain an insight into the advantages and disadvantages of alternative solutions for DSM-IV Axis II.

Summary:

Objective: Personality disorder not otherwise specified (PDNOS) is one of the most frequently used Axis II diagnoses. However, explicit guidelines for its assessment are lacking. This study examined the prevalence and construct validity of various definitions of PDNOS.

Method: The sample consisted of 1,064 psychotherapy patients. Personality disorders (PDs), including depressive, negativistic, self-defeating, and mixed type, were diagnosed using the Structured Interview for DSM-IV Personality Disorders (SIDP-IV). In addition, a construct validity battery was administered.

Results: Sixty percent had at least one of the 10 formal PDs. In addition, 22% met the criteria for PDNOS. Of these, 35% met the criteria for one or more of the appendix diagnoses, and 83% met the criteria for mixed PD (using cutoff of 10 criteria). Furthermore, we found few differences between those with a formal versus those with appendix or mixed PD in terms of severity of personality pathology, psychiatric symptoms, and social and occupational functioning.

Conclusions: In this large sample representative of psychotherapy patients, PDNOS was the single most prevalent PD (22%) and is characterized by largely similar severity and functional impairments as compared to the 10 formal PDs. The results suggest that DSM-IV lacks sufficient coverage.

References:

1. Verheul R, Widiger TA: A meta-analysis of the prevalence and usage of the personality disorder not otherwise specified (PDNOS) diagnosis. *Journal of Personality Disorders* 2004; 18(4):309-319.
2. Westen D, Arkowitz-Western L: Limitations of Axis II in diagnosing personality pathology in clinical practice. *Am J Psychiatry* 1998; 155:1767-1771.

NR618 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Risk Factors and Prevalence of Psychotic Symptoms in the General Population in Izmir, Turkey

Koksal Alptekin, M.D., *Department of Psychiatry, Medical School of Dokuz Eylul University, 505 Sok No 10/25, Bahcelievler Izmir 35340, Turkey*; Semih Semin, M.D., Berna Akdede, M.D., Gül Ergör, M.D., Yıldız Akvardar, M.D., Yücel Demiral, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the importance of detecting psychotic symptoms and related risk factors in the community.

Summary:

Objective: The aim of this study was to find risk factors and identify prevalence of psychotic symptoms in the general population in Izmir, Turkey.

Methods: The study group consisted of 1,280 adults above 18 years of age. The sample was selected with the systematic sampling method from the residents of the three districts of Izmir with the population of almost 100,000. Data were collected through a face-to-face questionnaire, including information on age, gender, marital status, education, medical history, use of medication, and tobacco, alcohol, and drug use. The Composite International Diagnostic Interview was administered to all the participants.

Results: Psychotic symptoms were found in 3.6% of the study group. In 19 individuals (1.5%) there was one symptom, in 15 (1.2%) two symptoms, and in 12 (1.0%) three or more symptoms were seen. Most frequent symptoms were thought disorder, such as "thoughts are being read by others" (1.4%), delusions of persecution (1%), catatonia (1%), visual hallucinations (0.7%), and olfactory hallucinations (0.7%). Logistic regression analysis showed that being female (OR = 2.4), having a first-degree family history of any mental disorders (OR = 13.9), lack of social support (OR = 4.5), and alcohol use (OR = 4.9) were all related to psychotic symptoms.

References:

1. Van Os J, Hanssen M, Bijl RV, Ravelli A: Strauss (1969) revisited: a psychosis continuum in the general population? *Schizophr Res* 2000; 45: 11-20.
2. Poulton R, Caspi A, Moffitt TE, Cannon M, Murray R, Harrington H: Children's self-reported psychotic symptoms and adult schizophreniform disorder: a 15-year longitudinal study. *Arch Gen Psychiatry* 2000; 57: 1053-1058.

NR619 Wednesday, May 25, 12:00 p.m.-2:00 p.m. Human Salivary Levels of Cortisol, DHEA, and Testosterone

Gerald L. Brown, M.D., *Psychiatric Medicine, University of Virginia, P.O. Box 800623, Charlottesville, VA 22908*; Adrienne Keller, Ph.D.

Educational Objectives:

At the conclusion of this presentation, participants will: 1) understand the methodology and assay techniques for salivary collection of biological markers; 2) be able to discuss the limitations of simple models and the advantages of multifactorial models of biological markers for aggressive behavior.

Summary:

Objective: To demonstrate the feasibility and relevance of using salivary assessments of biological markers to model a complex biological substrate of aggressive behavior.

Method: Five college-age males completed the State-Trait Anger Expression Inventory on enrollment and provided saliva samples at 2000, 0200 and 0800 hours one day per week for three consecutive weeks. Saliva samples were assayed for cortisol (C), dehydroepiandrosterone (DHEA), and testosterone (T).

Results: The pattern of diurnal variation for each individual across the weeks of the study was more stable for C ($F = 0.084$, $df = 2, 8$, $p = 0.92$) than for DHEA ($F = 2.72$, $df = 2, 8$, $p = 0.125$) or T ($F = 0.974$, $df = 2, 8$, $p = 0.418$). Examination of the relationship among C, DHEA, and T and the scales of the State-Trait Anger Expression Inventory provided preliminary evidence of complex interrelationships based on both levels and diurnal variations of all three biological measures.

Conclusions: This small pilot study demonstrated the feasibility of using salivary collection and assays to assess the level and stability of diurnal variation in biological markers and the necessity

of formulating complex models to investigate the relationship between biology and behavior.

References:

1. Brown GL, Linnoila M: CSF serotonin metabolite (5-HIAA) studies in depression, impulsivity, and violence. *J Clin Psychiatry* 1990; 5 (suppl):31-41.
2. Granger DA, Booth A, Johnson DR: Human aggression and enumerative measures of immunity. *Psychosomatic Medicine* 2000; 62:583-590.

NR620 Wednesday, May 25, 12:00 p.m.-2:00 p.m. New Research of Sleep and Dreams: Psychosis and Communication

Nikola Ilankovic, M.D., *Belgrade, Yugoslavia*; Tanja Lakovic, M.D., Andrej Ilankovic, M.D., Vera Ilankovic, Ph.D., Lana Marija Ilankovic, M.A.

Educational Objectives:

At the conclusion of this session the participants should understand the relationships between psychotic future, perturbation of internal sleep organization, and the level of communication capability.

Summary:

Objectives: Clinical and neurophysiological research and measurement of sleep (PSG) was used to investigate models of sleep disturbances in different psychotic states (altered states of consciousness).

Methods: Neurophysiological measurement of sleep (EEG, EOG, EMG, PSG) was done in subjects with psychotic states (depression, mania, schizophrenia) and altered states of consciousness. Scoring of sleep (according Rechtschaffen, Kales), statistical analysis, and estimating of discriminative models of sleep in psychosis and altered states of consciousness was done. The Electrophysiological Profile of Sleep (EPS) is derived from PSG and contained 130 variables of nocturnal sleep. Statistical analysis was by discriminative analysis "step by step." The most discriminative variable was the Index of Endogenous Periodicity/Perturbation (IEP-P1 = REM-1/NREM-1).

Results: 1. The index of Endogenous Perturbation (IEP-P1) was very HIGH (1): in A1. model—"delta deficit type" (with reduction of "delta-sleep") in endogenous depressed, manic, and paranoid states ("hyper-communication states"), IEP-P1 > 2.40; and in A2. model—"REM deficit type" (with REM predomination or absence of "delta-sleep") in delirium and other organic psychotic states ("dyscommunication states"); IEP-P1 > 2.40. 2. or very LOW (2): B model—"REM deficit type" (with reduction of "REM-1 phase") in schizophrenia-like states ("hypo- and a-communication states"), IEP-P1 < 0.3

Conclusions: The results of our investigations demonstrate that the Index of Endogenous Sleep Perturbation (IEP-P1=REM-1/NREM-1) is a highly reliable indicator of the development/regression of endogenous perturbation of sleep in depression, mania, schizophrenia, delusional state, organic brain syndromes, and other psychotic states/altered states of consciousness. The relationship between psychotic future and the level of communication capability may have its origin in perturbation of internal sleep organization.

References:

1. Ilankovic N, Ilankovic A: Sleep, dreams and psychosis. BNPA Annual Meeting, London 2004.
2. Ilankovic N, et al: Consciousness, sleep and dreams, Belgrade Institute of Psychiatry & Medical Faculty, 1999.

NR621 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Simulating the Effect of Antipsychotics on Serotonin and Norepinephrine Homeostasis

Supported by Janssen Pharmaceutica, Inc.

Hugo Geerts, Ph.D., *Computational Medicine, In Silico Biosciences, 686 Westwind Drive, Berwyn, PA 19312*; Athan Spiros, Ph.D., John Dani, Ph.D., Robert Carr

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand that a higher dose does not necessarily give better results.

Summary:

Objective: Many antipsychotics affect dopamine receptors in addition to a considerable number of serotonin (5-HT) and norepinephrine (NE) receptors. This makes prediction of clinical effects related to 5-HT homeostasis almost impossible.

Methods: A computer model based on the available pharmacological interaction between the locus coeruleus and dorsal raphe was constructed. This model includes the functional effect of six different subtypes of 5-HT, dopamine, and NE receptors and neurotransmitter transporters involved in 5-HT release and is validated with reported microdialysis experiments in preclinical models.

Results: The computer model allows reconstruction of the effects of the full dose-response of any antipsychotic on 5-HT release. Due to the complex pharmacology of compounds, the dose-response curve is of an inverse U-shape form, with an optimal dose often different from the maximal tolerable dose. The optimal dose is dependent upon the relative affinities of the drugs for 5-HT and NE receptors, in particular the alpha-1 adrenergic receptor. For example, the model suggests an optimal risperidone dose of 2 mg/day and 200 mg/day for quetiapine, but the decline after the optimum dose is much steeper for risperidone than for quetiapine.

Conclusion: The model helps in understanding the nonlinear pharmacodynamic dose-response of antipsychotics when considering the serotonergic deficit in human depression.

References:

1. Kasper S, Stamenkovic M, Letmaler M, Schreiner D: Atypical antipsychotics in mood disorders. *Int Clin Psychopharmacol* 2002; 17 Suppl 3:S1-10.
2. Siegle GJ, Steinhauer SR, Thase ME: Pupillary assessment and computational modeling of the Stroop task in depression. *Int J Psychophysiol* 2004; 52(1):63-76.

NR622 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Development and Implementation of an Interpersonal and Communication Skills Awareness and Training Program for Psychiatric Residents

Jennifer K. Penberthy, Ph.D., *Psychiatric Medicine, University of Virginia Health System, PO Box 801210, Charlottesville, VA 22908*; Zachariah Dameron, M.D.

Educational Objectives:

At the conclusion of this session, the participant will be able to identify and understand the impact and necessity of teaching effective therapeutic interpersonal and communication skills to resident physicians and will be introduced to an innovative and effective program to maximize the teaching and assessment of this core competency.

Summary:

Objective: Interpersonal and communication skills are listed among the six general competencies promoted by the ACGME and are defined as "the ability to develop a therapeutic relationship with patients and their families; use verbal and nonverbal skills

to communicate effectively with patients and their families; [and] work effectively as a team member or leader." These skills are crucial to the education of residents but have been difficult to quantify, teach, and assess via traditional medical education.

Methods: The presenters propose a program of instruction in interpersonal/communication skills training utilizing interpersonal theory and the Impact Message Inventory (IMI). This program includes assessment and feedback of interpersonal style, education regarding therapeutic styles, and research on impact of style upon patient satisfaction/outcome.

Results: The presenters discuss the results of the resident physicians' interpersonal and communication skills training and assessment program, including the content of the educational, feedback, assessment, and research components, and impact upon patient satisfaction/outcome.

Conclusions: The training and assessment program in interpersonal/communication skills promotes a well-rounded educational experience for resident physicians, as well as provides competency-based training and research quality assessment. This intervention can easily be adapted for use in general medical training.

References:

1. Kiesler DJ, Auerbach SM: Integrating measurement of control and affiliation in studies of physician-patient interaction: the interpersonal circumplex. *Social Science & Medicine* 2003; 57(9), 1707-1722.
2. Auerbach SM, Penberthy AR, Kiesler DJ: Opportunity for control, interpersonal impacts, and adjustment to a long-term invasive health care procedure. *Journal of Behavioral Medicine* 2003; 27 (1): 11-29.

NR623 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Clinical Presentation of Anxious Depression in Primary Care Settings

Francisco J. Arranz, M.D., *Medical Department, Laboratorios Dr. Esteve, S.A., Av. Mare de Déu de Montserrat, 221, Barcelona 08041, Spain*; José Luis Carrasco, M.D., Jousé Antonio Noya, M.D., Alfonso Moreno, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the clinical picture of anxious depression in primary practice settings and to discuss the utility of DSM-IV criteria as a diagnostic tool for depression and anxiety.

Summary:

Objective: To gain knowledge about the clinical picture of anxious depression among primary care patients as a part of a naturalistic study on the effectiveness of sertraline in this disorder.

Methods: Open multicenter pharmacoepidemiologic study with ambulatory patients with a current diagnosis of depressive syndrome based on DSM-IV criteria. Eligible patients should show a high level of anxiety, as demonstrated by a higher score on the Raskin depression scale than on the Covi anxiety scale and a score of at least 8 on both scales.

Results: Four thousand one hundred and nine of 4,308 evaluable patients were included in this analysis. The most frequent diagnosis was depression not otherwise specified (40.2% of cases). The other diagnoses were: dysthymic disorder (23.3%), major depression, single episode (22.7%) or recurrent (9.9%), and bipolar depression (3.2%).

Conclusions: In this study in primary care settings across a large sample of depressive patients with prominent anxiety, most of the cases were given a diagnosis of unspecified depression. These findings question the classificatory usefulness of DSM-IV in this population and reveal the current division between anxiety

and depression as inadequate, giving support to the clinical relevance of the mixed anxiety-depressive disorder.

Supported by Laboratorios Dr. Steve, S.A., Barcelona, Spain

References:

1. Jenkins R, Lewis G, Bebbington P, Brugha T, Farrell M, Gili B, et al: The national psychiatric morbidity surveys of Great Britain: initial findings from the household survey. *Psychol Med* 1997; 27:775-789.
2. Shorter E, Tyrer P: Separation of anxiety and depressive disorders: blind alley in psychopharmacology and classification of disease. *BMJ* 2003; 327:158-160.

NR624 Wednesday, May 25, 12:00 p.m.-2:00 p.m. **Impulse-Control Disorders in Psychiatric Outpatients: Prevalence and Comorbidity**

Christina A. Beccue, B.A., *Department of Psychiatry, Rhode Island Hospital, 235 Plain St. Suite 501, Providence, RI 02905*; Iwona Chelminski, Ph.D., Mark Zimmerman, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to better understand the prevalence and comorbidity of ICDs compared to those of anxiety disorders and substance use disorders in a psychiatric outpatient population.

Summary:

Objective: There are insufficient data on the prevalence and comorbidity of impulse-control disorders (ICD). To our knowledge, there are no studies on a range of ICDs in a heterogeneous sample of psychiatric outpatients using a semistructured diagnostic interview. The present report from the Rhode Island MIDAS project examined: 1) current and lifetime prevalence of nine ICD categories, 2) the likelihood of an ICD as a principal reason for seeking treatment, 3) the desire for treatment of a secondary diagnosis of an ICD, and 4) the differences in rates of comorbidity in ICDs compared to other classes of disorders.

Method: A sample of 1,709 outpatients was evaluated with the Structured Clinical Interview for DSM-IV supplemented by modules on ICDs.

Results: Of this sample 190 (11.1%) patients had a current ICD, and 349 (20.4%) had a lifetime ICD. Thirty patients (1.8%) received a principal diagnosis of an ICD. Additionally, 164 patients (86.3% of all ICD patients) received a secondary diagnosis, of which 111 (67.7%) expressed interest in treatment. Over 5% of all patients with a current ICD had more than one current ICD diagnosis. Within the same sample, 56.1% had a current anxiety disorder and 12.1% a current substance use disorder. Examining comorbidity among these disorders, 49.8% of patients with any current anxiety disorder had more than one anxiety disorder and 19.3% with any substance use disorder had a comorbid substance use disorder.

Conclusions: The findings suggest that ICDs are relatively common, although they are rarely the main reason for seeking psychiatric treatment. When offered, almost three-quarters of those with an ICD were interested in receiving treatment. Compared to anxiety and substance use disorders, the comorbidity rates among the ICDs appear to be much lower.

References:

1. Black DW, Moyer T: Clinical features and psychiatric comorbidity of subjects with pathological gambling behavior. *Psychiatric Services* 1998; 49:1434-1439.
2. McElroy S, Keck P, Pope H, Smith J, Strakowski S: Compulsive buying: A report of 20 cases. *Journal of Clinical Psychiatry* 1994; 55:242-248.

NR625 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Venlafaxine Versus SSRIs and Placebo in the Treatment of Anxious Depression

Supported by Wyeth Research

Maurizio Fava, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC-812, Boston, MA 02114*; Richard Entsuah, Ph.D., Raj Rummala, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to (1). describe anxious depression, a major depressive disorder subtype (2). discuss prevalence of anxious depression among patients in a large database of major depressive disorder clinical trials (3). compare the efficacy (remission rates) of venlafaxine, selected SSRIs, and placebo in anxious depression.

Summary:

Objective: Evaluate the efficacy of venlafaxine, selective serotonin reuptake inhibitors (SSRIs), and placebo in patients with anxious depression.

Method: Patient data from 31 randomized, double-blind trials comparing treatment with venlafaxine/venlafaxine XR (N = 3,273) and selected SSRIs (fluoxetine, paroxetine, sertraline, citalopram, or fluvoxamine; N = 3,217) in major depressive disorder were analyzed. Nine studies also included a placebo control arm (N = 932). The criteria for remission were a primary HAM-D17 total score of 7 or less, and a more stringent alternate HAM-D17 score of 5 or less. Week 8 was the common endpoint for all studies.

Results: Patients with anxious depression constituted 72% of the patient population (5,370/7,421). Remission rates (HAM-D17 score of 7 or less) at week 8 for patients with anxious depression were 39% for venlafaxine/venlafaxine XR, 33% for the SSRIs, and 24% for placebo (p < 0.001 for all pairwise comparisons). Using the HAM-D17 score of 5 or less, week 8 results for patients with anxious depression were 27% for venlafaxine/venlafaxine XR, 22% for the SSRIs, and 15% for placebo (p < 0.001 for all pairwise comparisons).

Conclusion: In patients with anxious depression, venlafaxine/venlafaxine XR and SSRIs were associated with significantly higher remission at week 8 with venlafaxine/venlafaxine XR, compared with the studied SSRIs, in this depression subtype.

References:

1. Fawcett J, Kravitz HM: Anxiety syndromes and their relationship to depressive illness. *J Clin Psychiatry* 1983; 44(8 Pt 2):8-11.
2. Stein MB, Kirk P, Prabhu V, Grott M, Terepa M: Mixed anxiety-depression in a primary-care clinic. *J Affect Disord* 1995; 34:79-84.

NR626 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Assessment of Depression and PTSD Symptoms After Low Voltage Electrical Injury

Jennifer S. Morse, M.D., *4849 Ocana Place, San Diego, CA 92124*; Michael S. Morse, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the need for ongoing mental health screening for symptoms of depression and PTSD in patients who have experienced low voltage peripheral contact electrical injuries.

Summary:

Objective: Research regarding the psychological impact of electrical injury due to low voltage (< 1000 volts) is very limited, and some types of electrical injuries are so rare as to make recruiting subjects difficult. The purpose of this study was to assess the

presence of symptoms of depression and PTSD up to five years after electrical injury.

Methods: Thirty subjects who experienced an electrical injury completed a Web-based interactive survey that assessed demographic factors, prior traumatic experiences, and current symptoms of PTSD and depression (IES-R and PHQ-9). All subjects had peripheral electrical contacts only. Subjects with evidence by history of direct mechanical contact with the head or secondary closed head injury were excluded from this study.

Results: Thirty subjects completed the survey. Ten subjects (33%) reported previous exposure to a traumatic event. The mean IES-R score for PTSD symptoms was 57.32 (SD = 21.7), and the mean PHQ-9 score was 14.18 (SD = 7.8), indicating potential need for treatment. Subjects responding at 18-60 months post-injury had higher mean scores. Over 50% of the subjects reported seeing some type of mental health provider only once.

Conclusions: Results show the importance of ongoing mental health screening of this group of patients to ensure appropriate treatment.

References:

1. Primeau M, Engelstatter G, Bares K: Behavioral consequences of lightning and electrical injury. *Seminars Neurol* 1995; 15(3):279-285.
2. Pliskin NH, Capelli-Schellpfeffer M, Law RT, et al: Neuropsychological symptom presentation after electrical injury. *J Trauma: Injury Infection and Critical Care* 1998; 44(4):709-715.

NR627 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Effects of Tiagabine on Sleep in Patients With Primary Insomnia

Supported by Cephalon

James K. Walsh, Ph.D., *Sleep Medicine and Research Center, St. Luke's Hospital, 232 S. Woods Mill Road, Chesterfield, MO 63017*; Murray H. Rosenthal, D.O.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the effect of tiagabine on objective measures of sleep in adult patients with primary insomnia.

Summary:

Objective: Since gamma-aminobutyric acid (GABA) plays a central role in promoting sleep, increased availability of GABA may have therapeutic use in insomnia. The effects of tiagabine, a selective GABA reuptake inhibitor (SGRI), on sleep in adult patients with primary insomnia were studied.

Methods: Adult patients (N = 232; 18-64 years) with primary insomnia were randomly assigned to receive tiagabine 4, 6, 8 or 10 mg, or placebo on two consecutive nights of polysomnography.

Results: Efficacy data were obtained from 230 patients. The mean change from baseline in minutes of slow-wave sleep (SWS) was greater with tiagabine than with placebo (4 mg, +18.4 min; 6 mg, +31.7 min; 8 mg, +39.6 min; 10 mg, +52.9 min; placebo, +10.5 min), with the 6-, 8-, and 10-mg doses being significant versus placebo ($p < 0.001$ for each). No significant differences ($p > 0.05$) were observed between any dose of tiagabine and placebo on latency to persistent sleep or total sleep time. The tolerability profile of tiagabine was similar to placebo, with dizziness, nausea, and somnolence being the most common adverse events, primarily at the two higher doses.

Conclusion: Tiagabine enhanced SWS in adult patients with primary insomnia. Investigation into the clinical correlates of this effect on sleep is warranted.

Reference:

1. Mathias S, Wetter TC, Steiger A, Lancel M: The GABA uptake inhibitor tiagabine promotes slow wave sleep in normal elderly subjects. *Neurobiol Aging* 2001; 22(2):247-53.

NR628 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Is a Longer Duration of Untreated Illness a Risk Factor for Poor Outcome in Bipolar Disorder?

Emanuela Mundo, M.D., *Department of Psychiatry, Division of Clinical Sciences "L. Sa, University of Milan, via G.B. Grassi 74, Milan 20157, Italy*; Annalisa Santini, M.D., Daniele Salvadori, M.D., A. Carlo Altamura, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize and discuss the impact of a longer duration of untreated illness on the clinical course of bipolar disorder and to recognize the importance of early diagnosis and treatment.

Summary:

Objective: The aim of this study was to investigate the effects of the duration of untreated illness (DUI) on the clinical course of bipolar disorder (BD). As in a previous report on a smaller sample of BD patients, the presenters hypothesized that a longer DUI was correlated with a more severe course of BD, as identified by a higher rate of comorbid Axis I diagnoses, a higher number of hospitalizations, and a higher frequency of rapid cycling course.

Methods: Three hundred and one patients with a DSM-IV diagnosis of BD I (N = 115) or BD II (N = 186), with a mean age of 44.9 (SD = 12.4) years, mean age at onset 29.7 (SD = 10.4) years and a well-documented good compliance to mood stabilizers were studied. All patients had an SCID-I diagnosis and gave their informed consent to participate in the study. The DUI was defined as the time between the onset of BD and the beginning of treatment with mood stabilizers. The main clinical variables were compared between patients with $DUI \leq$ one year and patients with $DUI >$ one year (chi-square tests and t-tests).

Results: BD patients with $DUI >$ one year (N = 265) were more likely to develop comorbid substance abuse or dependence (chi-square = 4.69, df = 1, $p = 0.03$). With respect to the other clinical variables investigated, no significant differences were found.

Conclusions: These results suggest the critical importance of early diagnosis and intervention in BD in order to avoid later comorbid complications in the course of BD.

References:

1. Altamura AC, Bassetti R, Sassella F, Salvador D, Mundo E: Duration of untreated psychosis as a predictor of outcome in first episode schizophrenia: a retrospective study. *Schizophrenia Res* 2001; 52: 29-36.
2. Mundo E, Salvadori D, Madaro D, Bassetti R, Altamura CA: Duration of untreated illness and clinical course in bipolar disorder. Presented at the 155th Meeting of the American Psychiatric Association, Philadelphia (PA), May 18-23 2002.

NR629 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

The Effect of Tiagabine on Sleep: A 30-Day, Placebo-Controlled Pilot Study *Supported by Cephalon*

Andrew D. Krystal, M.D., *Department of Psychiatry, Duke University Medical Center, Box 3309, Durham, NC 27710*; James K. Walsh, Ph.D., Russell Rosenberg, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the 30-day treatment effect of tiagabine on sleep in adult and elderly patients with primary insomnia.

Summary:

Objective: To evaluate the effects of tiagabine, a selective gamma-aminobutyric acid (GABA) reuptake inhibitor (SGRI), on polysomnographic sleep measures in adults and elderly persons with primary insomnia.

Methods: This 30-day exploratory study randomly assigned 31 patients (15 adults, 18-64 years; 16 elderly patients, 65-85 years) with primary insomnia to receive nightly tiagabine 8 mg (eight adults), tiagabine 4 mg (10 elderly), or placebo (seven adults and six elderly). Polysomnograms were obtained on nights 1-2, 15-16, and 29-30.

Results: Slow-wave sleep (SWS) was increased in patients receiving tiagabine at all three study visits. At nights 29-30, median SWS increase from baseline in adults was 32.0 min for tiagabine vs. 6.3 min for placebo, and in the elderly, 6.8 min for tiagabine vs. 2.8 min for placebo. At nights 29-30, median WASO decrease from baseline in adults was 46.0 min for tiagabine vs. 28.8 min for placebo, and in the elderly, 16.8 min for tiagabine vs. 10.3 min for placebo. Tiagabine did not decrease sleep latency or increase total sleep time. Tiagabine was generally well tolerated.

Conclusion: At three study visits spanning 30 nights of administration, tiagabine increased SWS and decreased WASO. The investigation of the potential clinical benefit of these effects is warranted.

References:

1. Mathias S, Wetter TC, Steiger A, Lancel M: The GABA uptake inhibitor tiagabine promotes slow wave sleep in normal elderly subjects. *Neurobiol Aging* 2001; 22(2):247-53.

NR630 Wednesday, May 25, 12:00 p.m.-2:00 p.m. Effect of Religious Activities in Psychiatric Ward on Compliance of Outpatient

Shin Kyungchul, M.D., *Department of Psychiatry, Saint Andrew's Neuropsychiatric Hospital, 586-2 Pyogyo2ri Majang-myun, Icheon 467-813, South Korea*; Kim Jae Hwan, Ph.D., Park Ejin, M.D., Choi Samwook, M.D., Kim Euijung, M.D., Jeong Jongil, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be aware that an environment for religious life in inpatients of psychiatric hospitals can be helpful in improving compliance of outpatients after discharge.

Summary:

Objectives: The author examined the impact of the religious life of psychiatric inpatients on adherence to outpatient treatment and also investigated correlation with the change of some clinical characteristics.

Methods: A total of 225 patients discharged January 1, 2001 to December 31, 2001 from Saint Andrew Psychiatric Hospital were recruited as subjects and were classified as active religious life group, passive religious life group, and no religious life group. Adherence to outpatient treatment was evaluated by whether the patient visited an outpatient clinic at four points: one, three, five, and twelve months after discharge.

Results: The adherence of outpatients in the three groups showed no significant difference one month after discharge. In the active religious life group, adherence at three, five, and 12 months after discharge showed a significant difference, compared with the passive religious life group and no religious life group.

Insight, kind of psychiatric diseases, etc., in three groups showed no significant difference.

Conclusions: This study shows that active religious life in psychiatric inpatients influences adherence of outpatients positively regardless of religious thought or varieties of religion. This implies that an environment for religious life for inpatients in psychiatric hospitals can be helpful in improving adherence of outpatients after discharge.

References:

1. Allport GW, Ross JM: Personal religious orientation and prejudice. *J Pers Soc Psychol* 5:432-443.
2. American Psychiatric Association: Guidelines regarding possible conflict between psychiatrists' religious commitments and psychiatric practice. *Am J Psychiatry* 1990; 147:542.

NR631 Wednesday, May 25, 12:00 p.m.-2:00 p.m. A Predictive Model on Weight Gain Induced by Antipsychotics in Schizophrenia Inpatients

Hsien-Jane Chiu, M.D., *Department of Psychiatry, Yu-Li Hospital, DOH, 448 Chung-Hwa Road, Hualien 981, Taiwan*; Meng-Shien Wu, Ph.D., Guang-Chyi Liu, M.D., Tsuo-Hung Lan, M.D., Hung-Chieh Hsieh, M.D., Fan-Chin Kung, M.D., C.L. Yueh, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate how to predict the weight gain of schizophrenic patients by using a computerized statistical model.

Summary:

Objective: The aim of this study was to establish a predictive model of body weight gain in schizophrenic patients.

Method: Weight gain due to antipsychotics exposure was chosen as the main clinical outcome in this study in two different forms: dichotomous and continuous data type. Two-hundred chronic schizophrenic patients with at least six months' hospitalization were enrolled from two Taiwan psychiatric hospitals. The dichotomous outcome for weight gain was predicted by the logistic regression model, which was established from 67 schizophrenic patients. Data from another 230 schizophrenic patients were utilized to establish the linear regression model and to test its accuracy of weight gain prediction. For the convenience of users, neuro-fuzzy techniques were applied to simplify the procedure of prediction of the clinical outcome for most clinicians with no thorough knowledge background of biostatistics.

Results: The reliability of the logistic regression model was warranted by good sensitivity (90%) and specificity (83%). The accuracy of weight gain prediction by the linear regression model reached 92%, compared to the observed values (within 5% confidence interval). The prediction rate of the neuro-fuzzy techniques ranged from 80% to 98% after appropriate equation learning and training.

Conclusions: Throughout these three different approaches, the clinical outcome prediction by algorithms for decision-making was proven effective and provided an evidence-based approach in medical practice.

References:

1. National Institute of Health: Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. *Obes Res* 1998; 6(suppl. 2):51-209.
2. Maurice MO: Improving decision-making procedures with the fuzzy logic approach in the epidemiology of sleep disorders. *J Psychosom Res* 1999; 47:297-311.

NR632 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Modification of Saliva Cortisol Level by Psychological Debriefing After Trauma Exposure

Georges Brousse, M.D., *Emergency, Chu Clermont Ferrand, Place Henri Dunant, Clermont-Ferrand 63000, France*; A Chamoux, M.D., G. Lac, M.D., PM Llorca, M.D., Jeannot Schmidt, M.D., F. Ducrocq, M.D., G. Vaiva, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the importance of early intervention after trauma exposure.

Summary:

Objective: Debriefing is an early intervention after acute stress to limit the emergence of posttraumatic stress disorder. But the clinical and biological impact of this intervention is still controversial. Several studies have found increased cortisol after acute stress. The aim of this study was to demonstrate the effect of a debriefing intervention on cortisol level.

Method: Ten employees who encountered suicide by immolation of one of their colleagues received a debriefing intervention one week after this acute stress. Saliva samples were collected before and after debriefing. IESR, PDEQ, mini interview were completed. PTSD was evaluated one month after this event.

Result: No patients had a psychiatric history. Before debriefing all the subjects showed high score on scales that are usually considered as positive predictors of PTSD. One month later no PTSD occurred. Moreover before debriefing, cortisol levels were higher than usual circadian levels. After debriefing, cortisol levels were significantly decreased relative to circadian level. Thus debriefing could lead to the decrease of cortisol level and to diminution of the incidence of PTSD.

Conclusion: Early intervention after acute stress could decrease cortisol level. Lower cortisol levels after debriefing might be a predictor for less PTSD emergence.

References:

1. Young EA, Tolman R, Witkowski K, Kaplan G: Salivary cortisol and posttraumatic stress disorder in a low-income community sample of women. *Biol Psychiatry* 2004; 55(6):621-626.
2. Bakke M, Tuxen A, Thomsen CE, Bardow A, Alkjaer T, Jensen BR: Salivary cortisol level, salivary flow rate, and masticatory muscle activity in response to acute mental stress: a comparison between aged and young women. *Gerontology* 2004; 50(6):383-92.

NR633 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Performance Improvement of Patients With Schizophrenia Participating in the Computer-Based Cognitive Training With X-Cog

Supported by Astra Zeneca

Matthias Dobmeier, M.D., *Department of Psychiatry, Bezirksklinikum/Tagesklinik, August-Holzstr1, Regensburg/Cham, Germany*, Alexander Hasmann, Wolfgang Trapp

Educational Objectives:

At the end of the presentation the participant should be able to recognize that there are first indications that the computer-based cognitive training software X-Cog can be a useful tool to remediate cognitive deficits in schizophrenic patients.

Summary:

The goal of this study was to examine performance improvement of schizophrenic patients participating in computer-based cognitive training with X-Cog. forty subjects (10 women, 30 men; N = 20 control group, "placebo": work therapy, sports therapy,

art therapy; N = 20 experimental group) with the diagnosis of schizophrenia (ICD10 F20.X) were trained for 10 weeks (twice a week, duration one hour per session) using the software X-Cog in different wards of the Bezirksklinikum Regensburg. In two-factorial MANOVAS ("treatment" as group factor, "pre-/posttest" as within-subjects factor), significant interaction effects were found for errors and preservation errors in the WCST 1616, the amount of learning and recall short delay in the German version of the CVLT, and "tonic alertness" on the "Testbatterie zur Aufmerksamkeitsprüfung" (German test, similar to the CPT task). In addition, a significant decline in relevant psychopathology (negative and positive symptoms measured by PANSS and PDS-P [German self-rating scale for paranoid symptoms]) was discovered. Numeric effects for "depression" (BDI) and PDS-D [German self-rating scale for depressive symptoms]) did not reach statistical significance. No differences in state and trait anxiety (measured by the STAI) were found. This study gives first indications that X-Cog could be a useful way to increase performance of cognitive functioning in patients trained with this computer-based software.

References:

1. Sharma, T. Antonova L: Cognitive function in schizophrenia: deficits, functional consequences and future treatment. *Psychiatric Clinics of North America* 2003; 26 (1): 25-40.
2. Suslow T, Schonauer K, Arolt V: Attention training in the cognitive rehabilitation of schizophrenic patients: a review of efficacy studies. *Acta Psychiatrica Scandinavica* 2001; 103: 15-23.

NR634 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Virtual Reality in Addiction Research

Supported by the National Institute on Drug Abuse and the National Institute on Alcohol Abuse and Alcoholism

Patrick S. Bordnick, Ph.D., *University of Georgia, 1000 University Center Lane, Building B Room, Lawrenceville, GA 30043*; Ken Graap, M.Ed., Hilary Copp, M.S.W., Amy Traylor, M.S.W.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the role of virtual reality in addiction research, assessment, and treatment.

Summary:

Objectives: To test virtual reality (VR) cue reactivity assessment systems in nicotine- and alcohol-dependent persons using a within-subjects design. The presenters hypothesized that VR drug stimuli/cues would lead to increased craving and corresponding physiological reactivity, compared to neutral cues.

Method: In pilot case studies and controlled research trials, VR environments were developed and tested to assess reactivity in cigarette smokers and alcohol-dependent subjects. Tested VR environments consisted of inanimate (smoking and drinking paraphernalia) and animate (social interactions) in which the subject is offered an alcohol drink or cigarettes. A neutral VR environment containing non-drug stimuli/cues was developed to serve as a control condition. Subjects were monitored for physiological reactivity and drug craving in each VR cue environment.

Results: Data from research trials conducted on alcohol and smoking samples are presented. Specifically, data on standardization of physiological reactivity (GSR, HR) in VR addiction environments and drug craving are reported.

Conclusion: VR offers a valuable tool to standardize assessment of drug cue reactivity in both nicotine- and alcohol-dependent persons. VR cue reactivity environments elicited craving and physiological reactivity.

References:

1. Bordnick PS, Graap KM, Copp H, Brooks J, Ferrer M, Logue B: Standardization of cue reactivity for nicotine dependence using virtual reality. *Addictive Behaviors* 2004; 29: 1889-1894.
2. Bordnick PS, Graap KM, Copp HL, Brooks J, Ferrer M, Logue B: Utilizing virtual reality to standardize nicotine craving research: a pilot study. *Addictive Behaviors* 2004; 29: 1889-1894.

NR635 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Diagnostic Coding for Patients on Second-Generation Antipsychotics in the Real World *Supported by Bristol-Myers Squibb*

Diana I. Brixner, Ph.D., *Department of Pharmacotherapy, University of Utah, 30 South 2000 East Room 258, Salt Lake City, UT 84112*; Qayyim Said, Ph.D., John Newcomer, M.D., Vickie Tuomari, M.S., Gary Oderda, Pharm.D., Bill Stockdale, M.B.A., Gilbert L'Italien, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to discuss how various social factors, from the patient's perspective, and uncertainty or economic drivers, from the physician's perspective, may impact the diagnostic coding of patients taking SGAs.

Summary:

Objective: The second-generation antipsychotics (SGAs) are primarily indicated for schizophrenia but primarily used in patients with bipolar disorder. Due to the stigmatization of either disease, or potential reimbursement issues, actual coding in a primary care setting may vary.

Methods: This study evaluated a national electronic medical record (EMR) research database (GE Logician) in a primary care setting to determine coding patterns for patients taking SGAs.

Results: Of 25,396 patients identified as taking SGAs, only 10,374 (40.9%) had a diagnosis code for a psychotic disorder. Of the patients where a diagnosis code did exist, 8,596 (82.8%) had a diagnosis of depression, 2,879 (27.8%) had a diagnosis of schizophrenia or schizoaffective disorder, 3,725 (35.9%) had a diagnosis of bipolar disorder, and 2,643 (25.5%) had other diagnoses related to the use of SGAs. These numbers indicate that patients may have multiple diagnoses. Further, of the patients who had a diagnosis of depression, 6,386 (74.3%) had diagnosis of depressive disorder not elsewhere classified.

Conclusion: Patients taking SGAs are often undiagnosed or misdiagnosed in primary care. This may have an impact on the continuity of care in optimizing patients' outcomes.

References:

1. Torgersen T, Rosseland LA, Malt UF: Coding guidelines for ICD-9 section on mental disorders and reliability of chart clinical diagnoses. *Acta Psychiatr Scand* 1990; 81(1):62-7.

NR636 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Effect of ORTHO TRI-CYCLEN® on Bone Mineral Density in Pediatric Females With Anorexia Nervosa *Supported by Ortho-McNeil Pharmaceutical, Inc.*

Andrew J. Friedman, M.D., *Internal Medicine, Johnson & Johnson Pharmaceutical R & D, 920 Route 202, Raritan, NJ 08869*; William Yates, M.D., Jill Zweig, D.O., Robert Dahmes, M.D., Debra Karvois, M.S.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to evaluate the effect of ORTHO TRI-CYCLEN® on lumbar spine (LS) (L1 L4) BMD in pediatric subjects with anorexia nervosa (AN)

Summary:

Objective: This study evaluated the effect of Ortho Tri-Cyclen on lumbar spine (LS) (L1 L4) bone mineral density (BMD) in pediatric subjects with anorexia nervosa (AN).

Methods/Results: A total of 123 females, post-menarcheal through age 17 with AN, were enrolled and randomly assigned (1:1) to Ortho Tri-Cyclen or placebo for 13 consecutive 28-day cycles; 88 subjects completed at least 12 treatment cycles (completer population). Treatment groups were similar for age (overall mean: 15.1 yrs) and body mass index (BMI) (overall mean: 17.77 kg/m²). In a completer population, the Ortho Tri-Cyclen group had a significantly greater increase in mean LS BMD, compared with the placebo group, at cycle 13 (0.0374 g/cm² and 0.0218 g/cm²; p = 0.018). The incidence of adverse events for subjects in the Ortho Tri-Cyclen group (N = 61 [78.7%]) was similar to the placebo group (N = 62 [79.0%]) except for worsening of AN (Ortho Tri-Cyclen: two; placebo: 11). Other adverse events observed were consistent with those in previous clinical studies with Ortho Tri-Cyclen.

Conclusions: In a completer population, the Ortho Tri-Cyclen group had a significantly greater increase in mean LS BMD, compared with the placebo group at cycle 13. The results of this study suggest that Ortho Tri-Cyclen may benefit adolescent females with AN by increasing LS BMD and potentially reducing future fracture risk.

References:

1. Klibanski A, Biller BM, Schoenfeld DA, Herzog DB, Saxe VC: The effects of estrogen administration on trabecular bone loss in young women with anorexia nervosa. *Journal of Clinical Endocrinology and Metabolism* 1995; 80(3):898-904.
2. Kanis JA, Melton LJ, Christiansen C, et al: The diagnosis of osteoporosis. *J Bone Miner Res* 1994; 9:1137-1141.

NR637 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Psychological Trauma in New York Japanese Communities Two Years After the 9/11 Terrorist

Takuya Saito, M.D., *Department of Psychiatry, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Room F103, Brooklyn, NY 10461*; Masako Mori, Ph.D., Shizuko Burnes, M.A., Yoshiko Nishimatsu, M.D.

Educational Objectives:

At the conclusion of the presentation, the participants should be able to understand long-term psychological effects from the September 11, 2001 terrorist attacks in a minority community.

Summary:

Objective: The presenters previously reported that approximately 10% of Japanese living in New York area presented with probable posttraumatic stress disorder (PTSD) three months after the WTC terrorist attacks. A follow-up study was to determine long-term effects from the terrorist attacks.

Method: A set of questionnaires was distributed to 502 Japanese families living in NY in September 2003 two years after the attacks. It included demographic and disaster-exposure questions and Impact of Event Scale—Revised (IES-R).

Results: A total of 137 families responded; 98 responders lived in NY before the attacks and 39 moved to NY after the attacks. In responders living in NY before the attack, 5.7% of the children, 6.5% of their fathers, and 8.1% of the mothers presented with

probable PTSD (IES-R score = 25). Over the two years the average of IES-R score in the children and the mothers decreased significantly ($p < 0.01$ and $p < 0.01$ respectively), but there was no significant decrease in ISR-R score in the fathers.

Conclusions: In the two years after the terrorist attacks, the psychological effects in the Japanese community in NY appeared to be abated. The degree of the recovery appeared different in the different subgroups.

References:

1. Saito T, Burns KS, Kakuma T: A survey of psychological reactions in the Japanese living in New York after the September 11, 2001 terrorist attacks, Part I: psychological reactions in the Japanese adults. *Japanese Journal of Clinical Psychiatry* 2004;33(11): 1473-1480.
2. Saito T, Burns KS, Kubota S, et al. A survey of psychological reactions in the Japanese living in New York after the September 11, 2001 terrorist attacks, Part II: psychological reactions in the Japanese children. *Japanese Journal of Clinical Psychiatry* (in press).

NR638 Wednesday, May 25, 12:00 p.m.-2:00 p.m. Virtual Relaxation Environment for Chronic Low Back Pain

Libby R. Tannenbaum, Ph.D., *Virtually Better, 2450 Lawrence Highway, Suite 101, Decatur, GA 30033*; Barbara Rothbaum, Ph.D., Elana Zimand, Ph.D., Mirtha Ferrer, M.S., Ken Graap, M.Ed., Stanley Chapman, Ph.D., Peter Campos, Ph.D.

Educational Objectives:

At the conclusion of this presentation, participants should be able to demonstrate knowledge of the application of virtual reality (VR) technology to the treatment of chronic low back pain, discuss the development and testing of this VR Relaxation Environment, and understand the utility of VR as a tool for facilitating relaxation and pain reduction.

Summary:

Objective: Chronic low back pain (CLBP) affects 25%-45% of adults at some time in their life. Psychological factors contribute to exacerbation and treatment of CLBP. Relaxation therapy is an empirically validated technique used as an alternative or adjunct to pharmacotherapy for CLBP. This study tested an innovative treatment for CLBP, delivering relaxation therapy within virtual reality (VR). VR provides a multisensory experience facilitating increased immersion and interaction and treatment standardization. In VR, CLBP participants complete progressive muscle relaxation and breathing exercises, selecting from virtual beach, forest, or garden environments, with virtual voiceover. VR's effectiveness in acute pain has been demonstrated; however, no studies have tested VR for chronic pain. In this controlled clinical trial, the presenters hypothesized lower pain and tension levels and increased relaxation among VR participants, compared to control at posttreatment.

Methods: Twenty adults with CLBP randomly assigned to VR treatment (five VR sessions over five weeks) or waitlist control complete standardized self-report measures of pain, relaxation, medication use, beliefs, coping, and anxiety, and physiological assessment of muscle tension, at pretreatment, post-, and three months.

Results: Posttreatment results for 20 participants using repeated-measures MANOVA with multiple outcome measures (self-report, physiological) are reported.

Conclusion: This study of the first VR program for chronic pain offers preliminary evidence of the utility of VR to facilitate relaxation

and pain reduction and a potential new medium for clinicians/researchers working in pain and related areas.

Supported by NIAMS grant #1-R43-AR050863-01.

References:

1. Block A, Gatchel R, Deardoff W, Guyer R: *The Psychology of Spine Surgery*. Washington, DC, American Psychological Association, 2003.
2. Turk DC: Clinical effectiveness and cost effectiveness of treatments for patients with chronic pain. *Clinical Journal of Pain* 2002; 18:355-365.

NR639 Wednesday, May 25, 12:00 p.m.-2:00 p.m. Diagnosing Bipolar Disorder in Primary Care Clinics

William Lawson, M.D., *Department of Psychiatry, Howard University Hospital, 2041 Georgia Avenue, Washington, DC 20060*; Ruth Graves, Ph.D., Chris Chrishon, M.P.H., Tanya Alim, M.D., Thomas Mellman, M.D.

Educational Objectives:

At the conclusion of the presentation the participant should be able to recognize the difficulties in diagnosing bipolar disorder in a medical setting.

Summary:

Objective: Bipolar affective disorder (BD) is a disabling Axis I disorder, often underrecognized in nonpsychiatric settings, especially in African Americans. The Mood Disorders Questionnaire (MDQ) is a screening instrument proposed to show adequate sensitivity and specificity for BD. The presenters examined the usefulness of this instrument in primary care clinics with primarily African American patients.

Method: Consenting patients in three academically affiliated primary care clinics were asked to complete the MDQ. Ninety percent of the clinic patients were African American. Diagnoses were determined with the Structured Clinical Interview for DSM-IV (SCID) as a gold standard within a larger study exploring traumatic stress exposure and psychopathology.

Results: Participation refusal rate overall was less than 50%. Sixty of 173 (34.7%) screened positive for BD on the MDQ, but only 18 (10.4%) were SCID-positive for BD. The sensitivity was 61.1% and specificity 68.4%, with a positive predictive value of 18.3% and negative predictive value of 93.8%. Six patients positive for BD were receiving psychiatric treatment but only one was taking a mood stabilizer.

Conclusion: The MDQ was not found to be a useful screening tool in this setting. The contribution of issues such as ethnicity, socioeconomic status, and substance abuse are discussed.

References:

1. Hirschfield RM, Calabrese JR, Weissman MM, et al: Screening for bipolar disorder in the community. *J. Clin Psychiatry* 2003; 64:53-59.
2. Ghaemi SN, Boiman EE, Goodwin FK: Diagnosing bipolar disorder and the effects of antidepressants: a naturalistic study. *J Clin Psychiatry* 2000; 6:344-348.

NR640 Wednesday, May 25, 12:00 p.m.-2:00 p.m. The Validity/Reliability of the Turkish Version IES-R

Muberra D. Dogan, M.D., *Medical Writing, Omega Cro, Guniz Sok No:32/9, Ankara 06700, Turkey*; Aytul C. Ozdemir, M.D., Ilhan Yargic, M.D., Pakize Geyran, M.D., Nese Kocabasoglu, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the Turkish version of IES-R as valid and reliable.

Summary:

Objectives: This study was designed to determine the validity and reliability of the Turkish version of the Impact of Event Scale-Revised (IES-R).

Method: A total of 104 subjects with a diagnosis of posttraumatic stress disorder (PTSD) and 65 subjects without PTSD were enrolled in the study. After the recording of sociodemographic characteristics, all subjects were assessed with both IES-R and Clinician Administered Post Traumatic Stress Disorder Scale (CAPS), for which reliability and validity of the Turkish version have been shown. The validity of IES-R referring to CAPS and internal consistency were determined using relevant statistical methods.

Results: Total IES-R score ($r = 0.705$, $p < 0.001$) and intrusion ($r = 0.693$, $p < 0.001$), hyperarousal ($r = 0.639$, $p < 0.001$), avoidance ($r = 0.491$, $p < 0.001$) IES-R subscale scores were found to be correlated with the corresponding scores of CAPS with Spearman analysis. The area under the ROC curve was defined as 0.878 ± 0.031 ($p < 0.001$). For cut-off points of IES-R between 24 and 33, both sensitivity and specificity were over 70%. Cronbach alpha was 0.937 ($p < 0.0001$).

Conclusion: This study demonstrated that the Turkish version of IES-R is valid and has good diagnostical performance for cut-off points of IES-R between 24 and 33 and high internal consistency.

References:

1. Horowitz M, Wilner N, Alvarez W: Impact of Event Scale: a measure of subjective stress. *Psychosomatic Medicine* 1979; 41:209-218.
2. Creamer M, Bell R, Failla S: Psychometric properties of the Impact of Event Scale-Revised. *Behav Res Ther* 2003; 41:1489-1496.

NR641 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

The Risk Factors for PTSD in Earthquake Survivors in Turkey

Muberra D. Dogan, M.D., *Medical Writing, Omega Cro, Guniz Sok No:32/9, Ankara 06700, Turkey*; Pakize Geyran, M.D., Nese Kocabasoglu, M.D., Ilhan Yargic, M.D., Aytul C. Ozdemir, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize PTSD risk factors in earthquake survivors.

Summary:

Objectives: The goal of this study was to evaluate the frequency and risk factors of PTSD among survivors of the 1999 earthquake in Turkey.

Method: People ($N = 144$, men 60%, mean age 33.3 ± 11.9) living in prefabricated houses in Kocaeli region were assessed for PTSD using IES-R. Sociodemographic variables for pretraumatic individual characteristics, subjective emotional feelings (subjective severity score/SSS, 0-8), objective experiences (objective severity score/OSS, 0-8), and number of post-disaster stressors (0-6) during earthquake were evaluated.

Results: A Total of 108 subjects (75%) had an IES-R score > 24 and a diagnosis of PTSD. The number of stressors (2.8 ± 1.4 vs. 2.2 ± 1.2 , $p = 0.05$), OSS (5.2 ± 1.6 vs. 3.4 ± 2.1 , $p < 0.001$), PDE-Q (27.1 ± 7.9 vs. 18.2 ± 6.2 , $p < 0.001$), and DIS-Q (153.4 ± 46.6 vs. 106.9 ± 36.3) scores of the PTSD (+) subjects were significantly higher than the PTSD (-). There was no significant difference between PTSD (+) and PTSD (-) subjects regarding age (34.1 ± 12.2 vs. 31.1 ± 11.0) and SSS (2.8 ± 1.6 vs. $2.1 \pm$

1.7). Significant correlations between the IES-R total score and OSS ($r = 0.214$, $p = 0.01$), SSS ($r = 0.476$, $p < 0.001$), and number of stressors ($r = 0.226$, $p = 0.007$) were found.

Conclusion: The risk factor for PTSD that showed the highest correlation with the IES-R total score was SSS. The OSS and the number of stressors were correlated less with the IES-R score.

References:

1. Basoglu M, et al: Traumatic stress responses in earthquake survivors in Turkey. *J Trauma Stress* 2002; 15(4):269-276.
2. Shalev AY, et al: Predictors of PTSD in injured trauma survivors: A prospective study. *Am J Psychiatry* 1996; 153(2):219-225.

NR642 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

The Role of Dissociation for the Development of PTSD in Earthquake Survivors in Turkey

Muberra D. Dogan, M.D., *Medical Writing, Omega Cro, Guniz Sok No:32/9, Ankara 06700, Turkey*; Aytul C. Ozdemir, M.D., Ilhan Yargic, M.D., Nese Kocabasoglu, M.D., Pakize Geyran, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the role of dissociation in the development of PTSD in earthquake survivors.

Summary:

Objectives: The goal of this study was to evaluate the role of dissociation for the development of PTSD among survivors of the 1999 Earthquake in Turkey.

Method: People ($N = 144$, men 60%, mean age 33.3 ± 11.9), living in prefabricated houses in Kocaeli region were assessed for PTSD using the IES-R. The relation between dissociation and PTSD was studied by analyzing the correlation of scores on the IES-R with scores on the PDE-Q and DIS-Q, which were the questionnaires used to define the level of dissociation of the subjects.

Results: A significant correlation between the IES-R total score and DIS-Q total score ($r = 0.612$, $p < 0.001$) was found. The correlations between scores on the subscales of the IES-R (intrusion, hyperarousal, and avoidance) and DIS-Q total score were also statistically significant ($r = 0.568$, $r = 0.676$, and $r = 0.417$, respectively, $p < 0.001$ for all). Similarly IES-R total and subscale scores were correlated significantly with the PDE-Q total score ($p < 0.001$). The correlation coefficients for the IES-R total, intrusion, hyperarousal, and avoidance scores with PDE-Q total score were 0.590, 0.615, 0.525, and 0.433.

Conclusion: General tendency for dissociation, which was assessed by DIS-Q, and the level of dissociation during trauma, which was assessed by PDE-Q, were found to be important factors for the development of PTSD.

References:

1. Shalev AY, et al: Predictors of PTSD in injured trauma survivors: a prospective study. *Am J Psychiatry* 1996; 153(2):219-225.
2. Marmar CR, et al: Peritraumatic dissociation and posttraumatic stress in male Vietnam theater veterans. *Am J Psychiatry* 1994; 151(6):902-907.

NR643 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

A Multicenter Validation of the Abbreviated Hamilton Depression Rating Scale (HAM-D-7) to Evaluate Remission in Primary Care

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008, Toronto, ON M5T 2S8, Canada; Roger McIntyre, M.D., Neil Maresky, M.D., Sagar V. Parikh, M.D., Larry Grupp, Ph.D., Sidney Kennedy, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to discuss the use of an abbreviated Hamilton Depression Rating Scale in primary care.

Summary:

Objectives: To validate the Hamilton Depression Rating Scale 7-item (HAMD-7) and operationalize a remission cut-score in depressed patients treated in primary care settings.

Methods: This cross-national, multicenter, randomized validation study was conducted in naturalistic primary-care settings (N = 50). Depressed patients (N = 379), meeting DSM-IV-TR criteria for major depressive disorder (MDD) received open-label antidepressant treatment at clinician discretion. Patients were randomly assigned to either the HAMD-7 (N = 189) or HAMD-17 scale (N = 190) as the primary metric to evaluate depressive symptoms and response to treatment at baseline, and repeatedly across eight weeks of observation. The main outcome measures were change from baseline in overall depressive symptom severity, response (>50% reduction from baseline to endpoint in total depressive symptoms), and remission (total HAMD-7 <3; total HAMD-17 score < 7, respectively) rates in patients evaluated with either the HAMD-7 or HAMD-17.

Results: Baseline to posttreatment changes in overall depressive symptom severity, evaluated with either the HAMD-7 or HAMD-17 scales, were highly correlated. The percentage of patients who achieved a-priori-defined response in the HAMD-7 and HAMD-17 groups (67%, 61%, respectively) and remission (46%, 42%, respectively) were similar (p = 0.199, p = 0.536, respectively). Overall depressive symptom improvements, as evaluated by either the HAMD-7 or HAMD-17 and a quantitative global measure (i.e., Clinical Global Impression scale) were also highly correlated.

Conclusion: The HAMD-7 is a brief, comprehensive, validated rating scale that quantifies depressive symptom severity and determines when full symptomatic remission has occurred. Guideline-concordant algorithmic care in depression is usefully augmented by quantitative outcome measures.

Supported by an unrestricted educational grant from Wyeth Pharmaceuticals.

References:

1. McIntyre RS, Kennedy SH, Bagby R, Bakish D: Assessing full remission. *J Psychiatry Neurosci* 2002; 27(4):235-9.
2. McIntyre RS, Fulton K, Bakish D, Jordan J, Bagby M, Kennedy SH: The HAMD-7: a brief depression scale to distinguish antidepressant response from symptomatic remission. *Primary Psychiatry* 2003; 10(1):39-42.

NR644 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

What Do Patients With Heart Failure Believe Regarding Depression and Depression Care?

Vei Jiang, M.D., *Department of Psychiatry, Duke University Medical Center, 811 Southshore Parkway, Durham, NC 27703*; David Whellan, M.D., Maragatha Kuchibhatla, Ph.D., Christopher M. O'Connor, M.D., Manuel Garcia, M.D., K. Ranga R. Krishnan, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that (1) CHF patients are knowledgeable about depression impact/care: (2) and that CHF patients prefer being treated for depression by their primary care physician or cardiolo-

gists, while most of their health providers believe it needs to be treated by psychiatrists.

Summary:

Objective: Depression is a prognostic factor in patients with chronic heart failure (CHF). Although SSRIs are effective and safe for these patients, depression treatment among them is far from optimal. We are conducting a study to understand the knowledge of CHF patients and their nonpsychiatric health providers regarding depression impact/care and to assess whether providing depression education materials may improve the knowledge of these patients.

Methods: Inpatients/outpatients with CHF were eligible. Participants were asked to perform a quiz. Half were randomly provided with answers to the quiz and depression education material; the other half were requested to just complete the assessment. Physicians involved in these patients' care were asked to answer questions. Preliminary analysis was performed to examine features of currently enrolled participants.

Results: Of the 98 participants are enrolled so far, 80% believed depression is common in CHF patients, 61.4% believed depression is due to CHF, and 78.2% knew CHF patients with depression are more likely to die or to be hospitalized. Although the majority believed depression is curable, 73.3% preferred to be treated by a primary care physician or cardiologist. In contrast, only one-third of their health care providers believed depression in CHF patients is better managed by nonpsychiatric providers (p = 0.028).

Supported by an unrestricted educational fund from Pfizer Inc.

References:

1. Jiang W, Alexander J, Christopher E, Kuchibhatla MN, Davenport C, O'Connor CM, Krishnan KR: Effect of depression on mortality and morbidity in patients with congestive heart failure. *Archives of Internal Medicine* 2001; 161:1849-56.
2. Glassman AH, O'Connor CM, Califf RM et al: Sertraline treatment of major depression in patients with acute MI or unstable angina. *JAMA* 2002; 288:701-9

NR645 Wednesday, May 25, 12:00 p.m.-2:00 p.m.

Divalproex, Lithium, and Suicide in a Medicaid Population

Supported by Abbot Laboratories

Jon C. Collins, Ph.D., *Mental Health and Addiction Services, Oregon Department of Human Services, 500 Summer Street NE, PO Box 14250, Salem, OR 97301*; Bentson McFarland, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to compare rates of suicide and suicide attempts between lithium versus divalproex users among Medicaid patients with bipolar disorder.

Summary:

It was recently reported by Goodwin et al. that for patients in two private health plans receiving treatment for bipolar disorder the risk of suicide attempt and suicide death is lower during treatment with lithium than during treatment with divalproex. However, it has remained unclear whether there is a differential impact on suicidal behavior among mood-stabilizing agents, as other studies have not demonstrated any differences from lithium (e.g., Yervanian et al.) This preliminary study examined electronic records for 12,770 Oregon Medicaid clients with bipolar disorder (66% female, average age 39) to generate detailed information about suicide and suicide attempts among clients using lithium versus divalproex and/or other mood-stabilizing agents. After adjusting for age, gender, time of diagnosis, and use of mood-stabilizing

agents taken independently vs. in combination with other stabilizing agents, the risk of suicide was no greater for divalproex, compared to lithium. The data does suggest a higher risk of suicide for individuals while using gabapentine. Further analysis will describe risk associated with suicide attempts and control for other confounding factors, such as physical illness and concurrent use of antipsychotics and antidepressants.

References:

1. Goodwin FK, et al: Suicide risk in bipolar disorder during treatment with lithium and divalproex. *JAMA* 2003; 290:1467.
2. Yerevanian BI, et al: Lithium, anticonvulsants and suicidal behavior in bipolar disorder. *J Affect Disord* 2003; 73:223-228.

NR646 **Wednesday, May 25, 12:00 p.m.-2:00 p.m.** **A Scale to Screen for DSM-IV Axis I Disorders in Psychiatric Outpatients**

Mark Zimmerman, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905*; Iwona Chelminski, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate knowledge of the diagnostic properties of the Psychiatric Diagnostic Screening Questionnaire.

Summary:

Objective: The Psychiatric Diagnostic Screening Questionnaire (PDSQ) is a reliable and valid self-report scale designed to screen for the most common DSM-IV Axis I disorders encountered in outpatient mental health settings. The present report is the second large-scale validation study of the PDSQ in psychiatric outpatients. Because some of the sizes of the diagnostic groups in the initial report were modest, it is important to determine whether the recommended cutoff scores to screen for psychiatric disorders remained the same in a replication study.

Method: Six hundred and seventy psychiatric outpatients presenting for treatment were evaluated with a semistructured diagnostic interview after completing the PDSQ.

Results: Based on receiver operating curve analysis, the PDSQ performed as well in the replication sample as in the initial validation study. For nine of the 13 PDSQ subscales the recommended cutoff score in the replication study was the same as in the initial study. After data from the two studies (N = 1,300) were combined the mean sensitivity across the 13 PDSQ subscales was 87% and the mean negative predictive value was 97%.

Conclusions: The PDSQ is a diagnostic aid designed to improve the efficiency of conducting initial diagnostic evaluations. From a clinical perspective it is important that a screening tool have good sensitivity so that most cases are detected, and high negative predictive value so that most noncases on the measure are indeed noncases. The results of this second large validation study indicated that most of the PDSQ subscales achieve this goal.

Supported by NIMH grants MH48732 and MH56404

References:

1. Zimmerman M, Mattia JI: Psychiatric diagnosis in clinical practice: Is comorbidity being missed? *Compr Psychiatry* 1999; 40:182-191
2. Zimmerman M, Mattia JI: A self-report scale to help make psychiatric diagnoses: The Psychiatric Diagnostic Screening Questionnaire (PDSQ). *Arch Gen Psychiatry* 2001; 58:787-794

NR647 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.** **Psychosis in Epilepsy: A Survey**

Christina M. Vanderfelt-Cornelis, Ph.D., *Department of Psychiatry, Free University Medical Center, Valeriusplein G, Amsterdam 1075 BG, Netherlands*

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize four clusters of psychotic symptoms in epilepsy patients, recognize the clinical relevance of left-sided cerebral pathology, mental retardation and PDD-NOS, and know a basic treatment algorithm for the several clusters.

Summary:

Objective: To establish the prevalence of psychotic disorder in clinical epilepsy patients, to describe the phenomenology, and to explore relevant predisposing variables.

Methods: In this survey, a two-stage screening method was followed to describe all cases of psychosis in 901 consecutive patients in a tertiary care epilepsy clinic.

Results: A total of 126 of these patients with epilepsy were deemed to have a mental disorder after CIDI screening. Of these, 49 (38.9%) received a diagnosis of a DSM-IV psychotic disorder after a standardized psychiatric interview. Four psychotic symptom clusters were found: affective (34.6%), seizure-related (30.7%), chronic (18.3%), and stressor-aggression-related (16.4%). The cluster of seizure-related psychosis shows psychotic symptoms associated with seizure frequency and severity. Stressor-aggression-related psychosis occurs in more than half of cases of left-sided cerebral pathology, in mentally retarded patients. Treatment with atypical neuroleptics was effective and did not have an adverse effect on seizure control or antiepileptic drug use.

Conclusions: The notion that psychosis occurs more often in patients with epilepsy than in the general population is confirmed in this study. The high number of affective psychoses confirms the view that psychotic symptoms in epilepsy patients are preceded or accompanied by mood disorder. The psychosis of epilepsy should be considered a complex cerebral disorder, involving epilepsy, left-sided cerebral pathology, chronic psychosis, mental retardation, and other developmental disorders, such as PDD-NOS, and resulting in chronicity of symptoms and gradually occurring severe impairment of general functioning.

References:

1. Slater E, Beard AW: The schizophrenia-like psychoses of epilepsy I. psychiatric aspects. *Brit J Psychiat* 1963; 109:95-150.
2. Van der Feltz-Cornelis CM: Treatment of interictal psychiatric disorder in epilepsy. II. chronic psychosis. *Acta Neuropsychiatrica* 2002; 14:1:44-48.

NR648 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.** **Methylphenidate in Adult ADHD Patients With Epilepsy: An Open Trial**

Christina M. Vanderfelt-Cornelis, Ph.D., *Department of Psychiatry, Free University Medical Center, Valeriusplein G, Amsterdam 1075 BG, Netherlands*

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the high prevalence of adult ADHD in epilepsy patients, recognize the concomitant psychiatric comorbidity, and know how to treat patients with adult ADHD in treatment-refractive epilepsy effectively and safely with methylphenidate.

Summary:

Objective: To establish the prevalence of adult ADHD in patients with epilepsy. To evaluate effectiveness and safety of methylphenidate treatment in adult ADHD patients with treatment-refractive epilepsy, compared with adult ADHD patients without epilepsy but presenting with pseudoseizures.

Method: In 156 consecutive patients admitted to an epilepsy clinic, 126 received a diagnosis of epilepsy, and six, a diagnosis of adult ADHD. An open treatment trial was performed. Three patients with epilepsy and three with pseudoseizures were included. Both groups received 10 mg of methylphenidate twice daily. Follow-up was performed after six weeks.

Results: A prevalence of 2.4% was found for adult ADHD in the patients with treatment-refractive epilepsy. The two patient groups in the open trial showed clinical improvement of ADHD symptoms during treatment with methylphenidate. In both groups one patient had to stop treatment because of reversible adverse effects. None of the patients experienced adverse effects on seizure control or antiepileptic drug use.

Conclusion: Prevalence of adult ADHD in patients with treatment-refractive epilepsy was higher than in the general population in this study. Methylphenidate was similarly effective in patients with treatment-refractive epilepsy as in patients without epilepsy and had no adverse effects on seizure control or antiepileptic drug use.

References:

1. Gucuyener K, Kemal Erdemoglu A, Senol S, Serdaroglu A, Soysal S, Kockar I: Use of methylphenidate for attention-deficit hyperactivity disorder in patients with epilepsy or electroencephalographic abnormalities. *J Child Neurol* 2003; 18:109-112.
2. Van der Feltz-Cornelis CM. Intractable obsessive-compulsive disorder: co-morbidity with unrecognized adult attention-deficit hyperactivity disorder? *J Nerv Ment Dis* 1999; 187:4:243-5.

NR649 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

EEG BIS-AD Correlates With Mild Cognitive Dysfunction in Elderly Subjects

Supported by Aspect Medical Systems, Inc

Vikas Saini, M.D., *Cardiovascular Specialists, 25 Main Street, Hyannis, MA 02601*; Charles Smith, B.S., Scott Greenwald, Ph.D., Philip Devlin, M.Eng.

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate whether a frontal EEG index developed to assess severity of dementia, BIS-AD, would correlate with assessments of cognitive function in presumably normal elderly subjects.

Summary:

Objective: BIS™ is a widely used monitor of depth of anesthesia that correlates with metrics of cognitive function (e.g., MMSE, memory recall, and sedation level.) BIS-AD, a novel revision (0.1), was designed to correlate with dementia severity assessed with the MMSE. This study evaluated BIS-AD in assessing cognitive function in elderly subjects.

Methods: Elders (age > 75) living independently in their community were enrolled in an ongoing longitudinal trial in which EEG and assessments (MMSE, ADAScog, BIMC) were measured quarterly. BIS-AD (At-Fpz) was extracted from a three-minute vigilant, eyes-closed period. One patient with MMSE <25 was excluded.

Results: Interim results: 229 assessments from 88 subjects (age = 80.0 +/- 3.5). Although the range of cognitive performance was small (MMSE, 28.7 +/- 1.2; ADAScog, 8.4 +/- 3.9; BIMC, 3.6 +/- 2.4), BIS-AD correlated with MMSE (0.17, p = 0.009),

ADAScog (-0.17, p = 0.013), and BIMC (-0.16, p = 0.027). At baseline, BIS-AD was higher in subjects who scored perfectly (MMSE = 30) than in those who made only one mistake (96.0 vs. 94.1, p < 0.05). Change in BIS-AD from baseline correlated with change in MMSE (0.15, p = 0.031)

Conclusions: BIS-AD correlated with cognitive performance in presumably normal elderly subjects. Follow-up assessments will evaluate whether BIS-AD may be an early marker for the development of dementia.

References:

1. Rampil IJ: A primer for EEG signal processing in anesthesia. *Anesthesiology* 1998; 89(4):980-1002.
2. Renna M, Handy J, Shah A: Low baseline bispectral index of the EEG in patients with dementia. *Anesthesia & Analgesia* 2003; 96(5):1380-1385.

NR650 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Geropsychiatry Clinical Database: How Can It Inform Us on Morbidity Patterns?

Sultan A. Lakhani, M.D., *Department of Psychiatry, Virginia Commonwealth University, P.O. Box 980710, 1300 East Marshall Street, Richmond, VA 23298*; Ananda K. Pandurangi, M.D., Nancy Wallace, N.P., Angela Revercomb, M.S., Bonnie Marrow, M.S., Robert Lewis, Ed.D., Walter V. Vieweg, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize prevalence and profiles of common psychiatric disorders seen in the elderly.

Summary:

Introduction: As the population in the U.S. ages, geropsychiatry assumes an increasing role. Whereas data on the prevalence of mental health disorders in elderly exist, data are scarce on access, racial/gender differences, comorbidity, etc. The geropsychiatry program at Virginia Commonwealth University began to study such factors from its clinical database. Data on 276 patients are the basis of this report.

Design: Demographic and clinical data are gathered from all patients in the community seeking prescribed medication from the GeroPsychiatry Program. Patients reside in nursing homes, assisted care living facilities, or family homes. A nurse, physician, or family member made the referral. Patients receive a standard workup and laboratory tests as indicated from a team of mental health professionals, including a geropsychiatrist, nurse practitioner, and social worker. Variables of interest are collected on a form and entered into an ACCESS database. Frequency distributions and group differences (t-test, chi-square) were examined with SPSS.

Results: Data are currently available on 276 patients (age = 80.7 years; males: 53, females: 223); males were significantly younger (78.2 vs. 81.3, t = 1.98, p < 0.06). Race: whites = 219, blacks = 55, other = 2; blacks were younger than whites (75.8 vs. 81.9).

Psychiatric Symptoms: Reasons for psychiatric referral were: depression = 64, medication evaluation = 34, agitation = 24, aggression = 20, anxiety = 18, dementia evaluation = 16, behavior problem = 16, psychosis = 14.

Diagnoses: Alzheimer and vascular dementia = 182 (age = 82 years, males = 31, females = 151; race: white = 140, black = 40); secondary dementia = 16 (age = 78.94 years, white = 11, black = 5); major depression = 55 (age = 80.3 years males = 11, females = 44; race: white = 49, black = 6); any psychotic disorder = 4, miscellaneous = 7.

Medications: All patients were receiving psychotropics as follows: atypicals = 135, typical = 13; ACh inhibitors = 91; benzodiaz-

zepine = 93; SSRIs = 112, SNRs = 39, TCAs = 5, hypnotics = 63, mood stabilizers = 22. Most patients were taking more than one psychotropic: one = 47 patients, two = 60, three = 59, four = 46, five = 14, six = 3, eight = 2. No difference in number of medication based on race or gender, however primary dementia patients were taking significantly more medications than other groups (2.5 vs 1.8, $t = 3.4$, $p < 0.001$).

Discussion: We examined demographic and diagnostic profiles of elderly patients seeking prescribed medication at a community program of a university hospital. The largest group is those with dementia, followed by depression. There was a preponderance of females and Caucasians. African Americans were underrepresented. This may be due to economic factors. Every patient was taking psychotropics, some as many as four different medications. The literature is replete with studies of polypharmacy in this population, and this is an area for improvement and implementation of evidence-based medicine. We are continuing to expand the database and expect to present complete information on 500 patients.

References:

1. Bartels SJ et al: Evidence-based practices in geriatric mental health care: an overview of systematic reviews and meta-analyses. *Psychiatr Clin North Am* 2003; 26(4):971-90, x-xi.
2. Stolee P et al: A community development and outreach program in geriatric mental health: four years' experience. *J Am Geriatr Soc* 1996; 44(3); 314-20.

NR651 Wednesday, May 25, 12:00 p.m.-5:00 p.m.

Localization of Cingulate Activity: Comparison of Four-Versus 24-Channel EEG

Supported by Aspect Medical Systems, Inc

Andrew F. Leuchter, M.D., *Department of Psychiatry, Neuropsychiatric Institute-UCLA, 760 Westwood Plaza, Room 37-426, Los Angeles, CA 90024-8300*; Timothy Kofol, Scott Greenwald, Ph.D., Philip Delvin, Ian A. Cook, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to compare the effectiveness of four-channel EEG monitoring with a traditional full electrode montage for localization of the source of prefrontal EEG activity.

Summary:

Objective: Prefrontal theta activity is associated with antidepressant medication response. These theta rhythms are thought to be generated by the anterior cingulate cortex (ACC). Full surface electrode montages typically are used to localize ACC sources, although large montages are problematic for routine use. This work evaluated whether a four-channel montage would perform similarly to a full-head montage.

Methods: EEGs (24 channels) were recorded from 24 subjects with major depressive disorder prior to reboxetine treatment. Fourteen subjects responded ($\text{HAM-D} \leq 10$) after eight weeks. Sources of prefrontal theta activity were estimated by using low resolution brain electromagnetic tomography (LORETA) of a four-second, EEG segment (band-passed 4-8 Hz). Images were made twice per subject: first with the original 24 channels (standard method), then with four channels (F7-Fpz, F8-Fpz, A1-Fpz, A2-Fpz) augmented with synthetic EEG for the remaining 20 channels (novel method).

Results: Both methods localized the source of prefrontal EEG activity to the voxels in the ACC with a high degree of correlation ($p > 0.05$). Images of group differences between responders and nonresponders were similar between methods, showing lower ACC activity in responders ($p < 0.05$ for both methods.)

Conclusions: These results demonstrate that ACC activity can be estimated with a simple-to-use four-channel EEG. Future work will refine the technique for the development of a clinical tool to aid management of antidepressant therapy.

References:

1. Pizzagalli D, Pascual-Marqui RD, Nitschke J, Oakes T, Larson C, Abercrombie H: Anterior cingulate activity as a predictor of degree of treatment response in major depression: evidence from brain electrical tomography analysis. *American Journal of Psychiatry* 2001; 158:405-415.
2. Pascual-Marqui RD, Michel CM, Lehmann D: Low resolution electromagnetic tomography: a new method for localizing electrical activity in the brain. *International Journal of Psychophysiology* 1994; 18:49-65.

NR652 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Psychological Aspects of the Mother-Child Relationship of Children With Cystic Fibrosis

Maria Gragas Lima, M.S., *Department of Psychology Services, Santa Casa Sao Paulo, Cesario Mota, Jr. 112, Sao Paulo, SP 01221-900, Brazil*; Isabel C. Gomez

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the intrinsic psychological processes of the mother-child relationship considering the context of a child with a chronic health condition.

Summary:

The present study was conducted to examine the psychological aspects of the mother-child relationship, considering the context of a child with a chronic health condition, specifically cystic fibrosis. It was hypothesized that the intrinsic psychological processes concerning the mother-and-child relationship would be vulnerable to the distressing factors resulting from this illness. Psychoanalysis was the theoretical framework used, particularly Winnicott's work, and a bibliographical survey was carried out concerning children with cystic fibrosis. The research was conducted at the Cystic Fibrosis Ambulatory Clinic of Santa Casa de Sao Paulo, and the methodology was the case study of three mothers ranging from 30 to 40 years old, whose children had cystic fibrosis and received treatment at that ambulatory clinic. They attended a semidirected interview and drawing-story procedures. The findings were coincident and complimentary, in the sense that they identified depressive anxiety, a sense of abandonment and solitude, and defense mechanisms of idealization, rationalization, and isolation in the mother-child relationship.

References:

1. Sarti, MHC: A Criança Hospitalizada: Contribuição do Desenho da Figura Humana para Avaliação do seu Estado Emocional. Dissertação de Mestrado, Universidade de São Paulo, São Paulo, 1988.
2. Trinca, AM: A Apreensão de Conteúdos Emocionais de Crianças em Situação Pré-Cirúrgica. Dissertação de Mestrado, Universidade de São Paulo, São Paulo, 1987.

NR653 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Impaired Recognition of Facial Emotional Expressions in Elderly

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss evidence that impairment of facial affect recognition in elderly may be part of the normal aging process.

Summary:

Objectives: It is well known that some cognitive function and perceptual abilities decline with aging. However, studies of change in emotion-related functions are rare across nations. This study investigated differences of facial emotional recognition between elderly person age 60 years and young persons age 30 years.

Methods: Korean facial expressions of emotion, including happiness, sadness, fear, anger, disgust, surprise, and neutral, were used as stimuli for the facial affect recognition test. A computerized facial affect recognition test that consisted of a facial affect identification test and a facial affect intensity test was done.

Results: A total of 120 persons (53 elderly persons) participated in this study. For the facial affect identification test, there was a significant difference between the groups ($F=3.986$, $p<0.01$) after controlling the effect of years of education. Elderly participants showed a significantly less correct recognition rate with sadness, anger, and disgust ($p<0.05$). For the facial affect intensity test, there was no significant difference between groups.

Conclusions: This study reports impairment of facial affect recognition in elderly persons in a study using Korean facial expressions. This study suggests that dysfunction of facial affect recognition may be part of the normal aging process.

References:

1. Calder AJ, Kean J, Manly T, Sprengelmeyer R, Scott S, Nimmo-Smith I, et al: Facial expression recognition across the adult life span. *Neuropsychologia* 2003; 41:195-202.
2. Phillips LH, Allen R: Adult aging and the perceived intensity of emotions in faces and stories. *Aging Clin Exp Res* 2004; 16:190-199.

NR654 Wednesday, May 25, 3:00 p.m.-5:00 p.m. Diagnostic Accuracy of Cognitive Screening in Emergent Psychiatric Patients

Zoya Simakhodskaya, Ph.D., *Department of Psychiatry, Bellevue Hospital Center, New York, NY 10016*; Steven P. Cery, Ph.D., Aaron Elliott, M.D.

Educational Objectives:

At the conclusion of this presentation, participants should be able to recognize that cognitive screening using the MMSE may be enhanced by supplementing it with three brief measures: Oral Trails, animal fluency, and Clock Drawing tests.

Summary:

Objective: The Mini-Mental State Examination (MMSE) is firmly established as a cognitive screening instrument. However, in certain clinical contexts, its sensitivity may be lower than is desirable. The presenters examined the diagnostic accuracy of a cognitive screening assessment designed to supplement the MMSE with minimal increased time expense.

Methods: The MMSE, Oral Trails, animal fluency, and Clock Drawing tests were administered to 18 patients presenting with emergent psychiatric conditions. Subsequent comprehensive neuropsychological evaluation served as the criterion for determining group membership. Three Z-score cutoffs (-1.0, -1.5, and -2.0) based on published norms were used to calculate standard diagnostic decision measures. Logistic regression analysis was conducted by using a prior probability of 0.50.

Results: Sensitivity (71.4%) and total diagnostic accuracy (72.2%) of the MMSE were optimal at $Z = -1.0$. Sensitivity (100%) and total diagnostic accuracy (83.3%) of the cognitive screen

were superior to the MMSE alone across all three Z-score cutoffs. Logistic regression yielded excellent sensitivity (92.9%), specificity (100%), and total diagnostic accuracy (94.4%).

Conclusions: Preliminary findings suggest that the cognitive screening assessment substantially enhances the clinical utility of the MMSE for detecting cognitive dysfunction in emergent psychiatric populations and may lead to improved treatment outcomes in those patients.

References:

1. Folstein et al: 'Mini-mental state': a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975; 12:189-198.
2. Tierney et al: Prediction of probable Alzheimer disease in patients with symptoms suggestive of memory impairment. *Arch Fam Med* 2000; 9:527-532.

NR655 Wednesday, May 25, 3:00 p.m.-5:00 p.m. Computerized Cognitive Tests Identify MCI in Urban Black Individuals

Supported by National Institutes of Health, SUNY Health Sciences Center at Brooklyn, and Institute for the Study of Aging

Ely S. Simon, M.D., *Neurotrax Corporation, 1133 Broadway Suite 706, New York, NY 10010*; Glen M. Doniger, Ph.D., Howard Crystal, M.D., *Mi-Yeoung Jo*

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the discriminant validity of a set of computerized cognitive tests in identifying mild cognitive impairment (MCI) in urban black individuals.

Summary:

Objective: To assess the validity of Mindstreams computerized cognitive tests in identifying mild cognitive impairment (MCI) in a largely Afro-Caribbean inner-city cohort.

Method: Elderly persons from an inner-city primary care clinic with conference diagnoses of cognitively healthy ($N=22$; age: 67.6 ± 4.6 ; years of education: 13.6 ± 3.2) or MCI ($N=27$; age: 69.2 ± 6.5 ; years of education: 10.3 ± 3.7) completed Mindstreams® (NeuroTrax Corp., NY) testing. Discriminant validity was assessed by analysis of covariance with age, education, gender, and computer experience as covariates in separate analyses when indicated both by a between-group difference and by correlation with performance. Area under the curve (AUC) was used as a measure of effect size. Primary outcomes were age- and education-normalized Memory, Executive Function, and Visual Spatial index scores and an MCI score score summarizing performance in domains most sensitive to MCI.

Results: The Memory index score ($AUC=0.816$) discriminated participants with MCI from healthy participants ($p<0.001$), even after adjustment for education ($p=0.002$) and computer use ($p<0.001$). The Executive Function ($AUC=0.737$) index score discriminated the two groups ($p=0.01$), as did the Visual Spatial ($AUC=0.683$) index score ($p=0.03$). The MCI score ($AUC=0.829$) discriminated MCI particularly well ($p<0.001$), even after adjustment for education ($p=0.001$) and computer use ($p<0.001$).

Conclusions: Mindstreams tests exhibit good discriminant validity for MCI in urban black individuals.

References:

1. Dwoletzky T, Whitehead V, Doniger GM, Simon ES, Schweiger A, Jaffe D, et al: Validity of a novel computerized cognitive battery for mild cognitive impairment. *BMC Geriatr* 2003; 3: 4.
2. Elstein D, Doniger GM, Guedalia J, Simon ES, Antebi V, Arnon Y et al: Computerized cognitive testing in patients with type I

Gaucher disease: effects of enzyme replacement and substrate reduction. *Genet Med* (in press).

NR656 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Computerized Assessment Reveals Common Deficits in Multinational MCI Cohort

Supported by Institute for the Study of Aging

Ely S. Simon, M.D., *Neurotrax Corporation, 1133 Broadway Suite 706, New York, NY 10010*; Felicia C. Goldstein, Ph.D., Tzvi Dwolatzky, M.D., Glen M. Doniger, Ph.D., Allan I. Levey, Ph.D., James J. Lah, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to appreciate: 1) the ability of a set of computerized cognitive tests to identify mild cognitive impairment (MCI) in individuals with varying ethnic backgrounds and 2) the common pattern of cognitive impairment in MCI.

Summary:

Objective: To examine the cognitive profile of mild cognitive impairment (MCI) in a two-site multinational cohort.

Method: Cognitively healthy (N=24; age: 73.4±10.9; education: 15.5±3.0 years) and MCI (Petersen's criteria; N=68; age: 73.8±9.3; education: 13.5±4.0 years) participants from U.S. and Israeli sites completed Mindstreams® (NeuroTrax Corp., NY) testing. The U.S. cohort was 81% white and 17% African American. The Israeli cohort was 36% Eastern European, 24% Western European, 20% Native Israeli, 12% American, and 8% Asian. Healthy and MCI participants were comparable in age, gender, handedness, and computer experience (p's>0.05); MCIs had fewer years of education (p=0.03). Analysis of variance included site and diagnosis as factors with education as a covariate when correlated with performance.

Results: No intersite performance differences were found other than poorer Verbal Function performance in U.S. participants (p=0.03). MCIs performed more poorly than healthy participants on Memory (p=0.001), Executive Function (p=0.004), Verbal Function (p<0.001), Attention (p=0.02), and Information Processing (p=0.01) index scores and on a Global Cognitive Score (p<0.001). The site-by-diagnosis interaction was not significant for any outcome.

Conclusions: Mindstreams validly identifies MCI in individuals with varying ethnic backgrounds as evidenced by similar extent of impairment and cognitive profile across sites in a multinational cohort.

References:

1. Dwolatzky T, Whitehead V, Doniger GM, Simon ES, Schweiger A, Jaffe D, et al: Validity of a novel computerized cognitive battery for mild cognitive impairment. *BMC Geriatr* 2003; 3: 4.
2. Elstein D, Doniger GM, Guedalia J, Simon ES, Antebi V, Arnon Y et al: Computerized cognitive testing in patients with type I Gaucher disease: effects of enzyme replacement and substrate reduction. *Genet Med* (in press).

NR657 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Caregiver Distress Behavioral Correlates in Alzheimer's Disease and Dementia

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Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the importance of specific behaviors contributing to caregiver distress in specific dementias.

Summary:

Objective: The presenters determined neuropsychiatric features contributing to caregiver distress in different dementia diagnoses.

Method: Twenty-four dementia facility subjects were evaluated by using the Neuropsychiatric Inventory (NPI-NH), Mini-Mental State Exam (MMSE), and DSM-IV-TR and NINCDS-ADRDA criteria for Alzheimer's disease (AD).

Results: In dementia (N=24), NPI total caregiver distress scores were independently related to delusions (r=.717, r²=.515, p=.00012), agitation (r=.657, r²=.432, p=.00066), disinhibition (r=.619, r²=.383, p=.0016), and irritability (r=.646, r²=.417, p=.00087). In multivariate regression, delusions, agitation, and irritability remained significant (r=.925, r²=.856, p=.0000024). In DSM-IV-TR AD (N=16), caregiver distress independently correlated with agitation (r=.749, r²=.562, p=.0013), disinhibition (r=.699, r²=.488, p=.0038), and irritability (r=.692, r²=.479, p=.0043). On multivariate regression, only agitation and irritability remained significant (r=.879, r²=.773, p=.00073). In NINCDS-ADRDA probable AD (N=11), caregiver distress independently correlated only with irritability (r=.739, r²=.546, p=.0094).

Conclusions: Irritability is a common source of caregiver distress across dementia types. In DSM-IV-TR AD, agitation was more a source of distress than in NINCDS-ADRDA AD. DSM-IV-TR AD may include a type of AD (e.g., executive variant AD) with greater ventral frontotemporal pathology, with more agitation and disinhibition and less depression than NINCDS-ADRDA AD, and fewer delusions than non-AD dementia. Confirmation will require larger samples.

References:

1. Dunkin JJ, Anderson-Hanley C: Dementia-caregiver burden: a review of the literature and guidelines for assessment and intervention. *Neurology* 1998; 51(1 Suppl 1):S53-60.
2. Senanarong V, Cummings JL, Fairbanks L, et al: Agitation in Alzheimer's disease is a manifestation of frontal lobe dysfunction. *Dement Geriatr Cogn Disord* 2004; 17:14-20.

NR658 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Dopaminergic Dysfunction in Schizophrenia: HPA, HPT, and Noradrenergic Correlates

Fabrice Duval, M.D., *Department of Psychiatry, Centre Hospitalier, 27 Rue du 4eme RSM, Rouffach 68250, France*; Marie-Claude Mokrani, Ph.D., Jose Monreal, M.D., Said Fattah, M.D., Christiane Champeval, Ph.D., Marie-Laure Souan, M.D., Jean-Paul Macher, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that dopamine dysfunction in paranoid schizophrenic patients (as reflected by blunted ACTH/cortisol and prolactin responses to apomorphine) is associated with relatively increased HPA axis activity, normal alpha 2-noradrenergic function, and normal HPT axis activity.

Summary:

Background: The aim of this study was to assess hypothalamic-pituitary dopaminergic (DA), noradrenergic (NA), thyroid (HPT), and adrenal (HPA) activity in schizophrenia.

Method: Hormonal responses to 8 AM and 11 PM TRH tests, dexamethasone suppression test (DST), apomorphine test (APO; a DA receptor agonist), and clonidine test (CLO; an alpha 2-adrenoreceptor agonist) were measured in 13 untreated male

inpatients with DSM-IV paranoid schizophrenia and 13 matched hospitalized healthy comparison subjects.

Results: Compared with the healthy subjects, patients showed 1) a decrease in APO-induced adrenocorticotropin (ACTH) and cortisol stimulation ($p < 0.04$ and $p < 0.01$ respectively), 2) a higher rate of blunted prolactin (PRL) suppression to APO ($p < 0.01$), 3) and a slight increase in post-dexamethasone cortisol values ($p < 0.02$). Blunted responses to APO were independent of DST status. On the other hand, TSH responses to TRH, growth hormone responses to CLO and APO, and PRL responses to TRH and CLO were not significantly different between schizophrenic patients and comparison subjects.

Conclusion: The results suggest that decreased hypothalamic DA receptor activity (possibly secondary to increased presynaptic DA release), together with relatively increased HPA axis activity, normal alpha 2-noradrenergic function, and normal HPT axis activity, characterize untreated male paranoid schizophrenic patients.

References:

1. Mokrani MC, Duval F, Crocq MA, Bailey P, Macher JP: Multi-hormonal responses to apomorphine in mental illness. *Psychoneuroendocrinology* 1995; 20:365-375.
2. Duval F, Mokrani MC, Monreal J, Bailey P, Vaidebenito M, Crocq MA, Macher JP: Dopamine and serotonin function in untreated schizophrenia: clinical correlates of the apomorphine and d-fenfluramine tests. *Psychoneuroendocrinology* 2003; 28:627-642.

NR659 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Thyroid Axis Activity and Suicidal Behavior in Depressed Patients

Fabrice Duval, M.D., *Department of Psychiatry, Centre Hospitalier, 27 Rue du 4eme RSM, Rouffach 68250, France*; Marie-Claude Mokrani, Ph.D., Jose A. Monreal Ortiz, M.D., Said Fattah, M.D., Christiane Champeval, Ph.D., Marie-Laure Souan, M.D., Jean-Paul Macher, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand that specific thyroid axis abnormalities distinguish between depressed patients with a suicide attempt history and those without such history.

Summary:

Background: The aim of this study was to investigate the relationship between suicidal behavior and hypothalamic-pituitary thyroid (HPT) axis activity in depressed patients.

Method: The presenters evaluated the serum levels of TSH, free thyroxine (FT4), and free triiodothyronine (FT3) before and after 8 AM and 11 PM TRH challenges (200 µg IV), on the same day, in 44 healthy hospitalized comparison subjects and 95 drug-free DSM-IV euthyroid major depressed inpatients (53 with a history of suicide attempts [SA], 42 without [NSA]).

Results: TRH-induced TSH responses were not significantly different between SAs and comparison subjects but were blunted in NSAs (at 8 AM: $p < 0.05$, at 11 PM: $p < 0.00001$). Owing to decreased FT4 basal levels, SAs showed lower FT4/FT3 ratios than comparison subjects (at 8 AM: $p < 0.004$, at 11 PM: $p < 0.001$) and than NSAs (at 8 AM: $p = 0.05$, at 11 PM: $p < 0.01$).

Conclusions: This study suggests that in NSAs, hypersecretion of hypothalamic TRH (as reflected by the decreased TRH receptor function) may represent a compensatory mechanism to maintain normal serum T3 and T4 concentrations. In SAs, this mechanism is not effective, but the reduced FT4/FT3 ratios suggest enhanced conversion of T4 to T3 to maintain normal T3 concentration.

References:

1. Duval F, Mokrani MC, Crocq MA, Jautz M, Bailey P, Diep TS, Macher JP: Effect of antidepressant medication on morning and evening thyroid function tests during a major depressive episode. *Arch Gen Psychiatry* 1996; 53:833-840.
2. Berlin I, Payan C, Corruble E, Puech AJ: Serum thyroid-stimulating-hormone concentration as an index of severity of major depression. *Int J Neuropsychopharmacol* 1999; 2:105-110.

NR660 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Dopamine Dysregulation in Bipolar Depressed Patients

Jose A. Monreal Ortiz, M.D., *Department of Psychiatry, Centre Hospitalier, 27 Rue Du 4 RSM, Rouffach 68250, France*; Fabrice Duval, M.D., Marie-Claude Mokrani, Ph.D., Said Fattah, M.D., Christiane Champeval, Ph.D., Marie-Laure Souan, M.D., Jean-Paul Macher, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand that dopamine (DA) dysfunction in bipolar depressed patients is not due to deficiency of pituitary lactotrophs and/or increased hypothalamic-pituitary-adrenal axis activity, but may reflect altered post-synaptic receptor sensitivity in the tuberoinfundibular DA system.

Summary:

Background: The purpose of this study was to assess the dopaminergic (DA) receptor sensitivity at the hypothalamic-pituitary level in relation to the clinical course in depressed patients.

Method: The presenters evaluated the multihormonal responses to the DA agonist apomorphine (APO, 0.75 mg SC) in 19 drug-free inpatients with DSM-IV major depression (10 with bipolar depression, nine with unipolar depression), compared with 15 sex- and age-matched healthy hospitalized comparison subjects. In the same subjects, prolactin (PRL) response to 8 AM and 11 PM protirelin challenges (TRH, 200 µg IV) and cortisol response to dexamethasone suppression test (DST, 1 mg orally) were examined.

Results: Responses to TRH tests and DST were comparable between healthy subjects, unipolar patients, and bipolar patients. No significant difference in cortisol, adrenocorticotropin and growth hormone values was found (i.e., at baseline and in response to APO) across the three diagnostic groups. However, the bipolar patients had lower APO-induced PRL suppression than the healthy subjects ($p = 0.0003$) and the unipolar patients ($p = 0.04$).

Conclusions: Taken together these results suggest that decreased APO-induced PRL suppression in bipolar depressed patients is not due to a deficiency of pituitary lactotrophs and/or increased HPA axis activity but may reflect an altered postsynaptic DA-D2 receptor sensitivity in the tuberoinfundibular dopamine system.

References:

1. Mokrani MC, Duval F, Crocq MA, Bailey P, Macher JP: Multi-hormonal responses to apomorphine in mental illness. *Psychoneuroendocrinology* 1995; 20:365-375.
2. Duval F, Mokrani MC, Bailey P, Crocq MA, Diep TS, Macher JP: Dopamine function in men with bipolar depression *Biol Psychiatry* 2000; 47:73S.

NR661 **Wednesday, May 25, 3:00 pm-5:00 p.m.**

The Cell Viability and the Proliferation Activity of Peripheral Lymphocytes in Patients With Alzheimer's Disease

Lee S. Kim D.K., M.D. *Department of Psychiatry, Samsung Medical Center, 50 Irwon-dong, Kangnam-gu, Seoul 135-710,*

Korea; Suzie Lee, M.D., Young-Ah Kwon, M.S., Hyeran Kim, M.D., Sung H. Chung, M.D., Dohk Kim

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that there is decreased peripheral lymphocytes cell viability and proliferation activity in AD patients.

Summary:

There is evidence of apoptotic neuronal cell death in Alzheimer's disease (AD). Recent studies suggests that AD pathogenesis in the central nervous system appeared as well as in peripheral lymphocytes. This study compared cell viability and proliferation activity in AD patients with those in healthy control subjects by using peripheral lymphocytes. The presenter analyzed the cell viability and proliferation activity of phytohemagglutinin (PHA)-activated lymphocytes from 73 AD patients and 31 control subjects. The cell viability and the proliferation activity were measured at baseline (T0), 24 hours (T24), 48 hours (T48), 76 hours (T76), and 92 hours (T92) by the trypan blue method and the BudU proliferation activity method, respectively. The cell viability of PHA-activated peripheral lymphocytes in AD patients was significantly decreased after 48 hours, compared with that in the healthy control subjects ($F = 13.0$, $p < 0.001$). In AD patients, the decline of the proliferation activity appeared earlier than in the control subjects. The results suggest that there is decreased peripheral lymphocytes cell viability and proliferation activity in AD patients. These findings may be related to increased apoptosis in AD.

References:

1. Hamdane M, Delobel P, Sambo AV, Smet C, Begard S, Violleau A, Landrieu I, Delacourte A, Lippens G: Neurofibrillary degeneration of Alzheimer-type: an alternate pathway to neuronal apoptosis? *Biochem Pharmacol* 2003; 15:66(8):1619-25.
2. Cummings JL, Cole G: Alzheimer Disease. *JAMA* 2002; 287(18):2335-2338.

NR662 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Validation of a Structured Instrument for the Diagnosis of Delirium and Its Measurement

Maricarmen Flores-Miranda, M.D., *Instituto NCMNSZ, Department of Neurology, Cuauhtemoc 46 Col Toriello-Guerra, Mexico City 14050, Mexico*; Juan J. Calva, M.S.C., Guillermo Dominguez-Cheritt, M.D., Adrian Gonzalez, M.D., Gabriel Alejo, M.D., Juan Gutierrez, M.D., Angeles Vargas, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that a delirium diagnosis can be obtained in a mechanically ventilated patient receiving sedative medications, with independence of professional experience or background.

Summary:

Objective: To develop and validate a structured instrument for diagnosis of delirium in critically ill patients.

Method: The presenters created a structured instrument to standardize the interview. The cross-sectional study was conducted at the adult intensive care unit at the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán. Participants were 291 patients, including both ventilated and nonventilated patients, who were also receiving sedative medication. Blind pair evaluations were conducted. The main outcome measure was interrater agreement obtained with the SIDDIM-ICU and concurrent validation of the SIDDIM-ICU with the Delirium Rating Scale-Revised-98 (DRS-R-98).

Results: The interrater agreement obtained with kappa statistics was 0.85 for ventilated patients, 0.94 for nonintubated patients, 0.81 for patients receiving sedative medication, 0.96 for patients

without sedatives, 0.86 among psychiatrists, 1.00 among intensivists, 0.90 among nurses, 1.00 between the nurses and intensivists, 0.94 between the nurses and psychiatrists, and 0.83 between the intensivists and psychiatrists. The sensitivity and specificity were 100%.

Conclusion: This structured instrument may be useful in this challenging population.

References:

1. Trzepacz P: Validation of the Delirium Rating Scale-Revised-98: comparison with the Delirium Rating Scale and the Cognitive Test for Delirium. *J Neuropsych Clin Neurosci*, 2001; 13: 229-242.
2. Ely W: Evaluation of delirium in critically ill patients: validation of the Confusio assessment method for the intensive care unit. *Crit Care Med* 2001; 29: 1370-1379.

NR663 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Switching From Risperidone to Quetiapine in Elderly Patients With Dementia

Supported by AstraZeneca Pharmaceuticals

Subamoni Madhusoodanan, M.D., *Peninsula Hospital, 327 Beach 19th Street, Far Rockaway, NY 11691*; Olivera J. Bogunovic, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that switching from one antipsychotic to another with a better safety profile can produce favorable outcomes for geriatric patients with dementia.

Summary:

Objective: To collect data on outcomes obtained when the medication of elderly nursing home residents with dementia is switched from risperidone to quetiapine.

Methods: Medical records were reviewed to identify dementia patients whose medication was switched from risperidone to quetiapine between May and December 2003. Demographic, efficacy, and safety data were collected. Clinical Global Impression (CGI) scores assigned retrospectively (at switch and weeks 4-6) assessed treatment.

Results: Data from 15 men and 52 women (mean age, 82.8 years) were evaluated. Alzheimer's disease was the primary diagnosis in 37 patients and a secondary diagnosis in 19 patients; other diagnoses included vascular dementia, schizophrenia, schizoaffective disorder, depression, anxiety, and alcohol-related dementia. Mean daily dose of risperidone at the switch was 1.42 mg (range, 0.25-6.0 mg). Switching was abrupt in all but two patients. Mean daily dose of quetiapine after the switch was 87.3 mg (range, 25-200 mg). After the switch, the CGI Severity of Illness score remained unchanged, but the CGI Global Improvement was positive. Fourteen patients reported somnolence; three patients discontinued quetiapine because of lack of response.

Conclusions: Most patients in this study had their medication switched from risperidone to quetiapine with no worsening of clinical status. Even the two patients whose medication was abruptly switched did not report significant adverse effects.

References:

1. Madhusoodanan S: Introduction: antipsychotic treatment of behavioral and psychological symptoms of dementia in geropsychiatric patients. *Ann J Geriatr Psychiatry* 2001; 9(3):283-8.
2. Liperoti R, Mor V, Lapane KL, Pedone C, Gambassi G, Bernabei R: The use of atypical antipsychotics in nursing homes. *J Clin Psychiatry* 2003; 64(9):1106-1112.

NR664 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Methylenetetrahydrofolate Reductase Variant and Schizophrenia

Maria P. G-Portilla, Ph.D., *Department of Psychiatry, Oviedo University, Julian Claveria 6-3, Oviedo 33006, Spain*; Pilar A. Saiz, Ph.D., Blanca Morales, M.D., Eliecer Coto, Ph.D., Victoria Alvarez, Ph.D., Juan M. Fernandez, M.D., Julio B. Bobes, M.D.

Educational Objectives:

At the conclusion of this presentation, participants should be able to recognize and discuss the role of the C667T methylenetetrahydrofolate reductase gene polymorphism in schizophrenia in Spanish population.

Summary:

Objective: To investigate the potential association between the C667T methylenetetrahydrofolate reductase (MTHFR) gene polymorphism and schizophrenia.

Method: The presenters genotyped 204 schizophrenic outpatients (Sc) (DSM-IV criteria) (mean age [SD] = 35.48 [11.72]; males = 59.3%) and 296 unrelated healthy volunteers (mean age [SD] = 37.37 [10.21]; males = 53.0%) from Asturias (Northern Spain) (same ethnic background). All individuals gave written informed consent. Genomic DNA was extracted from lymphocytes of peripheral blood samples. The target sequence was amplified with polymerase chain reaction by using the procedure of Fross et al. (1995). PCR products were digested with the restriction enzyme *Hinf*I.

Results: No significant differences in MTHFR genotype frequencies between patients and control subjects was found ($p = 0.307$). The genotype homozygous for the T667 allele was similar in both groups (9.3% vs. 13.9%; OR = 0.639, 95% CI = 0.359-1.136; $p = 0.163$). MTHFR T667 allele frequencies did not differ between both groups (34.1% vs. 37.5%; OR = 0.861, 95% CI = 0.661-1.121).

Conclusions: Polymorphic variations in the MTHFR gene were not associated with schizophrenia in the study population. Although no evidence of allelic or genotypic associations with schizophrenia was found, larger samples are needed to confirm or reject the current data.

References:

1. Arinami T, Yamada N, Yamakawa-Kobayashi K, Hamaguchi H, Toru M: Methylenetetrahydrofolate reductase variant and schizophrenia / depression. *Am J Med Genet* 1997; 74:526-528.
2. Virgos C, Martorell L, Simo JM, Valero J, Figuera L, Joven J, et al: Plasma homocysteine and the methylenetetrahydrofolate reductase C667T gene variant: lack of association with schizophrenia. *Neuroreport* 1999; 10:2035-2038.

NR665 Wednesday, May 25, 03:00 p.m.-5:00 p.m.

5HT 2A Receptor Gene Polymorphisms and Personality Traits in Healthy Subjects

Pilar A. Saiz, Ph.D., *Department of Psychiatry, University of Oviedo, Julian Claveria No 6-30, Oviedo 33006, Spain*; Rocio Herrero, M.D., Blanca Morales, M.D., Maria P. G-Portilla, Ph.D., Begona Paredes, M.D., Teresa Bascaran, M.D., Julio B. Bobes, M.D.

Educational Objectives:

At the conclusion of this presentation, participants should be able to recognize and discuss the role of two serotonin 2A receptor gene polymorphisms in personality traits in a mentally healthy Spanish population.

Summary:

Objectives: To investigate the relationship between personality traits and two polymorphisms (T102C / A-1438G) of the serotonin 2A receptor gene (5-HT2A).

Method: The participants included 343 healthy adults (mean age [SD] = 38.82 [10.67]; males = 45.8.3%) with no history of psychiatric disorder from Asturias (Northern Spain) (same ethnic background). All individuals gave written informed consent. All participants were tested with the Temperament and Character Inventory (TCI) and genotyped for serotonin 2A receptor gene polymorphisms. Genotyping was analyzed with polymerase chain reaction. Differences in TCI dimension and subscale scores among groups were examined with ANOVA.

Results: Both polymorphisms (T102C / A-1438G) were in complete linkage disequilibrium in our population. Observed genotype distributions were consistent with Hardy-Weinberg equilibrium. Frequencies of the 5-HT2A genotypes were: TT (AA), 22.2%, TC (AG), 48.7%, CC (AA), 29.2%. There was no significant relationship of the 5-HT2A genotypes with the seven personality dimension scores. In exploratory analyses, CC subjects scored higher in the S1 (responsibility) and C3 (helpfulness) subscales than TT individuals ($p = 0.042$, $p = 0.016$, respectively). However, these results would not withstand Bonferroni's correction for multiple testing.

Conclusions: Personality traits detected by TCI may not be directly related to the 5-HT2A receptor gene polymorphisms in the study population.

References:

1. Kusumi I, Suzuki K, Sasaki Y, Kameda K, Sasaki T, Koyama T: Serotonin 5-HT2a receptor gene polymorphism, 5-HT2A receptor function and personality traits in healthy subjects: a negative study. *J Affect Disord* 2002; 68:235-241.
2. Ham BJ, Kim YH, Choi MJ, Cha JH, Choi YK, Lee MS: Serotonergic genes and personality traits in the Korean population. *Neurosci Lett* 2004; 354:2-5.

NR666 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Parental Psychopathology and Childhood Atopic Disorders in the Community

Ramin Mojtabai, M.D., *Department of Psychiatry, Beth Israel Medical Center, First Avenue At 16th Street, New York, NY 10003*

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the relationship between common mental disorders in parents and atopic disorders in their children.

Summary:

Objective: To examine the association of parental psychopathology and childhood atopic disorders in the general population.

Methods: In a sample of 9,240 (8,686 biological and 554 nonbiological) parent-child dyads drawn from the 1999 U.S. National Health Interview Survey, the association of childhood atopic disorders with parental major depression, generalized anxiety disorder, and panic attacks was examined. Parental DSM-IV psychiatric diagnoses were ascertained by the Composite International Diagnostic Interview, Short-Form (CIDI-SF).

Results: Parental major depression and panic attacks were associated with childhood atopic disorders only in biological parent-child dyads, and among these, only in mother-child dyads (adjusted odds ratio = 1.87 and 1.55, respectively). Parental atopic disorders and parental psychopathology have an additive effect on the risk of atopic disorders in the offspring.

Conclusion: Findings from this study support the hypothesis of a shared genetic liability for childhood atopic disorders and parental major depression and panic attacks.

References:

1. Wamboldt MZ, Hewitt JK, Schmitz S, et al: Familial association between allergic disorders and depression in adult Finnish twins. *Am J Med Genet* 2000; 96:146-53.
2. Goodwin RD, Jacobi F, Thfeld W: Mental disorders and asthma in the community. *Arch Gen Psychiatry* 2003; 60:1125-30.

NR667 Wednesday, May 25, 3:00 p.m.-5:00 p.m.
Is Insomnia a Visiting Card for Psychiatric Disorders in General Hospitals?

Claudia Hara, M.S.C., *Department of Psychiatry, IPSEMG, Rio Grande Norte 921 AP 803, Belo Horizonte, MG 30130-131, Brazil*; Fabio L. Rocha, M.D., Cristina V. Rodrigues, M.D., Milena A. Santos, M.D., Erico C. Costa, M.S.C., Cintia Fuzikawa

Educational Objectives:

At the conclusion of this session, the participant should be aware of the relationship between insomnia and psychiatric disorders in general hospital inpatients.

Summary:

Objective: The prevalence of psychiatric disorders in general hospital inpatients is high. These disorders can negatively interfere with the evolution of clinical problems, increasing morbidity, mortality, and hospitalization time. Also, insomnia is a common but underrecognized problem in general hospitals. The aim of the study was to evaluate the relationship between insomnia and psychiatric disorders in general hospital inpatients.

Method: The information about insomnia was collected with a structured and codified questionnaire adapted from a previously validated one in Brazil. For DSM-IV psychiatric diagnosis, the Portuguese version of the International Neuropsychiatric Interview (MINI) was used.

Results: Of the 200 patients interviewed, 56.5% complained of insomnia and 50.0% had at least one psychiatric disorder. Only three (1.5%) of these patients had a psychiatric diagnosis in their medical records at the time of the interview. No record included mention of any symptom related to sleep. Major depressive episode ($p < 0.001$), generalized anxiety disorder ($p = 0.025$), and suicide risk ($p = 0.034$) were associated with insomnia in the univariate analysis. The results of the multivariate analysis of psychiatric disorders associated with insomnia showed that only major depressive episode had a statistically significant association with insomnia (OR = 3.6; 95% CI = 1.9-6.9).

Conclusions: This study found a high prevalence of psychiatric disorders and insomnia in a general hospital population. These problems had a low rate of detection by the clinician. Insomnia can be a "visiting card" for a major depressive episode.

References:

1. Jiang W, Alexander J, Christopher E, et al. Relationship of depression to increased risk of mortality and rehospitalization in patients with congestive heart failure. *Arch Intern Med* 2001; 161:1849-56.
2. Uldall KK, Koutsky LA, Bradshaw DH, et al: Psychiatric comorbidity and length of stay in hospitalized AIDS patients. *Am J Psychiatry* 1994; 151:1475-8.

NR668 Wednesday, May 25, 03:00 p.m.-5:00 p.m.

Fractal Analysis of EEG in Hypnosis and Its Relationship With Hypnotizability

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Educational Objectives:

At the conclusion of this session, the participant should understand that the hypnotic condition and hypnotizability can be defined by neurophysiological variations.

Summary:

Objectives: The differences in scales for accessing hypnotizability were investigated, and their relationships were examined on the basis of results of a fractal analysis of hypnotic EEG to clarify the physiological concomitant for hypnotizability.

Methods: The subjects in this study were 19 psychiatric outpatients in healthy medical condition. The hypnotist used the hypnotic induction profile (HIP) technique to induce hypnosis and to measure hypnotizability. EEG data were acquired by the Telefactor EEG monitoring device in an EEG recording room. Fifty-four sets were analyzed by detrended fluctuation analysis (DFA) a well-established fractal analysis technique. Repeated-measures ANOVA and correlation were used to determine any differences or relationships between the means of the conditions.

Results: Significant differences for scaling exponents, which are the results of fractal analysis, were found between waking and hypnotic conditions in most of the channels. The examination of the relationships between the scaling exponents in a hypnotic condition and scores on hypnotizability scales showed that only the eye-roll sign (ERS), which is a part of the HIP, significantly correlated with the scaling exponents at specific cerebral areas.

Conclusion: The scaling exponents of fractal analysis are significantly reduced toward white noise during hypnotic condition. Furthermore, the decrease in scaling exponents during hypnosis was associated with the ERS within specific cortical areas closely related to eye movements and selective attention.

References:

1. Lutzenberger W, Elbert T, Birbaumer N, Ray WJ, Schupp HT: The scalp distribution of fractal dimension of the EEG and its variation with mental task. *Brain Topogr* 1992; 5:27-34.
2. Peng CK, Havlin S, Stanley HE, Goldberger AL: Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series. *Chaos* 1995; 5:82-87.

NR669 Wednesday, May 25, 03:00 p.m.-5:00 p.m.

Assessing Depression in Frail, Community-Dwelling Elderly

Laura S. Britan, M.P.H., *Department of Psychiatry, Emory University, 1841 Clifton Road, NE, Atlanta, GA 30329*; Eve Byrd, Catherine Ivy, M.S.W., Kirk Easley, M.S., Paul E. Holtzheimer III, M.D., Renee Moore, B.S., William M. McDonald, M.D.

Educational Objectives:

At the conclusion of this session, the participant will have a better understanding of depression in a community sample of frail older adults.

Summary:

Objective: This pilot study tested an educational intervention for nonphysician health care workers to facilitate the detection of depressive symptoms among high-risk elderly clients. The rela-

tionship between demographic factors and depression prevalence before and after the intervention was also examined. We hypothesized that depression prevalence would initially increase (with increased recognition) then decrease (with treatment).

Methods: Nursing-home-eligible clients were evaluated for depression and use of psychotropic medication at three time points: baseline, year 2, and year 3. Logistic regression was used to identify factors associated with depression prevalence.

Results: A total of 2,264 clients were assessed at baseline (mean age, 79.2 years). Being older, white, female, and widowed/divorced/separated were associated with increased depression prevalence. As expected, the frequency of depressed clients increased then decreased over time from 13.0% to 17.3% to 15.8%. The prevalence of depression increased by 33.1% from baseline to year 2 and decreased by 8.7% from year 2 to year 3. The percentage of depressed clients receiving antidepressant medications also increased over time from 37.4% to 38.7% to 48%.

Conclusions: Educating nonphysician health care workers to screen for depression was effective in detecting depressive symptoms among high-risk elderly clients. Certain demographic variables are associated with increased depression prevalence in these clients. Antidepressant treatment may decrease depression prevalence over time.

References:

1. Blazer D, Hughes DC, George LK: The epidemiology of depression in an elderly community population. *Gerontologist* 1987; 27(3):281-287.
2. Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, et al: Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey. *Arch Gen Psych* 1994; 51(1):8-19.

NR670 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Does Efavirenz Produce Neuropsychological Disturbances in HIV-1 Infected Patients?

Jordi Blanch, M.D., *Department of Psychiatry, Hospital Clinic, Rossello 170, Barcelona 08036, Spain*; Toni Raspall, D.O., Jose L. Blanco, M.D., Josep Mallolas, Ph.D., Teresa Roget, Ph.D., Josep Gatell, Ph.D., Manel Salameo, Ph.D.

Educational Objectives:

At conclusion of this presentation, the participant should be able to know whether efavirenz produces neuropsychological disturbances in HIV-1 infected patients and if they correlate with efavirenz plasma levels.

Summary:

Objective: Neuropsychiatric disturbances are a well-known side effect related to efavirenz (EFV). The objective of this study was to assess whether the initiation of an EFV-containing regimen produced neuropsychological disturbances and if they correlated with EFV plasma levels.

Methods: Twenty-seven consecutive HIV-1-infected outpatients for whom EFV was prescribed (EFV group) and nine HIV-1-infected outpatients who started antiretroviral therapy not including EFV (control group) underwent a neuropsychological assessment. A comprehensive neuropsychological battery and a standardized questionnaire for anxiety and depression (HAD) were completed for all patients at baseline and at two, four, and 12 weeks. EFV plasma levels were obtained for patients in the EFV group at two, four, and 12 weeks.

Results: No differences were found between the EFV group and the control group on any of the cognitive domains assessed. Within EFV patients, a trend toward a significant correlation was obtained between anxiety and neuropsychiatric side effects

(NPSE). Patients who reported NPSE tended to feel more anxious than patients who did not report NPSE. EFV plasma levels did not correlate with performance on any neuropsychological test.

Conclusion: Neither neuropsychological disturbances nor impairment in the neuropsychological function were associated with the initiation of an EFV-containing regimen.

References:

1. Blanch J, Martinez E, Rousaud A, Blanco JL, Garcia-Viejo MA, Peri JM, Mallolas J, De Lazzari E, De Pablo J, Gatell JM: Preliminary data of a prospective study on neuropsychiatric side effects after initiation of efavirenz. *J Acquir Immune Defic Syndr* 2001; 27(4):336-43.
2. Marzolini C, Telenti A, Decosterd LA, Greub G, Biollaz J, Buclin T: Efavirenz plasma levels can predict treatment failure and central nervous system side effects in HIV-1-infected patients. *AIDS* 2001; 5:15(1):71-5. Comment in: *AIDS* 2001 Jun 15; 15(9):1192-4.

NR671 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Depressive Symptoms After Therapy in HIV Positive/HCV Positive Outpatients

Jordi Blanch, M.D., *Department of Psychiatry, Hospital Clinic, Rossello 170, Barcelona 08036, Spain*; Montse Lagundo, M.D., Teia Plana, M.D., Montse Serra, M.D., Soledad Romero, Josep Mallolas, Ph.D., Cristobal Gasto, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize and treat the psychiatric side effects after initiation of interferon therapy for HIV/HCV positive patients.

Summary:

Objectives: Interferon alpha (IFa) therapy for chronic hepatitis C (CHC) infection is commonly associated with neuropsychiatric side effects, including depressive symptoms. The presenters evaluated the incidence and management of depressive symptoms during IFa therapy in HIV-infected patients with CHC infection.

Methods: HIV-infected patients with CHC infection who began IFa and ribavirin between April 2001 and April 2003 were included in the study. Patients with a past personal history of major depressive disorder were excluded.

Results: Of 113 co-infected patients who started IFa therapy during the recruitment period, 40% reported depressive symptoms (sadness, tiredness, apathy). Twenty were treated with citalopram, a selective serotonin reuptake inhibitor antidepressant, and they showed improvement of their symptoms. Four patients needed hospitalization and IFa removal due to severe depressive symptoms. Most patients (60%) reported depressive side effects in the first three months after initiation of IFa.

Conclusions: The incidence of depressive symptoms in patients with HIV/HCV co-infection treated with IFa is high. Most of the depressive symptoms were not severe and improved with antidepressant therapy, without reduction or cessation of IFa therapy. During the first weeks after initiating IFa therapy in HIV/HCV co-infection, close assessment and preventive treatment of psychiatric symptoms is recommended.

References:

1. Dieperink E, Willenbring M, Ho SB: Neuropsychiatric symptoms associated with hepatitis C and interferon alpha: a review. *Am J Psychiatry* 2000; 157:867-876.
2. Bonaccorso S, Marino V, Blondi M, Grimaidi F, Ippoliti F, Maes M: Depression induced by treatment with interferon-alpha in patients affected by hepatitis C virus. *J Affect Disord* 2002; 72:237-241

NR672 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Group Psychotherapy Improves Psychosocial Adjustment to HIV Positive Infection

Jordi Blanch, M.D., *Department of Psychiatry, Hospital Clinic, Rossello 170, Barcelona 08036, Spain*; Araceli Rousaud, Esteban Martinez, Ph.D., Josep M. Peri, Ph.D., Joan De Pablo, Ph.D., Josep Gatell, Ph.D., Cristobal Gasto, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to show the efficacy of a structured time-limited cognitive-behavioral group psychotherapy program in improving adjustment to HIV-1 infection in an outpatient consultation-liaison psychiatry unit.

Summary:

Objective: To evaluate the immediate efficacy of a group therapy in improving psychosocial adjustment to illness in HIV-positive outpatients referred to a consultation-liaison psychiatry department.

Methods: Repeated-measures Friedman test was used to analyze changes on the Psychosocial Adjustment to Illness Scale (PAIS) administered to 48 participants at three time points T1 (one month before therapy), T2 (first session), and T3 (last session). The therapy consisted of 16 weekly two-hour sessions following a structured cognitive-behavioral group psychotherapy program.

Results: Significant improvement was observed during the intervention time (between T1/T2 and T3) in sexual functioning ($p < 0.001$), social functioning ($p = 0.003$), psychological distress ($p < 0.001$), and in the total scale ($p < 0.0001$). Improvement was also observed in the rest of the subscales (health care orientation, vocational environment, domestic environment, and extended family relationships), although it was not statistically significant. No changes were observed during baseline (between T1 and T2).

Conclusions: Psychosocial adjustment to HIV infection, especially in sexual and social relationships, can be improved by means of a structured group psychotherapy program in a heterogeneous sample of HIV-1-infected patients referred to a consultation-liaison psychiatry unit.

References:

1. Blanch J, Rousaud A, Hautzinger M, Martinez E, Peri JM, Andres S, Cirera E, Gatell JM, Gasto C: Assessment of the efficacy of a cognitive-behavioural group psychotherapy programme for HIV-infected patients referred to a consultation-liaison psychiatry department. *Psychother Psychosom*. 2002; 71:77-84
2. Bock J, Escobar-Pinzon LC, Riemer D, Blanch J, Hautzinger M: [EUROVIHTA Project-specific intervention program for HIV infected patients to support the coping process with this chronic illness]. *Psychother Psychosom Med Psychol* 2003 Jul; 53(7):310-8.

NR673 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Phylogenetic Framework of Memory Deficits in Alzheimer Dementia

Supported by the Manchester VAMC, Manchester, New Hampshire

Virginia O. Emery, Ph.D., *Department of Psychiatry, Dartmouth Medical, One Medical Center Drive, Lebanon, NH 03756*

Educational Objectives:

At the conclusion of this session, the participant will be able to better recognize that the pattern of Alzheimer memory decline involves retrophylogenesis across phyletic hierarchy of neocortical

memory, emotional memory, and motor memory and will be able to better diagnose and treat Alzheimer-type dementia.

Summary:

Objective: Phylogenetically, memory is a product of modified old brain parts and newer brain parts working together, having evolved over millions of years into a set of structural and functional systems enabling adaptation. Although there is nosologic concurrence that memory deficit is defining and necessary for a diagnosis of dementia of Alzheimer type (DAT), the next level of explanation relating to pattern of memory loss in DAT over time has not been investigated adequately. The research question addressed is: what is the diachronic pattern of DAT memory deficits in context of phylogenesis.

Method: Participants were 43 consecutive late-onset DAT patients recruited through VAMC and private nursing homes and 40 demographically equivalent normal elderly persons. Mean age of the DAT patients was 76.3 years; mean age of the normal elderly group was 74.9 years. Excluded from the DAT sample were patients with cardiovascular disease, stroke, tumors, substance abuse, and psychiatric disorders other than DAT. Memory measures included measures of motor memory, emotional memory, and neocortical memory, which correspond to the phylogenetic hierarchy in evolution of memory.

Results: Relative to themselves and normal aging, DAT memory deficits are significantly greater on neocortical memory tasks, compared to motor memory or tasks of emotional memory, in a pattern of "retrophylogenesis."

Conclusions: Memory decline in DAT involves fundamental primitivization and retrophylogenesis across the phyletic hierarchy of neocortical memory, emotional memory, and motor memory.

References:

1. Emery VOB: "Retrophylogenesis" of memory in dementia of the Alzheimer type; in *Dementia: Presentations, Differential Diagnosis, and Nosology*, Second Edition. Emery VOB, Oxman TE eds. Baltimore, Johns Hopkins University Press, 2003, pp 177-236.
2. Reisberg B: Towards a science of Alzheimer's disease management: a model based upon current knowledge of retrogenesis. *International Psychogeriatrics* 1999; 11: 9-10.

NR674 Wednesday, May 25, 03:00 p.m.-5:00 p.m.

Investigation of the Relationship Between BDD and Social Phobia

Meredith E. Coles, Ph.D., *Department of Psychology, Binghamton University, State University of New York, Binghamton, NY 13902-6000*; William Menard, B.A., Christina Fay, B.A., Risa B. Weisberg, Ph.D., Katharine A. Phillips, M.D.

Educational Objectives:

At the conclusion of this presentation, participants should be knowledgeable about the relationship between BDD and social phobia, informing the diagnosis and treatment of patients with these disorders.

Summary:

Objective: Much attention has been paid to the relationship between body dysmorphic disorder (BDD) and obsessive-compulsive disorder. However, to our knowledge, no published study has examined the relationship between BDD and social phobia (SP), even though they appear to more frequently co-occur than BDD and OCD.

Methods: The presenters examined the relationship between BDD and SP in 178 broadly ascertained subjects with current DSM-IV BDD using reliable and valid interviewer-administered and self-report measures. The interviewer-administered Brief So-

cial Phobia Scale (BSPS) was used to assess social anxiety independent of BDD symptoms, and the self-report Social Phobia Inventory (SPIN) was used to assess social anxiety generally (due to SP or BDD).

Results: A total of 39.3% of the BDD subjects had comorbid lifetime SP, and 34.3% met the criteria for current SP. Comparisons of BDD subjects with and without current comorbid SP revealed that BDD+SP subjects were significantly less likely to be employed and more likely to report suicidal ideation and had poorer social adjustment. However, the two groups did not differ on current age, age of BDD onset, gender distribution, probability of being in current treatment, or global functioning. There was a trend for BDD+SP subjects to have more severe BDD symptoms ($p = 0.098$). Finally, BDD+SP subjects were rated as having significantly more severe social anxiety independent of BDD symptoms (on the BSPS) and self-reported more social anxiety generally (due to SP or BDD) on the SPIN. Social anxiety independent of BDD and general social anxiety due to either BDD or SP were moderately correlated ($r = .53$, $p < 0.001$).

Conclusion: The findings support the need to further examine the comorbidity of BDD and SP.

References:

1. Phillips KA, Gunderson CG, Mallya G, McElroy SL, Carter W: A comparison study of body dysmorphic disorder and obsessive-compulsive disorder. *J Clin Psychiatry* 1998; 59:568-575.
2. Wilhelm S, Otto MW, Zucker BG, Pollack MH: Prevalence of body dysmorphic disorder in patients with anxiety disorders. *J Anx Dis* 1997; 11:499-502.

NR675 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Suicidal Ideation and Suicide Attempts in Body Dysmorphic Disorder

Katharine A. Phillips, M.D., *Department of Psychiatry, Butler Hospital/Brown University, 345 Blackstone Boulevard, Providence, RI 02906*; Meredith E. Coles, Ph.D., William Menard, B.A., Shirley Yen, Ph.D., Christina Fay, B.A.

Educational Objectives:

At the conclusion of this presentation, the participant should be knowledgeable about characteristics of suicidal ideation and suicide attempts in BDD, including predictors of these events.

Summary:

Objective: Because suicidality in body dysmorphic disorder has received little investigation, this study examined rates, correlates, predictors, and other aspects of suicidal ideation and attempts in this disorder.

Method: A total of 200 subjects with body dysmorphic disorder recruited from diverse sources were assessed with standard measures.

Results: Subjects had high rates of lifetime suicidal ideation (78.0%) and suicide attempts (27.5%). Body dysmorphic disorder was the primary reason for suicidal ideation in 70.5% of those with a history of ideation and nearly half of subjects with a past attempt. Suicidal subjects often did not reveal their body dysmorphic disorder symptoms to their clinician. In univariate analyses, both suicidal ideation and attempts were associated with lifetime impairment due to BDD ($p < 0.001$), current functional impairment ($p < 0.001-0.05$), and comorbid borderline personality disorder ($p < 0.01-0.001$). A history of suicidal ideation (but not attempts) was additionally associated with comorbid lifetime major depression ($p = 0.001$) and any personality disorder ($p = 0.003$). A history of suicide attempts (but not ideation) was additionally associated with delusional appearance beliefs ($p = 0.01$) and lifetime bipolar disorder, PTSD, an eating disorder, or a substance use disorder ($p < 0.001-0.05$). In logistic regression analyses, suicidal ideation

was significantly predicted by comorbid major depression ($p = 0.011$) and greater lifetime impairment due to body dysmorphic disorder ($p = 0.008$); suicide attempts were significantly predicted by PTSD ($p = 0.001$) and greater lifetime impairment due to body dysmorphic disorder ($p = 0.001$).

Conclusion: Individuals with body dysmorphic disorder have high rates of suicidal ideation and attempts. Lifetime impairment due to body dysmorphic disorder and certain comorbid disorders are associated with suicidality.

References:

1. Phillips KA: Body dysmorphic disorder: recognizing and treating imagined ugliness. *World Psychiatry* 2004; 3:12-17.
2. Phillips KA, Menard W, Fay C, Weisberg R: Demographic characteristics, phenomenology, comorbidity, and family history in 200 individuals with BDD. *Psychosomatics*, in press.

NR676 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

An Open-Label Trial of Escitalopram in Body Dysmorphic Disorder

Supported by Forest Laboratories, Inc.

Katharine A. Phillips, M.D., *Department of Psychiatry, Butler Hospital/Brown University, 345 Blackstone Boulevard, Providence, RI 02906*

Educational Objectives:

At the conclusion of this presentation, the participant will be familiar with results from the first study of the SRI escitalopram in body dysmorphic disorder.

Summary:

Objective: Body dysmorphic disorder (BDD), a preoccupation with an imagined or slight defect in appearance, is relatively common and impairing. While available data suggest that SRIs are often efficacious for BDD, pharmacotherapy research is limited, and there are no published reports on the SSRI escitalopram.

Methods: Fifteen subjects with DSM-IV BDD or its delusional variant were treated in a 12-week open-label escitalopram trial. Subjects were assessed at regular intervals with the Yale-Brown Obsessive Compulsive Scale Modified for BDD (BDD-YBOCS; the primary outcome measure), Clinical Global Impression scale (CGI), Brown Assessment of Beliefs Scale (BABS), 17-item Hamilton Depression Rating Scale (HAM-D), Global Assessment of Functioning (GAF) scale, and SOFAS (a measure of psychosocial functioning).

Results: BDD-YBOCS scores decreased from 30.3 ± 5.7 at baseline to 14.7 ± 9.0 at endpoint ($t = 6.1$, $df = 14$, $p < 0.001$); 73.3% ($N = 11$) of subjects were responders. On the CGI, 46.7% ($N = 7$) of subjects had very much improvement in BDD, and 33.3% ($N = 5$) were much improved. The delusional appearance beliefs significantly decreased, with the mean baseline BABS score in the poor insight range (15.3 ± 4.7) and the mean endpoint score reflecting good insight (6.9 ± 5.2 ; $t = 5.1$, $df = 14$, $p < 0.001$). HAM-D scores decreased from 18.1 ± 8.7 to 5.3 ± 4.7 ($t = 6.0$, $df = 14$, $p < 0.001$). GAF scores also significantly improved (from 48.3 ± 9.2 to 71.6 ± 16.3 ; $t = -6.2$, $df = 13$, $p < 0.001$), as did psychosocial functioning on the SOFAS (from 52.5 ± 13.1 to 76.6 ± 18.5 ; $t = -6.9$, $df = 13$, $p < 0.001$). The mean endpoint escitalopram dose was 28.0 ± 6.5 mg/day, and the mean time to BDD response was 4.7 ± 3.7 weeks. Escitalopram was generally well tolerated.

Conclusions: These preliminary data suggest that escitalopram is safe and effective for BDD. Delusional appearance beliefs, depressive symptoms, global symptom severity, and functioning also significantly improved.

References:

1. Phillips KA: Pharmacologic treatment of body dysmorphic disorder: review of the evidence and a recommended treatment approach. *CNS Spectrums* 2002; 7:453-460.
2. Phillips KA: Body dysmorphic disorder. In: Phillips KA, ed. *Somatoform and Factitious Disorders (Review of Psychiatry Series, Volume 20, Number 3; Oldham JM and Riba MB, series editors)*. Washington DC: American Psychiatric Publishing, 2001.

NR677 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.** **The Impact of Medical Comorbidity on Cognitive Function in Late-Life Depression**

Shwu-Hua Lee, M.D., *Department of Psychiatry, Chan Gung Memorial Hospital, 5, Fu-Shing Road, Kuei-San, Taoyuan, Taiwan*; Min-Ching Wen, M.S.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss the relationship between cardiovascular disease and cognitive impairment in elderly depressive patients.

Summary:

Objective: The comorbidity of medical illnesses and cognitive impairment is common in late-life depressive patients. Previous studies revealed depression with cognitive impairment was found to be associated with disability and poor prognosis. The aim of this study was to investigate the impact of medical comorbidity on cognitive function in late-life depression.

Method: The presenters enrolled 70 late-life depressive patients from an outpatient memory clinic at a medical center. All the patients were nondemented and met the DSM-IV criteria for major depressive disorder. The Cumulative Illness Rating Scale was used to measure medical comorbidity, and a comprehensive neuropsychological battery to assess cognitive function. The 17-item Hamilton Depression Rating Scale was used to assess depression symptoms and severity. The impact of medical illness of different organ system categories on cognitive function in late-life depression was analyzed.

Results: Medical illnesses in the cardiovascular organ categories are associated with cognitive impairment in elderly depressive patients.

Conclusions: This study explored the clinical depression-executive dysfunction syndrome in late-life depression and provided further support for the vascular depression concept in late-life depression. Identification of modifiable risk factors should be integrated in the prevention and treatment of late-life depression.

References:

1. Lichtenberg PA, Ross T, Millis SR, et al. The relationship between depression and cognition in older adults: a cross-validation study. *Journals of Gerontology Series B-Psychological Sciences & Social Sciences*. 50(1): P25-P32, 1995.
2. MA, Whyte EM, Nebes RD et al. The nature and determinants of neuropsychological functioning in late-life depression. *Archives of General Psychiatry*. 61(6): 587-95, 2004 Jun.

NR678 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.** **Apathy and Neuropsychological Deficits in Late-Life Depression**

Min-Ching Wen, M.S., *Department of Psychiatry, Chang Gung Hospital, No. 5 Fu-Hsing St. Kueishan, Taoyuan 333, Taiwan*; Shwu-Hua Lee, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that apathy is distinct from depression in late life.

Summary:

Objective: Apathy and cognitive dysfunction are often linked together in persons with dementia, but few studies have examined this relationship in late-life depression. The purpose of this study was to explore whether apathy is associated with worse cognitive performance, especially with frontal lobe dysfunction.

Method: Seventy-five elderly patients without dementia who met the DSM-IV criteria for major depressive disorder were given a comprehensive neuropsychological battery and the Hamilton Depression Rating Scale, including apathy-related items measuring diminished work/interest, psychomotor retardation, anergy, and lack of insight.

Result: Apathy was significantly correlated with verbal executive measures (verbal fluency of category, digit span subtest from the WAIS-III), nonverbal executive measures (Trail Making A and B), and a measure of information processing speed (digit-symbol substitution subtest from the WAIS-III). Stepwise regression analyses of the executive function and information processing speed data showed that apathy plus age or education accounted for a significant amount of the variance.

Conclusions: In late-life depression, apathy is associated with poor executive function. Apathy may be a specific neuropsychiatric syndrome and might be distinct from depression. Further studies clarifying the relationship of apathy, depression, and neurobehavioral functioning are needed.

References:

1. Marin RS, Butters MA, Mulsant BH, Pollock BG, Reynolds CF: Apathy and executive function in depressed elderly. *Journal of Geriatric Psychiatry and Neurology* 2003; 16(2): 112-116.
2. Feil D, Razani J, Boone K, Lesser I: *International Journal of Geriatric Psychiatry* 2003; 18: 479-485.

NR679 **Wednesday, May 25, 03:00 p.m.-5:00 p.m.** **Change in Prevalence Over Five Years in Metabolic Syndrome Risk Factors in SPMI Patients**

Terrance J. Bellnier, M.P.A., *Department of Pharmacy, State University of New York at Buffalo, 36 Forest Meadow Trail, Rochester, NY 14624*; Sarah Bingel, Ph.D., Kashinath B. Patil, M.D., Tulio R. Ortega, M.D., Adam Decatur, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the importance of having severe and persistently mentally ill treatment include the same health strategies (ongoing nutrition education, exercise, and medication) utilized in the general population.

Summary:

Objective: Atypical antipsychotics have been associated with metabolic disorders. The study goal was to evaluate the change in prevalence of risk factors for metabolic syndrome in severe and persistently mentally ill patients (SPMI) over five years.

Method: A chart review of inpatients (N=239) was conducted in 1999 and again in 2004 (N = 232). All subjects had a physical examination. The groups were matched for age, sex, ethnicity, and psychiatric diagnosis and compared to national general population norms (GP).

Results:

Subject Characteristics: N = 224; age 48 ± 5 years (range = 19-77); 138 males; 196 with schizophrenia

Prevalence:

	1999 %		2004 %		Change	
	SPMI	GP	SPMI	GP	SPMI	GP
Diabetes	10.1	6.7	10.3	6.6	0.2	-0.1
Hypertension	19.8	32.2*	26.3	39.2*	6.5	7.0
Hypertipidemia	26.1	24.4	29.3	28.1	3.2	3.7
Obesity	36.7	22.9*	38.8	30.5	2.1	7.6*
Metabolic syn- drome	21.2	20.3	24.8	23.3	3.6	3.0

*p < 0.05 chi-square test

Conclusion: SPMI patients have greater rates of diabetes, hyperlipidemia, obesity, and metabolic syndrome. Change in prevalence was similar between SPMI and GP, suggesting that similar factors contribute to both populations. The sample size limits the ability to make population inferences, yet the role of atypical antipsychotics contributing to these rates maybe limited. Findings suggest that health care strategies for SPMI patients should not differ from those for GP.

References:

1. Ford ES, Giles WH, Mokdad AH: Increasing prevalence of the metabolic syndrome among US adults. *Diabetes Care* 2004; 27(10):2444-2449.
2. Heiskanen T et al: Metabolic syndrome in patients with schizophrenia. *J Clin Psychiatry* 2003; 64(5):575-579.

NR680 Wednesday, May 25, 03:00 p.m.-5:00 p.m. Nutrition and Exercise in SPM: An Effect on Metabolic Syndrome Risk Factors

Kashinath B. Patil, M.D., *Department of Psychiatry, University of Rochester, 36 Forest Meadow Trail, Rochester, NY 14624*; Terrance J. Bellnier, M.P.A., Jill Pearce, M.S., Tulio R. Ortega, M.D., Adam Decatur, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to realize the importance of ongoing good nutrition and regular exercise in reducing metabolic syndrome risk in severe and persistently mentally ill.

Summary:

Objective: The study goal was to evaluate the effect on metabolic syndrome risks of a nutrition/exercise program designed for severe and persistently mentally ill (SPMI) patients.

Method: The study had a acute (one hour three times a week) phase for three months and a maintenance phase (one hour once a month) for three months. Vital signs and laboratory tests were obtained every three months.

Results:

Subject Characteristics: N = 18; age 39 ± 10 years (range = 22-59); five males; 15 with schizophrenia; BMI ≥ 30.

	Baseline	Acute	Maintenance
Waist (male > 40 in)	100%	60%*	60%*
(female >35 in)	100%	77%*	77%*
Weight (lbs)	259	247	250
Cholesterol	203	185*	186*
Triglycerides	151	113*	144
HDL	41	54*	47*
Glucose	94	85*	91
Exercise compliance (three times a week)	11%	89%*	33%*
Metabolic syndrome	50%	11%*	39%

*p < 0.05 (student t or chi-square test)

Conclusion: SPMI subjects had reductions in metabolic syndrome risks demonstrated by decreases in waist size, glucose, cholesterol, and triglycerides and an increase in HDL. Some benefits were lost when subjects curtailed exercise compliance in the maintenance phase. The sample size limits the ability to make

population inferences, yet the findings suggest that nutrition/exercise programs should be universally available, encouraged, and ongoing to have maximum health benefit.

References:

1. Menza M et al: Managing atypical antipsychotic-associated weight gain: 12 month data on a multimodal weight control program. *J Clin Psychiatry* 2004; 65(4):471-477.
2. Desai MM et al: Receipt of nutrition and exercise counseling among medical outpatients with psychiatric and substance abuse disorders. *J Gen Internal Medicine* 2002; 556-560.

NR681 Wednesday, May 25, 3:00 p.m.-5:00 p.m. Illness Severity and Length of Stay Prediction for Psychiatric Inpatients

Ronald H. Beach, M.D., *UBH, 12125 Woodcrest Executive Drive, St. Louis, MO 63119*; George I. Viamontes, M.D., Robert Fusco, M.D., Michael Powell, Ph.D., Brett A. Hart, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the factors that determine length of stay in psychiatric inpatients and understand how neural network predictive models can be created and used for predicting the duration of psychiatric hospitalizations.

Summary:

The prediction of psychiatric inpatient lengths of stay (LOS) from clinical and demographic data has numerous applications, ranging from establishment of DRGs to treatment plan development. Demographic and clinical data (115 variables) were collected on 6,052 inpatients over a two-year period and used to construct a LOS predictive model. Factors most highly correlated with length of stay were empirically determined and used as inputs to a classification neural network. These included: age, violent behavior, psychotic symptoms, manic symptoms, self-care deficits, problems with orientation, psychiatric diagnosis, chemical dependence parameters, and the type and number of psychiatric medications. A set of 2,000 patients was selected at random and reserved for validating the network's performance. The network was trained with the remaining 4,052 cases. Based on the 2,000 entry validation set, the neural network was able to identify 72.5% of patients with a LOS < five days (72.5% sensitivity, 65% specificity) and 65% of patients with a LOS ≥ five days (65% sensitivity, 72.5% specificity). The study database permits construction of an empirical severity of illness index, and the neural network model provides a practical tool for clinical work. This work has applications in case mix analysis, DRG development, and resource allocation.

References:

1. Durbin J, Goering P, Pink G, and Murray M: Classifying psychiatric inpatients: seeking better measures, *Med Care* 1999; 37(4):415-423.
2. Keebler J, Duder S, and Lechman C: Predicting length of stay in an acute care hospital: the role of psychosocial problems. *Soc Work Health Care* 2001; 33(2):1-16.

NR682 Wednesday, May 25, 03:00 p.m.-5:00 p.m. Migraine and Depression Comorbidity Supported by Medical Research Council, U.K.

Zainab A. Samaan, M.D., *Department of Genetics, SGDP at Maudsley, DeCrespigny Park, POB 8, London SE5 8AF, United Kingdom*; Anne Farmer, M.D., Peter McGuffin, M.D., Ailbne

Burke, B.A., Richard Williamson, Ph.D., Pak Sham, M.D., Nick Craddock, M.D., Mike Owen, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that migraine and depression are closely linked and have a possible common etiology. Psychiatrists must be vigilant in enquiring about the symptoms of migraine in depressed patients.

Summary:

Objectives: Migraine and depression have been reported to have an association that is specific to migraine. The nature of the association remains unclear. This study investigated the comorbidity of migraine and depression and tested the hypothesis that this relationship is specific to migraine.

Methods: Subjects with recurrent depression were compared to healthy control subjects to investigate the presence of migraine and other headaches in each group. Participants were interviewed to generate ICD-10 and/or DSM-IV diagnoses of depression, and the International Headache Society criteria were used for the diagnosis of migraine. Chi-square tests and logistic regression were used.

Results: A total of 1,494 depressed subjects and 863 healthy control subjects were included. Migraine with and without aura occurred in 8.9% of the cases and 2.9% of the control subjects. Migraine and other headache types were more prevalent in the cases than in the control subjects (Pearson $\chi^2 = 217.5$, $df = 5$, $p < 0.0001$). The odds ratio for having migraine with aura in depressed subjects was 6.73 (95% CI = 3.8-12).

Conclusion: There is a strong association between depression and migraine confirmed in this large cohort; however, this relationship was not specific to migraine. Any headache type was also significantly associated, although a trend showing the strongest association was for migraine with aura.

References:

1. Swartz KL, Pratt LA, Armenian HK, Lee LC, Eaton WW: Mental disorders and the incidence of migraine headaches in a community sample: results from the Baltimore Epidemiologic Catchment area follow-up study. *Archives of General Psychiatry* 2000; 57(10):945-50
2. Breslau N, Lipton R, Stewart W, Schultz L, Welch K: Comorbidity of migraine and depression: investigating potential etiology and prognosis. *Neurology* 2003; 60:1308-1312.

NR683 Wednesday, May 25, 03:00 p.m.-5:00 p.m. Physical Illness in Mentally Ill: A Quality Assurance Program

Jens I. Larsen, M.D., *Department of Psychiatry, Aalborg Hospital, Moelleparkvej 10, Aalborg, DK 9000, Denmark*; Ib Rasmussen, M.D., Kai R. Andersen, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize comorbid physical illness in the mentally ill and take into consideration the influence of physical well-being on the outcome of the psychiatric illness.

Summary:

Objective: Physical illness is common among patients with a psychiatric disorder and often undiagnosed. Substance abuse, including use of tobacco, is common and predisposes these patients to cardiovascular diseases. These patients also have a high degree of obesity and diabetes mellitus type 2. The aim of the study was to investigate the predictors for conspicuous versus hidden physical morbidity, including a description of the pathways to psychiatric care.

Methods: All persons admitted through an assessment unit during one year were included. After collection of all available information and an interview with a physical examination, and again after three months or at discharge, patients' status was determined.

Results: Of a sample of 458 patients, 251 patients (54.8%)/245 (53.9%) were found to have a known/final somatic diagnosis. Known/final somatic diagnoses related to cardiovascular disease, obesity, and diabetes were found in 75 (16.4%)/69 (15.7%), eight (1.8%)/72 (15.7%), and 11 (2.4%)/12 (2.6%) patients. Furthermore, a correlation with the pathways to admission was found; the patients admitted via other services than GP or somatic departments had a lower degree of known somatic disease.

Conclusion: It is relevant to talk about a burden of somatic disease. Lifestyle and pathways to care are important for identifying, treating, and preventing physical illness among mentally ill patients.

References:

1. Goldman LS: Medical illness in patients with schizophrenia. *J Clin Psychiatry* 1999; 60:10-15.
2. Jeste DV et al: Medical co-morbidity in schizophrenia. *Schizophrenia Bulletin* 1996; 22:413-430.

NR684 Wednesday, May 25, 03:00 p.m.-5:00 p.m. rEEG-Guided Pharmacotherapy for Severely Ill, Dually-Diagnosed Patients

Jay H. Shaffer, M.D., *Rancho L'Abri, 1809 Bee Canyon Road, Dulzura, CA 91917*; John E. Milner, M.D., Mark J. Schiller, M.D.

Educational Objectives:

At the end of this session, the participant should be able to understand the basic technology and premises of referenced electroencephalography (rEEG), how it is used to guide pharmacotherapy, the general results of prior studies and the specific findings of this first use of rEEG-guided prescribing in a severely ill population of dually diagnosed patients.

Summary:

Objective: Free of drugs and alcohol for at least 21 days, 58 severely ill residents at Rancho L'Abri were treated with referenced electroencephalography (rEEG)-guided prescribing. In seven prior studies using rEEG-guided pharmacotherapy to treat nonpsychotic DSM-IV diagnoses (N = 422), 338 patients (80%) were rated "much improved" or "very much improved." There are no prior reports of rEEG-guided pharmacotherapy in treating severely ill patients meeting both DSM-IV nonpsychotic psychiatric illness and DSM-IV alcoholism/substance abuse criteria.

Methods: After 21 days drug/alcohol free, patients age 17 to 62 years were evaluated for DSM-IV diagnoses and severity of illness on a 7-point scale. After more than six weeks taking medication, patients were rated on a 7-point CGI Scale by the treatment team. Physicians rated rEEG helpfulness in prescribing.

Results: Forty-eight patients (83%) were rated at least "markedly ill;" 10 (17%) were rated "mildly ill or moderately ill." Thirty-five (73%) "markedly ill" or worse patients were rated "very much improved." Nine (80%) "mildly ill or moderately ill" patients were rated "very much improved." rEEG guidance was rated "essential" in 56 cases (85%).

Conclusions: rEEG-guided prescribing yields both high quality and frequent clinical improvement in numbers greater than would be expected from conventional treatment in this severely ill and dually diagnosed population. While these findings compare to rEEG results in other populations, randomized, double-blind studies are needed to validate rEEG efficacy.

References:

1. Suffin SC, Emory WH: Neurometric subgroups in attentional and affective disorders and their association with pharmacotherapeutic outcome. *Clin EEG Neurosci* 1995; 26:73-83.
2. Emory WH, Schiller M, Suffin SC: Referenced-EEG in the treatment of eating disorders, in *New Clinical Drug Evaluation Unit 2004 Program Abstracts*. Washington, DC, NCDEU, 2004, poster 221.

NR685 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.** **Psychoeducation in Health Care Delivery Settings**

Joel L. Nitzkin, M.D., J.L.N., M.D. Associates, 4939 Chestnut, New Orleans, LA 70115-2941; Shelagh A. Smith, M.P.H.

Educational Objectives:

At the conclusion of this session, the participant will recognize the value of psychoeducational programming in health care settings to improve outcomes and restrain health care costs. The participant will be able to play a lead role in developing psychoeducational interventions and educate medical/surgical staff to more effectively recognize psychiatric comorbidities.

Summary:

Objective: Psychoeducation is a preventive behavioral service consisting of health education and behavioral counseling. The counseling component deals with emotions, fears, expectancy, and coping skills. Despite ample evidence of effectiveness and cost-efficiency, psychoeducation and other preventive behavioral services are inadequately provided in health care settings.

Methods: A structured review of the literature (1964-2003) for psychoeducational services in health care settings was conducted.

Results: Psychoeducation is effective for three categories of patients.

1) Presurgical psychoeducation can reduce postoperative pain, improve breathing in the immediate postsurgical period, and accelerate ambulation.

2) Psychoeducation for patients with chronic diseases, such as diabetes and asthma, can reduce anxiety, improve coping skills, and improve adherence to prescribed regimens of care. While the medical details vary by disease, the behavioral counseling process can be consistent across a broad array of diseases.

3) Psychoeducation can improve quality of life and reduce health care expenditures for some high-cost patients, whose use of services cannot be explained on the basis of mental or physical illness.

The interactive nature of psychoeducational programming can facilitate recognition of psychiatric comorbidities in medical/surgical patients who could benefit from psychiatric care.

Conclusion: Psychoeducation in health care settings can secure 5% to 30% improvements in selected clinical and cost-related outcome measures.

References:

1. Nitzkin J, Smith S: *Clinical Preventive Services in Substance Abuse and Mental Health Update: From Science to Services*. DHHS Publ No. (SMA) 04-3906. Rockville, MD, Center for Mental Health Services, SAMHSA, 2004.
2. Lorig K, Sobel D, Ritter P, Laurent D, Hobbs M: Effect of a Self-Management Program on Patients with Chronic Disease. *Effective Clinical Practice* Nov/Dec 2001 (<http://www.acpmonline.org/journals/ecp/novdec01/lorig.htm>) (Accessed 27 April 2004).

NR686 **Wednesday, May 25, 03:00 p.m.-5:00 p.m.** **Psychiatric Morbidity in Chinese Patients Suffering From Chronic Pain**

Pui Tat Ho, M.R.C., Department of Psychiatry, Kwai Chung Hospital, 3-15 Kwai Chung Hospital Road, New Territories, Hong Kong

Educational Objectives:

At the conclusion of this session, the participants should be able to recognize that depression and somatoform disorders are highly prevalent among chronic pain patients. They should be vigilant to specific patient factors associated with psychiatric disorders so as to improve recognition.

Summary:

Objective: Psychiatric disorders are highly prevalent among Western chronic pain patients. However, the scenario in the Chinese population is unknown. This study investigated the prevalence of psychiatric disorders in Chinese chronic pain patients and their associated patient factors.

Method: All consecutive Chinese patients attending an university-based chronic pain clinic were eligible for recruitment during a six-month period. Psychiatric diagnoses were made with the Structured Clinical Interview for DSM-IV axis I disorders.

Results: Eighty-nine subjects were recruited, with a response rate of 90%. The prevalence of psychiatric disorders was 63%. Current major depressive disorder was diagnosed in 31.5% of the subjects. One-third of the patients had somatoform disorders. Pain disorder in particular was found in 28.1%. Anxiety disorders and substance use disorders also constituted 18% respectively. After logistic regression, psychiatric morbidity was found to be highly associated with younger age and younger age of onset of pain. Depression was also significantly associated with orthopedic illness, ADL dependence, higher pain intensity, negative pain cognition, and problems with social and leisure activities.

Conclusion: Depression and somatoform disorders were highly prevalent among Chinese chronic pain patients. Clinicians should be vigilant to specific patient factors associated with psychiatric disorders so as to improve recognition.

References:

1. Fishbain DA: Approaches to treatment decisions for psychiatric comorbidity in the management of the chronic pain patient. *Medical Clinics of North America* 1999; 83:737-60.
2. Polatin PB, Kinney RK, Gatchel RJ, Lillo E, Mayer TG: Psychiatric illness and chronic low-back pain: the mind and the spine—which goes first? *Spine* 1993; 18:66-71.

NR687 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.** **Personality Profile and Affective State With Inflammatory Bowel Disease**

Angela Vidal, Department of Psychiatry, Hospital Clinic, Rossello 140 Baixos, Barcelona, Spain; Esther Gomez-Gil, M.D., Julia Panes, Anna Torres, M.D., Nuria Sanchez

Educational Objectives:

At the conclusion of this session, the participant should be able to assess the affective state and the profile of personality in inflammatory bowel disease patients, and their association with the active disease.

Summary:

Objective: The literature on the association between inflammatory bowel disease (IBD) and a specific profile of personality and psychiatric illness is controversial. This study assessed the affective state and the personality profile of IBD patients.

Method: One hundred and thirty-seven patients attending a clinic for IBD (72 with Crohn's, 65 with ulcerative colitis) who had at least one relapse in the last 24 months were assessed for the presence of anxiety and depression using the HAD scale, and their personality profile was assessed with the Character and Temperament Inventory (TCI).

Results: The overall prevalence of psychiatric illness (HAD \geq 8) in Crohn's disease and ulcerative colitis was 46% and 38%, respectively. Psychiatric illness was not more common in patients who had an exacerbation, compared with those who were in remission (42% vs. 42%). All the TCI subscales scored in the normality range, and there were no differences between Crohn's and ulcerative colitis patients. There was an association between personality (harm avoidance, persistence) and higher scores on the HAD.

Conclusion: IBD patients who recently had an exacerbation did not differ from IBD patients who had a relapse in anxiety and depressive symptoms. Their affective state does not depend on the activity of the disease but on their personality profile. IBD patients with high scores in harm avoidance and persistence are more vulnerable to psychological disorder.

References:

1. Sewitch MJ, Abrahamowicz M, Bitton A, et al: Psychological distress, social support, and disease activity in patients with inflammatory bowel disease. *Am J Gastroenterol* 2001; 96:1470-9.
2. Robertson DAF, Ray J, Diamond I, et al: Profile and affective state of patients with inflammatory bowel disease. *Gut* 1989; 30:623-6.

NR688 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.** **Investigation of Religious Habits and Mental Health in the Elderly Living in the Community**

Adriana D.S. Baptista, M.D., UNIFESP-EPM, Miguel Pierro, 61, Campinas, SP 13083-300, Brazil; Sergio L. Blay, D.R.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the association between religious habits and mental health.

Summary:

Objective: To investigate religious habits and their association with mental health in elderly persons living in the community.

Method: The design is a cross-sectional study. The sample had as participants 6,961 people age 60 years and over, not institutionalized, both sexes, living in an urban area, residents in the State of Rio Grande do Sul. The data were collected by trained interviewers who completed a structured interview face-to-face consisting of closed-ended questions contained in thematic blocks. Mental health status was assessed by using the Short Psychiatric Evaluation Schedule; demographic, social, and cultural—religious information was collected in specific blocks.

Results: A total of 75.7% of the sample followed the Catholic religion, 15.5% had evangelical beliefs, 48.9% did not change their religious behavior over time, 71.5% were active participants in their religion. A multivariate analysis indicated that evangelic subjects were at increased risk for mental disorders (OR = 0.97, CI = 0.835 to 1.146).

Conclusion: Religious practice, particularly evangelic religion, seemed to be associated with mental disorders among elderly people. The results highlight the need for further investigation of the underlying effects of religion beliefs on psychiatric morbidity among elderly people.

References:

1. Braam AW, Eeden VD, Prince MJ, Beekman ATF, Kivela SL, Lawlor BA et al: Religion as a cross-cultural determinant of

depression in elderly Europeans: results from the EUROPE collaboration. *Psychol Med* 2001; 31:803-14.

2. Koenig HG, Larson DB: Religion and mental health: evidence for an association. *Int Rev Psychiat* 2001; 13:67-78.

NR689 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.** **Medical System Utilization and Its Relation to Mental Health in Elderly Patients**

Sergio L. Blay, D.R., UNIFESP, R Botucato 740, Sao Paulo, SP 04023-900, Brazil; Sergio B. Andreoli, Ph.D., Fabio L. Gastal, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that elderly subjects with previous outpatient consultations and increasing number of hospital admissions are at increasing risk of late-life mental disorder.

Summary:

Objective: The aim of this study was to assess the use of health services in elderly persons living in the community and the role of mental health in services utilization.

Method: In a cross-sectional design, a representative sample of 7,000 subjects, age 60 years and over was examined to estimate the frequency of six-month outpatient consultations, one-year hospital admissions, and psychiatric morbidity in Brazil. A validated reduced version of the SPES was used to detect mental distress, along with other questionnaires.

Results: The frequency of outpatient consultations was 30.7% for men and 69.3% for women. The hospital admission rate was 52% among psychiatric cases with one admission, jumping to 82.1% with subjects with \geq 4 hospitalizations. A logistic regression indicated that female gender, less education, unmarried status, previous outpatient treatment (OR = 1.5, 95% CI = 1-1.7), and number of inpatient admissions (OR = 8.5, 95% CI = 5.0-14.7) were related to risk for developing mental distress.

Conclusion: The data indicate that gender, marital status, education, and pattern of medical service utilization, particularly the number of hospital admissions, substantially increase the risk of mental morbidity in older subjects.

References:

1. Brugha et al: Trends in service use and treatment for mental disorders in adults throughout Great Britain. *British Journal of Psychiatry* 2004; 185:378-84.
2. Blay et al: Validity of a Brazilian version of the OARS mental health screening questionnaire. *Journal of the American Geriatrics Society* 1988; 36:687-692.

NR690 **Wednesday, May 25, 03:00 p.m.-5:00 p.m.** **Tobacco Use Among the Elderly: A Systematic Review of General Population Surveys**

Valeska Marinho, M.D., Department of Psychiatry, Federal University of São Paulo, R. Botucatu 740, São Paulo 04023-900, Brazil; Sergio L. Blay, D.R.

Educational Objectives:

At the conclusion of this session, the participant should be able to assess the prevalence and patterns of tobacco use in the elderly living in community through a systematic review.

Summary:

Methods: Well-designed cross-sectional and follow-up investigations were searched. The following electronic databases were used: MEDLINE (1994-2004), LILACS (1994-2004), EMBASE

(1994-2004). Hand searching of journals most likely to contain surveys in this area was done.

Results: No epidemiological studies specifically dealing with tobacco use in elderly persons living in the community were found. The search generated 78 studies measuring tobacco use in adults living in the community, and 20 included more than 200 elderly individuals in the sample and were selected for this review. The reported prevalence rates varied enormously (1.9%-30.1%). There is evidence for higher prevalence rates for men (11%-58%) than for women (0.8%-21%).

Conclusion: In general, the prevalence of tobacco use in elderly persons ranged from 1.9% to 30.1%. Moreover these data emerged from adult samples with a small proportion of elderly persons in the samples. Tobacco consumption was defined and evaluated in different ways. Therefore, it was difficult to precisely measure patterns of current use and lifetime use. In addition, no data were collected through studies focused in aged populations.

References:

1. White V, Hill D, Slahpush M, Bobevski I: How has the prevalence of cigarette smoking changed among Australian adults? Trends in smoking prevalence between 1980 and 2001. *Tob Control* 2003; 12 Suppl 2:1167-74.
2. Steyn K, Bradshaw D, Norman R, Laubscher R, Saloojee Y: Tobacco use in South Africans during 1998: the first demographic and health survey: *J Cardiovasc Risk* 2002; 9(3):161-70.

NR691 Wednesday May 25, 03:00 p.m.-5:00 p.m. SPECT Brain Imaging: Validity of Scoring

Robert D. Hunt, M.D., *Center for Attention, 2129 Belcourt Avenue, Nashville, TN 37212*; Isaac L. Meek, B.S., Brandon S. Vestal, B.A.

Educational Objectives:

At the conclusion of this session, the participants will recognize that SPECT images can be reliably scored across cognitive and affective diagnoses. This reliability constitutes an essential step in determining the ultimate clinical potential for functional imaging.

Summary:

Objective: The clinical utility of SPECT brain imaging has been limited by a lack of validation of scoring and correlation with diagnosis and treatment outcome. This study assessed the interrater reliability of scoring SPECT images in adult patients with attention and mood disorders.

Method: Patients' diagnoses were determined by diagnostically appropriate rating scales (e.g. Conner's scale for ADHD, Hamilton Depression Rating Scale for depression) and the SCID standardized interview. Thirty patients who received SPECT brain imaging as a component of their overall clinical assessment were independently rated by three experienced reviewers utilizing visual scoring of 18 definable brain areas using a computer-generated color code that visually distinguishes 5% increments in brain blood flow.

Results: The SPECT scores were 94% congruent across raters ($p > 0.05$) and were not a function of patients' diagnoses or comorbidities.

Conclusion: The data suggest that if raters are trained at the same site, their margin of scoring error is minimal. A reliable method of SPECT scoring is the first step toward validating the potential clinical utility of SPECT imaging. These images are being submitted to independent sites for cross-validation.

References:

1. Ren H-P, Jia Y-Y, Wu W-K: A scoring system for Certification and Interlaboratory Comparison of QC Test of SPECT. Peking Union Medical College Beijing (China)

NR692 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Are Clinical Data Matched With Empirical Ones? Comparison After an Empowerment Course

Nir Essar, M.D., *Psagot Institute, Tel-Aviv, Israel*; Menachem Ben-Ezra

Summary:

To enable ENOSH (Israeli equivalent to NAMI-National Alliance for the Mentally Ill) rehabilitated patients to work with fellow mentally handicapped that are home bound, the presenters taught the patients how to recognize motivational cognitive mistakes and how to reduce them among patients and their family members. The course included 19 meetings, each six hours long, of teaching and role playing. During the course, the students were treated as colleagues, and there was an emphasis on the common biases of all the handicapped people (mentally and physically). Learning was expected to improve self-awareness, self-esteem and social and occupational functioning. The SQLS (Schizophrenia Quality of Life Scale), CBI (Care Burden Inventory), social adaptation and demographic questionnaires were administered at the beginning (25 students) and at the end (18) of the course. Psychosocial and diagnostic measures were obtained, and the students were filmed three month, before the course ended. Assignment to the experimental (study) group was in addition to their regular treatment. Clinical results indicated that their self-awareness of the disease had increased and their self-image was improved as comprehended by themselves and by their peers. Seventeen students had begun working in the free market. However, although the administered questionnaires did not yield any significant result or show any improvement, the clinical state was improved drastically. This improvement was apparent both to the students themselves and to their peers and also to the clinical staff who taught them. These results are presented in a sample video. The lack of correlation between the results of the questionnaires and the clinical state will be discussed.

References:

1. Lecomte T, Cyr M, Lesage AD, Wilde J, Leclerc C, Ricard N: Efficacy of a self-esteem module in the empowerment of individuals with schizophrenia. *J Nerv Ment Dis* 1999; 187:406-13.
2. Openshaw C, Waller G, Sperlinger D: (2004). Group cognitive-behavior therapy for bulimia nervosa: statistical versus clinical significance of changes in symptoms across treatment. *Int J Eat Disord* 2004; 36:363-375.

NR693 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Level of Agitation of Patients Presenting to an Emergency Department

Leslie Zun, M.D., *Emergency Department, Mount Sinai Hospital, 15th & California, Chicago, IL 60608*; Lavonne Downey, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to determine the level of agitation of psychiatric patients who present to an emergency department.

Summary:

Objective: To determine the level of agitation seen in psychiatric patients presenting to an emergency department (ED) and the change in the level over time.

Methods: A convenience prospective, observation trial was conducted. The Agitation-Behavior and the Richmond Agitation-Restraint scales were used to determine the level of agitation of psychiatric patients who presented to the ED upon entry and every 30 minutes for three hours. The setting was a Level I adult and pediatric trauma center in an inner city with 45,000 visits. Data

for patients who were restrained or chemically modulated or both were analyzed.

Results: There were a total of 94 subjects, 48 without restraint and 46 with restraint. Restrained patients had significantly higher agitation levels upon entry to the ED than unrestrained patients. ($F = 6.810$, $df = 3$, $p < 0.001$). Those requiring restraints or chemical modulation maintained a significantly higher agitation level for the entire three-hour observation, compared to those who were not restrained ($F = 4.829-19.134$, $df = 3$, $p = 0.001-0.01$). All subjects moved to lower levels of agitation (restrained group 31% to 57% and unrestrained group 0% to 58% in category of least amount of agitation) by the end of the observation period.

Conclusion: Restrained and chemically modulated patients are more agitated and remained that way over the time of observation compared with those who were not.

References:

1. Battaglia J, Moss S, Rush J, et al: Haloperidol, lorazepam, or both for psychotic agitation? a multicenter, prospective, double blind, emergency department study. *Am J Emerg Med* 1997; 15:335-340.
2. Dubin WR: Evaluating and managing the violent patient. *Am Emerg Med* 1981; 10:481-484.

NR694 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Effects of Isotretinoin on Brain Function in Acne Patients

J. Douglas Bremner, M.D., *Department of Neuroscience Unit, Emory University, West Campus, 1256 Briarcliff Road, Room 308, Atlanta, GA 30306*; Negar Fani, B.S., Ali Ashraf, M.D., John Votaw, Ph.D., Lai Reed, Ph.D., Viola Vaccarino, M.D., Charles Nemeroff, M.D.

Educational Objectives:

At the conclusion of the presentation participant should be able to identify the potential role for isotretinoin in the development of depression and possible brain pathways by which this may occur.

Summary:

Although there have been case reports suggesting a relationship between treatment with the acne medication isotretinoin (Accutane) and the development of depression and suicide, this topic remains controversial. In order for isotretinoin to cause depression it must have an effect on the brain; however no studies to date have examined the effects of isotretinoin on brain function in acne patients. The purpose of this study was to assess the effects of isotretinoin on brain function in acne patients. Brain function was measured with [$F-18$]-2-fluoro-2-deoxyglucose (FDG) positron emission tomography (PET) before and after four months of treatment with isotretinoin ($N = 13$) and antibiotic ($N = 15$). Isotretinoin (but not antibiotic) treatment was associated with decreased brain metabolism in the orbitofrontal cortex (-21% change versus a +2% change for antibiotic) ($p < 0.05$), a brain area known to mediate symptoms of depression. There were no differences in severity of depressive symptoms between the isotretinoin and antibiotic treatment groups before or after treatment. This study suggests that isotretinoin treatment is associated with changes in brain function.

Funding from Mr. Liam Grant of the Roaccutane Action Group and attorneys involved in litigation regarding accutane.

References:

1. Bremner JD: Does isotretinoin cause depression and suicide? *Psychopharmacology Bulletin* 2003; 37:5-9.
2. Crandall J, Sakai Y, Zhang J, Koul O, Mineur Y, Crusio WE, McCaffery P: 13-cis-retinoic acid suppresses hippocampal cell division and hippocampal-dependent learning in mice. *Pro-*

ceedings of the National Academy of Sciences USA 2004; 101(14):5111-5116.

NR695 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Superoxide Dismutase and Thiobarbituric Acid Reactive Substances Associated With Subtypes and Clinical Course of Schizophrenia

Clarissa S. Gama, M.D., *Department of Psychiatry, HCPA, Rua Ramiro Barcelos, 2350, Porto Alegre/RS 90035-000, Brazil*; Mirian Salvador, Ph.D., Ana Cristina Andreatza, Pharm.D., Flavio P. Kapczinski, Ph.D., Paulo S. Belmonte-de-Abreu, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize some neurobiological markers in schizophrenia.

Summary:

High levels of superoxide dismutase (SOD) - a key enzyme in antioxidant defense mechanisms — were associated with positive symptoms in neuroleptic-free schizophrenic patients. SOD activity also seems to be increased in the residual schizophrenia subtype, compared to the paranoid subtype. Recent studies provided some evidence of increased levels of lipid peroxidation products, measured by the thiobarbituric acid reactive substances (TBARS), in schizophrenic patients. Animal studies found evidence among females of higher levels of antioxidant enzymes and products of lipid peroxidation. The presenters examined serum SOD and TBARS levels in different subtypes, gender, and outcome of schizophrenia in 88 chronically medicated schizophrenic patients. Fifty-one patients were classified as schizophrenic paranoid type, 31 as disorganized, and six as undifferentiated. There were 22 subjects with partial remission, 28 with marked symptoms, and 38 with deterioration. Mean serum SOD and mean serum TBARS concentrations were not significantly different among different schizophrenia subtypes and between the three different outcomes. Stratification by gender failed to show any difference in SOD levels. TBARS levels were significantly higher in the male subgroup with marked symptoms, compared to the deteriorated group. Serum SOD and TBARS levels failed to show any correlation with BPRS scores. TBARS levels in male patients might be considered as a biological marker of state (a warning sign long before deterioration). This highly speculative conclusion can be examined in further studies of the association of increased lipid peroxidation and disturbed behavior.

Funding from CAPES, FIPE-HCPA

References:

1. Zhang XY, Zhou DF, Cao LY, Zhang PY, Wu GY: Elevated blood superoxide dismutase in neuroleptic-free schizophrenia: association with positive symptoms. *Journal of Psychiatric Research* 2003; 117(1):85-8.
2. Herken H, Uz E, Ozyurt H, Sogut S, Virit O, Akyol O. Evidence that the activities of erythrocyte free radical scavenging enzymes and the products of lipid peroxidation are increased in different forms of schizophrenia. *Molecular Psychiatry* 2001; 6(1):66-73.

NR696 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Economic and Disability Outcomes Among Near Elderly Americans With Depression and Pain

Rebecca Robinson, M.S., *Health Outcome Department, Eli Lilly and Company, Lilly Corporate Center, DC1850, Indianapolis, IN 46285*; Tian Haijun, Ph.D., Roland Sturm, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be aware that 1) depression with pain was associated with worse labor market, financial, insurance, and disability outcomes among near elderly Americans than either single condition. 2) Individuals with depression and pain receiving government supports may have worse access to care due to leaving employment early.

Summary:

Objective: The presenters analyzed associations between depression and pain on labor market, financial, insurance, and disability outcomes among Americans age 55-65, using Wave 3 of the Health and Retirement Survey, a nationally representative sample of the general population age 55-65 in 1996.

Methods: Multivariate regression analyses, controlling for sociodemographics and health conditions, estimated the association between depression and pain on outcomes of work and retirement status, household income and wealth, health care costs, government health insurance, Social Security, health limitations, and activities of daily living (ADLs) affecting work. Independent variables included the presence or absence of depression with or without self-reported pain.

Results: In this sample, depression with pain predicted work status, retirement, household income, total wealth, total medical expenditures, government insurance, Social Security earnings, limitations in ADLs, and limitations affecting work (all $p < 0.01$). Compared to depression-only or pain-only, individuals with depression and pain were less likely to work for pay, had higher total medical expenditures, and were more likely to report health limitations in ADLs and on work (all $p < 0.01$).

Conclusion: Depression with pain was associated with worse labor market, financial, insurance, and disability outcomes in a sample of near elderly adults. Treatment should address the duality of these conditions.

References:

1. Bao Y, Sturm R, Croghan TW: A national study of the effect of chronic pain on the use of health care by depressed persons. *Psychiatr Serv* 2003; 54:693-697.
2. Bair MJ, Robinson RL, Katon W, Kroenke K: Depression and pain comorbidity. *Arch Intern Med* 2003; 163:2433-2445.

NR697 Wednesday, May 25, 3:00 p.m.-5:00 p.m. Association of the TAP2 Gene With Schizophrenia in the Korean Population

Won Kim, M.D., *Department of Psychiatry, St. Mary's Hospital, 62 Youido-dong Youngdengpo-gu, Seoul 150-713, South Korea*; Tae-Youn Jun, M.D., Jeong-Ho Chae, M.D., Won-Myong Bahk, M.D., Byung-Wook Lee, M.D., Seung-Kyu Bang, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the association of the TAP2 gene and schizophrenia.

Summary:

Objectives: A number of reports have recently been published about the genetic association of human leukocyte antigens (HLA) with schizophrenia. The genes for transporters associated with antigen processing (TAP) are located near HLA class II coding regions and related to antigen presentation. Therefore, polymorphisms of TAP might alter the T-cell mediated immune response and influence on the susceptibility to schizophrenia, which is known to have alterations in T-cell immunity. The aim of this study was to verify the relationship between schizophrenia and polymorphisms of TAP2 genes.

Methods: Among Korean patients with a diagnosis of schizophrenia by DSM-IV, 257 patients without neurological illness, hormonal disorder, or comorbid mental illness were selected. Blood was obtained from 184 age- and sex-matched control subjects with no history of autoimmune and psychiatric disease. TAP2 polymorphic residues at positions 379, 565, and 665 in the TAP2 gene were found using amplification refractory mutation system-polymerase chain reaction (ARMS-PCR). The resulted products, TAP2379, TAP2565, TAP2665 were assessed.

Results: There were significant differences in genotype frequencies of TAP2565 and TAP2665 between the patients with schizophrenia and the control group ($p < 0.001$ and $p < 0.001$, respectively). The allele frequencies of TAP2565 and TAP2665 were significantly different between the patients and the controls ($p < 0.001$ and $p < 0.001$).

Conclusions: These findings suggest that the TAP2 gene may be associated with susceptibility to schizophrenia in the Korean population. Further studies are needed to determine the functional implications of these genes.

References:

1. Ozean ME, Taskin R, Banoglu R, Babacan M, Tuncer E: HLA antigens in schizophrenia and mood disorders. *Biol Psychiatry* 1996; 39:891-895.
2. Zhang SL, Chabod J, Penforis A, Reviron D, Tiberghien P, Wendling D, Toussiot E: TAP1 and TAP2 gene polymorphism in rheumatoid arthritis in a population in eastern France. *Eur J Immunogenet* 2002; 29:241-9.

NR698 Wednesday, May 25, 3:00 p.m.-5:00 p.m. No Association of the LMP Gene With Schizophrenia in the Korean Population

Won Kim, M.D., *Department of Psychiatry, St. Mary's Hospital, 62 Youido-dong Youngdengpo-gu, Seoul 150-713, South Korea*; Tae-Youn Jun, M.D., Jeong-Ho Chae, M.D., Won-Myong Bahk, M.D., Byung-Wook Lee, M.D., Seung-Kyu Bang, M.D., Han Yong Jung, M.D., Sa-Bong Roh, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the association of LMP gene and schizophrenia.

Summary:

Objective: A number of reports have recently been published about the genetic association of human leukocyte antigens with schizophrenia. Low-molecular weight polypeptide (LMP) genes, located between HLA-DQ and HLA-DP, are closely linked to MHC class II genes. LMP, the LMP2 and LMP7 gene products, are beta type subunits of the multicatalytic protease complex. It has been suggested that the LMP2 and LMP7 proteins may favor degradation of endogenous proteins and influence the spectrum of peptides suited for binding to class I molecules. Therefore, polymorphisms of LMP might alter the antigen processing pathway and influence the susceptibility of schizophrenia. Thus, the presenters investigated the possible role of LMP polymorphism in the genetic susceptibility to schizophrenia.

Method: Among Korean patients with a diagnosis of schizophrenia by DSM-IV, 261 patients without neurological illness, hormonal disorder, or comorbid mental illness were selected. Blood was obtained from 184 age- and sex-matched control subjects with no history of autoimmune and psychiatric disease. DNA was extracted from whole blood using proteinase K, and LMP2 and LMP7 gene were amplified by polymerase chain reaction. The genotypes and alleles were determined with restriction fragment length polymorphism.

Results: The genotype and allele distribution of LMP2 and LMP7 in patients with schizophrenia were not significantly different from those of control subjects.

Conclusion: This study did not show the association of the LMP2 and LMP7 gene with schizophrenia in the Korean population. Further studies are needed to determine the role of LMP in the pathophysiology of schizophrenia.

References:

1. Maksymowych WP, Jhangri GS, Gorodezky C, Luong M, Wong C, Burgos-Vargas R, Morenot M, Sanchez-Corona J, Ramos-Remus C, Russell AS: The LMP2 polymorphism is associated with susceptibility to acute anterior uveitis in HLA-B27 positive juvenile and adult Mexican subjects with ankylosing spondylitis. *Ann Rheum Dis* 1997; 56(8):488-492.
2. Lee HJ, Ha SJ, Han H, Kim JW: Distribution of HLA-A, B alleles and polymorphisms of TAP and LMP genes in Korean patients with atopic dermatitis. *Clin Exp Allergy* 2001; 31(12):1867-74.

NR699 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

A 52-Week Study of the Efficacy and Safety of Divalproex Sodium ER Augmentation of Donepezil for Cognition and Behavior in Mid/Moderate Alzheimer's Disease

Supported by Abbott Laboratories

Peter M. Aupperle, M.D., *Department of Psychiatry, UMDNJ, Robert Wood Johnson Medical School, 667 Hoes Lane, Piscataway, NJ 08854*; Julie Coleman, R.N., Steve Sohnle, Ph.D., Anjali Patel, B.S.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to conclude that a double-blind placebo-controlled study and this protocol provides open label extension data on the use of divalproex sodium ER as an augmenting agent to donepezil.

Summary:

Divalproex sodium ER (extended release) has been studied in terms of decreasing the behavioral complications in AD patients; however, little clinical data exist on the cognitive enhancing ability of divalproex sodium ER, despite some positive basic science data. The authors previously presented positive cognitive and behavioral data in a six-month, double-blind placebo-controlled study, and this protocol provides open-label extension data on the use of divalproex sodium ER as an augmenting agent to donepezil. Subjects were enrolled if they met NINCDS/ADRA criteria for the diagnosis of AD. No concomitant psychotropic medications were allowed. Cognition was assessed with the MMSE and the ADAS-Cog, and changes in behavioral complications were examined via the NPI and the Behave-Ad. At baseline the mean ADAS-Cog was 23.5, and the MMSE was 15.5. The NPI was 16; the Behave-Ad was 2. At week 52 the mean ADAS-cog was 29.5, and the MMSE was 13. The NPI was 4.5; Behave-ad was 2.5. There were no adverse events noted during this extension protocol. Participants who were augmented with divalproex sodium ER for the entire 52-week period showed improvement in cognition and behavior as demonstrated by the ADAS-cog, MMSE, NPI, and Behave-Ad. Cognitive scales declined less rapidly than would be typical in this population and behavioral rating scales showed improvement. Of also of interest was that divalproex sodium ER was well tolerated.

References:

1. Tariot PN, Loy R, Ryan JM, Porsteinsson A, Ismail S: Mood stabilizers in Alzheimer's disease: symptomatic and neuropro-

TECTIVE RATIONALES. *Advanced Drug Delivery Reviews* 2002; 54(12):1567-77.

2. Tariot PN: Valproate use in neuropsychiatric disorders in the elderly. *Psychopharmacology Bulletin* 2003; 37 Suppl 2:116-28.

NR700 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Negative and Affective Symptom Response to Antipsychotics Is Predicted by a 5-HT1A Receptor Genotype

Gavin P. Reynolds, Ph.D., *Division of Psychiatry and Department of Neuroscience, Queen's University Belfast, Whitla Medical Building, Belfast BT9 7BL, United Kingdom*; Lucy Templeman, Ph.D., Sofia Fertuzinhos, B.S., Belen Arranz, M.D., Luis San, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand that a common genetic factor, via effects on serotonin neurotransmission, strongly predicts the outcome of the treatment of schizophrenia with antipsychotic drugs.

Summary:

Objective: Negative symptoms of schizophrenia respond poorly to antipsychotic treatment, although some atypical antipsychotics may have an improved effect on these symptoms. One possible mechanism associated with antipsychotic effects on negative and affective symptoms is an action at the 5-HT1A receptor. A common genetic polymorphism of the 5-HT1A receptors is associated with depression and suicide. The presenters investigated the association of this polymorphism with symptom response to antipsychotic drug treatment.

Method: Drug-naive psychotic patients were assessed by PANSS and Calgary depression scale before and following antipsychotic drug treatment for a first psychotic episode and genotyped for the -1019C/G 5HT1A receptor gene polymorphism.

Results: Improvement in total PANSS at three months was significantly associated with genotype, whereby the G allele predicted poorer response to treatment. This reflected a highly significant association with improvement in negative symptoms and an effect on general psychopathology symptoms, with no significant effect on positive symptoms. A very strong association of 5-HT1A genotype with the response of symptoms of depression to antipsychotic drugs was also observed.

Conclusion: These findings demonstrate a strong genetic association with the response of the negative syndrome and depressive symptoms to treatment with antipsychotic drugs, indicating the role played by 5-HT system and the 5-HT1A receptor in negative and affective symptoms and their treatment.

Partially supported by a grant from Fundació La Marató (01/5330).

References:

1. Lemonde S et al: Impaired repression at a 5-HT1A receptor gene polymorphism associated with major depression and suicide. *J Neurosci* 2003; 23: 8788-8799.
2. Reynolds GP et al: Pharmacogenetics of treatment in first-episode schizophrenia: D3 and 5-HT2C receptor polymorphisms separately associate with positive and negative symptom response. *Eur Psychopharmacol* (in press).

NR701 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Efficacy and Tolerability of Fixed, Low Dose Paroxetine CR in the Treatment of Major Depression in the Elderly

Supported by GlaxoSmithKline

Desiree Schaefer, B.A., *Department of Psychiatry, GlaxoSmithKline, 2301 Renaissance Boulevard Bldg 510, King of Prussia, PA 19406-2772*; Cornelius Pitts, Pharm.D., Alan Lipschitz, M.D., Malini Iyengar, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the use of paroxetine CR 12.5 mg and 25 mg in the treatment of MDD in elderly patients.

Summary:

Objective: To evaluate the efficacy and tolerability of low doses of paroxetine CR in the treatment of major depressive disorder (MDD) in elderly patients.

Method: A total of 528 outpatients (ages 60-91; mean = 67) with MDD were randomly assigned to 10 weeks of fixed doses of paroxetine CR 12.5 mg or 25 mg/day or placebo.

Results: Baseline-endpoint change for drug vs. placebo demonstrated efficacy for both paroxetine 12.5 mg (-1.8, 95% CI = 3.41 to -0.19, $p = 0.029$) and 25 mg (-3.3, 95% CI = -4.84 to -1.68, $p < 0.001$) as measured by the primary variable (HAM-D [LOCF]) Remission rates (HAM-D total score <7 at endpoint) were 33% for paroxetine 12.5 mg ($p = 0.280$) and 41% for paroxetine CR 25 mg ($p = 0.008$), relative to placebo (28%). Efficacy was demonstrated for paroxetine CR 12.5 mg and 25 mg by the LOCF CGI-S and the HAM-D depressed mood item. Both active treatment groups had a low incidence of AEs. There was a low incidence of withdrawals due to AEs (12.5 mg = 6%; 25 mg = 8%; placebo = 7%).

Conclusion: These data show that the administration of paroxetine CR 12.5 mg and 25 mg daily is efficacious and well tolerated in the treatment of elderly depressed patients.

References:

1. Trivedi M, et al: Paroxetine CR Efficacy and Tolerability at Low Doses in the Treatment of Major Depression. US Psychiatric and Mental Health Congress, 2002.
2. Rapaport M: Efficacy of controlled-release paroxetine in the treatment of late-life depression. *J Clin Psychiatry* 2003; 64:9, 1065-1074.

NR702 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Qualitative Analysis of Eight Suicide Notes in Old Age

Daniel Matusevich, M.D., *Av Del Libertador 2306 #1B, Buenos Aires 1425, Argentina*; Carolina Vairo, M.D., Martin Ruiz, M.D., Carlos Finkelsztejn, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to discuss suicide notes and consider that suicide notes are one important way to understand suicidal behavior.

Summary:

The presenters analyzed and classified eight suicide notes left by elderly patients who attempted suicide; older adults more frequently leave suicide notes. The typology created by Jacobs in 1967 was used to classify notes in five categories. The issues that frequently appear are physical illness, chronic pain, loneliness, disability, depression, and isolation.

References:

1. Leenaars A: Suicide notes of the older adult, in *Suicide and the Older Adult*. Leenaars A, Maris R, Mc Intosh J, Richman J. (eds). New York, Guilford, 1992; pp 62-79.
2. Leenaars A: *Suicide Notes*. New York, Human Sciences Press, 1988.

NR703 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Dementia, Suicide Attempts, and Suicide: A Case Study

Daniel Matusevich, M.D., *Av Del Libertador 2306 #1B, Buenos Aires 1425, Argentina*; Martin Ruiz, M.D., Carolina Vairo, M.D., Carlos Finkelsztejn, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to discuss the risk of suicide attempts in patients with dementia

Summary:

The prevalence of suicide attempts and suicide in patients with any sort of dementia has not been well established. The only data found through a bibliographic research in MEDLINE belong to a paper by Larson dated 1963, who points out that only 0.8% of men and 0.3% of women with dementia commit suicide. Although people over 65 years old are less than 13% of the world's total population, they actually commit between 17% and 25% of all suicides among all ages. It has been usually claimed that people with dementia do not commit suicide, because of failure in executive abilities and in their capacity to carry it out and because of the loss of insight. Both would act as protective factors from suicide. The aim of this study was to analyze five clinical cases of patients with dementia who were hospitalized in a psychiatric unit of a general hospital after attempting suicide and to compare them with four other cases of patients with dementia who committed suicide reported in international literature.

References:

1. Shneidman E, Farberow N: Comparaciones estadísticas entre intentos de suicidio y suicidio consumados, in Farberow N, Shneidman Y. *Estudio sobre el suicidio y su prevención*. Mexico City, Prensa Medica Mexicana, 1969.
2. Larson T, Sjogren T, Jacobson G: Senile dementia: a clinical, socio-medical and genetic study. *Acta Psychiatr Scand* 1963; suppl 167:1-259.

NR704 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Suicide Attempts in Old Age: Data From the Hospital Italiano of Buenos Aires, Argentina

Daniel Matusevich, M.D., *Av Del Libertador 2306 #1B, Buenos Aires 1425, Argentina*; Martin Ruiz, M.D., Carolina Vairo, M.D., Carlos Finkelsztejn, M.D., Eugenia Dabi, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the characteristics of patients over 60 who attempts suicide.

Summary:

Objective: The aim of this study was to analyze some characteristics of 25 patients, over 60 years old, who attempted suicide and were hospitalized in the Department of Psychiatry of a general hospital in Buenos Aires.

Methods: This retrospective study used data from the medical records of patients (1999 to 2002) based on a protocol comprising

an analysis of attempted suicides and demographic and clinical variables. Patients' diagnoses following the DSM-IV criteria were made by two trained GPs and were confirmed by MMPI and Rorschach.

Results: A total of 72% were women. The average age was 73.8, 16% were divorced, 20% never married, 32% widowed, and 32% married. The most frequent diagnosis was major depressive disorder of late onset followed by personality disorder (96%; 48%). The most frequent method was intoxication (68.75% BDZ). Almost half of the attempts were highly severe.

Conclusions: Elderly people who attempt suicide are likely to be female, 68-78 years old, without a partner, and living with someone. They are likely to have major depressive disorder (half had a personality disorders) and a clinical disease. The attempt is likely to be the first and to occur when the person is alone at home; the person does not advise others. Reduced hearing is a very frequent comorbidity.

References:

1. Cattell H, Jolley D: One hundred cases of suicide in elderly people. *British Journal of Psychiatry* 1996; 166: 451-457.
2. Szanto K, Reynolds Ch, Conwell Y, Begley A, Houck P: High levels of hopelessness persist in geriatric patients with remitted depression and a history of attempted suicide. *Journal of the American Geriatrics Society* 1998; 46 (11):1401-1406.

NR705 Wednesday, May 25, 03:00 p.m.-5:00 p.m.

Remission in Depressed Outpatients: More Than Just Symptom Resolution?

Mark Zimmerman, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905*; Joseph McGlinchey, Ph.D., Michael Posternak, M.D., Michael Friedman, M.D., Daniela Boerescu, M.D., Naureen Attiullah, M.D.

Educational Objectives:

At the conclusion of the presentation the participant should be able to recognize that remission should be defined according to both symptom levels and functioning.

Summary:

Objective: In treatment studies of depression, remission is defined according to scores on symptom severity scales. Normalization of functioning has often been mentioned as an important component of the definition of remission, although it is not used to identify remitted patients in studies of treatment efficacy. Conceptually, the return of normal functioning should be as fundamental to the concept of remission as is symptom resolution, because both symptoms and impaired functioning are core constructs in the diagnosis of mental disorders. In the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project the presenter examined the independent and additive association between level of severity of depressive symptoms and functional impairment in predicting depressed patients' subjective evaluation of their remission status.

Methods: Five hundred and fourteen depressed psychiatric outpatients filled out a questionnaire on which they rated the severity of the symptoms of depression, the level of impairment due to depression, and their quality of life.

Results: Symptom severity, functional impairment from depression, and quality of life were significantly and highly intercorrelated, and each was significantly associated with remission status. The results of a logistic regression analysis indicated that each of the three variables was a significant, independent, predictor of remission status.

Conclusions: In treatment studies of depression, remission is narrowly defined in terms of symptom resolution. Our results sup-

port broadening the concept of remission beyond symptom levels to include assessments of functioning and quality of life.

References:

1. Ballenger J: Clinical guidelines for establishing remission in patients with depression and anxiety. *J Clin Psychiatry* 1999; 60 suppl 22:29-34.
2. Rush A, Trivedi M: Treating depression to remission. *Psych Annals* 1995; 25:704-709.

NR706 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

To What Extent Do the PANSS and CGI-S Overlap?

Jonathan Rabinowitz, Ph.D., *Bar Ilan University, Ramat Gan 91000, Israel*

Educational Objectives:

At the conclusion of this presentation the participant should be able to understand the extent to which the CGI-S and PANSS overlap in measuring psychopathology and change in clinical trials.

Summary:

Objectives: Because they are regarded as complementary but not completely overlapping measures, both the PANSS (Positive and Negative Syndrome Scale; 30 items) and the CGI (Clinical Global Impression) items for severity and for change are used together as measures of severity of psychotic illness in clinical trials. However, little is known about the extent to which they overlap. The PANSS is the "gold standard" measure in efficacy studies of antipsychotic medication. However, it is often not possible or even desirable to use the PANSS, yet the validity of the CGI has yet to be explored. The aim of this study was to examine the extent to which the PANSS and CGI overlap.

Methods: Analysis was conducted on baseline and endpoint data from four large randomized clinical trials of antipsychotic drugs used to treat persons with schizophrenia. Linear regression was used to predict CGI severity scores at baseline based on the PANSS items. Crosstabs were used to examine the association of clinical improvement on the PANSS (20% or better decline) and change on the CGI-S.

Results: In descending order of variance explained by trial, the PANSS items, explained 59% (N = 523), 53% (N = 555), 46% (N = 594), and 24% (N = 1,362) of the variance in the CGI-S. Clinical improvement on the PANSS corresponded best to a 1-point decline on the CGI-S (N = 1,362, sensitivity = 89.6%, specificity = 65.8%, kappa = 0.054; N = 523, sensitivity = 75.7%, specificity = 82.8%, kappa = 0.58; N = 555, sensitivity = 85.8%, specificity = 72.4%, kappa = 0.57; N = 594, sensitivity = 86.6%, specificity = 72.0%, kappa = 0.59).

Conclusions: While the CGI-S and PANSS are strongly correlated, they are not synonymous. However, both measures show substantial agreement in detecting change.

Some funding for travel from Janssen Research Foundation

References:

1. Guy W: Clinical Global Impression (CGI), In *Handbook of Psychiatric Measures*. Edited by Rush AJ. Washington, DC, American Psychiatric Association, 2000, pp 100-102

NR707 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Trends in Psychiatric Emergency Admissions of Older Adults in the U.S.

Daniel P. Chapman, Ph.D., *Division of Adult and Community Health, Centers for Disease Control and Prevention, 4770 Buford Highway N.E., MS-K67, Atlanta, GA 30341*; Robert Anda, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to describe trends in the emergency admissions of older adults with a primary diagnosis of a psychiatric disorder.

Summary:

Objective: While believed to underutilize psychiatric services relative to their younger peers, older adults are more likely to be hospitalized with psychiatric disorders following an emergency room visit. Given the aging of the U.S. population, a better understanding of trends in the psychiatric emergency hospitalization of older adults is warranted.

Method: Using Medicare Part A claims data, the presenters assessed the prevalence of psychiatric disorders as admitting diagnoses among persons age 65 years or older in the U.S. during the years 1997 and 2000.

Results: A greater number of psychiatric emergency admissions were reported among older adults in the U.S. in 2000 (N = 110,043) than in 1997 (N = 96,359). Dementia, delirium, and amnesic disorders comprised a greater percentage of psychiatric admitting diagnoses in older adults in 2000 than in 1997 (44.4% vs. 38.8%), as did schizophrenia and psychotic disorders (21.0% vs. 19.8%). Conversely, decreased percentages of mood disorders (24.4% vs. 29.5%) and anxiety disorders (2.0% vs. 2.3%) were reported in 2000 than in 1997, as well as decreased percentages of substance abuse disorders (7.7% vs. 8.9%) and medication-induced disorders (0.4% vs. 0.7%).

Conclusions: With the aging of the U.S. population, the number of older adults hospitalized for psychiatric emergencies will likely increase. Assessment of the proportion of diagnoses precipitating emergency hospitalization may suggest areas for further investigation and intervention in this population.

References:

1. Chapman DP, Currier GW, Miller JK, Anda RF: Medication-induced emergency hospitalizations for psychiatric disorders among older adults in the US. *Int J Geriatr Psychiatry* 2003; 18:185-186.
2. Puryear DA, Lovitt R, Miller DA: Characteristics of elderly persons seen in an urban psychiatric emergency room. *Hosp Community Psychiatry* 1991; 42:802-807.

NR708 Wednesday, May 25, 3:00 p.m.-5:00 p.m. A Case of Behcet's Disease With Atypical Psychosis

SungBin Choi, M.D., *Department of Psychiatry, Keyo hospital, 280-1 Wanggok-dong, Uiwang city 437-020, South Korea*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the importance of careful evaluation of the patient's history, clinical symptoms, process, and biological data to make a diagnosis of Behcet's disease.

Summary:

Behcet's disease is a multisystemic inflammatory disease—oral ulcer, genital ulcer, uveitis etc.—of unknown etiology. The patient described here developed psychiatric symptoms with physical symptoms of Behcet's disease. She had oral ulcers, uveitis, and arthritis as physical symptoms. She also had atypical psychotic symptoms affected by neurological involvement of Behcet's disease. Psychiatric episodes in Behcet's disease may be misdiagnosed and mistreated as functional psychiatric diseases such as schizophrenia. The psychiatrist should be aware of the possibility of neurological and/or psychiatric involvement in Behcet's disease. Careful evaluation of the patient's history, clinical symptoms, process, and biological data may be important to make a diagnosis and give proper treatment.

References:

1. Borson S: Behcet's disease as psychiatric disorder: a case report. *Am J Psychiatry* 1982; 139:10:1348-1349.
2. Chiba S, Takahashi S, Miyagishi T: Psychiatric manifestation as an early symptom of Behcet's disease. *Br J Psychiatry* 1986; 148:752-753.

NR709 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Psychometric Properties of the Geriatric Depression Scale-Short Form (GDS-SF) in Parkinson's Disease

Daniel Weintraub, M.D., *Geriatric Psychiatry Division, University of Pennsylvania, 3535 Market St, Philadelphia, PA 19104*; Katherine Oehlberg, B.A.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate that the GDS-SF, a brief and easily-administered depression rating scale, has good sensitivity and specificity for a DSM-IV diagnosis of depression in PD, performing comparably to the Hamilton Depression Rating Scale. These results suggest the GDS-SF is appropriate to use as a screening instrument for depression in PD.

Summary:

Objective: To compare the psychometric properties of the Geriatric Depression Scale-Short Form (GDS-SF) and the Hamilton Depression Rating Scale (HDRS-24) in Parkinson's disease (PD).

Methods: A convenience sample of 148 PD patients at the Parkinson's Disease Centers at the Philadelphia VA Medical Center and the University of Pennsylvania were administered the 15-item GDS (GDS-SF), the 24-item HDRS (HDRS-24), and the Structured Clinical Interview for DSM-IV (SCID) depression module by a research psychiatrist or trained research assistant. Receiver-operating characteristic (ROC) curves were plotted for the GDS-SF and HDRS-24 scores, with a SCID diagnosis of a depressive disorder as the "gold standard."

Results: Thirty-two subjects (22%) received a diagnosis of depression. The area under the curve (AUC) for the two scales were comparable (GDS-SF = 0.92, HDRS-24 = 0.91), with maximal discrimination for the GDS-15 at a cutoff of 4/5 (87% accuracy; 88% sensitivity; 85% specificity) and for the HAMD-24 at a cutoff of 9/10 (83% accuracy; 88% sensitivity; 78% specificity).

Conclusions: The GDS-SF performs comparably to the HDRS-24 in discriminating between depressed and nondepressed patients in PD, making it suitable for use in this population. Because it is a brief instrument and can even be self-administered, it is an excellent tool for depression screening in PD.

References:

1. Lenntjens AFG, Verhey FRJ, Lousberg R, et al: The validity of the Hamilton and Montgomery-Asberg Depression Rating Scales as screening and diagnostic tools for depression in Parkinson's disease. *International Journal of Geriatric Psychiatry* 2000; 15:644-649.
2. Lenntjens AFG, Verhey FRJ, Luijckx G-J, et al: The validity of the Beck Depression Inventory as a screening and diagnostic instrument for depression in patients with Parkinson's disease. *Movement Disorders* 2000; 15:1221-1224.

NR710 Wednesday, May 25, 3:00 p.m.-5:00 p.m. Daily Affect in Parkinson's Disease: Responsive to Life Events and Motor Symptoms

Daniel Weintraub, M.D., *Geriatric Psychiatry Division, University of Pennsylvania, 3535 Market St, Philadelphia, PA 19104*; Donna Taraborelli, B.A.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss daily affect reporting, to demonstrate that Parkinson's disease (PD) patients are not anhedonic, in contrast with previous findings. However, they do experience worse affect overall due to a combination of low participation in positive events and the impact of core PD symptoms.

Summary:

Objectives: To determine if Parkinson's disease (PD) patients are anhedonic, by using daily affect and life event rating scales.

Methods: Nondepressed male subjects, either with PD (N = 24) or healthy elderly control (N = 23), completed the Lawton Daily Affect Rating Scales for 28 consecutive days. The effect of daily life events and PD-related symptoms on daily affect was examined by using linear and logistic mixed regression models.

Results: PD patients reported significantly less positive affect ($B = -0.013$, $p = 0.0002$), more negative affect (odds ratio = 1.063, $p = 0.0039$), and greater affective variability than controls over time. PD patients reported far fewer days with active participation events than control subjects (52 vs. 177), but they reported greater improvement in affect in response to them ($B = 0.240$, $p = 0.0275$). Increasing severity of core motor symptoms was independently associated with worse affect in the PD group ($B = -0.060$, $p = 0.0066$ for positive symptoms; odds ratio = 1.587, $p < 0.0001$ for negative symptoms).

Conclusions: PD patients report worse daily affective experiences than healthy elderly control subjects, but they do not demonstrate anhedonia in response to positive life events. The gross intergroup difference in positive events suggests the potential value of increased participation in positive experiences on emotional tone.

References:

1. Cantello R, Aguggia M, Gilli M, et al: Major depression in Parkinson's disease and the mood response to intravenous methylphenidate: possible role of the "hedonic" dopamine synapse. *Journal of Neurology, Neurosurgery, and Psychiatry* 1989; 52:724-731.
2. Persico AM, Reich S, Henningfield JE, et al: Parkinsonian patients report blunted subjective effects of methylphenidate. *Experimental and Clinical Psychopharmacology* 1998; 6:54-63.

NR711 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

The Association Between Psychosis and Depression in Parkinson's Disease

Daniel Weintraub, M.D., *Geriatric Psychiatry Division, University of Pennsylvania, 3535 Market St, Philadelphia, PA 19104*; Donna Taraborelli, B.A.

Educational Objectives:

At the conclusion of this presentation, the participant should be aware that an association exists between psychosis and depression in Parkinson's disease (PD) and that psychosis alone in this population is related to PD medication exposure, while psychosis comorbid with depression is associated with the combination of dopaminergic stimulation and executive impairment.

Summary:

Objective: Psychosis and depression are common and frequently comorbid in Parkinson's disease (PD), but the nature of this association is not known. The aim of this study was to probe for clinical characteristics associated with comorbid psychosis and depression in PD.

Methods: PD patients (N = 147) were divided into four groups based on a psychiatric assessment: (1) psychotic (P; N = 14); (2)

depressed (D; N = 37); (3) psychotic and depressed (P-D; N = 19); and (4) nonpsychotic and nondepressed (NP-ND; N = 77). The groups were compared by using univariate ANOVA with post hoc t tests and χ^2 tests.

Results: There were no between-group differences in PD duration ($F = 1.4$, $df = 3$, $p = 0.24$) or severity ($F = 1.6$, $df = 3$, $p = 0.20$). P patients were significantly younger ($F = 3.0$, $df = 3$, $p = 0.03$) and more likely to be treated with a dopamine agonist ($\chi^2 = 8.0$, $df = 3$, $p < 0.05$), and both P and P-D patients were taking higher levodopa dosages ($F = 4.6$, $df = 3$, $p < 0.01$). In spite of similar MMSE scores, P-D subjects performed worse on all measures of an executive function test (the Tower of London-Drexel), including having significantly more rule violations ($F = 3.5$, $df = 3$, $p = 0.02$).

Conclusions: Increased exposure to dopaminergic medication is associated with uncomplicated psychosis in PD, but comorbid psychosis and depression is more complicated and associated with both dopaminergic stimulation and executive impairment.

References:

1. Aarsland D, Larsen JP, Cummings JL, et al: Prevalence and clinical correlates of psychotic symptoms in Parkinson's disease: a community-based study. *Archives of Neurology* 1999; 56:595-601.
2. Marsh L, Williams JR, Rocco M, et al: Psychiatric comorbidities in patients with Parkinson disease and psychosis. *Neurology* 2004; 63:293-300.

NR712 Wednesday, May 25, 03:00 p.m.-5:00 p.m.

G-Protein $\beta 3$ Subunit C825T SNP Is Associated With Seasonal Mood Variation

Heon-Jeong Lee, M.D., *Department of Psychiatry, Korea University Hospital, 126-1, 5-KA, Anam-Dong, Sungbuk-Ku, Seoul 136-705, Korea*; Seung-Mo Sung, M.D., Leen Kim, M.D., Min-Soo Lee, M.D., Seung-Hyun Kim, M.D., Sook-Haeng Joe, M.D., In-Kwa Jung, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate genetic effects on the seasonal variation of mood and behavior in humans.

Summary:

This study investigated the relationship between the G protein $\beta 3$ subunit (GNB3) C825T polymorphism and seasonal variation in young healthy male subjects. A total of 189 young Korean male medical students were recruited in this study. They were genotyped for C825T and evaluated for seasonal variation in mood and behavior with the Seasonality Pattern Assessment Questionnaire (SPAQ). Global Seasonality Score (GSS) ($F = 4.51$, $p = 0.012$) and some subscale scores such as sleep ($F = 5.08$, $p = 0.007$), social behavior ($F = 4.00$, $p = 0.02$), and energy level ($F = 5.37$, $p = 0.005$) were significantly different between three genotypes. The heterozygotes (CT) showed the higher seasonal variations in GSS ($p = 0.003$), sleep ($p = 0.002$), social behavior ($p = 0.005$), mood ($p = 0.028$), and energy level ($p = 0.003$) than homozygotes (CC/TT). The comparison between seasonals (syndromal plus subsyndromal seasonal affective disorder according to SPAQ) and normal subjects showed significant difference in frequencies of CT and CC/TT genotypes ($\chi^2 = 5.95$, $p = 0.015$; odds ratio = 2.27; 95% confidence interval, 1.17-4.43). These results suggest that the GNB3 C825T polymorphism is related to seasonal variation in mood and behavior in a normal population. Heterozygotes had significantly increased seasonality, which may represent an example of heterosis.

References:

1. Willeit M, Praschak-Rieder N, Zill P, Neumeister A, Ackenheil M, Kasper S, Bondy B: C825T polymorphism in the G-protein beta3-subunit gene is associated with seasonal affective disorder. *Biol Psychiatry* 2003; 54: 682-686.
2. Johansson C, Willeit M, Aron L, Smedh C, Ekholm J, Paunio T: Seasonal affective disorder and the G-protein beta-3-subunit C825T polymorphism. *Biol Psychiatry* 2004; 55: 317-319.

NR713 Wednesday, May 25, 03:00 p.m.-5:00 p.m. **Diagnosis and Assessment of Alzheimer's Disease in Routine Clinical Practice**

Francisco J. Arranz, M.D., *Medical Department, Laboratorios Dr. Esteve, S.A., Av. Mare de Déu de Montserrat, 221, Barcelona 08041, Spain*; Carlos Martinez Parra, M.D., Sonia Pons, M.D., Lluís Tàrraga, Psy.D., Ana Frank, M.D., Mercè Boada, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the strategies for the diagnosis and assessment of Alzheimer's disease most frequently used in routine clinical practice.

Summary:

Objective: As a part of a study on the pattern of use of rivastigmine in clinical practice, it was intended to gain information about the habits of Spanish neurologists regarding the diagnosis and assessment of Alzheimer's disease (AD).

Methods: An open multicenter prospective naturalistic study in ambulatory patients with AD was conducted. All patients were receiving rivastigmine in accordance with the drug's package insert. Patients were assessed at baseline and after six months of treatment, although intermediate visits were allowed according to the doctor's criterion.

Results: One hundred and forty-two neurologists recruited 989 patients, 774 of whom completed the treatment. The criteria most frequent applied for the diagnosis of AD were those of the DSM-IV (76.7%) and NINCDS-ADRDA (32.3%). In most cases (88%), at least one clinical assessment scale of AD was used, but a depression rating scale was employed only in 38% of patients. Only 46.6% of patients were seen at one or more follow-up visits before six months of the first consultation.

Conclusions: In this large sample of patients with AD seen in real clinical practice settings, most of them were not administered a scale for the evaluation of depression, and follow-up visits were scarce.

Funding from Laboratorios Dr. Esteve, S.A.; Av. Mare de Déu de Montserrat, 221. 08041 Barcelona Spain.

References:

1. Cummings JL: Alzheimer's disease. *N Engl J Med* 2004; 351:56-67.
2. Richard SS, Hendrie HC: Diagnosis, management and treatment of Alzheimer disease: a guide for the internist. *Arch Intern Med* 1999; 159(8):789-98.

NR714 Wednesday, May 25, 3:00 p.m.-5:00 p.m. **Effectiveness and Pattern of Use of Rivastigmine in Real Clinical Practice Settings**

Francisco J. Arranz, M.D., *Medical Department, Laboratorios Dr. Esteve, S.A., Av. Mare de Déu de Montserrat, 221, Barcelona 08041, Spain*; Lluís Tàrraga, Psy.D., Carlos Martinez Parra, M.D., Ana Frank, M.D., Mercè Boada, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the way doctors use rivastigmine in routine clinical practice.

Summary:

Objective: This study was designed to provide information about the doses and posologic schedules of rivastigmine most frequently used in the treatment of Alzheimer's disease (AD) in routine clinical practice.

Method: In an open multicenter prospective study, ambulatory patients with a current diagnosis of AD were given rivastigmine at usual clinical practice doses according to the drug's package insert. To assess the efficacy of the treatment, MMSE, NPI-Q, and IDDD were all administered at baseline and after six months of treatment.

Results: Seven hundred and seventy-four of 989 patients included were completers. Ninety-two percent of the patients were taking a dose within the therapeutic window (3-6 mg b.i.d.) at the end of the study. The drug was slowly titrated, with 82 days the mean time to reach the final dose. Patients improved slightly, but in a statistically significant manner, on the MMSE and both NPI-Q severity and NPI-Q stress scales. Only 6% of patients withdrew due to intolerance.

Conclusions: In real clinical practice settings doctors titrate the dose of rivastigmine very slowly. This procedure provided rivastigmine with effectiveness and allowed most of the patients to receive therapeutic doses with very good tolerability.

Funding from Laboratorios Dr. Esteve, S.A. Av. Mare de Déu de Montserrat, 221, 08041 Barcelona Spain;

References:

1. Corey-Bloom J, Anand R, Veach J et al: A randomized trial evaluating the efficacy and safety of ENA 713 (rivastigmine tartrate), a new acetylcholinesterase inhibitor, in patients with mild to moderately severe Alzheimer's disease. *Int J Geriatr Psychopharmacol* 1998; 1:55-65.
2. Rösler M, Anand R, Cicin-Sain A, et al: Efficacy and safety of rivastigmine in patients with Alzheimer's disease: international randomised controlled trial. *BMJ* 1999; 318:633-63.

NR715 Wednesday, May 25, 03:00 p.m.-5:00 p.m. **A PET Study Examining Pharmacokinetics, Likeability, and Dopamine Transporter Receptor Occupancy of Methylphenidate Formulations in Adults**

Thomas J. Spencer, M.D., *Pediatric Psychopharmacology, Massachusetts General Hospital, 55 Fruit Street, Warren 705, Boston, MA 02114*; Joseph Biederman, M.D., Patrick Ciccone, M.D., Bertha Madras, Ph.D., Darin Dougherty, M.D., Alan Fischman, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the underlying central effects of MPH in humans.

Summary:

Objective: It has been hypothesized that the abuse potential of methylphenidate (MPH) is due to the rapid onset of blockade of the presynaptic dopamine transporter (DAT) in the brain. Since the newly formulated OROS formulation of MPH has a slower rise of MPH concentration, it is hypothesized that it will also have a slower onset of blockade of the presynaptic DAT and a lower risk for detection and likeability than immediate release (IR) MPH.

Method: Twelve healthy adults were randomly assigned to either single doses of IR-MPH or OROS-MPH. Doses were chosen to

match Cmax (40 mg IR-MPH, 90 mg OROS-MPH). Plasma d-MPH levels and detection/likeability questionnaires were obtained hourly for 10 hours, twice for each subject. DAT occupancies were measured at hours 1, 3, 5, and 7 using C-11 altropane and positron emission tomography (PET).

Results: Despite similar Cmax for both formulations, treatment with OROS-MPH was associated with a greater Tmax, a later time to maximum CNS DAT occupancy, and no detection/likeability, compared with IR-MPH.

Conclusion: Findings indicate that abuse liability risk of oral MPH is due to the rate of delivery and not the magnitude of plasma concentration or brain transporter occupancy.

Funding: This study was supported by funding from NIMH grant RO1MH064019 (Dr. Spencer) and McNeil Consumer & Specialty Pharmaceuticals.

References:

1. Volkow ND, Wang G-J, Fowler JS, Gatley SJ, Logan J, Ding Y-S, Hitzemann R: Dopamine transporter occupancies in the human brain induced by therapeutic doses of oral methylphenidate. *Am J Psychiatry* 1998; 155:1325-1331.
2. Kollins SH, Rush CR, Pazzaglia PJ, Ali JA: Comparison of acute behavioral effects of sustained-release and immediate-release methylphenidate. *Experimental and Clinical Psychopharmacology* 1998; 6:367-374.

NR716 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.** **Delirium Incidence and Prevalence in Terminally Ill Cancer Patients**

Supported by National Cancer Institute of Canada

Pierre Gagnon, M.D., *Psychiatric Department, Hotel-Dieu de Québec, 11 Côte du palais, Quebec City G1R 2J6, Canada*; Francois Tardif, M.S.C., Bruno Gagnon, M.D., Pierre Allard, Ph.D., Chantal Mérette, Ph.D., Claudia Emond, M.S.C., Colette Soulard, R.N.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to (1) describe delirium occurrence in terminal cancer patients and associated morbidity and demographics and (2) discuss the use of delirium screening and diagnosis instruments for clinical and research purposes in palliative medicine.

Summary:

Background: Delirium is a major diagnosis encountered by the consultant psychiatrist in palliative medicine. Prevalence rates described in previous studies vary widely. This is the largest study reporting epidemiological data based on a rigorous methodology in this population.

Objective: To assess delirium incidence and prevalence in terminal cancer.

Methods: A total of 1,460 patients in seven palliative care units in Canada, who survived longer than 48 hours, were followed prospectively from October 2001 to September 2004 from admission until patient's death. The Confusion Rating Scale (CRS) was used for delirium screening, and the Confusion Assessment Method (CAM) for diagnosis.

Results: Among the 1,460 patients evaluated, 216 reached the CRS threshold for delirium at admission for a delirium prevalence of 14.8%, while 362 patients free of delirium at admission reached the CRS delirium threshold before death, for an incidence of 31.9%. Hence, the prevalence from admission to death was 46.7%. Due to the patients' debilitated condition, CAM interviews could only be performed in 39% of patients positive on screening.

Conclusions: (1) Delirium is highly prevalent in terminal cancer, although 50% will not show signs of delirium before death. (2)

Delirium instrument selection must be carefully adapted to palliative care conditions.

References:

1. Casarett DJ, Inouye SK: Diagnosis and management of delirium near the end of life. *Ann Intern Med* 2001; 135(1): 32-40.
2. Gagnon P, Allard P, Mâsse B, de Serres M: Delirium in terminal cancer: a prospective study using daily screening, early diagnosis, and continuous monitoring. *Journal of Pain and Symptom Management* 2000; 19:412-426.

NR717 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.** **Quetiapine Use in Nursing Home Residents** *Supported by AstraZeneca LP*

Jacqueline Pesa, Ph.D., *Health Economics, AstraZeneca LP, 1800 Concord Pike B3B-315, Wilmington, DE 19850*; Sandra Molotsky, B.S.N., Lawrence Helbers, Leesa Gentry, M.S., Jacqueline Pesa, Ph.D., David Duff, B.A., Luis Silva, B.A.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that, in the nursing home setting, the atypical antipsychotic quetiapine is prescribed primarily to treat behavioral disturbances associated with dementia, psychotic mood disorders, and schizophrenia. This chart review provides "real-world" evidence that quetiapine is used to treat acceptable conditions and is within OBRA guidelines.

Summary:

Objective: Atypical antipsychotic use in nursing homes must be within guidelines outlined by the 1987 Omnibus Budget Reconciliation Act (OBRA). This study was initiated to describe quetiapine use in nursing homes and to determine if diagnoses, targeted behaviors, and dosages were acceptable per OBRA guidelines.

Methods: Charts of nursing home residents for whom quetiapine was prescribed over three months were reviewed.

Results: Charts of 2,231 nursing home residents in 255 facilities in Massachusetts, New York, Ohio, and Tennessee were reviewed. In 2,120 cases (95%), quetiapine was prescribed to treat acceptable diagnoses. Organic syndrome and psychotic mood disorders occurred most frequently and were treated with scheduled doses of 50-100 mg/day. Targeted behaviors resulting from these diagnoses were documented on 88% of charts. The most common acceptable targeted behavior prompting quetiapine use was agitation (44%). Scheduled and maximum as-needed dosages ranged from <50 to >400 mg/day. Other psychotropics currently prescribed with quetiapine were selective serotonin reuptake inhibitors (N = 809; 42.7%), anxiolytics (N = 804; 42.5%), and cognition enhancers (N = 608; 32.1%). Sleep agents were prescribed simultaneously with quetiapine more frequently than prior to quetiapine initiation.

Conclusions: Quetiapine was prescribed primarily to treat behavioral disturbances associated with dementia, psychotic mood disorders, and schizophrenia and fell within OBRA guidelines for "acceptable use."

References:

1. Stoudemire A, Smith DA: OBRA regulations and the use of psychotropic drugs in long-term-care facilities: Impact and implications for geropsychiatric care. *Gen Hosp Psychiatry* 1996; 18: 77-94.
2. Ruby CM, Kennedy DH: Psychopharmacologic medication use in nursing home care: indicators for surveyor assessment of the performance of drug regimen reviews, recommendations for monitoring, and non-pharmacologic alternatives. *Clin Fam Pract* 2001; 3:577-98.

NR718 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Effect of Depression on Physical Health in Patients: Patients With Stomach or Breast Cancer

Sang-Ick Han, M.D., *Department of Neuropsychiatry, Our Lady of Mercy Hospital, 665 Pupyung-Dong, Pupyung-Gu, Incheon 403-720, Korea*; Yang-Whan Jeon, M.D., E-Jin Park, M.D., Seung-Man Park, M.D., Se-Jung Oh, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to aware that depression is common in cancer patients, and it is associated with reduced quality of life and makes the outcome of cancer poor. This study demonstrated the relationship between depression and the physical health in cancer patients.

Summary:

Objective: This study was designed to investigate the effect of depression on physical health in cancer patients. The hypothetical model is that depressive symptoms and environment affect physical and psychological health and social relationships.

Methods: Thirty-five outpatients with stomach or breast cancer who underwent curative surgery at the department of surgery, Our Lady of Mercy Hospital, the Catholic University of Korea, were selected randomly. Depressive symptoms were assessed with the 17-item Hamilton Depression Rating Scale (HAM-D) and quality of life was measured with the Korean version of WHOQOL (physical, psychological, social, and environmental domains). Structural equation model was employed with LISREL (version 8.12a).

Results: Under the hypothetical model, depressive symptoms significantly affected physical health ($r_s = 0.154$, $t = 2.224$), but did not affect psychological health ($r_s = 0.005$, $t = 0.132$) and social relationships ($r_s = 0.032$, $t = 0.414$). Environment had an effect on social relationships ($r_s = 0.541$, $t = 3.231$), but not on physical health ($r_s = 0.300$, $t = 1.705$). Thus, depressive symptoms had a direct, negative effect on a physical health in cancer patients ($r_s = 0.157$, $t = -2.286$) in the revised model.

Conclusions: Due to the direct, negative effect of depression on physical health, it is very important to evaluate thoroughly and treat intensively depression in cancer patients after curative surgery.

References:

1. McDaniel JS, Musselman DL, Porter MR, et al: Depression in patients with cancer. *Arch Gen Psychiatry* 1995; 52:89-99.
2. Endicott J: Measurement of depression in patients with cancer. *Cancer* 1984; 53:2243-2248

NR719 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Weight Change in Elderly Patients With Dementia During Olanzapine Treatment

Supported by Eli Lilly and Company

Ilya Lipkovich, Ph.D., *Department of Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Jonna Ahl, Ph.D., Russell Nichols, Pharm.D., Thomas Hardy, M.D., Vicki Hoffman, Pharm.D.

Educational Objectives:

At the conclusion of this presentation, the participant will have a better understanding of the relationship between weight gain in elderly dementia patients and treatment with antipsychotic medication.

Summary:

Objective: Although atypical antipsychotics do not have an indication for dementia, these medications are used to treat behavioral disturbances in these patients. Several atypical antipsychotics are associated with treatment-emergent weight gain in patients with

schizophrenia or bipolar mania, but less is known about weight gain in dementia.

Methods: This is a post hoc analysis of seven olanzapine clinical trials in dementia. Baseline weight was categorized according to body mass index (BMI, kg/m^2): underweight (< 18.5), normal (18.5-24.9), overweight (25.0-29.9), and obese (≥ 30).

Results: Olanzapine-treated patients ($N = 1,267$) were 80.1 ± 6.9 years old, and most (62.6%) were underweight or normal weight at baseline. After 20 weeks treatment with olanzapine (1-20 mg/day), mean weight change was $+1.3 (\pm 3.7)$ kg ($N = 671$). Underweight patients who received olanzapine gained the most weight (2.26 kg). Most patients receiving active comparator ($N = 296$) lost weight (-1.3 kg). Greater than 7% of initial body weight was gained in 12.9% of patients receiving olanzapine, 5.4% active comparator, and 4.5% placebo.

Conclusions: Weight gain in olanzapine-treated elderly patients with dementia was less than that reported in younger patients and was more common in individuals with baseline BMI < 25 .

References:

1. Gurevitz SL, Costakis T, Leiter J: Do atypical antipsychotics cause weight gain in nursing home dementia residents? *Consult Pharm* 2004; 19(9):809-12.
2. Street JS, Clark WA, Kadam DL, et al: Long-term efficacy of olanzapine in the control of psychotic and behavioral symptoms in nursing home patients with Alzheimer's dementia. *Int J Geriatr Psychiatry* 2001; 16:S62-S70.

NR720 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

An Item Response Analysis of the Positive and Negative Syndrome Scale (PANSS)

Supported by Eli Lilly and Company.

Jean-Pierre Lindenmayer, M.D., *Psychopharmacology Research Program, Manhattan Psychiatric Center, East 125th Street, Wards Island, NY 10035*; Haya Ascher-Svanum, Ph.D., Darcy Santor, Ph.D., Robert Obenchain, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to differentiate among items of the Positive and Negative Syndrome Scale (PANSS) based on their usefulness in assessing the severity of schizophrenia.

Summary:

Objectives: To assess how each item on the Positive and Negative Syndrome Scale (PANSS) differs in its usefulness in assessing the severity of schizophrenia.

Method: Data included baseline PANSS item scores of 9,205 schizophrenia patients enrolled in 13 studies. Using a nonparametric item response model, option characteristic curves were produced to examine how the probability of endorsing a particular option changes with increasing overall severity of illness, as measured by the PANSS total score. Illness severity was defined as the total score on the PANSS and on its subscales (Positive, Negative, and General Psychopathology).

Results: Option characteristic curves identified nine PANSS items that performed very well (e.g., delusions), seven items that were good (e.g., grandiosity), and 14 items that performed less well (e.g., somatic concerns). The Positive and the Negative subscales were more discriminating than the General Psychopathology subscale or the PANSS total score.

Conclusions: Most of the PANSS items appear to be very good or good at assessing overall severity illness. Results did show where a number of items and options might be improved and suggest that the Positive and the Negative subscales may be more sensitive to change than the General Psychopathology subscale or the PANSS total score.

References:

1. Lindenmayer JP, Grochowski S, Hyman RB: Five factor model of schizophrenia: replication across samples. *Schizophr Res* 1995; 14:229-34.
2. Santor DA, Ramsay JO, Zuroff DC: Nonparametric item analyses of the Beck Depression Inventory: examining item bias and response option weights in clinical and nonclinical samples. *Psychological Assessment* 1994; 6: 255-270.

NR721 Wednesday, May 25, 3:00 p.m.-5:00 p.m. **Interim Psychiatric Care by Emergency Staff and Completion of Outpatient Referrals**

Lynda B. Grogan, N.P., MHD, VAMC, PO BOX 1034, Portland, OR 97207; Thomas Hansen, M.D., Laura Ross, B.A.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to describe the use of emergency psychiatry staff in provision of interim care and the influence of this interim care on subsequent attendance at first clinic visit.

Summary:

Objective: In response to long waits for outpatient appointments, the presenters' emergency psychiatry team provides interim care. Evidence suggests that completion rates (attendance for first appointment) improve with shorter waiting periods. This project assessed whether interim care (APIC) improves completion rates for outpatient referral.

Method: The presenters collected demographic and clinical data, duration until first clinic appointment, and completion rate for APIC patients seen from June to August 2003. They also determined completion rates for the clinic from the clinic's appointment database for July to September (to approximate when APIC patients would be seen).

Results: Fifty-four APIC patients (average age 49, diagnoses typical for VA) were seen on average twice while waiting a mean of 72 days for the first clinic appointment, with 85% completion. The clinic had 250 new patient appointments during the overlapping months, with 65% completion. The time to first clinic appointment was significantly associated with completion rate for patients without interim contact ($p = 0.03$), but not when interim care had been provided ($p = 0.34$).

Conclusion: Completion of clinic referral appears to be improved by interim contact. Utilizing emergency psychiatry staff can be an efficient method for providing interim care while patients await first clinic appointments.

References:

1. Craig TJ, Huffine CL, Brooks M: Completion of referral to psychiatric services by inner city residents. *Arch Gen Psychiatry* 1974; 31:353-357.
2. Kruse GR, Rohland BM: Factors associated with attendance at a first appointment after discharge from a psychiatric hospital. *Psychiatric Services* 2002; 53:473-476.

NR722 Wednesday, May 25, 3:00 p.m.-5:00 p.m. **Video Testimony of Long-Term Hospitalized Psychiatrically Ill Holocaust Survivors**

Rael D. Strous, M.D., Beer Yaakov Mental Health Center, Tel Aviv University, PO Box 1, Beer Yaakov 70350, Israel; Mordechai Weiss, M.D., Irit Felsen, Ph.D., Boris Finkel, M.D., Yuval Melamed, M.D., Dori Laub, M.D.

Educational Objectives:

At the conclusion of this session, the participants should be able to recognize the importance of chronic PTSD symptomatology even 60 years following a severely traumatizing event such as the Holocaust and that the option of managing these symptoms exists in the context of a unique "Video Testimony" treatment program.

Summary:

Many Holocaust survivors, suffering from both psychotic disorders and residual posttraumatic-stress disorder (PTSD) symptoms, remain chronically hospitalized in psychiatric institutions. This study investigated clinical benefits of a therapeutic process facilitating a detailed videotaped account of traumatic experience ("testimony method") in elderly long-term hospitalized Holocaust survivors. Twenty-four schizophrenia patients (mean age = 72.2) chronically hospitalized in psychiatric hospitals underwent a battery of blinded psychiatric ratings, including PANSS, CGI, MMSE, CAPS-2, and SIDES scales, prior to, and four months post, an extensive videotaped interview. Results indicated that 38% of patients met the criteria for PTSD at the first interview and only 19% at the second. There was a significant reduction of functional impairment, symptom severity, and intensity of all posttraumatic clusters, especially "avoidance." Eleven subjects indicated a 30% improvement or more in total posttraumatic severity score. Females showed higher prevalence of PTSD symptoms. There was an inverse correlation between total CAPS-2 and total PANSS scores. Study observations indicate the clinical benefits of the testimony interview in the alleviation of many posttraumatic symptoms, but not psychosis, in a cohort of psychiatrically ill Holocaust survivors, despite the lapse of up to 60 years since the traumatic event, and suggest implications for the care and rehabilitation of such a patient subpopulation.

References:

1. Robinson S, Rapaport J, Durst R, Rapaport M, Rosca P, Metzger S, Zilberman L: The late effects of Nazi persecution among elderly Holocaust survivors. *Acta Psychiatr Scand* 1990; 82:311-5.
2. Weine SM, Kulenovic AD, Pavkovic I, Gibbons R: Testimony psychotherapy in Bosnian refugees: a pilot study. *Am J Psychiatry* 1998; 155:1720-6.

NR723 Wednesday, May 25, 3:00 p.m.-5:00 p.m. **Association Study Between 5 SNPs of DBH Gene in Korean Patients With Schizophrenia**

Ahrang Cho, M.D., Department of Psychiatry, Kyunghee University Hospital, 1 Hoegi-Dong Dongdae Moon-Gu, Seoul 130-872, South Korea; Seokyoung Lee, M.D., Jiyoung Song, M.D., Jinkyung Park, M.D., Kyungkyu Lee, M.D., Geonho Ban, M.D., Wonserb Kang, M.D.

Educational Objectives:

At the conclusion of this session, the participants should be able to recognize that the DBH gene is a candidate gene and can be associated with the pathogenesis of schizophrenia.

Summary:

Objective: The structural gene encoding the enzyme dopamine beta-hydroxylase (DBH) is closely related to DBH activity and to psychotic symptoms in several psychotic disorders. This study was designed to examine other SNPs around exon 4 with DBH444G/A in the DBH gene in Korean schizophrenia patients.

Method: Genotypic and allelic distributions of these five polymorphisms using sequencing and restriction fragment length polymorphism were compared between 109 Korean control subjects

and phenotypic groups of 89 Korean schizophrenia patients stratified according to gender and subtype.

Results: No significant differences were found in the genotype distribution and allele frequencies between the patients and the control subjects for each four polymorphisms (DBHrs 161112, DBHrs5320, DBHrs161121, DBHrs1548). However, genotype distribution of DBH444G/A in the disorganized schizophrenia patients was significantly different than that for the control subjects.

Conclusions: These results suggest that genotype distribution of DBH444G/A may support the relation of phenotype variation to DBH variants in Korean schizophrenia patients. Our data provide no direct evidence of an association between four SNPs in the DBH gene and schizophrenia with phenotype variation.

References:

1. Yamamoto K, Cubells JF, Gelernter J, Benkelfat C, Lalonde P, Bloom D, Lal S, Labelle A, Turecki G, Rouleau GA, Joobor R: Dopamine beta-hydroxylase (DBH) gene and schizophrenia phenotypic variability: a genetic association study. *Am J Med Genet* 2003; 117B(1):33-8.
2. Jonsson EG, Abou Jamra R, Schumacher J, Flyckt L, Edman G, Forslund K, Mattila-Evenden M, Rylander G, Asberg M, Bjerkenstedt L, Wiesel FA, Propping P, Cichon S, Nothen MM, Sedvall GC: No association between a putative functional promoter variant in the dopamine beta-hydroxylase gene and schizophrenia. *Psychiatr Genet* 2003; 13(3):175-8.

NR724 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.** **Functional Neuroimaging Evidence for Explicit Memory Deficits in Depressed Patients**

Jong-Chul Yang, M.D., *Department of Psychiatry, Chonnam National University Hospital, 8 Hak-dong, Dong-gu, Gwangju 501-757, South Korea*; Sung-Jong Eun, B.A., Jin-Sang Yoon, M.D., Moo-Suk Lee, M.D., Hyung-Young Lee, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the neuroanatomical mechanism of memory deficits in depressed patients.

Summary:

Objectives: Memory deficits are a very common symptom in depressed patients, and they were found in many clinical studies. However, there has been little neuroimaging research. The purpose of this study was to investigate the cerebral regions associated with memory deficits in depressive patients by using blood-oxygenation-level-dependent functional magnetic resonance imaging (fMRI).

Methods: Thirteen depressed patients who met DSM criteria for major depressive disorder and 14 healthy control subjects matched for sex, age, and educational level participated in the study. All subjects underwent brain fMRI during the memory tasks: encoding of two-syllable words, and explicit (cued recall test) and implicit (word completion test) retrieval of previously learned words under the levels with conceptual and perceptual processing. The fMRI data were analyzed with SPM 99.

Results: Depressive patients were impaired on explicit memory tasks, compared with healthy control subjects. They showed significantly less cerebral activation in the hippocampus, parahippocampal gyrus, posterior cingulate gyrus, precuneus, and middle temporal gyrus ($p < 0.001$). However, there was no difference in implicit memory tasks.

Conclusions: These results provide experimental evidence and suggest a neuroanatomical mechanism for explicit memory deficits in depressive patients.

References:

1. Bazin N, Perruchet P, De Bonis M, Feline A: The dissociation of explicit and implicit memory in depressed patients. *Psychol Med* 1994; 24:239-45.
2. Burt DB, Zembar MJ, Niederehe G: Depression and memory impairment: a meta-analysis of the association, its pattern, and specificity. *Psychol Bull* 1995; 117:285-305.

NR725 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Treatment of Depressed or Anxious Primary Care Patients With Multisomatoform Disorder: A Pilot Study Comparing Venlafaxine XR Versus Placebo Supported by Wyeth Pharmaceuticals

Kurt Kroenke, M.D., *Regenstrief Institute, 1050 Wishard RG6, Indianapolis, IN 46202*; Isma Benattia, M.D., Jeff Musgnung, Jay Graepel, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to evaluate the efficacy and tolerability of treatment with venlafaxine XR, a serotonin-norepinephrine reuptake inhibitor (SNRI), in patients with multisomatoform disorder.

Summary:

Objective: To evaluate efficacy and safety of venlafaxine XR in anxious and/or depressed patients with multisomatoform disorder (MSD).

Methods: This 12-week, multicenter, randomized, double-blind study assessed adult primary care outpatients with MSD diagnosed using the 15-item patient health questionnaire (PHQ-15), who met DSM-IV criteria for major depressive disorder, generalized anxiety disorder, or social anxiety disorder. Of 117 patients randomly assigned to treatment with flexible-dose venlafaxine XR or placebo, 112 were included in the ITT population (venlafaxine XR = 55; placebo = 57). The primary efficacy outcome was the baseline-to-endpoint change in PHQ-15 score. Secondary measures included baseline-to-endpoint changes in HAM-D17, HAM-A, CGI Severity of Illness (CGI-S) and Improvement (CGI-I) scales, McGill Quality of Life Questionnaire Physical Symptoms Scale (MQOL-PS), and Medical Outcomes Study Short-Form 36-Item Questionnaire (SF-36).

Results: Differences between the venlafaxine XR and placebo groups in PHQ-15 total scores were statistically nonsignificant at endpoint ($p = 0.09$). The venlafaxine XR group indicated significantly ($p < 0.05$) greater improvement than the placebo group on the PHQ-15 pain subscale and on the CGI-I, MQOL-PS, and SF-36 mental health domain. Venlafaxine XR was generally well tolerated.

Conclusions: Venlafaxine XR may improve some types of somatic symptoms, particularly pain, in MSD patients with depression and/or anxiety disorders.

References:

1. Kroenke K, Spitzer RL, deGruy FV 3rd, Hahn SR, Linzer M, Williams JB, Brody D, Davies M: Multisomatoform disorder: an alternative to undifferentiated somatoform disorder for the somatizing patient in primary care. *Arch Gen Psychiatry* 1997; 54:352-8.
2. Kroenke K, Spitzer RL, Williams JB: The PHQ-15: validity of a new measure for evaluating the severity of somatic symptoms. *Psychosom Med* 2002; 64:258-66.

NR726 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Quetiapine for the Treatment of Agitation in Patients With Dementia

Supported by AstraZeneca, Wilmington, Delaware, USA

Kate Zhong, M.D., AstraZeneca, 1800 Concord Pike, Wilmington, DE 19850-5437; Pierre Tariot, M.D., Margaret C. Minkwitz, Ph.D., Nancy A. Devine, M.S., Jacobo Mintzer, M.D.

Educational Objectives:

At the conclusion of the presentation, participants should recognize that quetiapine 200 mg/day is more effective than placebo in treating patients with agitation associated with dementia, and that quetiapine can be safely titrated to 200 mg/day by day 8 and has a favorable tolerability profile in this patient population.

Summary:

Objective: To evaluate the efficacy, tolerability, and safety of quetiapine compared to placebo in treating patients with agitation associated with dementia.

Method: In this multicenter, double-blind, placebo-controlled, fixed-dose, 10-week study, eligible patients were randomly assigned (3:3:2) to quetiapine 100 mg/day, 200 mg/day, or placebo. Quetiapine was initiated at 25 mg/day and titrated in 25 mg/day increments, reaching target doses of 100 mg/day by day 4 or 200 mg/day by day 8. Key efficacy measures were PANSS-Excitement Component (EC), CGI-C score, and response rate (percentage of patients with $\geq 30\%$ reduction in PANSS-EC or 'much' or 'very much improved' on CGI-C). Key safety and tolerability measures were the incidence of treatment-emergent adverse events, including cerebrovascular effects (CVAEs), postural hypotension, and falls.

Results: The baseline characteristics of patients (N = 333) were comparable among treatment groups and 63%-65% completed the entire study. Compared to placebo, quetiapine 200 mg/day was associated with statistically significant improvements in PANSS-EC and CGI-C scores, and significantly higher response rates ($p < 0.05$ for all measures). No CVAEs were reported in either quetiapine group. The incidences of postural hypotension and falls were similar among all treatment groups.

Conclusions: Quetiapine 200 mg/day is effective and well tolerated in treating patients with agitation associated with dementia.

References:

1. Tariot PN et al: Long-term use of quetiapine in elderly patients with psychotic disorders. *Clin Ther* 2000; 22: 1068-1084.
2. Tariot PN et al: Quetiapine in nursing home residents with Alzheimer's dementia and psychosis. Poster presented at the 15th Annual Meeting of the American Association for Geriatric Psychiatry, February 24-27, 2002, Orlando FL, USA.

NR727 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Duloxetine Versus Placebo in the Treatment of Elderly Patients With MDD

Supported by Eli Lilly and Company

Joel Raskin, M.D., Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Curtis Wiltse, Ph.D., James Dinkel, Alan Siegal, M.D., Javaid Sheikh, M.D., Jimmy Xu, Ph.D., Benjamin Rotz, Ph.D.

Educational Objectives:

At the conclusion of the presentation, audience participants will better understand the effects of duloxetine on cognition in the treatment of MDD in the elderly.

Summary:

Objective: To compare effect of duloxetine vs. placebo on cognition in elderly (age ≥ 65) MDD patients.

Methods: Patients were randomly assigned to duloxetine 60 mg QD (N = 207) or placebo (N = 104) treatment for eight weeks. Primary outcome measure was a prespecified composite cognitive score based on five cognitive tests that measured verbal learning and memory, selective attention, and executive functioning. Secondary measures included Geriatric Depression Scale (GDS), HAMD17, VAS for pain, CGI-Severity, and SF-36.

Results: Duloxetine demonstrated significantly greater improvement in cognitive composite score vs. placebo (1.95 vs. 0.76, $p = 0.013$). Duloxetine showed significantly greater reductions in both HAMD17 and GDS score. Duloxetine HAMD17 response and remission rates were approximately twice those of placebo. Duloxetine demonstrated greater improvement vs. placebo on CGI-severity, VAS for back pain and pain while awake, and five SF-36 measures. Discontinuation rates due to AE did not differ between duloxetine and placebo (9.7% vs. 8.7%), and more placebo than duloxetine patients discontinued due to lack of efficacy (9.6% vs. 2.9%). Common treatment-emergent AEs included dry mouth, nausea, constipation, dizziness, diarrhea, fatigue, and somnolence. Rates of discontinuation-emergent adverse events were similar for duloxetine and placebo (14.2% vs 10.0%).

Conclusions: Duloxetine improved cognition and depression measures and was well tolerated in elderly MDD patients.

References:

1. Cassano GB, Puca F, Scapicchio PL, Trabucchi M: Paroxetine and fluoxetine effects on mood and cognitive functions in depressed nondemented elderly patients. *J Clin Psychiatry* 2002; 63(5):396-402.
2. Ressler KJ, Nemeroff CB: Role of norepinephrine in the pathophysiology of neuropsychiatric disorder. *CNS Spectrums* 2001; 6:63-670.

NR728 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Pharmacotherapy of Alzheimer's Disease in 2004: What Clinicians Know and Need to Know

Hareesh Tharwani, M.D., Department of Psychiatry, Duke University Medical Center, 4323 Ben Franklin Boulevard, Suite 700, Durham, NC 27704; P. Murali Doraiswamy, M.D., Ashwin Patkar, M.D., Rajnish Mago, M.D., Prakash S. Masand, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize knowledge gaps in the treatment of Alzheimer's disease that could benefit from further education.

Summary:

Objective: To better understand clinicians' preferences regarding the treatment of Alzheimer's disease (AD).

Method: Clinicians attending a psychiatry CME conference organized by Duke University were surveyed. Questions included patterns of use of medications (cholinesterase inhibitors, atypical antipsychotics) to treat AD.

Results: Of the 149 respondents, 70.3% were psychiatrists. The most effective treatment for mild-moderate AD was cholinesterase inhibitors (CEI) (67.4%), followed by lipids and blood pressure control (13.6%), exercise (7.9%), vitamins (7.2%), and ginkgo biloba (4.5%). A total of 17.1% of respondents did not consider CEI to be first or second line treatment. In mild-moderate AD, donepezil was ranked the most effective by 42%, followed by no preference (40.6%), rivastigmine (9.8%), and galantamine (7.7%). Respondents were split between three months (46%) or six months (34%) as the optimal duration of treatment in AD. When one CEI failed, 71.4% would switch to another CEI, 18.6% would stop CEI, 7.9% would use higher than recommended doses, and 2.1% would add another CEI ($p < 0.05$). Risperidone (57.9%) was ranked higher

than olanzapine (24.3%), haloperidol (10.7%), or quetiapine (7.1%) to treat psychosis of AD.

Conclusions: A significant proportion of clinicians may benefit from further education. Certain knowledge gaps could be filled with better evidence or expert consensus guidelines.

References:

1. Ritchie CW, Ames D, Clayton T, Lai R: Meta-analysis of randomized trials of the efficacy and safety of donepezil, galantamine, and rivastigmine for the treatment of Alzheimer disease. *Am J Geriatr Psychiatry* 2004; 12(4):358-69.
2. Mintzer JE: What are the challenges faced by psychiatrists in the management of Alzheimer's disease? *CNS Spectr* 2004; 9(7 Suppl 5):13-5.

NR729 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Differences in Peripheral Mu-Opioid Receptors Among Substance Abusers

Supported by National Institute on Drug Abuse

Amanda N. Lindsay, B.S., *Department of Psychiatry, Duke Clinical Trials Program, 4323 Ben Franklin Blvd., Durham, NC 27704*; Allen Zeiger, Ph.D., Phillip Matthews, B.S., Paolo Mannelli, M.D., Kathleen Peindl, Ph.D., Leonard Handelsman, M.D., Ashwin Patkar, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the effects of various drugs of abuse on the opioid system.

Summary:

Objective: The mu opioid receptor (MOR) is considered a gateway to drug addiction. MOR are present in the brain as well as on red blood cells (RBC). The presenter investigated whether there were differences in MOR levels on RBC following chronic exposure to heroin, methadone, cocaine, and nicotine.

Method: Blood samples from eight heroin-dependent individuals, nine methadone-maintained patients, 27 cocaine-dependent persons, 20 tobacco smokers, and 15 drug-free control subjects were studied. MOR levels on RBC were measured using flow cytometry immunoassay.

Results: The MOR levels from heroin subjects (65.28 ± 38.78) were significantly higher, compared to control subjects (22.78 ± 30.89) ($t = 2.87, p < 0.01$). The MOR levels in control subjects did not significantly differ from methadone (31.52 ± 31.89), cocaine (27.35 ± 35.78), or nicotine (30.64 ± 40.19) subjects. There was a bimodal distribution of MOR levels in cocaine and nicotine subjects. This was not observed in control subjects or heroin and methadone patients.

Conclusion: The findings confirm that the MOR receptor is present on human RBC. Elevated MOR levels are associated with chronic heroin exposure, but methadone, cocaine, and nicotine do not appear to alter MOR levels. Longitudinal studies may clarify the influence of drugs on regulating the opioid system.

References:

1. Contet C, Kieffer BL, Befort K: Mu opioid receptor: a gateway to drug addiction. *Curr Opin Neurobiol* 2004; 14(3):370.
2. Zeiger AR, Patkar AA, Ballas S, et al: Changes in mu opioid receptors and rheological properties of erythrocytes among opioid abusers. *Addiction Biology* 2002; 7(2):207-217.

NR730 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Differential Serum Anticholinergic Activity of Antipsychotic Medications

Supported by Janssen Medical Affairs, L.L.C.

Benoit H. Mulsant, M.D., *Department of Psychiatry, University of Pittsburgh School of Medicine, 3811 O'Hara Street, Room 3-809, Pittsburgh, PA 15213-2593*; Mark Lehman, Ph.D., Georges Gharabawi, M.D., Margaret Kirshner, Ph.D., Byron Cumbie, Ph.D., Andrew Greenspan, M.D., Bruce Pollock, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participants should recognize that certain antipsychotic drugs show anticholinergic activity in vitro, and that this may correlate to clinical findings.

Summary:

Objective: Increasing age is associated with greater sensitivity to the effects of anticholinergic agents. This is especially true in dementia patients, who already have a cholinergic deficit and nevertheless may be exposed to medications with anticholinergic activity. This analysis compared in vitro serum anticholinergic activity (SAA) of the most commonly prescribed antipsychotic medications in the elderly.

Methods: Five antipsychotic medications were evaluated: risperidone, olanzapine, quetiapine, aripiprazole, and haloperidol. Radioreceptor assays using homogenate rat brain measured levels of anticholinergic activity for each drug at three therapeutic doses. Atropine was used as a standard. SAA was expressed as pmole/ml.

Results: Olanzapine (2.5, 5.0, and 7.5 mg) showed the highest SAA levels, yielding 43, 84, and 121 pmole/ml, respectively, followed by quetiapine (100, 150, and 200 mg), yielding 42, 50, and 74 pmole/ml, respectively. Both drugs showed a dose-dependant increase in SAA. For risperidone (0.25, 0.5, and 1.0 mg), aripiprazole (5, 10, and 15 mg), and haloperidol (1, 2, and 4 mg), assays detected no SAA.

Conclusions: Olanzapine and quetiapine showed concentration-related levels of SAA in vitro. SAA levels were not detected with risperidone, aripiprazole, or haloperidol. These findings are consistent with prior research on anticholinergic activity and may explain some of the differential effects of these drugs.

References:

1. Tune LE: Anticholinergic effects of medication in elderly patients. *J Clin Psychiatry* 2001; 62 Suppl 21:11-4.
2. Mulsant BH: Gharabawi G, Bossie C, Mao L, Greenspan A, Basteau J, Pollock BG. Correlates of anticholinergic burden to behavioral and psychological symptoms of dementia in patients treated with risperidone or olanzapine. Poster presented at the 42nd ACNP annual meeting. Puerto Rico, December 2003.

NR731 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Association Study of Angiotensin-Converting Enzyme Gene Polymorphism in Patients With Schizophrenia

Seokyoung Lee, M.D., *Department of Psychiatry, Kyunghee University Hospital, 1 Hoegi-Dong Dongdae Moon-Gu, Seoul, 130-872, South Korea*; Jiyoung Song, M.D., Junho Noh, M.D., Jooho Chung, M.D., Jinkyung Park, M.D., Heejae Lee, M.D.

Educational Objectives:

At the conclusion of this session, the participants should be able to recognize that the ACE gene is a candidate gene for modulating dopamine turnover in brain. This study showed negative results; however this work would be one of the steps for conquering the pathogenesis of schizophrenia.

Summary:

Objective: Angiotensin-converting enzyme (ACE) is a candidate gene for psychiatric disorders. ACE is known to modulate dopamine turnover in the brain. The aim of the present study was to evaluate the role of the ACE gene insertion/deletion polymorphism in patients with schizophrenia.

Methods: The presenters examined the frequency of a polymorphism characterized by the insertion of a 287-bp Alu repeat sequence in intron 16 of the angiotensin-converting enzyme gene (located on chromosome 17q23) in a patient group (N = 123) and healthy control group (N = 295). ACE genotype was determined by the size-analysis of polymerase chain reaction products.

Results: Allelic frequencies and genotypic distribution of the ACE gene I/D polymorphism did not show any differences between schizophrenia patients and control subjects.

Conclusion: The present study found no association of the ACE gene I/D polymorphism in schizophrenia patients. These negative findings suggest that the ACE gene I/D polymorphism may not be involved in the pathogenesis of schizophrenia.

References:

1. Ouyang WC, Wang YC, Hong CJ, Cheng CY, Tsai SJ: Association study of angiotensin-converting enzyme gene polymorphism with schizophrenia and polydipsia. *Neuropsychobiology* 2001; 44(1):31-5.
2. Segman RH, Shapira Y, Modai I, Hamdan A, Zislin J, Heresco-Levy U, Kanyas K, Hirschmann S, Karni O, Finkel B, Schlafman M, Lerner A, Shapira B, Macchiardi F, Lerer B: Angiotensin converting enzyme gene insertion/deletion polymorphism: case-control association studies in schizophrenia, major affective disorder, and tardive dyskinesia and a family-based association study in schizophrenia. *Am J Med Genet* 2002; 114:310-314.

NR732 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.** **Dopamine Beta-Hydroxylase Gene and Phenotypic Variation in Schizophrenia Patients**

Seokyoung Lee, M.D., *Department of Psychiatry, Kyunghee University Hospital, 1 Hoegi-Dong Dongdae Moon-Gu, Seoul, 130-872, South Korea*; Jinkyung Park, M.D., Jiyoung Song, M.D., Jongwoo Kim, M.D., Heejae Lee, Ph.D., Ahrang Cho, M.D., Wonserb Kang, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that the DBH gene may be involved in modifying the psychiatric symptoms of schizophrenia and timing to develop schizophrenia.

Summary:

Objective: The dopamine beta-hydroxylase (DBH) gene is closely related to psychiatric symptoms in several psychiatric disorders. This study examined the association between two polymorphisms (rs1611131G/A and rs3025422T/C) of the DBH gene and phenotypic variation in Korean schizophrenia patients.

Method: Allelic and haplotype distributions of these two polymorphisms using automatic sequencing were compared between 144 Korean control subjects and phenotypic groups of 104 Korean schizophrenia patients stratified by onset age, presence of auditory hallucination, and persecutory delusion.

Results: Genotype and allele frequencies of the rs1611131G/A polymorphism showed significant differences between schizophrenia patients whose onset age was under 20 and control subjects ($p = 0.025$; $p = 0.039$). Allele frequency of rs3025422T/C polymorphism also showed a significant difference between those whose onset age was under 20 and control subjects ($p = 0.039$). Significant differences were found in the allele frequency of

rs3025422T/C polymorphism between schizophrenia patients with auditory hallucinations and control subjects ($p = 0.039$) and between those with persecutory delusion and control subjects ($p = 0.008$). Significant pairwise associations between the two polymorphisms were observed between schizophrenia patients and control subjects ($p = 0.004$) and between those with auditory hallucination and control subjects ($p = 0.007$). Estimated frequency of rs1611131A-rs3025422T haplotype of schizophrenia patients, especially of those with auditory hallucination, was higher than that of control subjects.

Conclusions: These findings suggest that the DBH gene may be involved in modifying the psychiatric symptoms of schizophrenia and timing of developing schizophrenia.

References:

1. Meszaros K, Lenzinger E, Fureder T, Hornik K, Willinger U, Stompe T, Heiden AM, Resinger E, Fathi N, Gerhard E, Fuchs K, Miller-Reiter E, Pfersmann V, Sieghart W, Aschauer HN, Kasper S: Schizophrenia and the dopamine-beta-hydroxylase gene: results of a linkage and association study. *Psychiatr Genet* 1996; 6(1):17-22.
2. Yamamoto K, Cubells JF, Gelernter J, Benkelfat C, Lalonde P, Bloom D, Lal S, Labelle A, Turecki G, Rouleau GA, Joobor R: Dopamine beta-hydroxylase (DBH) gene and schizophrenia phenotypic variability: a genetic association study. *Am J Med Genet*. 2003; 117B(1):33-8.

NR733 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.** **Care Burden of Caregivers According to Cognitive Status of Elderly People**

Sung-Wan Kim, M.D., *Department of Psychiatry, Chonnam National University Medical School, 5 Hak-Dong, Dong-Gu, Kwangju 501-746, South Korea*; Jae-Min Kim, M.D., Il-Seon Shin, M.D., Su-Jin Yang, M.D., So-Yeon Lim, M.D., Jin-Sang Yoon, M.D., Hyung-Yung Lee, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize strategy to reduce care burden for the elderly people according to their cognitive status.

Summary:

Objective: This study investigated the level of care burden of caregivers and compared the factors associated with the care burden according to the cognitive status of elderly people.

Methods: The study sample consisted of 484 elderly people and their caregivers in Korea. Care burden was measured by the Korean version of the Zarit Burden Interview. According to the evaluation of cognitive status and diagnosis of dementia for the elderly people, the participants were classified in three groups: normal (N = 319), cognitive impairment no dementia (CIND, N = 104), and dementia (N = 61)

Results: The level of care burden was significantly higher in caregivers of the dementia group than in the normal and CIND groups. Higher care burden was independently associated with severe depressive symptoms and alcoholism in the normal group, with alcoholism in the CIND group, and with urban living, cognitive impairment, and severe depressive symptoms, and caregivers' higher education, being an offspring, and lower social support in the dementia group.

Conclusion: In persons with dementia, improving cognitive function and depressive symptoms as well as providing social support for caregivers, is necessary. In those with normal and CIND cognitive states, management of alcoholism is mandatory. In addition, treatment of depression is important in normal elderly people.

References:

1. Zarit SH, Todd PA, Zarit JM: Subjective burden of husbands and wives as caregivers: a longitudinal study. *Gerontologist* 1986; 26(3):260-6.
2. Donaldson C, Tarrrier N, Burns A: Determinants of carer stress in Alzheimer's disease. *Int J Geriatr Psychiatry* 1998; 13:248-256.

NR734 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

The Effect of Cimetidine or Omeprazole on the Pharmacokinetics of Escitalopram

Dorte Malling, M.S.C., *H. Lundbeck A/S, Ottiliavej 9, Valby-Copenhagen 2500, Denmark*; Mette Nøhr Poulsen, M.S.C., Birgitte Søgaard, M.S.C.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to discuss the pharmacokinetics of changes following co-administration of escitalopram with cimetidine or omeprazole.

Summary:

Objective: Escitalopram is mainly metabolised by CYP3A, CYP2D6, and CYP2C19. The effect of co-administration of cimetidine or omeprazole on the pharmacokinetics of escitalopram was investigated.

Methods: Sixteen healthy volunteers were administered cimetidine (400 mg b.i.d.) or placebo for five days or omeprazole (30 mg o.d.) or placebo for six days in two randomized placebo-controlled crossover studies. On the second to last day, a single dose of escitalopram 20 mg was administered. Serum levels of escitalopram and its demethylated (S-DCT) metabolite were determined.

Results: Co-administration with cimetidine caused a moderate increase in the systemic exposure (AUC_{0-inf}) of escitalopram (geometric least square means ratio: 1.72; 90% CI = 1.41-2.11). There was an associated increase of t_{1/2} from 23.7 to 29.0 hours. S-DCT formation was delayed but there was no marked change in systemic exposure or t_{1/2}. Co-administration with omeprazole also resulted in a moderate increase in the systemic exposure of escitalopram (1.51, 95% CI = 1.41-1.62) and a small increase in elimination half-time from 26.5 to 34.8 hours. There was no significant change in systemic exposure of S-DCT. Co-administration of cimetidine or omeprazole had no effect on the safety and tolerability of escitalopram.

Conclusion: The pharmacokinetic changes observed following co-administration with cimetidine or omeprazole are not considered to be of clinical concern.

Funding from Lundbeck

References:

1. Gutierrez MM, Rosenberg J, Abramowitz W: An evaluation of the potential for pharmacokinetic interaction between escitalopram and the cytochrome P450 3A4 inhibitor ritonavir. *Clin Ther* 2003; 25:1200-1210.
2. von Moltke LL, Greenblatt DJ, Giancarlo GM, Granda BW, Harmatz JS, Shader RI: Escitalopram (S-citalopram) and its metabolites in vitro: cytochromes mediating biotransformation, inhibitory effects, and comparison to R-citalopram. *Drug Metab Dispos* 2001; 29:1102-1109.

NR735 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Safety and Efficacy of Ziprasidone in Over 100 Geriatric Patients

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Cleveland (Middleburg Heights), OH 44130; Douglas Deutschman, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the attendees should be able to demonstrate knowledge of the efficacy and safety of ziprasidone in geriatric patients treated in inpatient, consultation-liaison and outpatient settings in a busy clinical practice.

Summary:

Objective: The presenters report on a retrospective review of > 100 patients treated in an open-label, naturalistic design with ziprasidone during a three-year period in clinical practice.

Methods: Symptom severity was tracked on a five-point Likert scale. Efficacy was determined by comparing symptom severity and GAF scores at each patient's last visit to the severity at their first visit using paired t-tests. Safety was determined by analyzing reported side effects supplemented with clinical monitoring of key variables (e.g. QTc's).

Results: Most patients received 80 or 160 mg/day. The most common diagnoses were organic, psychotic, and affective. Most patients improved significantly in severity across a broad range of symptoms as measured by clinicians on a Likert scale (t = 3.17, df = 22, p = 0.004). Decreasing symptoms measured on the Likert scale were correlated with improvement in patients' GAF scores. Patients' GAF scores improved an average of 19.8 points (t = 6.97, p < 0.001). Sedation was reported in 13% of patients. Vivid nightmares include two cases of high dose ziprasidone (240 mg/day) in an 83 and 85 year-old and one case of a 93 year-old receiving 20 mg IM for delirium.

Conclusion: Ziprasidone appears safe and effective in elderly patients.

References:

1. Leso L, Schwartz TL: Ziprasidone treatment of delirium. *Psychosomatics* 2002; 43: 61-62.
2. Molsinger CD, et al: Use of atypical antipsychotic drugs in patients with dementia. *Am Fam Physician* 2003; 67: 2335-2340.

NR736 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

The Importance of Rater Experience on Ratings Competence in CNS Trials

Supported by PharmaStar, GlaxoSmithKline, Forest Labs, Cephalon, AstraZeneca, Johnson and Johnson, Janssen Medical Affairs, Organon

Steven D. Targum, PharmaStar, 575 E Swedesford Road, suite 101, Wayne, PA 19087; Evan Braxton

Educational Objectives:

At the conclusion of this presentation, the participant should be able to: 1) describe experience factors that impact upon ratings competence in CNS clinical trials, and 2) recognize the importance of scoring accuracy as contributors to successful clinical trials.

Summary:

Objective: Many raters who participate in CNS trials have limited clinical experience and little or no ratings experience with the rating instruments chosen for the trial. In this study, the ratings competence of novice raters was compared to that of more experienced raters.

Method: A total of 706 potential raters scored videotaped interviews with the Hamilton Anxiety Scale (Ham-A), Hamilton Depression Scale (Ham-D), and Young Mania Rating Scale (YMRS) during nine different rater qualification programs conducted for clinical trials by PharmaStar. Individual item scores were compared to established acceptable scores and analyzed relative to each raters' previous clinical and ratings experience.

Results: Clinical experience differentiated ratings competence on the YMRS but not on the Ham-A or Ham-D. Novice raters (first time at a PharmaStar qualification session) revealed significantly greater scoring variance and absolute deviations from acceptable scores on all three scales than experienced raters who had attended five or more PharmaStar qualification programs. Novice raters with five or more years of clinical experience still performed significantly poorer on the Ham-A, Ham-D, and YMRS than experienced raters. Thus, clinical experience did not compensate for a lack of ratings experience.

Conclusions: The findings reinforce the need for more stringent criteria for rater eligibility and effective training programs for novice raters.

References:

1. Bullinger AL, Targum, SD: Rater experience in CNS clinical trials, 44th Annual NCDEU meeting, Phoenix, AZ, June 2, 2004.
2. Sachais BA, Targum SD, West MD: Previous experience and qualification of raters for CNS clinical trials. 17th ECNP Congress, Stockholm, Sweden, October 10, 2004.

NR737 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Family-Based Association Study and Meta-Analysis of the Association Between Dopamine Beta-Hydroxylase and Attention Deficit-Hyperactivity Disorder

Roy H. Perlis, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street WACC 812, Boston, MA 02114*; Stephen Faraone, Ph.D., Jordan Smoller, M.D., Alysa Doyle, Ph.D., Pamela Sklar, M.D., James Gusella, Ph.D., Joseph Biederman, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize a small but significant association between ADHD and DBH and the need for further studies to identify the functional polymorphism in this gene (or a nearby gene) that contributes to this ADHD liability.

Summary:

Objectives: Several family-based studies have reported an association between attention deficit-hyperactivity disorder (ADHD) and the TaqI A2 allele of the dopamine beta-hydroxylase (DBH) gene, the primary enzyme responsible for the conversion of dopamine to nonrepinephrine, while others found no such association.

Methods: The presenters performed a family-based association analysis of the DBH TaqI polymorphism in 66 families, including 84 affected children and 244 unaffected individuals, as determined by DSM-III-R or DSM-IV criteria. They then applied meta-analysis to family-based association studies of ADHD and DBH to assess their joint evidence for association, the influence of individual studies, and evidence for publication bias.

Results: Among 66 newly-genotyped families, no significant association between TaqI A2 and ADHD was found (OR = 1.20, $p = 0.71$, 95% CI = 0.45-3.21). However, when the results were combined with other family-based studies using random effects meta-analysis, there was support for the association between ADHD and DBH that was not accounted for by any single study (pooled OR = 1.26, 95% CI = 1.07-1.50).

Conclusions: The results indicate a small but significant association between ADHD and DBH. Further studies are needed to identify the functional polymorphism in this gene (or a nearby gene) that contributes to this ADHD liability.

Supported in part by grants R01MH57934, R01HD37694, R13MH59126 (Dr. Faraone), and R01MH41314 (Dr. Biederman) from the National Institutes of Health.

References:

1. Daly G, Hawi Z, Fitzgerald M, Gill M: Mapping susceptibility loci in attention deficit hyperactivity disorder: preferential transmission of parental alleles at DAT1, DBH and DRD5 to affected children. *Molecular Psychiatry* 1999; 4:192-196.
2. Roman T, Schmitz M, Polanczyk GV, Eizirik M, Rohde LA, Hutz MH: Further evidence for the association between attention-deficit/hyperactivity disorder and the dopamine-beta-hydroxylase gene. *Am J Med Genet* 2002; 114(2):154-158.

NR738 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Risperidone in the Treatment of Psychosis of Alzheimer's Disease (PAD): A Meta-Analysis of Four Controlled Trials

Supported by Janssen Medical Affairs, L.L.C.

Ira R. Katz, M.D., *Department of Geriatric Psychiatry, University of Pennsylvania, 3535 Market Street, Room 3001, Philadelphia, PA 19104*; Jacobo Mintzer, M.D., Henry Brodaty, M.D., Peter P. De Deyn, M.D., Andrew Greenspan, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that PAD is a distinct treatable clinical entity and that risperidone has been shown to be effective in treating psychosis of AD.

Summary:

Objective: Patients with PAD are commonly treated with atypical antipsychotics. This meta-analysis examined risperidone in the treatment of PAD.

Methods: Data were from four placebo-controlled trials of risperidone (0.5-2.0 mg/day) in dementia patients. PAD was defined as a diagnosis of AD/mixed dementia and a rating ≥ 2 on any delusion/hallucination item of the Behavioral Pathology in Alzheimer's Disease (BEHAVE-AD) rating scale at baseline. Assessments included BEHAVE-AD psychosis and Clinical Global Impression-Change (CGI-C).

Results: A total of 894 patients met PAD criteria (risperidone N = 515, placebo N = 379). Mean \pm SD baseline BEHAVE-AD psychosis scores were 8.1 ± 4.8 for placebo and 7.5 ± 4.0 for risperidone patients. Risperidone treatment significantly reduced psychotic symptoms at endpoint, compared to placebo (change \pm SE: 3.4 ± 0.2 vs 2.7 ± 0.2 ; $p = 0.009$). At endpoint, CGI-C distribution scores showed significantly greater improvement with risperidone than placebo ($p = 0.024$); 48.7% of risperidone and 29.7% of placebo patients showed some (minimal/much/very much) clinical improvement (much/very much improvement for 27.9% and 16.9%). Reported AEs (>10% overall) were: injury (20.3%), somnolence (14.1%), fall (13.9%), urinary tract infection (12.5%), and agitation (10.2%). Cerebrovascular AEs were reported in eight (1.6%) risperidone and eight (0.8%) placebo patients ($p = 0.37$).

Conclusions: This meta-analysis provides further evidence that risperidone is effective for improving psychotic symptoms and overall clinical status in patients with PAD.

References:

1. De Deyn PP, Rabheru K, Rasmussen A, et al: A randomized trial of risperidone, placebo, and haloperidol for behavioral symptoms of dementia. *Neurology* 1999; 53:946-955.
2. Katz IR, Jeste DV, Mintzer JE, et al: Comparison of risperidone and placebo for psychosis and behavioral disturbances associated with dementia: a randomized, double-blind trial. *J Clin Psychiatry* 1999; 60:107-115.

NR739 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Association Between the 5HT1B Receptor Gene and the Inattentive Subtype of ADHD

Jordan W. Smoller, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WANG ACC 812, Boston, MA 02114*; Joseph Biederman, M.D., Lori Arbeitman, B.S., Jes Fagerness, B.S., Alysa Doyle, Ph.D., Roy Perlis, M.D., Stephen Faraone, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that variation in the HTR1B locus may primarily affect the inattentive subtype of ADHD.

Summary:

Objective: Attention-deficit/hyperactivity disorder (ADHD) is a highly heritable disorder thought to be influenced by multiple genes. Preclinical studies implicate the 5HT1B receptor in hyperactivity phenotypes, and a region of chromosome 6q that includes HTR1B has been linked to ADHD. Association between an HTR1B SNP (G861C) and ADHD has been reported in two studies.

Method: Using a linkage disequilibrium (LD) mapping approach, the authors genotyped 21 SNPs in and around HTR1B (approximately 1SNP/5kb) in 12 multigenerational CEPH pedigrees. They performed SNP-wise and haplotype-association analyses in 229 families of probands ascertained for DSM-II-R or DSM-IV ADHD using FBAT. Because previous studies have suggested that susceptibility loci may influence specific ADHD subtypes, they also examined the inattentive and combined subtypes.

Results: The authors observed nonsignificant overtransmission of the G861 allele to offspring with ADHD (one-tailed $p = 0.058$). Single-marker and haplotype tests of a haplotype block encompassing the HTR1B locus revealed no other associations with the ADHD phenotype. However, this six-marker block was associated with the inattentive subtype (global test $p < 0.01$). Additionally, three SNPs in this block were nominally ($p < .05$) associated with the inattentive subtype, but did not remain significant after correction for multiple testing.

Conclusions: These analyses suggest that variation in the HTR1B locus may primarily affect the inattentive subtype of ADHD.

References:

1. Quist JF, Barr CL, Schachar R, Roberts W, Malone M, Tannock R, Basile VS, Beitchman J, Kennedy JL: The serotonin 5-HT1B receptor gene and attention deficit hyperactivity disorder. *Mol Psychiatry* 2003; 8(1):98-102.
2. Hawi Z, Dring M, Kirley A, Foley D, Kent L, Craddock N, Asherson P, Curran S, Gould A, Richards S, Lawson D, Pay H, Turic D, Langley K, Owen M, O'Donovan M, Thapar A, Fitzgerald M, Gill M. Serotonergic system and attention deficit hyperactivity disorder (ADHD) a potential susceptibility locus at the 5-HT(1B) receptor gene in 273 nuclear families from a multi-centre sample. *Mol Psychiatry* 2002; 7(7):718-25.

NR740 **Wednesday, May 25, 03:00 p.m.-5:00 p.m.**

Functional MRI Findings of EMDR for PTSD: A Case Series Using Script-Driven Imagery Procedure

Supported by Astra Zeneca Inc.

Choi Joonho, M.D., *Department of Neuropsychiatry, Hanyang University, 17 Haengdang Sungdong-Gu, Seoul 133-792, Korea*; Daeho Kim, M.D., Seok Hyun Kim, M.D., Jang-Han Lee, M.D., Dong-Woo Park, M.D., Seun-Kyung Choi, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate knowledge of EMDR for PTSD.

Summary:

Objectives: The study sought to assess the change in activation patterns of brain after EMDR through functional MRI technique.

Methods: Before and after three sessions of EMDR, six PTSD subjects underwent fMRI at 1.5 Telsa field strength during traumatic script-driven symptom provocation. Data from six subjects were separately analyzed according to multiplicity of trauma: acute and single trauma (N = 3) and chronic and multiple trauma (N = 3).

Results: Three singly traumatized subjects demonstrated activation in the left middle frontal gyrus (Brodmann area 9) initially and after EMDR in the parahippocampal gyrus (BA 27) and left anterior cingulate gyrus (BA 32). In subjects with multiple trauma, the activated brain area before EMDR was the left superior frontal gyrus (BA 6) and no significant activation was found after treatment. All three subjects with single traumas improved more than 30% from baseline scores on the CAPS (responder), while only one of three with multiple trauma improved.

Conclusion: These findings may suggest successful regulation of emotional arousal evoked by traumatic stimuli after successful EMDR treatment.

References:

1. Lanius RA et al: Neural correlates of traumatic memories in PTSD: a functional MRI Investigation. *Am J Psychiatry* 2001; 158:1920-1922.
2. Levin P, Lazrove S, van der Kolk B: What psychological testing and neuroimaging tells us about the treatment of PTSD by EMDR. *J Anxiety Dis* 1999; 13: 159-172.

NR741 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**

Efficacy of Memantine on Cognition in Mild to Severe Alzheimer's Disease

Supported by Forest Laboratories, Inc.

Frederick A. Schmitt, Ph.D., *Department of Neurology, University of Kentucky, KY Clinic (Wing D)-L445, Lexington, KY 40536-0284*; Christopher van Dyck, M.D., Howard Feldman, M.D., Pierre N. Tariot, M.D., Elaine R. Peskind, M.D., E. Malca Resnick, Ph.D., Joanne M. Bell, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to assess the efficacy of memantine for cognitive deficits in Alzheimer's disease patients across disease severity.

Summary:

Objective: Memantine, a low-moderate affinity, uncompetitive NMDA-receptor antagonist, is approved for moderate to severe Alzheimer's disease (AD) in the U.S. and is available in Europe. This report provides additional analyses from two clinical trials.

Methods: A 24-week, double-blind, placebo-controlled trial in mild to moderate AD patients (N = 403) randomly assigned to memantine or placebo assessed cognition with the ADAS-cog. Another 24-week, double-blind, placebo-controlled trial conducted in moderate to severe AD patients treated with ongoing donepezil therapy (N = 404) and randomly assigned to memantine or placebo assessed cognition using the SIB. ANCOVAs were performed on total score, items, and subscales (LOCF).

Results: Memantine-treated patients showed statistically significant improvement, compared to placebo-treated patients. For mild to moderate AD, significant ($p < 0.05$) ADAS-cog items were: commands, orientation, comprehension, recall of instructions. Previously published factor analytically derived subscales revealed a significant effect of memantine on language and memory. For moderate to severe AD, three SIB subscales revealed significant effect: language, memory, praxis.

Conclusions: These findings support the efficacy of memantine in moderate to severe AD and suggest that memantine may pro-

vide cognitive benefits across disease severity through effects on memory, language, and possibly praxis.

References:

1. Tariot P, Farlow M, Grossberg G, et al: Memantine treatment in patients with moderate to severe Alzheimer disease already receiving donepezil: a randomized controlled trial. *JAMA* 2004; 291(3):317-324.
2. Peskind E, Potkin S, Pomara N, et al: Memantine monotherapy is effective and safe for the treatment of mild to moderate Alzheimer's disease: a randomized, controlled trial (abstract). *Eur J Neurol* 2004; 11(Suppl 2)186.

NR742 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Aripiprazole Treatment of Agitation in Inpatients With Psychosis of Alzheimer's Dementia

Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd.

Dusan Kostic, Ph.D., *Bristol-Myers Squibb Company, PO Box 4000, Route 206 and Province Line Road, Lawrenceville, NJ 08453-4000; Christopher Breder, M.D., Ronald Marcus, M.D., Andy Forbes, Ph.D., Andrei Pikalov, M.D., Rene Swanink, M.S.*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate understanding of efficacy of aripiprazole for treatment of agitation in institutionalized patients with psychosis of Alzheimer's dementia.

Summary:

Objective: To describe the efficacy of aripiprazole for reduction of symptoms of agitation in institutionalized patients with psychosis of Alzheimer's dementia (AD).

Method: Two 10-week, placebo-controlled randomized trials with 743 patients with psychosis of AD, evaluated aripiprazole for treatment of institutionalized patients with psychosis of AD. Data on agitation, including Neuropsychiatric Inventory (NPI) agitation/aggression and Cohen-Mansfield Agitation Inventory (CMAI) scores, were collected in both trials and are reported here.

Results: In the flexible-dose trial, the reductions from baseline in NPI agitation/aggression score were -1.18 for placebo and -2.63 for aripiprazole ($p = 0.001$). The reductions in CMAI scores were -6.2 and -10.2, respectively ($p < 0.05$). In the fixed-dose trial, the NPI agitation/aggression scores were significantly reduced with the 5 and 10 mg/day doses of aripiprazole (-2.32 and -2.42, respectively) vs. placebo (-1.32, $p < 0.05$ for both). The reductions in CMAI score were -11.8 in the 5 mg/day group, -11.0 in the 10 mg/day group, and -6.6 with placebo ($p < 0.05$ for both effective-dose aripiprazole groups vs. placebo).

Conclusions: In two trials enrolling institutionalized patients with psychosis of AD, aripiprazole was significantly superior to placebo for reduction of symptoms of agitation, as measured both by NPI and by CMAI.

References:

1. Liston H, Streim J, Breder C, Swanink R, McQuade R, Iwamoto T, Carson W, Stock E: Treating psychosis of Alzheimer's dementia: a flexible-dose aripiprazole study. *Int J Neuropsychopharmacol* 2004; 7(Suppl 1):S21116.
2. Kostic D, Breder C, Swanink R, Marcus R, Iwamoto T, Carson W, McQuade R: Aripiprazole treatment for institutionalized patients with psychosis associated with Alzheimer's disease: a dose-ranging study. *Int J Neuropsychopharmacol* 2004; 7(Suppl 1):S38616.

NR743 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Quetiapine Treatment for Institutionalized Patients With Alzheimer's Disease and Dementia: A Cost-Effectiveness Analysis

Supported by AstraZeneca

Jacqueline Pesa, Ph.D., *AstraZeneca LP, 1800 Concord Pike, Wilmington, DE 19850; Denis Getsios, B.A., Judith A. O'Brien, R.N., J. Jaime Caro, M.D.*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the cost and health implications of treating institutionalized patients with dementia with atypical antipsychotics.

Summary:

Objective: To evaluate quetiapine's cost-effectiveness as treatment for Alzheimer's disease (AD) with accompanying behavioral and psychological signs of dementia (BPSD) in nursing home patients.

Methods: A discrete event simulation model evaluated treatment of patients with AD, comparing quetiapine 200 mg/day to no pharmacological treatment. Patients were followed over one year, and changes in BPSD severity and resulting cost impact were tracked, using data from a randomized, double-blind, controlled clinical trial of quetiapine in AD patients, a state case-mix database, and published information. Costs included nursing home per diems, physician visits, psychiatric/behavioral services, and quetiapine costs. The primary effectiveness outcome was time without BPSD.

Results: Costs for untreated patients averaged \$49,350/year. Quetiapine reduced nondrug costs by almost \$1,200/patient; when drug costs were included, quetiapine generated savings of roughly \$50 per patient per year. Quetiapine patients spent an additional 50 days/year without BPSD. Repeated simulations found quetiapine cheaper and more effective than no treatment in 54% of replications, producing incremental costs of <\$2,500 per patient year with BPSD in 80% of replications.

Conclusions: These analyses indicate that quetiapine in patients with AD and BPSD is cost-effective and may even lead to overall health care system savings.

References:

1. Ballard CG, Margallo-Lana M, Fossey J et al: A 1-year follow-up study of behavioral and psychological symptoms in dementia among people in care environments. *J Clin Psychiatry* 2001; 62:631-636.
2. Murman DL, Chen Q, Powell MC, et al: The incremental direct costs associated with behavioral symptoms in AD. *Neurology* 2002; 59:1721-1729.

NR744 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Effect of Memantine on Behavior in Mild-to-Severe Alzheimer's Disease

Supported by Forest Laboratories, Inc.

Jeffrey L. Cummings, M.D., *Department of Neurology, UCLA Alzheimer's Disease Center, 710 Westwood Plaza, Ste. 2238, Los Angeles, CA 90095; Eugene Schneider, M.D., Elaine R. Peskind, M.D., Pierre N. Tariot, M.D., Stephen M. Graham, Ph.D., Joanne M. Bell, Ph.D.*

Educational Objectives:

At the conclusion of this presentation, the participant should be able to determine the effect of memantine on behavioral outcomes in Alzheimer's disease patients across disease severity, from mild to severe stages of the illness.

Summary:

Objective: Memantine is a low-moderate affinity, uncompetitive NMDA receptor antagonist approved for the treatment of moderate to severe Alzheimer's disease (AD) and currently under investigation for mild AD; it is also available in Europe. The effect of memantine on behavior was assessed in two 24-week, double-blind, placebo-controlled trials, one in moderate to severe AD patients in stable donepezil therapy (study MD-02; N = 404) and one in mild to moderate AD patients (study MD-10; N = 403).

Methods: Behavioral symptoms were assessed using the Neuropsychiatric Inventory (NPI). The statistical analysis (ANCOVA) was based on the ITT population (LOCF).

Results: Baseline characteristics between treatment groups were comparable within each trial. Statistical significance in favor of memantine was observed in both trials at endpoint (NPI total). Several NPI domains demonstrated statistical significance in favor of memantine (MD-02: agitation/aggression, irritability/lability, appetite/eating; MD-10: irritability/lability, aberrant motor behavior, appetite/eating). Significantly fewer memantine patients asymptomatic at baseline exhibited agitation/aggression, irritability/lability, and nighttime behavioral disturbances (MD-02), and delusions and irritability/lability (MD-10) at study endpoint. Patients with baseline symptoms exhibited significantly less worsening of agitation/aggression, apathy, irritability (MD-02), and delusions and apathy (MD-10) at study endpoint.

Conclusions: These results support the use of memantine to reduce behavioral symptoms associated with AD.

References:

1. Tariot P, Farlow M, Grossberg G, et al: Memantine treatment in patients with moderate to severe Alzheimer disease already receiving donepezil: a randomized controlled trial. *JAMA* 2004; 291(3):317-324.
2. Peskind E, Potkin S, Pomara N, et al: Memantine monotherapy is effective and safe for the treatment of mild to moderate Alzheimer's disease: a randomized, controlled trial (abstract). *Eur J Neurol* 2004; 11(Suppl 2) 186.

NR745 Wednesday, May 25, 03:00 p.m.-5:00 p.m.

Update of Memantine Safety in Short- and Long-Term Treatment of Dementia

Supported by Forest Laboratories, Inc. and Merz Pharmaceuticals GmbH

Gustavo Alva, M.D., *Department of Psychiatry and Human Behavior, University of California, Irvine, 101 The City Drive South, Building 3 Route 88, Orange, CA 92868-3201*; Martin R. Farlow, M.D., Anton Porsteinsson, M.D., Stephen M. Graham, Ph.D., Eugene Schneider, M.D., Jeffrey M. Jonas, M.D., Albrecht Stöfler, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to assess the safety and tolerability of memantine in the short- and long-term treatment of dementia.

Summary:

Objective: Memantine, a low-moderate affinity, uncompetitive NMDA-receptor antagonist, is approved for the treatment of moderate to severe Alzheimer's disease (AD) in the U.S. and is available in Europe. Safety and tolerability of memantine for dementia was assessed in eight controlled trials and five open-label extension studies.

Methods: Short-term safety of memantine in mild to moderate AD (N = 1306; 24 weeks) and moderate to severe AD (N = 734; 12-28 weeks) was assessed in six double-blind, placebo-controlled trials. Two 28-week, double-blind trials examined 900 mild to moderate vascular dementia (VaD) patients. Long-term safety

was assessed by pooling data from five open-label extension studies in moderate to severe AD and VaD (N = 1416; 24-104 weeks).

Results: Headache, confusion (AD trials), and constipation (VaD trials) were reported in $\geq 5\%$ of memantine-treated patients at an incidence at least twice that in placebo-treated patients. The overall AE profile in the long-term trials was similar to the short-term studies in moderate to severe AD. Overall, most AEs reported were not judged by the investigator to be related to memantine and were not rated severe. No clinically relevant differences between memantine and placebo patients in vital signs or laboratory values were observed.

Conclusion: Short- and long-term treatment of dementia with memantine is safe and well tolerated.

References:

1. Reisberg B, Doody R, Stöfler A, et al: Memantine in moderate-to-severe Alzheimer's disease. *N Engl J Med* 2003; 348(14):1333-1341.
2. Peskind E, Potkin S, Pomara N, et al: Memantine monotherapy is effective and safe for the treatment of mild to moderate Alzheimer's disease: a randomized, controlled trial (abstract). *Eur J Neurol* 2004; 11(Suppl 2)186.

NR746 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

APAF1 is a Predisposition Gene for Major Depression in Males

Supported by Abbott Laboratories, Myriad Genetics

Donna Shattuck, Ph.D., *Myriad Genetics, 320 Wakara Way, Salt Lake City, UT 84108*; Victor Abkevich, Ph.D., Chris Neff, B.S., David A. Katz, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the evidence that APAF1 is a gene linked to major depression in males.

Summary:

Objective: A highly significant linkage to major depression disorder (MDD) in males has been reported on chromosome 12 with HLOD = 6.1.

Methods: Resequencing of all genes within the 7.0 Mb linkage region to identify the underlying predisposing gene.

Results: The authors identified several missense variants (C450W, Q465R, E777K, N782T) in the protein Apaf-1 (apoptotic protease activating factor-1) that segregate with the disease among affected males in four of the seven pedigrees with the highest LOD-scores in the region ($p = 0.00003$). Independently, the authors determined that two of these variants (E777K and N782T) segregate with the disease among males in two smaller pedigrees ($p = 0.004$). Four additional variants (S357L, L415P, T953A, and 1297insT resulting in a stop at codon 439) were detected among 180 unrelated affected males but not in 768 control subjects.

Conclusion: Apaf-1 is a key protein in the intrinsic apoptotic pathway, and a role for altered apoptosis is supported by the available data that link major depression and morphologic brain changes.

References:

1. Abkevich V, et al: Predisposition locus for major depression at chromosome 12q22/12q23.2. *Am J Hum Genet* 2003; 73:1271-1281.
2. Zou H, et al: Apaf-1, a human protein homotologous to *C. elegans* CED4, participates in cytochrome c dependent activation of caspase 3. *Cell* 1997; 90:405-413.

NR747 Wednesday, May 25, 03:00 p.m.-5:00 p.m.

Variants in Apaf-1 Linked to Major Depression Promote Apoptosome Function

Supported by Abbott Laboratories

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Victor Abkevich, Ph.D., Chris Neff, B.S., Donna Shattuck, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that increased apoptosis has an etiologic role in certain major depression patients.

Summary:

Objective: APAF1, encoding the protein apoptosis protease activating factor 1 (Apaf-1), has recently been established as the chromosome 12 gene conferring predisposition to major depression in humans.

Methods: The molecular phenotypes of Apaf-1 variants were determined by in vitro reconstruction of the apoptosome complex in which Apaf-1 activates caspase 9 and thus initiates a cascade of proteolytic events leading to apoptotic destruction of the cell. Cellular phenotypes were measured using a yeast heterologous expression assay in which human Apaf-1 and other proteins necessary to constitute a functional apoptotic pathway were overexpressed.

Results: Apaf-1 variants encoded by APAF1 alleles that segregate with major depression in families linked to chromosome 12 shared a common gain-of-function phenotype in both assay systems. In contrast, other Apaf-1 variants showed neutral or loss-of-function phenotypes. The depression-linked alleles thus have a common phenotype that is distinct from that of nonlinked variants.

Conclusion: This result suggests an etiologic role for enhanced apoptosis in major depression.

References:

1. Abkevich V et al: Predisposition locus for major depression at chromosome 12q22-12q23.2. *Am J Hum Genet* 2003; 73:1271-128.1
2. Acehan D et al: Three dimensional structure of the apoptosome: implications for assembly, procaspase-9 binding, and activation. *Molec Cell* 2002; 9:423-432.

NR748 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Psychiatric History as a Predictor of Drug Response in Irritable Bowel Syndrome

Supported by GlaxoSmithKline

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Indira Varia, M.D., Prakash S. Masand, M.D.

Educational Objectives:

At the conclusion of this presentation the participants should be able to recognize the clinical relevance of psychiatric disorders in the treatment of irritable bowel syndrome.

Summary:

Objective: The authors investigated whether history of depressive and anxiety disorders predicted response to treatment in a double-blind, randomized, placebo-controlled trial of an SSRI (paroxetine CR) in irritable bowel syndrome (IBS).

Method: A total of 110 subjects were screened, and 72 subjects were randomly assigned to paroxetine CR (12.5-50 mg/day) or placebo for 12 weeks. Current and lifetime psychiatric diagnoses based on DSM-IV criteria were obtained using the Mini Interna-

tional Neuropsychiatric Interview. Patients with current depressive or anxiety disorders were excluded. Treatment response was defined as a Clinical Global Impression-Improvement (CGI-I) score of 1 or 2 at the end of treatment.

Results: A total of 24.2% of randomly assigned subjects had a lifetime diagnosis of depressive and/or anxiety disorders. Seventy percent in the drug group responded on the CGI-I versus 15% in the placebo group ($\chi^2 = 18.3$, $p < 0.001$). In logistic regression, there were main effects of both the drug ($\beta = 13.9$, $p < 0.001$) and psychiatric history ($\beta = 8.2$, $p < 0.05$). Moreover there was a significant interaction between the drug and psychiatric history ($\beta = 20.1$, C.I. = 4.3-93.8, $p < 0.001$). The mean paroxetine CR dose was 30 mg/day.

Conclusions: Psychiatric comorbidity is common in IBS. It appears that a history of depression or anxiety predicts a more favorable response to paroxetine CR in IBS.

References:

1. Masand PS, Gupta S, Schwartz TL, Kapan D, Virk S, Hameed A, Lockwood K: Does a preexisting anxiety disorder predict response to paroxetine in irritable bowel syndrome? *Psychosomatics* 2002; 43(6):451-5.
2. Folks DG. The interface of psychiatry and irritable bowel syndrome. *Curr Psychiatry Rep* 2004; 6(3):210-5.

NR749 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Consumers' Perspectives and Satisfaction with the Quality Service in an Ambulatory Mental Health Clinic

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Carlos Cruz, M.D., Ana Maria Rodriguez, Ph.D., Paula Aguirre, Ph.D.

Educational Objectives:

At the end of this presentation, the participant will be able to recognize that the unspecific aspects of the assistance are more important components from, the consumer's point of view, than the technical specific aspects in the consumer's satisfaction.

Summary:

The consumer's satisfaction is an important factor in the continuity of the treatment. The goal of the study was to identify factors that determine the consumer's satisfaction from the patient's point of view. A telephone survey was used (previously designed by the authors) in which the professional care, the administrative staff, and physical infrastructure of the clinic center were evaluated. Seventy patients were interviewed, selected at random from a total of 189 patients seen in the last six months; 80% were women. The gathered information was analyzed with the program SPSS, version 10.4, using models of regression, ANOVA, and factor analysis with a $p < 0.05$ of significance. Three groups of variables accounted for 72.3% of the variety: support system that includes infrastructure and secretarial services (36.6%); empathic support, which considers characteristics of a good support relationship (25.4%); and the cooperative relationship that occurs between the therapist and patient and includes technical knowledge and its use (10.3%). Satisfaction of the consumer with unspecific factors, the infrastructure and reception, and empathy on the professional side contribute greatly to general satisfaction, over the specific and technical aspects of the professional care received by the patient.

References:

1. Bennett MJ, Feldstein ML: Correlates of patient satisfaction with mental health services in a health maintenance organization. *Am J Prev Med* 1986; 2(3):155-62.

2. Johansson H, Eklund M: Patients' opinion on what constitutes good psychiatric care." *Scand J Caring Sci* 2003; 17(4):339-46.

NR750 Wednesday, May 25, 3:00 p.m.-5:00 p.m.
Obesity in Psychiatric Outpatients

Iwona Chelminski, Ph.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street Suite 501, Providence, RI 02905*; Mark Zimmerman, M.D.

Educational Objectives:

At the conclusion of this presentation the audience will have a better understanding of obesity in psychiatric population.

Summary:

Objective: Since 1980 obesity among adults has doubled, and it is becoming a serious and a very costly national problem. Research from this area describes high rates of psychopathology among the obese individuals. They report less positive mood states, worse self-esteem, and higher rates of depression and anxiety. It is unclear, however, how prevalent the problem of obesity is in populations presenting for treatment in routine clinical psychiatric practice. The authors examined body mass index (BMI) in patients from a large community clinical practice and examined the prevalence of psychiatric problems as a function of BMI.

Method: Eighteen hundred psychiatric outpatients were evaluated with the Structured Clinical Interview for DSM-IV. Information regarding their weight and height was also recorded, except for four participants. The authors compared the frequencies of major Axis I disorders in three nonoverlapping groups: nonobese (BMI < 30, N = 1,378), obese but not morbidly (N = 354), and morbidly obese (N = 64).

Results: Slightly over 50% of patients were within the limits of normal body weight (BMI < 25), 29.1% were overweight (BMI > 25 but <30), and 23.3% obese. Of the obese, 15.3% were morbidly obese. There were no gender differences between the three groups. Compared to the nonobese patients, the obese and morbidly obese patients were significantly more likely to receive a diagnosis of an eating disorder (10.5% and 15.6% vs. 5.1%, $\chi^2 = 22.4$, $p < 0.001$) and social phobia (32.5% and 39.1% vs. 27.4%, $\chi^2 = 6.9$, $p < 0.05$).

Conclusions: Obesity rates in the sample were lower than the national rates. Even though excess weight contributes to emotional stress in general, the findings indicate that obesity is not more common in psychiatric patients. Besides eating disorders, social phobia was the only disorder positively associated with BMI indicating obesity.

References:

1. Flegal KM, Carroll MD, Ogden CL, Johnson CL: Prevalence and trends in obesity among US adults, 1999-2000. *Journal of the American Medical Association* 2002; 288:1723-1727.
2. Glinksi J, Wetzler S, Goodman E: The psychology of gastric bypass surgery. *Obesity Surgery* 2001; 11:581-588.

NR751 Wednesday, May 25, 3:00 p.m.-5:00 p.m.
Impulsivity and Personality Traits in Pathological Gambling Disorder (PGD) Versus OCD

Joshua F. Boverman, M.D., *Department of Psychiatry, OHSU, 3181 SW Sam Jackson Park Rd#OP02, Portland, OR 97239*; Vanessa B. Wilson, B.A., Suzanne H. Mitchell, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand differences/similarities of OCD and PGD on measures of personality and impulsive decision-making.

Summary:

Objective: Abnormal impulse control and unusual decision-making styles are hallmarks of both OCD and PGD. However, the disorders have marked differences (e.g., PGD has a much higher comorbidity with substance abuse). To characterize differences and similarities between the disorders, the authors studied OCD and PGD subjects on measures of personality and impulsivity. They hypothesized that OCD and PGD subjects would show similar abnormalities of personality and impulsivity.

Methods: Subjects with PGD (N = 14) or OCD (N = 7) were recruited. Two control groups were matched to these subjects based on drug and alcohol use (nine substance users and seven abstinent). All subjects completed personality questionnaires (Sensation-Seeking Scale, Tridimensional Personality Questionnaire, Barratt's Impulsiveness Scale) and measures of impulsive decision-making (risk taking, inhibition, delay discounting).

Results: PGD and OCD subjects exhibited marked and statistically significant differences on several measures of personality and impulsivity. In particular PGD subjects had markedly higher impulsivity scores than OCD subjects. When compared to their respective drug-use control groups, few significant differences were seen.

Conclusions: These data suggest that persons with PGD have high levels of impulsivity, approximating those seen in substance abusers. These data further suggest that persons with OCD have low levels of impulsivity, approximating those seen in nonsubstance abusers. Substance abuse may be a confounding variable in measuring impulsivity differences between OCD and PGD. Alternatively, high impulsivity may make persons vulnerable to PGD and to substance abuse, but not to OCD.

References:

1. Kim SW, Grant JE: Personality dimensions in pathological gambling disorder and obsessive-compulsive disorder. *Psychiatry Research* 2001; 104(3):205-12.
2. Evenden JL: Varieties of impulsivity. *Psychopharmacology* 1999; 146, 348-361.

NR752 Wednesday, May 25, 3:00 p.m.-5:00 p.m.
Effects of Risperidone on Psychosis of Alzheimer's Disease (PAD) and Nursing Staff Burden
Supported by Janssen Medical Affairs, L.L.C.

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that symptom relief in patients with psychosis of Alzheimer's disease may reduce caregiver burden.

Summary:

Objective: Data from a 12-week randomized, placebo-controlled trial showed that risperidone is effective in reducing psychotic symptoms in dementia patients with general behavioral and psychological symptoms and in a subpopulation of PAD patients. This study measured the effect of risperidone treatment on the relative burden of PAD-related symptoms to nursing-home staff.

Methods: PAD was defined as a diagnosis of Alzheimer's disease (AD) or mixed dementia with a rating ≥ 2 on any delusion/hallucination item of the Behavioral Pathology in AD rating scale at baseline. The Modified-Nursing Care Assessment Scale measured the degree to which dementia-associated behaviors are exhibited by patients (attitude domain) and the difficulty nurses have in "coping" with these (strain domain). ANCOVA was used to examine treatment differences.

Results: A total of 93 patients met PAD criteria (risperidone: N = 46, placebo: N = 47). Risperidone significantly reduced strain domain scores at endpoint, compared to placebo ($p = 0.045$). This was driven by significant decreases on two of the five strain subscales (affect, job satisfaction, neediness, predictability, self direction; $p < 0.022$, $p < 0.138$, $p < 0.020$, $p = 0.063$, $p = 0.533$). The attitude domain revealed no differences ($p = 0.290$).

Conclusions: Although limited by small numbers, these results indicate that risperidone efficacy in PAD may reduce strain experienced by nursing staff in coping with the symptoms of these patients.

References:

1. Brodaty H, Ames D, Snowdon J, et al: A randomized placebo-controlled trial of risperidone for the treatment of aggression, agitation, and psychosis of dementia. *J Clin Psychiatry* 2003; 64:134-143.
2. Brodaty H, Katz I, De Deyn PP, et al: Risperidone is effective in treating psychotic symptoms in patients with psychosis of Alzheimer's disease. Poster presented at The International College of Geriatric Psychoneuropharmacology (ICGP) 2004 Annual Meeting, October 14-17, 2004. Basel, Switzerland.

NR753 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Cognitive and Behavioral Effects of Lamotrigine and Topiramate in Healthy Volunteers *Supported by GlaxoSmithKline*

Kimford J. Meador, M.D., *Department of Neurology, University of Florida, 100 South Newell Drive, Gainesville, FL 32610*; David Loring, Ph.D., James Fessler, M.D., Mary Ann Werz, M.D., Patty Ray, Ph.D., Victoria Vahle, M.P.H., James Miller, Pharm.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the effects of lamotrigine and topiramate on neuropsychological function in healthy adults.

Summary:

Objective: Antiepileptic drugs (AEDs) are used for a variety of indications. Cognitive side effects of AEDs are common. A variety of factors contribute to cognitive dysfunction in patients. Evaluating the cognitive effects of AEDs in healthy volunteers minimizes the confounding factors and allows extrapolation of the results to various clinical populations.

Methods: This was a randomized, double-blind, double-dummy, two-period crossover study in healthy adults. Subjects were randomly assigned (1:1) in the first treatment period to receive either lamotrigine or topiramate for 12 weeks (7 weeks of dose escalation followed by 4 weeks of maintenance therapy, and then 1 week of tapering off study drug). The initial dose was 25 mg/day, and the target maintenance dose was 300 mg/day for both AEDs. Subjects then received the alternate therapy for 12 weeks in the second treatment period with the same dosing format. Neuropsychological evaluation included 17 measures yielding 41 variables of cognitive function and subjective behavioral effects. The measures included: Selective Reminding Test (SRT), MCG Paragraph Memory, Boston Naming Test, Animal Naming, Controlled Oral Word Association (COWA), Stroop Test, Symbol Digit Modalities Test (SDMT), Digit Cancellation, Grooved Pegboard, Choice Reaction Time (CRT), Visual Serial Addition Test (VSAT), Continuous Performance Task (CPT), A-B Neurotoxicity Scale, QOLIE-89 Attention, Language and Memory subscales, SEALS inventory, Profile of Mood States (POMS), and SF-12. Evaluations were conducted at screening, at the end of the first maintenance phase, at the end of the second maintenance phase, and in the posttreatment period.

Results: A total of 47 adults (19 men and 28 women) with a mean age of 37 years completed both phases of the study. An analysis by paired t-tests revealed significant differences for 33 of the 41 variables, all in favor of lamotrigine. Significant differences were seen in CPT, Digit Cancellation, VSAT, Grooved Pegboard, CRT (initiation and total), Boston and Animal Naming, COWA, SRT (continuous long term recall), MCG Paragraphs, SDMT, Stroop (words and color), A-B Neurotoxicity, POMS (vigor, fatigue, confusion, and overall), all three cognitive subscales for QOLIE-89, four of the five SEALS factors, and the SF-12 mental summary.

Conclusion: Lamotrigine produces significantly fewer untoward cognitive and subjective side effects than topiramate in monotherapy at the dosages, titrations, and timeframes employed in this study.

References:

1. Meador KJ, Loring DW, Ray PG et al: Differential cognitive and behavioral effects of carbamazepine and lamotrigine. *Neurology* 2001; 8:1177-82.
2. Lee S, Sziklas V, Andermann F, et al: The effects of adjunctive topiramate on cognitive function in patients with epilepsy. *Epilepsia* 2003; 44:339-47.

NR754 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Decreased Temporal Lobe Volume in Panic Disorder: A Quantitative-MRI Study

Thomas Sobanski, M.D., *Department of Psychiatry and Psychotherapy, Thuringen-Klinik Saalfeld-Rudolstadt, Rainweg 68, Saalfeld 07318, Germany*; Gerd Wagner, Ph.D., Uwe Gruhn, M.D., Gregor Peikert, Ph.D., Heinrich Sauer, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that local brain alterations (decreased temporal lobe volumes) occur in patients with panic disorder.

Summary:

Objective: Vythilingam et al. (2000) reported a bilateral reduction of temporal lobe volume in patients with panic disorder. In other studies conflicting results were reported. The aim of the present study was to assess regional brain volume alterations in panic disorder.

Methods: Magnetic resonance imaging (MRI) scans were performed in a group of 16 inpatients with panic disorder and a control group matched for age and gender. Volumetric analyses of regions of interest were made semi-automatically by two blinded raters. The following structures were measured: temporal and frontal lobes, amygdala-hippocampus complexes, caudate nucleus, putamen, and whole brain volume. The differences between groups were calculated with MANCOVA (covariate brain volume).

Results: Patients with panic disorder had a significantly smaller temporal lobe volume on both sides. The amygdala-hippocampus complexes of the patients and healthy control subjects did not differ.

Conclusions: The results of Vythilingam et al. (2000) are confirmed by the findings, and the hypotheses of a pathogenetic involvement of the temporal lobes in panic disorder are supported. At present it can not be decided whether the volume reduction observed represents a primary phenomenon or a secondary alteration due to the disease process.

Supported by Ministry of Science and Education, Thuringia, Germany (research grant) and AstraZeneca (travel expenses).

References:

1. Massana G, Serra-Grabulosa JM, Salgado-Pineda P, Gasto C, Junque C, Massana J, Mercader JM, Gomez B, Tobena

A, Salamelo M: Amygdalar atrophy in panic disorder patients detected by volumetric magnetic resonance imaging. *Neuroimage* 2003; 19:80-90.

2. Vythilingam M, Anderson ER, Goddard A, Woods SW, Staib LH, Charney DS, Bremner JD: Temporal lobe volume in panic disorder—a quantitative magnetic resonance imaging study. *Psychiatry Res* 2000; 99:75-82.

NR755 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**
HIV Infection and Hepatitis in an Outpatient Psychiatric Clinic Population

John L. Beyer, M.D., *Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine, 4098 Hospital South, Durham, NC 27710*; Kenneth Gersing, M.D., Laura Taylor, Ph.D., K. Ranga R. Krishnan, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the prevalence of HIV infection and hepatitis in a general psychiatric outpatient clinic.

Summary:

Objective: The incidence of HIV infection in people with severe mental illness has been reported to be between 3.1% and 22.9%, markedly higher than comparable estimates of HIV infection in the general U.S. adult population (0.3%-0.4%). The high rate of HIV infection in persons with severe mental illness may be due in part to sampling issues, such as an overrepresentation of inpatients, urban mental health clinic patients, or those in socioeconomic circumstances associated with higher HIV exposure. The incidence of HIV infection in a general psychiatric outpatient population has not been assessed.

Methods: Using the Duke University Medical Center clinical database, an anonymized database of over 23,000 unique patients seen in the Duke psychiatric outpatient clinics since 2001, the authors evaluated the prevalence and primary psychiatric diagnoses of patients who had a comorbid diagnosis of HIV and/or hepatitis.

Results: The initial review of all primary psychiatric diagnoses demonstrated that rates of HIV infection and hepatitis were increased compared to the general U.S. population, but not to the level seen in studies that focused on the severely mentally ill. Patients with substance abuse disorders and bipolar and depressive disorders remained at higher risk of HIV and hepatitis infection. Specific prevalence rates and analyses of psychiatric/substance abuse comorbidity will be presented after a complete analysis of the database.

Conclusions: Elevated rates of HIV infection are seen in general psychiatric outpatient clinics. Clinical psychiatrists in all settings should be aware of the potential prevalence of HIV infection and hepatitis, especially among patients with certain primary psychiatric diagnoses.

Supported by a grant from the NIMH Bipolar Disorders in Late Life Project.

References:

1. Rosenberg SD, Goodman LA, Osher FC, Swartz MS, Essock SM, Butterfield MI, Constantine NT, George LW, Salyers MP: Prevalence of HIV, hepatitis B, and hepatitis C in people with severe mental illness. *Am J Pub Health* 2001; 91(1):31-37.
2. Dausey DJ, Desai RA : Psychiatric comorbidity and the prevalence of HIV infection in a sample of patients in treatment for substance abuse. *J Nerv Ment Dis* 2003; 191(1):10-17.

NR756 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**
Neuroleptic-Induced Catatonia: Catatonic Subtypes, Symptom Patterns, and Treatment Responses

Joseph W. Lee, M.D., *Department of Psychiatry, Graylands Hospital, Brockway Road Mt. Claremont, Perth 6010, Australia*

Educational Objectives:

At the conclusion of the session, the participant should recognize that neuroleptic-induced catatonia is similar to schizophrenic catatonia in symptom patterns and to manic catatonia in responses to benzodiazepines.

Summary:

Objective: Neuroleptic-induced catatonia (NIC) is a rare reaction to antipsychotic medications, sparsely reported in the literature. This study examined 18 episodes of NIC and compared their catatonic subtypes, symptom patterns, and treatment responses with episodes of manic and schizophrenic catatonia.

Methods: A total of 127 patients with catatonia were prospectively identified, with their catatonic (excited/retarded) subtypes determined based on research criteria. Most were treated with benzodiazepines. Catatonic symptoms were assessed with the Bush Francis Catatonia Rating Scale. The presence of the four catatonic symptom factors proposed by Kruger et al (2003) was retrospectively determined. In 18 episodes catatonic and prominent extrapyramidal symptoms developed following exposure to antipsychotic medications. These episodes of NIC were compared with 51 episodes of schizophrenic catatonia and 16 episodes of manic catatonia, noting their catatonic subtypes, symptom patterns based on Kruger et al's proposed symptom factors, and responses to benzodiazepines.

Results: Similar to schizophrenic catatonia, NIC manifested predominantly in the retarded form associated with factor 3 and 4, while manic catatonia was predominantly in the excited form, associated with factor 1 and 2. Three episodes fulfilled the criteria for neuroleptic malignant syndrome with fever, delirium, and autonomic disturbances. NIC showed good responses to benzodiazepines, comparable to manic catatonia (78% with full responses vs. 75%). Three with partial response responded promptly to amantadine.

Conclusions: NIC is similar to schizophrenic catatonia but different from manic catatonia in symptom patterns. Benzodiazepines and amantadine are effective treatments for NIC.

References:

1. Gelenberg AJ, Mandel MR: Catatonic reactions to high-potency neuroleptic drugs. *Arch Gen Psychiatry* 1977; 34:947-950.
2. Kruger S, Bagby RM, Hoffler J, et al: Factor analysis of the Catatonia Rating Scale and catatonic symptom distribution across four diagnostic groups. *Compr Psychiatry* 2003; 44:472-482.

NR757 **Wednesday, May 25, 3:00 p.m.-5:00 p.m.**
Comparative Neurocognitive Effects of Six Mood Stabilizers

Marshal Folstein, M.D., *Department of Radiology, Massachusetts General Hospital, Building 149-2301, 13th St, Charlestown, MA 02129*; Thomas Gualtieri, M.D.

Educational Objectives:

At the end of the presentation, the participant should appreciate the comparative cognitive effects of six mood stabilizers commonly used in patients with severe mood disorders. The participant will also learn about the clinical utility of computerized neurocognitive testing in the clinic setting.

Summary:

Objective: Many of the new antiepileptic drugs have psychiatric indications, and most are prescribed by psychiatrists for patients with mood disorders, even absent a specific indication. Epileptic drugs in general, even the newer ones, are known to effect cognition, sometimes in untoward ways. Research on the neurocognitive effects of antiepileptic drugs, however, has been done exclusively in normal volunteers and in patients with seizure disorders.

Method: A naturalistic, cross-sectional study of patients taking one of five different psychotropic anticonvulsants or lithium. Cognition was measured by a computerized neurocognitive screening battery, CNS Vital Signs. Subjects were 159 patients with bipolar disorder, age 18-70, treated with carbamazepine (N = 16), lamotrigine (38), oxcarbazepine (19), topiramate (19), and valproic acid (37); 30 bipolar patients taking lithium were included for comparison.

Results: Significant group differences were detected in tests of memory, psychomotor speed, processing speed, reaction time, cognitive flexibility, and attention. Rank order analysis indicated superiority for lamotrigine (1.8) followed by oxcarbazepine (2.1), lithium (3.3), topiramate (4.3), valproic acid (4.5), and carbamazepine (5.0).

Conclusions: The relative neurocognitive effects of the various psychotropic antiepileptic drugs in patients with bipolar disorder are concordant with those described in the seminal literature in normal volunteers and patients with epilepsy. Lamotrigine and oxcarbazepine have the least neurotoxicity, and topiramate, valproate, and carbamazepine have the most. Lithium effects on neurocognition are intermediate. Choosing a mood-stabilizing drug with minimal neurocognitive effects may enhance patient compliance over the long-term.

References:

1. Meador KJ, Loring DW, Huh K, Gallagher BB, King DW: Comparative cognitive effects of anticonvulsants. *Neurology* 1990; 40:391-4.
2. Gualtieri CT: Brain Injury and Mental Retardation: Psychopharmacology and Neuropsychiatry. Lippincott, Williams and Wilkins, 2002.

NR758 Wednesday, May 25, 3:00 p.m.-5:00 p.m. **Differentiating Mild Cognitive Impairment From Early Dementia**

Supported by CNS Vital Signs LLC

Marshal Folstein, M.D., *Department of Radiology, Massachusetts General Hospital, Building 149-2301, 13th St, Charlestown, MA 02129*; Thomas Gualtieri, M.D.

Educational Objectives:

At the conclusion of the presentation, participants will be familiar with the use of computerized neurocognitive testing in differentiating between mild cognitive impairment and early dementia.

Summary:

Objective: The concept of Mild Cognitive Impairment (MCI) has been proposed to designate an early, but abnormal, state of cognitive impairment intermediate between normal aging and very early dementia. MCI has generated a great deal of research from both clinical and research perspectives. However, there has been controversy regarding the precise definition of the concept and its implementation in various clinical settings. The goal of the study was to validate the differentiation between MCI and mild dementia (MD), made on clinical grounds, by using a new, computerized neurocognitive screening battery.

Method: Patients at the NC Neuropsychiatry Clinics with clinical diagnoses, by standard criteria, of MCI (N = 36) or mild dementia

(N = 53) and 89 normal control subjects, matched for age, race, and gender were tested.

Results: As expected, test performance on the Vital Signs battery differed significantly among the three groups in tests of memory, psychomotor speed, reaction time, cognitive flexibility, and complex attention (General Linear Model). Then, a cluster analysis was performed to validate the clinical differentiation between MCI and MD patients. The cluster analysis empirically generated two groups that corresponded, broadly, to the clinical designations. There was 65% agreement between the clinical and the empirical methods. MD patients who were classified as MCI by cluster analysis were: (1) well-educated professionals, whose test performance did not capture the degree to which they were impaired in day-to-day activities; and/or (2) patients with disabling psychiatric symptoms secondary to their cognitive disorder. MCI patients who were classified as MD by cluster analysis tended to be less well-educated patients who tested poorly but whose day-to-day activities were not impaired.

References:

1. Nordberg A: Toward an early diagnosis and treatment of Alzheimer's disease. *International Psychogeriatrics* 2003; 15:223-37.
2. Scarpini E, Scheltens P, Feldman H: Treatment of Alzheimer's disease: current status and new perspectives. *Lancet Neurology* 2003; 2:539-47.

NR759 Wednesday, May 25, 3:00 p.m.-5:00 p.m. **A Plasma Homocysteine as a Risk Factor for Korean Patients With Vascular Dementia and Alzheimer's Disease**

Sang-Yeol Lee, M.D., *Department of Psychiatry, Wonkwang University, 144-23 Dongsan-Dong, Iksan, Chonbuk 570-060, Korea*; Je-Sun Lee, M.D., Young-Hun Cheon, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize that elevated homocysteine is a risk factor for Korean patients with vascular dementia and Alzheimer's disease.

Summary:

Objective: Recent studies suggest that vascular disease may contribute to the cause of Alzheimer's disease (AD). Since elevated plasma homocysteine (tHcy) level is a risk factor for vascular disease, it may also be relevant to AD. The author examined the association in Korean patients of vascular dementia (VD) and AD with blood level of tHcy, its biological determinants folate and vitamin B12.

Methods: Fasting plasma tHcy, folate, vitamin B12 levels, and e4 allele of apoprotein E genotype were determined in 40 patients with VD and 46 patients with AD, and the results were compared with those for 71 control subjects.

Results: A significant increase in plasma homocysteine and a significant decrease in plasma vitamin B12 were observed in the disease groups, compared with control subjects. There was no significant difference in tHcy and vitamin B12 between VD and AD. This remained significant after allowance for confounding factors (age, sex, hypertension, cholesterol, smoking, creatinine, and nutritional measures). The odds ratio of clinically confirmed AD and VD associated with a tHcy level (>11.9 $\mu\text{mol/L}$) compared with the lower quartile (<9.1 $\mu\text{mol/L}$) was 2.7 and 3.9, after adjustment for vascular risk factors, creatinine, and nutritional measurement. The prevalence of depression in patients with VD and AD was 40% and 28%, respectively.

Conclusion: Moderately high plasma levels of homocysteine are associated in Korean patients with VD and AD. This is not due to vascular risk factors or nutritional status. Psychiatric intervention for patients with VD and AD is needed.

References:

1. Clarke R, Smith AD, Jobst KA, et al: Folate, vitamin B12, and serum total homocysteine levels in confirmed Alzheimer disease. *Arch Neurol* 1998; 55:1449-1455.
2. Ramon DA: Homocysteine and neurologic disease. *Arch Neurol* 2000; 57:1422-1427.

NR760 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Is Chronological Age or Age of Onset Critical for the Prognosis of Depression? A Systematic Review

Alex J. Mitchell, M.D., *Liaison Psychiatry, Leicester Partnership Trust, Leicester General Hospital, Leicester LE4 5PW, United Kingdom*

Educational Objectives:

At the conclusion of this session, participants should gain a better understanding of the role of age vs age of onset from studies in late-life and mid-life depression.

Summary:

How does age effect the outcome of depression? Studies were identified that have directly compared the prognosis of depression in late-life with depression in mid-life under similar conditions. Age at presentation/recruitment was considered separately from studies of age at first episode of depression. Outcome was considered as (1) remission, (2) relapse, (3) dementia, (4) mortality. The presenter found 22 primary data studies for outcomes 1 and 2 but only six studies for outcomes 3 and 4. From these, evidence suggests that response and remission rates to pharmacotherapy and ECT are not sufficiently different in old age depressions and middle-age depressions to be clinically significant. Regarding relapse and recurrence, older patients at study entry appeared to have a higher risk of further episodes that informs the debate about the duration of continuation treatment for depression in older people. However, older patients and patients with a late age of first episode onset (late-onset depression) are at increased risk of medical comorbidity. Thus a late age of first onset is a risk factor for accelerated mortality in depression. Surprisingly it is an early age of first onset that appears to be a risk factor for late cognitive decline. Both chronological age and age of onset moderate the prognosis of depression, but the relationship differs by the outcome under study.

References:

1. Mitchell AJ, Subramanian H: Prognosis of depression in old age compared to middle age—a systematic review of comparative studies. *Am J Psychiatry* (in press).
2. Palsson S, Aevansson O, Skoog I: Depression, cerebral atrophy, cognitive performance and incidence of dementia population study of 85-year-olds. *British Journal of Psychiatry* 1999; 174:249-53.

NR761 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Clinical Characteristics and Prognosis of Patients on SSRIs Undergoing CABG Surgery

Supported by Pfizer Inc.

Glen Xiong, M.D., *Internal Medicine & Psychiatry, DUMC, Box 31047, Durham, NC 27710*; Wei Jiang, M.D., L. Kristin Newby, M.D., Bob Clare, M.S., Linda Shaw, M.S., K. Ranga R. Krishnan, M.D.

Educational Objectives:

At conclusion of presentation, the participants should be able (1) to appreciate that patients taking SSRIs prior to CABG have higher baseline medical comorbidities and worse prognosis post

CABG and (2) to explore the potential mechanisms underlying higher mortality in patients treated with SSRIs prior to CABG.

Summary:

Objective: Depression is a prognostic factor in ischemic heart disease (IHD). SSRIs are considered safe and effective for depression and have been suggested to reduce cardiac events in depressed IHD patients. This study describes clinical characteristics and outcomes of patients treated with SSRIs prior to coronary artery bypass graft (CABG) surgery.

Methods: The Duke Databank for Cardiovascular Diseases was searched for patients who underwent CABG from January 1, 1999 to December 31, 2003. SSRIs included fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, escitalopram, venlafaxine, and clomipramine. Chi-square, Wilcoxon test, and log-rank test (for Kaplan-Meier survival plot) were used for statistical analysis.

Results: Of 4,794 patients, 5.1% were taking SSRIs prior to CABG and 94.9% were not. Compared to the non-SSRI group, patients taking SSRIs were more likely to be white and female and to have diabetes, dyslipidemia, and hypertension ($p < 0.05$). The 30-day readmission rate was significantly higher in the SSRI (19.5%) than in the non-SSRI group (12.7%, $p < 0.002$). The Kaplan-Meier survival rates at 4 years were 75.1% in SSRI and 84.9% in the non-SSRI group ($p = 0.0065$).

Conclusions: Patients taking SSRIs prior to CABG had more medical comorbidities and worse outcome post CABG. More statistical analyses adjusting potential baseline confounding variables are pending.

References:

1. Frasure-Smith N, Lesperance F, Talajic M: Depression following myocardial infarction: impact on 6-month survival. *JAMA* 1993; 270:1819-1825.
2. Glassman AH, O'Connor CM, Califf RM et al: Sertraline treatment of major depression in patients with acute MI or unstable angina. *JAMA* 2002; 288:701-709.

NR762 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Fuld Object Memory Evaluation of Donepezil in African Americans

Supported by Eisai, Inc., Pfizer Inc.

Peter Lichtenberg, Ph.D., *Department of Psychology, Wayne State University, Detroit, MI 48202*; Patrick Griffith, M.D., Robert Goldman, Ph.D., Jennifer Payne-Parrish, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the value of treating Alzheimer's disease and recognize the value of measuring memory functioning with the Fuld Object Memory Evaluation.

Summary:

Objective: Common assessments of memory and cognition in Alzheimer's disease (AD) studies (e.g., ADAS-cog and MMSE) have been validated. However, their sensitivity may be influenced by education and language fluency. The Fuld Object Memory Evaluation (FOME) is not influenced by education or language and has been validated across many cultures.

Methods: A 12-week, open-label trial of donepezil in African Americans with mild to moderate AD was conducted using the FOME, MMSE, and CIBIC-plus as outcome measures.

Results: Mean FOME retrieval and MMSE scores were significantly improved from baseline at endpoint (LOCF, $p < 0.0001$). CIBIC-plus scores were also improved at endpoint (LOCF, $p < 0.0001$). Donepezil was safe and well tolerated in this patient population. FOME retrieval and MMSE scores were also analyzed post hoc to examine (1) effects of education and (2) relative sensi-

tivity. While the MMSE and FOME both showed robust improvement after donepezil treatment, the FOME was highly sensitive to detecting significant improvement in memory functioning.

Conclusions: This is the first study to demonstrate the utility of the FOME as a cognitive endpoint. The FOME could be used to measure memory functioning in future dementia studies.

References:

1. Wall JR: The FULD object memory evaluation, a useful tool in the assessment of urban geriatric patients. *Clin Gerontol* 1998; 19:39-49.
2. Mast RI, Fitzgerald J, Steinberg J, MacNeill S, Lichtenberg P: Effective screening for Alzheimer's disease among older African Americans. *Clinical Neuropsychol* 2001; 16:196-202.

NR763 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Behavioral Coping Preferences of Psychiatric Inpatients

David J. Hellerstein, M.D., *Department of Psychiatry, New York State Psychiatric Institute, 1051 Riverside Drive, Unit 101, New York, NY 10032, Goretti Almeida*

Educational Objectives:

At the conclusion of this session, the participant should be able to describe issues related to coping preferences of psychiatric inpatients, which may vary by gender and diagnosis among other factors.

Summary:

Background: Recently, there has been increased concern about excessive restraint and seclusion on inpatient psychiatric units, and resulting injuries and deaths. Congressional legislation and new JCAHO standards have been formulated. However, there is a lack of research on approaches that include active engagement of inpatients in behavioral coping plans.

Method: We have developed a Coping Agreement Questionnaire (CAQ), which consists of four questions asking inpatients for their preferences on how to help them prevent loss of control if they become agitated. Nurses review the CAQ with each patient to find alternatives to restraint and seclusion. 257 admissions were reviewed, with diagnoses of mood disorders (36.7%, N=115); schizophrenia or other psychotic disorders (25.6%, N=80); or substance use disorders (19.8%, N=62). 54.1% were male.

Results: CAQ answers differed by diagnosis and gender. When asked "what upsets you and/or causes you to lose control?" the most common answer was "too much noise" (25% of sample); however, female patients rated "being touched" as the second most upsetting item (22%), and males listed "not being able to go home" (19%). When asked how staff could help if they were about to lose control, both those with schizophrenia (64%) and mood disorders (55%) rated "talk to me" as the first preference, whereas 65% of substance abusers rated "allow me to sit...by myself in my room." More females (10%) than males (3%) noted a history of self-injury when upset, and more patients with schizophrenia (54%) than those with mood disorders (35%) preferred PRN medication if they were losing control.

Conclusions: Findings suggest that patients may be engaged as active partners in managing their behavior during inpatient hospitalization, with a goal of improving outcome.

References:

1. Fisher WA: Restraint and seclusion: a review of the literature. *American Journal of Psychiatry* 1994; 151:1584-91.
2. Public Law 106-310, Children's Health Act of 2000 (Section 3207 and 3208). (These restraint and seclusion requirements amend Title V of the Public Health Service Act (42 USC 290aa et seq.) by adding Section 591 and 595.)

NR764 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Resource Utilization in Substance and Alcohol Abuse Patients With Schizophrenia

Supported by Janssen Pharmaceutica Products

Reshmi M. Siddique, Ph.D., *Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, P.O. Box 200, Lawrenceville, NJ 08560*; Jeffrey Markowitz, Ph.D., *Luella Engelhart, M.A.*

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the significant cost burden to the public payer system of schizophrenia patients with substance and alcohol abuse.

Summary:

Objective: This study compared resource utilization patterns of schizophrenia patients with substance/alcohol abuse (e.g. dual diagnosis) versus schizophrenia patients without a dual diagnosis.

Methods: California Medicaid (Medi-Cal) claims data (1996-2002) were used to identify schizophrenia patients (aged 18 to 64 years) as well as substance/alcohol dependent patients within one year of their schizophrenia diagnosis. These two groups (SCHIZ and DUAL, respectively) were followed for one year. Medical (inpatients and outpatients) and prescription utilization were examined.

Results: 11,438 subjects were identified. 17.6% of all patients were DUAL (n=2,016) For all drugs prescribed, DUAL patients had a mean of 49.6 claims compared with 39.1 for SCHIZ (p<0.0001). The average cost per patient per year for all prescription medications was \$3,392 for DUAL and \$2,188 for SCHIZ (p<0.0001). DUAL patients had higher utilization than SCHIZ patients across all medical resource utilization with the exception of inpatient costs. Total costs (prescription and medical) averaged \$8,089 in DUAL compared with \$6,380 in SCHIZ (p<0.0001).

Conclusion: Dual-diagnosis patients add a significant cost burden to the public payer system. Further research is needed to determine predictors of such costs such as severity of illness, treatment effectiveness, and medication noncompliance.

References:

1. Regier DA, Farmer ME, Rae DS, et al: Comorbidity of mental disorders with alcohol and other drug abuse: results from the Epidemiologic Catchment Area (ECA) study. *JAMA* 1990; 264:2511-2518.
2. Fowler, et al: Patterns of current and lifetime substance abuse in schizophrenia. *Schizophr Bull* 1998; 24(3):443-55.

NR765 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Impact of Atypical Antipsychotic Drug Sedation on Quality of Life

Supported by Janssen Pharmaceutica and Research Foundation

Reshmi M. Siddique, Ph.D., *Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, P.O. Box 200, Lawrenceville, NJ 08560*; Jeffrey Markowitz, Ph.D., *Luella Engelhart, M.A.*

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the importance of atypical antipsychotic sedation on quality of life.

Summary:

Objective: Atypical antipsychotic drug sedation is a side effect that can impact patient QOL. This study examines the effect of atypical antipsychotic drug sedation on QOL as measured by the Psychological General Well-Being Scale (PGWB).

Method: Schizophrenia patients (N=519) who were identified through the National Alliance for the Mentally Ill and community

health centers completed a self-administered questionnaire. PGWB scale scores by sedation frequency (absent/low and high) were analyzed, as were demographics and antipsychotic drug use. Multivariate analysis was done to control for confounders.

Results: 36.6% had high sedation. High sedation frequency varied by antipsychotic drug type (quetiapine, 56.3%; clozapine, 41.5%; ziprasidone, 33.3%; risperidone, 30%, and olanzapine, 25.5%). Patients who had high sedation had significantly lower QOL (i.e., lower PGWB scale scores) than those with absent/low sedation for total PGWB scores (59.4 vs. 65.6, $p=0.0016$) as well as for all subscale scores [anxiety (13.2 vs. 14.6, $p=0.0094$), self-control (8.9 vs. 9.6, $p=0.0385$), depressed mood (9.0 vs. 9.8, $p=0.035$), general health (7.7 vs. 8.7, $p=0.0012$), vitality (9.9 vs. 11.5, $p=0.0003$)] except positive well-being (10.7 vs. 11.5, $p=0.087$).

Conclusion: Atypical antipsychotic sedation can have a negative effect on QOL. Its impact on patient QOL should be considered when prescribing atypical antipsychotics.

References:

1. Lader Malcolm: Some adverse effects of antipsychotics: Prevention and treatment. *Journal of Clinical Psychiatry* 1991; 60 (suppl. 12): p18-21, 1999.
2. Owens DG: Adverse effects of antipsychotics agents. do newer agents offer advantages. *Drugs* 1996; 51:(6) 895-930.

NR766 Thursday, May 26, 12:00 p.m.-2:00 p.m. **Frequent Users of Psychiatric Emergency Services**

Jagoda Pasic, M.D., *Harborview Medical Center, Department of Psychiatry & Behavioral Sciences, 325 Ninth Street Box 359896, Seattle, WA 98104-2499*; Joan Russo, Ph.D., Peter P. Roy-Byrne, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the sociodemographic and clinical characteristics of frequent utilizers of psychiatric emergency services. They will also be able to appreciate and value using different definitions of high utilization.

Summary:

This study's objective was to examine the sociodemographic and clinical characteristics of frequent users (FU) of psychiatric emergency services (PES).

Methods: Data were collected over a four-year period from 761 FU, identified by three definitions (2SD above the mean visit number in four years, six visits per year (YR6), and four visits per quarter (Q4)), and 1,585 non-frequent users (NFU). Regression models were used to determine the group differences.

Results: Two distinct FU groups emerged: FUQ4 and FU2SD. Compared with NFU, more FU patients were homeless, with developmental delay, enrolled in mental health plan, with history of hospitalizations, uncooperativeness, personality disorders, unreliable social support, and lifetime history of incarceration and detoxification. Compared with FUQ4, the FU2SD patients had more visits, were likely to have history of incarceration and psychiatric hospitalization, enrolled in mental health plan, and less likely to be homeless.

Conclusions: FU make up a small percentage of individuals seeking care in PES and disproportionately utilizing resources. Two distinct subpopulations of FU were identified: the more chronically and severely mentally ill (FU2SD) and the acutely sick, with a cluster of visits (FUQ4). The two definitions may be useful in guiding clinical interventions and mental health policies.

References:

1. Arfken C, Zeman L, Yeager L, et al.: Case-control study of frequent visitors to an urban psychiatric emergency service. *Psychiatric Services* 2004; 55:295-301.

2. Sullivan P, Bulik C, Forman S, et al.: Characteristics of repeat users of a psychiatric emergency service. *Hospital and Community Psychiatry* 1993; 44:376-380.

NR767 Thursday, May 26, 12:00 p.m.-2:00 p.m. **Impact of Educational Program on Adherence to Sertraline Therapy in the Primary Care Setting** *Supported by Pfizer Inc.*

Morgan Bron, Pharm.D., *Department of Outcome Research, Pfizer, Inc., 235 East 42nd Street, New York, NY 10017*; Ilan Fogel, M.D., John O'Neill, B.A.

Educational Objectives:

At the conclusion of this session, the participant should have an improved understanding of the importance of educational interventions to enhance adherence to prescribed therapies.

Summary:

Introduction: The objective of this study was to evaluate the impact of an educational program on adherence to prescribed treatment with sertraline in the primary care setting.

Methods: Consecutive patients from Verispan's Vector One pharmacy claim database who were prescribed sertraline (N=556; 83% female; mean age, 43 years) and who received an educational intervention ("Knowing More") were retrospectively matched along key demographic and clinical variables with concurrent patients who received no educational intervention. Pill consumption and patient therapy days were compared for both groups over a seven-month follow-up period.

Results: Participation in the program increased the length of sertraline therapy by a mean of 13.2 days compared with the control group (89.4 ± 7.0 vs. 76.1 ± 6.8 days; $P = 0.01$). The number of pills taken was also increased among program participants by a total of 19.7 (107.8 ± 9.4 vs. 88.1 ± 8.7 pills; $P < 0.01$). The program was most effective in increasing length of therapy in patients who had recently (in past three months) initiated treatment with sertraline (46.0 ± 8.1 vs. 64.2 ± 9.0 days; $P < 0.01$).

Conclusions: The educational program was associated with a significant increase in adherence to prescribed therapy in the primary care setting.

References:

1. Vergouwen AC, et al: Improving adherence to antidepressants: a systematic review of interventions. *J Clin Psychiatry* 2003; 64:1415-1420.
2. Lin EH, et al: Enhancing adherence to prevent depression relapse in primary care. *Gen Hosp Psychiatry* 2003; 25:303-310.

NR768 Thursday, May 26, 12:00 p.m.-2:00 p.m. **Efficacy of Pregabalin in Chronic Neuropathic Pain Syndromes** *Supported by Pfizer Inc.*

Teresa Griesing, Ph.D., *Pfizer Incorporated, 235 East 42nd Street, New York, NY 10017*; Krystof Strojek, M.D., Rainer Freynhagen, M.D., Michael Balkenohl, Ph.D.

Educational Objectives:

Participants in this presentation will garner a better understanding of pregabalin's efficacy for treating pain and associated sleep interference in patients who have diabetic peripheral neuropathy or postherpetic neuralgia.

Summary:

Objective: Neuropathic pain, resulting from injury to nerve tissue, is often chronic and can be intensely painful and debilitating.

This 12-week, double-blind, placebo-controlled trial of patients with chronic neuropathic pain (NeP) due to diabetic peripheral neuropathy (DPN, n=249) or postherpetic neuralgia (PHN, n=89) evaluated pregabalin's efficacy for the treatment of chronic NeP compared with placebo.

Methods: Patients were randomized to placebo (n=65), flexibly-dosed pregabalin (150-600 mg/day BID, n=141), or fixed-dose pregabalin (600 mg/day, n=132). Patients completed pain and sleep-interference diaries every morning on a waking. Primary efficacy parameter was endpoint mean pain score (from last seven diary entries). Pain-related sleep interference score was also evaluated.

Results: Both regimens of pregabalin significantly reduced endpoint mean pain score versus placebo (flexible, p=0.002 and fixed, p<0.001). Improvement was rapid: by week 1 in fixed-dose patients and by week 2 in flexible-dose patients. Both regimens of pregabalin also significantly improved sleep interference compared with placebo by week 1 (p≤0.01). The most common adverse events (AEs) for pregabalin-treated patients were dizziness, peripheral edema (non-CV/renal origin), weight gain (not affecting diabetes control), and somnolence.

Conclusions: Pregabalin quickly and efficaciously treats chronic NeP and associated sleep interference in patients with DPN or PHN.

References:

1. Sabatowski R, Gálvez R, Cherry DA, Jacquot F, Vincent E, Maisonobe P, et al: Pregabalin reduces pain and improves sleep and mood disturbances in patients with post-herpetic neuralgia: results of a randomized, placebo-controlled clinical trial. *Pain* 2004; 109:26-35.
2. Rosenstock J, Tuchman M, LaMoreaux L, Sharma U: Pregabalin for the treatment of painful diabetic peripheral neuropathy: a double-blind, placebo-controlled trial. *Pain* 2004; 110:628-638.

NR769 Thursday, May 26, 12:00 p.m.-2:00 p.m. Prevalence and Demographic Patterns of SAD in U.S. Adults

Supported by GlaxoSmithKline

Norman E. Rosenthal, M.D., *Department of Psychiatry, Georgetown University Medical School, 11110 Stephalee Lane, Rockville, MD 20852-3656*; Larry Anderson, Ph.D., Paul E. MacCosbe

Educational Objectives:

At the conclusion of this session, the participant should be able to determine the nationwide prevalence and demographic patterns of SAD among U.S. adults.

Summary:

Introduction: Estimates of the U.S. prevalence of SAD are 0.4% to 9.7% based on widely differing study sizes and methodology.

Objective: Determine the nationwide prevalence and demographic patterns of SAD among U.S. adults.

Methods: 30,000 adults (≥18yrs) were selected from a large volunteer panel (Ipsos-Insight) to achieve sample proportions similar to the U.S. Census using rim-weighting. An online, SPAQ-based questionnaire was sent to each volunteer. The respondent results were re-weighted by age within gender. SAD was identified using validated scoring.

Results: 13,359 questionnaires were completed (44.5% response). Estimated SAD prevalence was 7.8%(1042/13,359); 10.1% for women(700/6,933) and 5.3% for men (342/6,425). Prevalence by age categories ranged from 9.5%(30-39yrs) to 1.2% (70+yrs) and was highest between 18-59 yrs of age (7.3-9.5%). SAD was more prevalent among adults from lower income house-

holds(<\$50K/yr, 9.5-10.6% vs. \$50K/yr+, 5.7%) and among divorced adults(10.6% vs. 7.6% non-divorced). Prevalence of SAD followed an occupational trend: housewives, military, and unemployed (12.2%)>students (9.1%)>blue collar workers (8.0%)>retired (6.5%)>white collar workers (6.2%).

Conclusions: This is the first nationwide study to establish the prevalence of SAD in the U.S. using the SPAQ. The results of this study agree with previous regional estimates using the SPAQ. Clinical implications will be discussed.

References:

1. Blazer DG, Kessler RC, Swartz MS: Epidemiology of recurrent major and minor depression with a seasonal pattern. The National Comorbidity Survey. *Br J Psychiatry* 1998; 172:164-167.
2. Mersch PP, Middendorp HM, Bouhuys AL, Beersma DG, van den Hoofdakker RH: Seasonal affective disorder and latitude: a review of the literature. *J Affect Disord* 1999; 53(1):35-48.

NR770 Thursday, May 26, 12:00 p.m.-2:00 p.m. SAD: Environmental and Demographic Predictors in U.S. Adults

Supported by GlaxoSmithKline

Jack G. Modell, M.D., *GlaxosmithKline, Five Moore Drive, Research Triangle Park, NC 27713*; Larry Anderson, Ph.D., Paul E. MacCosbe

Educational Objectives:

At the conclusion of this presentation, the participant will have an understanding of the environmental and demographic variables associated with the prevalence of SAD in U.S. adults.

Summary:

Introduction: It has been suggested that the prevalence of seasonal affective disorder (SAD) in the U.S. is primarily driven by latitude, but contributory or confounding factors remain to be elucidated.

Objective: To develop a predictive model of SAD prevalence based on geographic, climatologic, and demographic variables.

Methods: 30,000 adults (≥18yrs) in the continental U.S. were selected from a large volunteer panel (Ipsos-Insight) to match U.S. census proportions. Each received an online questionnaire based on the Seasonal Pattern Assessment Questionnaire (SPAQ). SAD was identified using standard SPAQ scoring. Each respondent's address was coded to latitude and longitude. Binary logistic regression was used to develop a model containing both categorical and continuous variables.

Results: 13,359 surveys were completed (44.5% response). A strong association was found between SAD prevalence and seasonal variation in the number of hours of day-length (latitude). Associations were also found with climatologic averages for cloudiness, size of the city where the respondent lives, age, gender, marital status, and employment status. Other potential contributors were also identified.

Conclusions: Seasonal variation in day-length (latitude) is a strong contributor to the prevalence of reported SAD, but independent demographic climatologic and other factors also play a significant role.

References:

1. Low KG, Feissner JM: Seasonal Affective disorder in college students: prevalence and latitude. *J Am Coll Health* 1998; 47(3):135-137.
2. Mersch PP, Middendorp HM, Bouhuys AL, Beersma DG, van den Hoofdakker RH: Seasonal affective disorder and latitude: a review of the literature. *J Affect Disord* 1999; 53(1):35-48.

NR771 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Analog Classroom Study of Amphetamine and Atomoxetine in Girls With ADHD

Supported by Shire US, Inc.

Joseph Biederman, M.D., *Department of Psychiatry, Massachusetts General Hospital, 55 Fruit Street, Warren Building 705, Boston, MA 02114*; Sharon B. Wigal, Ph.D., Thomas J. Spencer, M.D., James J. McGoough, M.D., David A. Mays, Ph.D., Garrick Fiddler, M.D.

Educational Objectives:

After reviewing this poster, the participant should be able to compare the behavioral effects of mixed amphetamine salts extended release (MAS XR) and atomoxetine for the treatment of girls aged 6 to 12 years with attention-deficit/hyperactivity disorder (ADHD).

Summary:

Objective: To compare the time course and efficacy of mixed amphetamine salts extended release (MAS XR; Adderall XR[®]) with a once-daily selective norepinephrine reuptake inhibitor (atomoxetine; Strattera[®]) in school-aged girls (6-12 years) with attention-deficit/hyperactivity disorder (ADHD).

Methods: This is a subanalysis of girls who participated in a multicenter, randomized, double-blind, forced-dose-escalation analog classroom study. Subjects were randomized in a 1:1 ratio to receive once-daily MAS XR (maximum dose, 30 mg/d) or atomoxetine (maximum dose, 1.2 mg/kg/d). Efficacy measures included the SKAMP Teacher Rating Scale and an objective math test assessed at baseline and again at three weekly laboratory school visits.

Results: The girls ITT sample included 57 subjects (MAS XR, n=26 and atomoxetine, n=31). Improvements in mean SKAMP deportment and attention scores were significantly greater for the MAS XR group compared with atomoxetine overall (deportment, -0.48 vs -0.04, respectively, $P < 0.0001$; attention, -0.45 vs -0.05, respectively, $P = 0.0004$) and at each week ($P < 0.05$). Overall, girls receiving MAS XR attempted significantly more math problems than girls receiving atomoxetine ($P = 0.04$). Both MAS XR and atomoxetine were well tolerated by girls, and most AEs were mild or moderate.

Conclusion: MAS XR improved behavior, attention, and academic productivity significantly more than atomoxetine in school-aged girls with ADHD.

References:

1. Biederman J, Mick E, Faraone SV, et al: Influence of gender on attention deficit hyperactivity disorder in children referred to a psychiatric clinic. *Am J Psychiatry* 2002; 159:36-42.
2. Biederman J, Heiligenstein JH, Faries DE, et al: Efficacy of atomoxetine versus placebo in school-age girls with attention-deficit/hyperactivity disorder. *Pediatrics* 2002; 110:e75.

NR772 Thursday, May 26, 12:00 p.m.-2:00 p.m.

A Ten Year Follow-Up Study of Males With ADHD

Joseph Biederman, M.D., *Department of Psychiatry, Massachusetts General Hospital, 55 Fruit Street, Warren Building 705, Boston, MA 02114*; Stephen Faraone, Ph.D., Eric Mick, Sc.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to see the high morbidity associated with ADHD and the importance of early recognition of this disorder for prevention and early intervention strategies.

Summary:

Introduction: Despite the clinical importance of understanding the long-term outcome of children with attention-deficit/hyperactivity disorder (ADHD), there is a lack of research following ADHD children into adulthood.

Methods: Using DSM-IV structured diagnostic interviews and blind raters, we re-examined psychiatric diagnoses as well as evaluated cognitive, social, and other areas of functioning at 10-year follow-up into young adult years of male ADHD and control subjects.

Results: At the ten-year follow up into young adult years, 112 (80%) and 105 (88%) of the ADHD and control children, respectively, were re-assessed at a mean age of 22 years. The lifetime prevalence for all categories of psychopathology (i.e., major psychopathology, antisocial disorders, developmental disorders, and substance dependence disorders) was significantly greater in ADHD young adults compared with controls.

Conclusions: By their young adult years, ADHD youth were at very high risk for a wide range of comorbid outcomes including markedly elevated rates of antisocial and addictive disorders as well as mood and anxiety disorders. These prospective findings provide further evidence for the high morbidity associated with ADHD and the importance of early recognition of this disorder for prevention and early intervention strategies.

References:

1. Biederman JS, Faraone, et al: A prospective 4-year follow-up study of attention-deficit hyperactivity and related disorders. *Archives of General Psychiatry* 1996; 53(5):437-46.
2. Seidman LJ, Biederman J, et al: Learning disabilities and executive dysfunction in boys with attention deficit hyperactivity disorder. *Neuropsychology* 2001; 15(4):544-556.

NR773 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Females With ADHD: A Five-Year, Follow-Up Study

Joseph Biederman, M.D., *Department of Psychiatry, Massachusetts General Hospital, 55 Fruit Street, Warren Building 705, Boston, MA 02114*; Stephen Faraone, Ph.D., Eric Mick, Sc.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the severity of ADHD in females.

Summary:

Introduction: Literature about ADHD is almost exclusively based on male subjects. The aim of this study was to examine the course and outcome of ADHD in females assessed at baseline and five years later.

Methods: At five year follow up 80% of control (n=96) and 90% of ADHD (N=126) girls (age 16.7 ± 3.4 yrs) were reassessed. Subjects were assessed with structured diagnostic interviews and psychometric tests assessing multiple domains of functioning by blinded raters.

Results: At follow up, our longitudinal analyses indicated that the syndromic remission (no longer meeting full DSM-IV criteria) of ADHD in girls aged 13-15 was 10% and of girls aged 19-21 was 50%. However, 80% of the oldest subjects continued to report residual symptoms of the disorder associated with clinically significant impairment. Girls with ADHD had lower IQ and achievement scores and more impairment on measures of various domains of functioning. Over the course of follow-up the incidence of psychiatric comorbidity was significantly greater in ADHD girls: They were more likely to onset with major depression, conduct disorder, and bipolar disorder than were control subjects.

Conclusions: These results support the severity of ADHD in females.

References:

1. Biederman J, Faraone SV, et al: Clinical correlates of ADHD in females: findings from a large group of girls ascertained from pediatric and psychiatric referral sources. *Journal of the American Academy of Child and Adolescent Psychiatry* 1999; 38(8):966-975.
2. Faraone SV, Biederman J, et al: Family study of girls with attention deficit hyperactivity disorder. *American Journal of Psychiatry* 2000; 157(7):1077-83.

NR774 Thursday, May 26, 12:00 p.m.-2:00 p.m. **An Open-Label Study of Ziprasidone in Children With Bipolar Disorder**

Joseph Biederman, M.D., *Department of Psychiatry, Massachusetts General Hospital, 55 Fruit Street, Warren Building 705, Boston, MA 02114*; Theresa Harpold, M.D., Paul Hammerness, M.D., Eric Mick, Sc.D., Meghan Dougherty, B.S., Megan Aleardi, B.A., Edin Randall, B.A.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the relative impact of ziprasidone in children and adolescents with bipolar disorder.

Summary:

Introduction: Bipolar disorder in children is associated with high levels of severity of illness and functional impairments. This study aimed to assess the impact of ziprasidone in youth with BPD.

Methods: This was an open-label, eight-week, prospective study of ziprasidone monotherapy in the treatment of youth with DSM-IV bipolar disorder manic, mixed, and NOS. Severity of manic symptomatology was rated using the Young Mania Rating Scale at baseline and weekly throughout the study. Improvement was rated using the Clinical Global Impression. Medication was titrated according to response and tolerability. At endpoint, the mean dose was 56.2 ± 34.3 mg/day.

Results: Twenty-one subjects were enrolled in the study with a mean age of 10.6 ± 3.4 years. At baseline the mean YMRS score was 26.2 ± 7.4 . Over eight weeks of treatment, there were significant reductions in symptoms of mania with mean change score of 10.8 ± 8.4 , $p < 0.0001$. Clinical ratings on the CGI indicate that 57% of subjects were much or very much improved. There was a moderate increase in prolactin levels associated ziprasidone (9.5 ± 9.5 ng/dL). The mean weight gain was 0.6 ± 2.1 kg.

Conclusions: This pilot, open-label study suggests that ziprasidone reduces manic symptomatology in youth with bipolar disorder. Future placebo-controlled, double-blind studies of ziprasidone are warranted in this population.

References:

1. Keck PE Jr., Versiani M, et al: Ziprasidone in the treatment of acute bipolar mania: a three-week, placebo-controlled, double-blind, randomized trial. *Am J Psychiatry* 2003; 160(4):741-8.
2. Perlis R, Miyahara HS, et al: Long-term implications of early onset in bipolar disorder: Data from the first 1000 participants in the systematic treatment enhancement program for bipolar disorder (STEP-BD). *Biological Psychiatry* 2004; 55(9):875-81.

NR775 Thursday, May 26, 12:00 p.m.-2:00 p.m. **A Double-Blind, Placebo-Controlled, Randomized Study of OROS Methylphenidate in the Treatment of Adults With ADHD: An Interim Analysis**

Joseph Biederman, M.D., *Department of Psychiatry, Massachusetts General Hospital, 55 Fruit Street, Warren Building 705, Boston, MA 02114*; Thomas Spencer, M.D., Craig

Surman, M.D., Eric Mick, Sc.D., Stephanie Dunkel, B.A., Meghan Dougherty, B.S., Megan Aleardi, B.A.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that treatment with OROS methylphenidate is effective and well tolerated in adults with ADHD.

Summary:

Introduction: Despite increasing recognition of the safety and efficacy of OROS®-methylphenidate (MPH) in the treatment of children with ADHD, there is little information on its safety and efficacy in the management of adults with this disorder.

Methods: This was a double-blind, placebo-controlled, six-week randomized clinical trial of OROS MPH versus a placebo, administered once a day in the morning, in the treatment of 65 adults with DSM-IV ADHD using standardized instruments for the assessment of ADHD symptoms. OROS MPH or placebo was initiated at 36 mg per day and increased by 36 mg per week based on response and tolerability up to a maximum daily dose of 1.3 mg/kg/day.

Results: LOCF analysis revealed that treatment with OROS MPH at a mean dose of 88.1 ± 27.4 mg/day significantly reduced the symptoms of ADHD and was very well tolerated. Treatment with OROS MPH at daily doses below 72 mg was numerically better for OROS MPH vs. placebo; however, the difference between the two groups did not reach statistical significance.

Conclusion: Treatment with OROS MPH at daily doses above 72 mg was effective and well tolerated in the acute treatment of adults with ADHD.

References:

1. Spencer T: ADHD treatment across the life cycle. *Journal of Clinical Psychiatry* 2004; 65 (Suppl 3):22-26.
2. Wilens T: Safety and efficacy of OROS methylphenidate in adolescents with ADHD. *American Psychiatric Association 2004 Annual Meeting, New York, NY, APA, 2004.*

NR776 Thursday, May 26, 12:00 p.m.-2:00 p.m. **A Workplace Simulation: Performance in ADHD Versus Control Subjects**

Joseph Biederman, M.D., *Department of Psychiatry, Massachusetts General Hospital, 55 Fruit Street, Warren Building 705, Boston, MA 02114*; Ronna Fried, Ed.D., Eric Mick, Sc.D., Megan Aleardi, B.A., Anya Potter, B.S., Katie Herzig, B.A.

Educational Objectives:

At the conclusion of this session, the participant should (1) be able to identify the underlying skills that have been documented to be necessary to be successful in today's workplace, (2) Be able to understand how the core symptoms of ADHD may have an effect of achievement in the work environment.

Summary:

Introduction: The main goal of this study was to evaluate adults with and without ADHD in a full day work simulation experience. We hypothesized that ADHD adults would show impairments on work simulated tasks, be observed with more off-task behavior, and relate more feelings of ADHD symptoms than matched controls.

Methods: We compared 18 adults with ADHD and 18 controls in a simulated workday on measures of self-reported ADHD symptoms, objective observations utilizing a structured instrument, and a variety of written tasks. All ADHD subjects were asked to abstain from taking their stimulant medication on the day that they took part in the simulation. Continuous data were analyzed with t-

tests and categorical data were analyzed using Pearson's chi-square test.

Results: Compared with controls, subjects with ADHD demonstrated impaired performance on reading comprehension and math fluency. Overall, there was a significant difference in the observer-rated and self-report for decompensation, but not attention. ADHD subjects reported subjective difficulty with hyperactivity on the majority of tasks completed.

Conclusion: These findings demonstrate that ADHD in adults is associated with significant deficits in performance on structured work-related tasks as well as on internal experiences and external observations of core symptoms of ADHD.

References:

1. Faraone SV, Biederman J, Spencer T, et al: Attention deficit hyperactivity disorder in adults: an overview. *Biological Psychiatry* 2000; 48:9-20.
2. Hinshaw SP, Peele P, Danielson L: Public health issues in ADHD: Individual, system, and cost burden of the disorder workshop. National Center on Birth Defects and Developmental Disabilities.

NR777 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Characterizing Impaired Driving in Adults With ADHD: A Controlled Study

Joseph Biederman, M.D., *Department of Psychiatry, Massachusetts General Hospital, 55 Fruit Street, Warren Building 705, Boston, MA 02114*; Carter Petty, M.A., Ronna Fried, Ed.D., Megan Aleari, B.A., Craig Surman, M.D., Karl Schweitzer, B.A.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to better understand the mechanisms that underlie poor driving behavior in individuals with ADHD.

Summary:

Introduction: Individuals with ADHD have been shown to have poor driving behavior compared with those without ADHD. We sought to confirm these previous findings as well as determine the correlates of poor driving behavior within the adults with ADHD.

Methods: We compared 26 adults with ADHD and 23 without ADHD on driving history using the Driver Behavior Questionnaire (DBQ).

Results: ADHD subjects had significantly poorer driving histories and driving behavior compared with control subjects. When ADHD subjects were stratified into high (N=15) and low (N=11) risk drivers based on their scores on the DBQ, ADHD high risk drivers had higher rates of ADHD combined type and nearly all comorbid disorders compared with the ADHD low risk drivers. Medium to large effects were found for processing speed and inhibition scores when comparing ADHD high and low risk drivers.

Conclusion: Our findings suggest that high and low risk drivers with ADHD can be identified using the DBQ. High-risk drivers differ from other drivers with ADHD by slow processing speed, higher rates of comorbidity, and high number of ADHD symptoms.

References:

1. Barkley R, Murphy K, et al: What contributes to the elevated driving risks in ADHD adults. *ADHD Report* 2003; 11(2):1-5.
2. Cox DJ, Merkel L, et al: Impact of methylphenidate delivery profiles on driving performance of adolescents with attention-deficit/hyperactivity disorder: A pilot study. *Journal of the American Academy of Child and Adolescent Psychiatry* 2004; 43(3):269-275.

NR778 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Cognitive Rehabilitation in Patients With Multiple Sclerosis

Silvia F. Balsimelli, *Department of Psychology Services, Santa Casa Sao Paulo, Cesario Mota Jr. 112, Sao Paulo, SP 01221-900, Brazil*; Maria Gragas Lima, M.S., Wilze L. Bruscato, D.R.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the importance of rehabilitation programs directed to patients with multiple sclerosis.

Summary:

Introduction: Multiple sclerosis may lead to cognitive impairments in young adults, generating strong impact in social and familiar life, and in work. These alterations vary from individual to individual. Rehabilitation programs directed to this pathology are scarce, but of great importance to the improvement of patients' quality of life. The aim of this study is to develop a rehabilitation program directed to the most frequent difficulties of this pathology.

Methods: 05 patients with relapsing-remitting M.S., with cognitive complaints, were selected, all with clinical and laboratorial diagnosis, defined by the Poser and cols. criteria. Patients were evaluated by neurologists, and incapacity was measured by the EDSS (Expanded Disability Status Scale), and by psychologists, through interviews and the application of the HAD Scale. A neuropsychological battery was applied, with the following tests: Digit Span, Trail Making, Stroop Test, Logical Memory, List of Words, and Analogue Visual Scale. The program developed involves restorative and ecological strategies. In the restorative strategy the Rehacom Program was utilized, adapted for the Portuguese language.

Results: 05 patients were evaluated by the Neuropsychological Battery, and no difference was observed as to cognitive performance, in the beginning and in the end of the rehabilitation. In the 06 dimensions evaluated by the Analogue Visual Scale, we observed an improvement of the cognitive functions labored on in the rehabilitation, acting in a positive way, in patients' performance.

Conclusion: Through the Analogue Visual Scale, we observed an improvement of the cognitive performance of the patients. These findings are important for the implement of a cognitive rehabilitation work for M.S. patients, leading to an adequate performance in professional, social, and familiar activities.

References:

1. Peyser JM, Edwards KR, Poser CM, Filskov SB: Cognitive function in patients with multiple sclerosis. *Archives of Neurology*, 1980; 37:577-579.
2. Rao SM: Cognitive and neuroimaging changes in multiple sclerosis. In Habreich U., *Multiple Sclerosis: A Neuropsychiatric Disorder*. American Psychiatric Press, Washington, 1993.

NR779 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Psychosocial Aspects Pre- and Post-Hepatic and Renal Transplantation

Rosana T. Rodrigues, M.S., *Department of Psychology Services, Santa Casa Sao Paulo, Cesario Mota Jr 112, Sao Paulo, SP 01221-900, Brazil*; Maria Gragas Lima, M.S., Sandra F. Amorim, M.S., Wilze L. Bruscato, D.R.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the importance to evaluate the psychosocial aspects in adults who underwent hepatic and renal transplantation.

Summary:

This study intended to describe psychosocial aspects pre and post hepatic and renal transplantation. A descriptive-transversal study evaluated 20 patients: 10 hepatic transplanted patients (5 men, 5 women) and 10 renal transplanted patients (5 men, 5 women), ages between 20 and 55 years old, with one to six years transplantation history. It was taken semistructured interviews with 40 minutes long in a private room at the Hepatic and Renal Transplantation Ambulatory. The data collected had been divided into different categories and then they were quantified. The major results found were related to pre-transplantation period: 30% (N=6) of the patients were involved in working activities and, after transplantation, 75% (N=15) of the patients had working activities involvement ($p < 0,0001$). Emotional conditions have been taken as positive in 15% (N=3) of the patients pre-transplantation and 75% (N=15) post-transplantation. The perception about the transplantation impact on life quality was considered positive for 80% (N=16) of the patients. Leisure activities at pre-transplantation period was taken as satisfactory for 60% (N=12) and 45% (N=11) for post-transplantation period. It was concluded that psychosocial aspects reported by the patients had been clearly better after transplantation and it appeared to have a positive influence at life quality and emotional condition of the patients. Leisure activities were not significantly better after transplantation what could be related to social and economical aspects as well as personality structure aspects of the patients.

References:

1. Bravata DM, Olkin I, Barnato AE, Keeffe EB Owens, DK: Health related quality of life after liver transplantation: a meta-analysis. *Liver Transplantation Surgery* 1999; 5(4):318-331.
2. Holzner B, Kemmler G, Kopp M, Dachs E, Kaserbacher R, Spechtenhauser B, Vogel W, Spermer-Unterweger B: Preoperative expectations and postoperative quality of life in liver transplant survivors. *Archives of Physical Medicine and Rehabilitation* 2001; 82(1):73-79.

NR780 Thursday, May 26, 12:00 p.m.-2:00 p.m. The Grasp of Life Experience of the Family Facing Hepatic Transplantation

Rosana T. Rodrigues, M.S., *Department of Psychology Services, Santa Casa Sao Paulo, Cesario Mota, Jr. 112, Sao Paulo, SP 01221-900*, Maria Gragas Lima, M.S., Wilze L. Bruscato, D.R., Ana Lucia M. Horta, Ph.D. *Brazil*

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the psychological aspects experienced by the family facing hepatic transplantation in one of its members.

Summary:

The aim of this study was to identify the life experience of a family facing hepatic transplantation in one of its members. It involves a qualitative analysis of the case of a four-member family in which one of the children has been through liver transplantation four years ago. It was taken five semi-structured interviews, which lasted approximately one hour long, in private rooms, during the period between September and November/2002. The first interview question intended to acquaint the life-experience process of transplantation. The interviews were recorded and transcribed and the contents were taken through the "Systemic Vision" as theoretical basis. It was verified, as major results, the anticipatory mourning experience which is responsible for stoppages at the family-system hindering individual development as well as affecting life quality. It was found out the built of a triangle process between the parents and the transplanted child which structure seems to work as a shield against couple detachment. Its conse-

quence for the child is the difficulty of achieving self-sufficiency. Since the beginning of the child's disease process, the family has become away from social conviviality which reduced the contact with the family's support net. It was taken the report of parental blame in relation with the child's disease process, loss of employment because of the treatment, financial difficulties, constant pressure and death fear. This study presents the difficulties faced by the family experiencing such situation and presents the proposal of family therapy during the attendance process of these patients and their families.

References:

1. McGoldrick M, Walsh F: Um Tempo para Chorar: A Morte e o Ciclo de Vida Familiar. In: Walsh, F, McGoldrick, M. *Morte na Familia: Sobrevivendo às Perdas*. Artmed. Porto Alegre, 1998.
2. Minuchin S: *Familias-Funcionamento e Tratamento*. Artes Médicas. Porto Alegre, 1990.

NR781 Thursday, May 26, 12:00 p.m.-2:00 p.m. Remission in Depression After Treatment Failure Supported by Wyeth Pharmaceuticals

Carmen Garcia-Caluo, M.D., *Medical Department, Wyeth Farma, CTRA Burgos KM 23, Madrid 28080, Spain*; Rita Prieto, M.D., Jose Giner, M.D., Enrique Baca-Baldomero, Jucio Vallejo

Educational Objectives:

Management of patients with antidepressant treatment failure.

Summary:

Objective: To compare the effectiveness of venlafaxine extended release (VXR) and conventional antidepressants (CA) in patients referred to psychiatry from primary care due to intolerance or lack of response after a minimum of four weeks of CA treatment.

Methods: Randomized, open-label, multicenter study on depressive patients with a Hamilton Depression Rating Scale (HAM-D₁₇) score ≥ 17 . Patients received six months of treatment with VXR or another CA different from the one taken previously. Remission was defined as a HAM-D₁₇ score ≤ 7 .

Results: Analysis of remission rates of 1,632 patients treated with VXR and 1,245 patients treated with the five CA most frequently used: paroxetine (312 patients), citalopram (294 patients), sertraline (279 patients), fluoxetine (248 patients) and mirtazapine (116 patients). After six months of treatment, VXR achieved a rate of remission of 59.3%, higher than the one achieved by paroxetine (51.6%; $p = 0.015$), citalopram (52.0%; $p = 0.024$), sertraline (52.7%; $p = 0.042$), fluoxetine (52.0%; $p = 0.032$) and mirtazapine (44.8%; $p = 0.003$).

Conclusions: Results suggest that venlafaxine extended release may be more effective in the treatment of depression than conventional antidepressants, mainly selective serotonin reuptake inhibitors (SSRIs), in patients who have failed a previous CA treatment.

References:

1. Thase ME: Remission rates during treatment with venlafaxine or selective serotonin reuptake inhibitors. *Br J Psychiatry* 2001; 178(3):234-241.
2. Einarson TR, Arikian SR, Casciano J, Doyle JJ: Comparison of extended-release venlafaxine, selective serotonin reuptake inhibitors, and tricyclic antidepressants in the treatment of depression: a meta-analysis of randomized controlled trials. *Clin Ther* 1999; 21:296-308.

NR782 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Symptom Excursions During Initial Mood Stabilization in Bipolar I Studies

Supported by GlaxoSmithKline

Ronald E. Westlund, M.S., Department of Department of Neuroscience, GlaxoSmithKline, 5 Moore Drive, Research Triangle Park, NC 27709; Theodore C. Spaulding, Ph.D., Thomas R. Thompson, M.D., Gary E. Evoniuk, Ph.D., Robert A. Leadbetter, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to develop an appreciation that in bipolar I disorder, symptoms of opposite polarity than the presenting mood can occur during stabilization of mood. Stabilization is affected by the severity of symptom excursions.

Summary:

Objective: Determine the incidence and severity of symptom excursions of opposite polarity and their influence on stabilization (randomization) for subjects entering clinical trials with episodes of depression (DEP) or mania (MAN).

Methods: Preliminary phases of lamotrigine trials GW605/2003 and GW606/2006 were assessed post-hoc. Subjects with DEP (N=911) were evaluated for manic excursions (MRS-11 \geq 10) and with MAN (N=216) for depressive excursions (HAMD-17 \geq 10). Symptom excursion categories were based on the maximum symptom score achieved (10 to <14, and \geq 14). A score maintained below 10 was considered no symptom excursion.

Results: For DEP, 22% exhibited manic excursions, and 42% of subjects with MAN exhibited depressive excursions. In subjects with DEP, the incidence of manic excursions were 13% (\geq 14), 9% (10 to <14), and 78% (no excursion) with respective stabilization rates of 34%, 47% and 50% (p=0.007). In subjects with MAN, the incidence of HAMD excursions were 25% (\geq 14), 17% (10 to <14), and 58% (no excursion) with respective stabilization rates of 28%, 57% and 65% (P<0.001). Baseline mood severity was similar among excursion categories in DEP and MAN.

Conclusion: Depressive excursions during MAN are more frequent than manic excursions during DEP and excursions may serve as a predictive marker of mood stabilization.

References:

1. Judd L, Akiskal H, Schettler P, Endicott J et al: Archives of General Psychiatry 2003; 60:392-400
2. Goodwin G, Bowden C, Calabrese J, Grunze H et al: Journal of Clinical Psychiatry 2004; 65:432-441.

NR783 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Concomitant Lamotrigine and Atypical Antipsychotics in Bipolar I Disorder

Supported by GlaxoSmithKline

Charles L. Bowden, M.D., Department of Psychiatry, University of Texas, Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78229-3900; Joseph R. Calabrese, M.D., Ronald E. Stewart, M.S., Angela M. Deveaugh-Geiss, M.S., Thomas R. Thompson, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to have an understanding of the safety and efficacy of concomitant use of lamotrigine and atypical antipsychotics.

Summary:

Objective: To retrospectively evaluate the clinical response and tolerability of concomitant lamotrigine and atypical antipsychotics in bipolar I disorder.

Methods: Pooled data from the eight- to 16-week, open-label preliminary phase (OLPP) of two maintenance trials (GW605/606) in bipolar I disorder were examined, including psychiatric rating scales and adverse events for all patients enrolled in the OLPP. Patients were administered lamotrigine as adjunctive or monotherapy.

Results: 196 of 1,305 (15%) patients received lamotrigine and atypical antipsychotics (olanzapine, risperidone, quetiapine fumarate, and clozapine) (median duration=6.9 weeks). Mean \pm SD observed CGI-S and GAS scores for patients on lamotrigine and atypical antipsychotics were 4.5 \pm 0.8 and 46.6 \pm 10.3, respectively, at study entry and 3.2 \pm 1.4 and 61.6 \pm 17.9, respectively, at the end of the OLPP. Adverse events were similar in patients who received lamotrigine and atypical antipsychotics and those on lamotrigine without atypical antipsychotics; the most common adverse events (>10%) were headache (19% vs. 25%), nonserious rash (9% vs. 10%), infection (8% vs. 11%), nausea (8% vs. 12%), and dizziness (7% vs. 10%). No serious rash was reported by patients on concomitant lamotrigine and atypical antipsychotics.

Conclusion: Lamotrigine appears to be safe and effective when used in combination with atypical antipsychotics in patients with bipolar I disorder.

References:

1. Bowden C, Calabrese J, Sachs G, Yatham L, et al: A placebo-controlled 18-month trial of lamotrigine and lithium maintenance treatment in recently manic or hypomanic patients with bipolar I disorder. Archives of General Psychiatry 2003; 60(4):392-400.
2. Calabrese J, Bowden C, Sachs G, Yatham L, et al: A placebo-controlled 18-month trial of lamotrigine and lithium maintenance treatment in recently depressed patients with bipolar I disorder. Journal of Clinical Psychiatry 2003; 64(9):1013-24.

NR784 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Amisulpride Versus Quetiapine Treatment of Delirium: A Prospective, Randomized, Open Trial

Kyoung-UK Lee, St. Mary's Hospital, 65-1 Kumoh-Dong, Uijeongbui-Si, Gyeonggi-Do 480-130, South Korea; Hae-Kook Lee, M.D., Yong-Sil Kweon, M.D., Chung Tae Lee, M.D., In-Chul Choi, M.D.

Educational Objectives:

Amisulpride as well as quetiapine may be useful drugs in the treatment of delirium due to its efficacy and relative lack of adverse events.

Summary:

Objective: The purpose of the present study is to provide preliminary data on the efficacy and tolerability of atypical antipsychotics amisulpride and quetiapine, for patients with delirium.

Methods: Forty patients were randomly assigned to either amisulpride (AMSP) or quetiapine (QTP) group. All the subjects were given with a flexible dose. Treatment was terminated as the CGI score had reached 2 or less. The Delirium Rating Scale-revised-98 (DRS-R-98), total sleep time and quality of sleep were assessed every day.

Results: Sixteen subjects in AMSP group and 15 subjects in QTP group completed the study. After treatment, DRS-R-98 score was significantly decreased from 10.6 \pm 4.3 to 3.6 \pm 1.4 in AMSP group and from 10.1 \pm 4.1 to 3.5 \pm 2.6 in QTP group (P<0.001), but there was no group difference. The mean duration of treatment was 6.5 \pm 4.5 days for AMSP group and 7.8 \pm 4 days for QTP group, and there was no group difference (P<0.001). There was no group difference in the mean quality of sleep score and the mean total sleep time.

Conclusions: Amisulpride as well as quetiapine may be useful drugs in the treatment of delirium due to its efficacy and relative lack of adverse events.

References:

1. Sasaki Y, Matsuyama T, Inoue S, Sunami T, Inoue T, Denda K, Koyama T: A prospective, open-label, flexible-dose study of quetiapine in the treatment of delirium. *J Clin Psychiatry* 2003; 64:1316-1321.
2. Parellada E, Baeza I, de Pablo J, Martinez G: Risperidone in the treatment of patients with delirium. *J Clin Psychiatry* 2004; 65:348-353.

NR785 Thursday, May 26, 12:00 p.m.-2:00 p.m.
DBT Skills Group for Treatment of Patients With Bipolar Disorders: A Retrospective Chart Review

Jenifer Culver, Ph.D., *Department of Psychiatry and Behavioral Science, Stanford University School of Medicine, 401 Quarry Road, Stanford, CA 94305*; Bruce Arnow, Ph.D., Adrienne Clark, Po Wang, M.D., Terence Ketter, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize DBT skills group as possible adjunctive psychosocial treatment for patients with bipolar disorders.

Summary:

Objective: To assess the effectiveness of Dialectical Behavior Therapy (DBT) skills group in treatment of patients with bipolar disorders.

Method: Retrospective chart review of patients assessed with the Systematic Treatment Enhancement Program (STEP-BD) Affective Disorders Evaluation (ADE) and followed with the STEP-BD Clinical Monitoring Form (CMF).

Results: Sixteen female patients (age 40.0 ± 12.0) with bipolar disorders (5 type I, 9 type II, 2 NOS) received DBT skills group for 17.1 ± 8.7 sessions over a period of 22.9 ± 12.4 weeks. Patients showed a 28% decrease in days spent with depressed mood ($29.4\% \pm 34.3$ to $21.3\% \pm 29.2$, $p < .01$), a 37% decrease in days spent with anhedonia ($35.6\% \pm 39.5$ to $22.5\% \pm 30.7$, $p < .01$), a 29% decrease in severity of anhedonia ($1.06 \pm .93$ to $.75 \pm .93$, $p < .01$), a 27% decrease in distractibility scores ($.41 \pm .46$ to $.30 \pm .36$, $p = .03$), and a 7% increase in Global Assessment of Functioning scores (61.5 ± 7.8 to 65.9 ± 6.7 , $p < .001$). A subanalysis of patients reporting suicidal ideation at the beginning of treatment ($n=5$) indicated an 83% decrease in suicidal ideation scores ($.60 \pm .22$ to $.10 \pm .22$, $p = .03$).

Conclusion: Results suggest that patients with bipolar disorders may benefit from participation in DBT skills groups. Controlled studies are warranted to systematically explore these preliminary observations.

References:

1. Linehan MM: Skills training manual for treating borderline personality disorder. New York, Guilford, 1993.
2. Johnson SL, Leahy RL (eds): Psychological treatment of bipolar disorder. New York, Guilford, 2003.

NR786 Thursday, May 26, 12:00 p.m.-2:00 p.m.
A 12-Week, Randomized Study of Dermatological Precautions With Lamotrigine in Patients With Bipolar Disorder
Supported by GlaxoSmithKline

Terence A. Ketter, M.D., *Department of Psychiatry, Stanford University, School of Medicine, 401 Quarry Road, Room 2124,*

Stanford, CA 94305-5723; Jay Graham, Pharm.D., Jeremy Roberts, M.S.C., Angela M. Deveaugh-Geiss, M.S., Thomas R. Thompson, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the limitations of dermatology precautions (limiting antigen exposure) during the first three months of treatment with lamotrigine in efforts to yield a low incidence of rash.

Summary:

Objective: Rash has been reported in about 10% of patients receiving lamotrigine. An open, uncontrolled case series suggested that utilizing dermatology precautions (DP, precautions to decrease environmental sources of rash) may yield a lower (5/100, 5%) incidence of lamotrigine treatment-emergent rash. We assessed DP versus usual care precautions (UCP) in a randomized trial.

Methods: Adult bipolar disorder patients were randomized to receive either blinded DP or UCP for 12 weeks while open lamotrigine was initiated, titrated adjusting for concomitant bipolar medications to a target dose of 200 mg/day, and maintained. Rates of rash, tolerability, and clinical responses (CGI-BP) were compared with DP versus UCP.

Results: 180 sites enrolled 1,175 subjects. No serious rash was reported. Rates of non-serious rash were 50/584 (8.6%) with DP and 52/591 (8.8%) with UCP. Adverse events included headache (8%), dizziness (5%), and insomnia (5%). Mean CGI-BP scores improved or remained stable similarly in both groups.

Conclusions: Lamotrigine was generally well-tolerated. DP and UCP had similar (8.6%-8.8%) rates of non-serious rash, that were marginally lower than the approximately 10% rate reported previously. Possible reasons for the lack of replication of the even lower (5%) rate reported in an open, uncontrolled case series will be discussed.

References:

1. Ketter TA, Wang PW, Chandler RA, Alarcon AM, Becker OV, Nowakowska C, O'Keeffe CM, Schumacher MR: Dermatology precautions yield low incidence of lamotrigine treatment-emergent rash. *J Clin Psychiatry*, in press.
2. Calabrese JR, Sullivan JR, Bowden CL, et al.: Rash in multicenter trials of lamotrigine in mood disorders: clinical relevance and management. *J Clin Psychiatry* 2002; 63(11):1012-1019.

NR787 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Wellbutrin XL Treatment of Adults With MDD
Supported by GlaxoSmithKline

A. John Rush, M.D., *Department of Psychiatry, University of Texas, SW Medical Center, 5323 Harry Hines Boulevard, MC9086, Dallas, TX 75390-9086*; Donna Wightman, R.Ph., Alok Krishen, M.S.C., Susan A. Vanmeter, M.D., Jack G. Modell, M.D., Kenneth D. Hampton, B.S.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that Wellbutrin XL appears to provide adequate treatment for Major Depressive Disorder in adult outpatients with the specific symptomatology of decreased energy, pleasure, and interest. In this placebo-controlled, randomized, double-blind 8-week study, Wellbutrin XL was generally well-tolerated and no serious adverse events were reported.

Summary:

Objective: The purpose of this study was to evaluate Wellbutrin XL versus placebo in adults with MDD and the specific symptomatology of decreased energy, pleasure, and interest.

Methods: A total of 274 adult outpatients with a DSM-IV diagnosis of MDD including decreased energy, pleasure, and interest, as measured by a minimum total score of 7 on the general interest, energy, pleasure, sexual interest, and physical energy items of the Inventory of Depressive Symptomatology (IDS) were enrolled in this placebo-controlled, randomized, double-blind, eight-week study. Patients received 300 to 450 mg per day of Wellbutrin XL or matching placebo.

Results: The IDS-Self Report (IDS-SR) and Clinician Rated (IDS-C) versions were used to measure efficacy. Changes from randomization in both IDS-SR total score and IDS-C total score at week 8 were significantly different between the two treatment groups, $p = .018$ and $p < .001$, respectively. IDS-SR remission rate was 41% in the Wellbutrin XL group compared with 27% in the placebo group, $p = .01$. Wellbutrin XL was generally well-tolerated and no serious adverse events were reported.

Conclusions: These data indicate that Wellbutrin XL is an effective and well-tolerated treatment for adults with MDD including symptoms of decreased energy, pleasure, and interest.

References:

1. Rush AJ, Giles DE, Schlessner MA, Fulton CL, Weissenburger J, Berns C: The Inventory for Depressive Symptomatology (IDS): Preliminary Findings. *Psychiatry Research* 1986; 18:65-87.
2. Rush AJ, Gullion CM, Basco MR, Jarrett RB, Trivedi MH: The Inventory of Depressive Symptomatology (IDS): psychometric properties. *Psychological Medicine* 1996; 26: 477-486.

NR788 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Adjunctive Ziprasidone for Resistant Depression: An Eight-Week Pilot Study

Supported by Pfizer Inc.

David L. Dunner, M.D., *Department of Psychiatry, University of Washington, 4225 Roosevelt Way NE, 306C, Seattle, WA 98105-6099*; Jay D. Amsterdam, M.D., Richard C. Shelton, M.D., Antony D. Loebel, M.D.

Educational Objectives:

At the conclusion of this presentation, participants should understand the role of ziprasidone augmentation in patients with treatment-resistant depression and its specific use with high-dose sertraline therapy.

Summary:

Objective: To evaluate adjunctive ziprasidone with sertraline (ZIP/SER) in treatment-resistant major depression without psychotic features.

Methods: Adults who failed ≥ 4 weeks of adequate therapy with ≥ 1 SSRI or non-SSRI antidepressants entered six-week, open trial of sertraline 100-200 mg/d (phase 1). Nonresponders were randomized to eight weeks of open-label sertraline (100-200 mg/d), SER/ZIP 80 mg/d, or SER/ZIP 160 mg/d (phase 2). Efficacy measures: LS mean change from baseline (phase 1 end) to endpoint (phase 2 end) in MADRS Total (primary), CGI-S, individual MADRS items, and MADRS responder rates.

Results: Phase 2 subjects included 20 on sertraline, 22 on ZIP/SER 80 mg/d, and 19 on ZIP/SER 160 mg/d. At endpoint, MADRS Total change was greater with ZIP/SER 80 mg/d (-6.8) and 160 mg/d (-7.9) than with sertraline only (-4.1) ($P=NS$). Response rates ($\geq 50\%$ MADRS decrease) were 19%, 32%, and 10%, respectively ($P=NS$). Subjects given ZIP/SER 160 mg/d demonstrated greater mean change in MADRS Apparent Sadness ($P<0.05$), Lassitude ($P<0.01$), and CGI-S ($P<0.05$) than those on sertraline only. Combination therapy raised no specific safety concerns.

Conclusions: In treatment-resistant major depression, ziprasidone augmentation was associated with greater improvement in efficacy measures than sertraline monotherapy. Improvements and response rates were more robust with ziprasidone 160 mg/d vs 80 mg/d.

References:

1. Daniel DG, Zimbroff DL, Potkin SG, et al: Ziprasidone 80 mg/day and 160 mg/day in the acute exacerbation of schizophrenia and schizoaffective disorder: a 6-week placebo-controlled trial. *Neuropsychopharmacology* 1999; 20:491-505.
2. Papakostas GI, Petersen TJ, Nierenberg AA, et al: Ziprasidone augmentation of selective serotonin reuptake inhibitors (SSRIs) for SSRI-resistant major depressive disorder. *J Clin Psychiatry* 2004; 65:217-221.

NR789 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Branded Clozaril Versus Generic Clozapine: Economic and Clinical Outcomes

Supported by Ivax Pharmaceuticals

Michael J. Reinstein, M.D., *Department of Psychiatric Research, Forest Foundation, 4755 North Kenmore Avenue, Chicago, IL 60640*; John G. Sonnenberg, Ph.D., Sangarapillai C. Mohan, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to better understand the economic and clinical impact of switching from a branded drug to a generic equivalent.

Summary:

Objective/Background: Ivax brand clozapine is a generic equivalent to Novartis' Clozaril. Economic advantages of generics depend upon clinical interchangeability. This study compares economic and clinical outcomes for subjects before and after a switch to Ivax's clozapine from Novartis's Clozaril.

Methods: 190 mentally ill subjects residing in the same long-term care facility switched from Clozaril to generic clozapine. Clinical Global Inventories, clozapine blood levels, and medication costs were compared for the two-week period before and after the switch.

Results: The sample (148 males and 42 females) carried a mean age of 45.1 years (range=23-68, SD=9.6). The daily mean dose pre-switch was 341.0mg and post-switch was 338.4mg. The mean blood level pre-switch was 335.8 (SD=245.2) and post-switch was 343.8 (SD=240.0). The mean blood levels were statistically equivalent ($p>0.20$) differing 2.3%. The CGI-Severity score averaged 4.4 (SD=1.2), indicating subjects were moderately-markedly ill at baseline. The CGI-Improvement scale average 3.9 (SD=0.5), indicating no change from baseline. Calculated at the same dose for comparison, switching 190 subjects to the generic reduced the cost (paid by Illinois Medicaid) of a two-week supply from \$40,071 to \$25,204.

Conclusion: Novartis brand Clozaril and Ivax brand clozapine were clinically equivalent and the generic cost 36% less.

References:

1. Greenwood-Smith C, Lubman D, et al: Serum clozapine levels: a review of their clinical utility. *J Psychopharmacology* 2003; 17:(2) 234-238.
2. Makela EH, Cutlip WD II, et al: Branded vs. generic clozapine for treatment of schizophrenia. *Ann Pharmacother* 2003; 37:350-353.

NR790 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Link Between Adherence and Rehospitalization in Patients With Schizophrenia

Supported by Bristol-Myers Squibb and Otsuka Pharmaceuticals Co, Ltd

Gillis Carrigan, Ph.D., *Department of Epidemiology, Bristol-Myers Squibb, 5 Research Parkway, Wallingford, CT 06492*; Paul Cislo, M.S., Saurabh Ray, Ph.D., Vickie Tuomari, M.S., William H. Carson, Jr., M.D., Patricia Corey-Lisle, Ph.D.

Educational Objectives:

At the conclusion of this session, participants will have a better understanding of the relationship between treatment discontinuation and relapse, and to recognize significant predictors of rehospitalization from a large, generalizable managed care database.

Summary:

Objective: Research demonstrates antipsychotic tolerability impacts treatment adherence. Linking non-adherence and rehospitalization would establish real-world consequences. We examined the association between adherence and rehospitalizations using a large managed care database.

Methods: Antipsychotic-treated schizophrenic patients ≥ 18 years, hospitalized for psychosis between November 2002 and May 2004 ($n = 480$) were categorized as non-adherent either at time of switch from initial medication or medication discontinuation. Patients were followed from treatment initiation until rehospitalization, loss to follow-up, or end of study. Hazard ratios (HR) for the time-to-rehospitalization were estimated for adherent and non-adherent patients. Analyses were controlled for age, gender, region, and physician specialty, diagnosis, and initial hospital length of stay.

Results: Non-adherence was a statistically significant predictor of re-hospitalization (Adjusted H.R. = 4.6, 95% CI: 1.9-10.6). Other factors associated with risk of rehospitalization included age (≥ 65 years vs. 18-35 yrs, HR = 3.6, 95% CI: 1.24-10.58) and region (western region vs. Midwest, HR = 1.8, 95% CI: 1.07-2.95). Psychiatric-specialty treatment was protective against rehospitalizations (HR = 0.55, 95% CI: 0.35-0.87).

Conclusions: Non-adherence to initial antipsychotic regimens is a strong predictor of rehospitalization. Given the economic burden associated with rehospitalization, comprehensive strategies for improving adherence may lead to substantial cost savings.

References:

1. Valenstein M, Copeland LA, Blow FC, McCarthy JF, Zeber JE, Gillon L, Bingham CR, Stavenger T: Pharmacy data identify poorly adherent patients with schizophrenia at risk for admission. *Medical Care* 2002; 40:630-639.
2. Rabinowitz J, Lichtenberg P, Kaplan Z, Mark M, Nahon D, Davidson M: Rehospitalization rates of chronically ill schizophrenic patients discharged on a regimen of risperidone, olanzapine, or conventional antipsychotics. *Am J Psychiatry* 2001; 158(2):266-269.

NR791 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Ziprasidone Safety and Tolerability in Bipolar Mania: Review of Trial Data

Supported by Pfizer Inc.

Lewis Warrington, M.D., *Medical Department, Pfizer Incorporated, 235 East 42nd Street, New York, NY 10017-5755*; Judith Dunn, Ph.D., Francine Mandel, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be knowledgeable about the safety and tolerability of ziprasidone in patients with bipolar mania.

Summary:

Objective: To evaluate ziprasidone's safety/tolerability in bipolar mania.

Method: Dataset included 619 subjects from five Phase III trials—three randomized, 21-day, placebo-controlled trials, and two open-label extensions (≤ 104 weeks). Short-term subjects received flexibly-dosed ziprasidone (80, 120, or 160 mg/d) as monotherapy ($n=279$) or with lithium ($n=101$); extension subjects ($n=216$) received 40-160 mg/d. Analyses included incidence of treatment-emergent AEs, discontinuations, laboratory abnormalities, vital signs, ECGs.

Results: In short-term trials, AEs $\geq 10\%$ included somnolence, dizziness, akathisia, EPS, headache, and nausea with monotherapy; somnolence, EPS, tremor, insomnia, dizziness, agitation, and nausea with lithium. Serious AEs were mostly psychiatric and attributable to disease under study. Mean weight change was comparable for ziprasidone (1.5 lb men, 0.04 lb women) and placebo (0.02 and 0.31 lb, respectively) with short-term monotherapy, and was -2.6 lb in extensions. With short-term monotherapy, median changes in TChol and TG were -1.6 and 3.6 mg/dL for ziprasidone, 0 and -8 mg/dL for placebo. Median changes in other labs were comparable to placebo and not clinically meaningful in any group. There was no $QTc \geq 500$ msec.

Conclusions: Ziprasidone, with or without lithium, was well tolerated in both short- and long-term treatment of bipolar disorder, and exhibited weight/lipid-neutrality. These data are consistent with schizophrenia trials.

References:

1. Keck PE Jr, Versiani M, Potkin S, et al: Ziprasidone in the treatment of acute bipolar mania: a three-week, placebo-controlled, double-blind, randomized trial. *Am J Psychiatry* 2003; 160:741-748.
2. Keck PE Jr, Potkin S, Lombardo I, Batzar E: Efficacy and safety of ziprasidone in bipolar disorder: long-term data. Presented at the 56th Institute on Psychiatric Services. October 6-10, 2004; Atlanta, Georgia, USA.

NR792 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Sequential IM/Oral Ziprasidone Versus Haloperidol for Acute Psychotic Agitation

Supported by Pfizer Inc.

Leslie L. Citrome, M.D., *Nathan Kline Institute, 140 Old Orangeburg Road, Building 37, Orangeburg, NY 10962*; Shlomo Brook, M.D., Antony D. Loebel, M.D., Francine Mandel, Ph.D.

Educational Objectives:

At the conclusion of this presentation, participants should be able to recognize the potential for sequential IM/oral ziprasidone to reduce agitation with good tolerability in patients with acute psychotic disorder.

Summary:

Objective: To compare ziprasidone with haloperidol for reducing agitation in acute psychosis.

Methods: Two studies compared reductions in Brief Psychiatric Rating Scale (BPRS) hostility, agitation, activation/aggression, anxiety/depression, positive, and negative scores over the first three and seven treatment days. Mixed-model repeated measures analysis assessed effect, with dependent variables being BPRS items or factors over time. Independent variables were treatment group and time, whose interaction was included in the model.

Results: On treatment Day 1, ziprasidone was superior to haloperidol in reducing agitation and hostility, co-varied with akathisia and positive factor ($P < 0.0001$). Haloperidol's effect on akathisia (worsening) was greater than ziprasidone's ($P = 0.0023$). In the

first three treatment days, ziprasidone was superior to haloperidol in reducing hostility ($P=0.0279$), agitation ($P=0.0013$), activation/aggression ($P=0.0276$), and anxiety/depression ($P=0.0256$). No differences were seen in positive and negative factors. After three days, efficacy measures in the two groups converged, and further improvement was likely due to a time effect. Results demonstrated ziprasidone's and haloperidol's specific anti-hostility effects by study end, with confounds corrected for (BPRS positive symptoms, akathisia, sedation, and ethnicity).

Conclusions: Anti-hostility effects occurred with both treatments, but ziprasidone was superior to haloperidol for agitation because of equal, if not superior, efficacy and greater tolerability.

References:

1. Citrome L, Nolan KA, Volavka J: Science-based treatment of aggression and agitation: in *The Science, Treatment, and Prevention of Antisocial Behaviors Volume 2*, edited by Fishbein D. Kingston, NJ: Civic Research Institute, Inc, 2004.
2. Citrome L, Volavka J, Czobor P, et al: Effects of clozapine, olanzapine, risperidone, and haloperidol on hostility among patients with schizophrenia. *Psychiatr Serv* 2001; 52:1510-1514

NR793 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Relation of Change in Clinical Symptoms to Cognitive Improvement

Supported by Pfizer Inc.

Philip D. Harvey, Ph.D., *Department of Psychiatry, Mt. Sinai Medical Center, 1425 Madison Avenue, New York, NY 10029*; Michael F. Green, Ph.D., Christopher Bowie, Ph.D., Antony D. Loebel, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand if there is any correlation between improvement in the major clinical symptoms of psychosis and schizophrenia and improvement in cognition following short- and long-term treatment with ziprasidone.

Summary:

Objective: To empirically identify dimensions of change in schizophrenia symptoms and assess correlations with cognitive improvement.

Method: 185 subjects who were switched from conventional antipsychotics, risperidone, or olanzapine to open-label ziprasidone were rated with PANSS and administered a cognitive battery measuring functions known to improve with atypical antipsychotics. A composite score was created by standardizing and averaging baseline scores. Assessments occurred at six weeks and six months.

Results: PANSS scores and cognitive performance improved significantly at six-week and six-month endpoints. Factor analyses identified four dimensions of clinical change with Eigen values > 1.0 —psychosis, negative symptoms, hostility/aggression, anxiety/depression. While all four of the symptom change factors were significantly ($P<.05$) correlated with each other, baseline scores, endpoint scores, and baseline-to-endpoint changes on cognitive functioning were uncorrelated with the four symptom change factors ($r<0.08$, $P>0.5$).

Conclusion: Switching to ziprasidone was associated with independent improvements in positive and negative symptoms, hostility, affective symptoms, and cognition. Improvements were detected by six weeks and sustained at six months. Change in cognitive functioning was not consequent to other clinical changes, indicating that cognitive change in schizophrenia can be discriminated from other treatment-associated clinical changes.

References:

1. Weiden PJ, Simpson G, Potkin SG, Romano SJ: Effectiveness of switching to ziprasidone for stable but symptomatic outpatients with schizophrenia. *J Clin Psychiatry* 2003; 64:580-588.
2. Keefe RS, Silva SG, Perkins DO, Lieberman JA: The effects of atypical antipsychotic drugs on neurocognitive impairment in schizophrenia: a review and meta-analysis. *Schizophr Bull* 1999; 25:201-222.

NR794 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Hormone Endophenotype Pre- and Post-Sildenafil Treatment of SRI Antidepressant Female Sexual Dysfunction: Response Associated Changes Supported by Pfizer Inc.

H. George Nurnberg, M.D., *Department of Psychiatry, University of New Mexico, 2400 Tucker NE, MSC 095030, Albuquerque, NM 87131*; Paula L. Hensley, M.D., Susan Paine, M.P.H., Linda Sparks

Educational Objectives:

At the end of this presentation, the attendee will understand pre/post treatment hormone profiles distinguishing responders from non-responders to sildenafil treatment of serotonin reuptake inhibitor antidepressant-associated female sexual dysfunction (SRI-AAFSD).

Summary:

Objective: To extend a previous report with pre/post treatment hormone profiles distinguishing responders and non responders to double-blind, placebo-controlled (DBPC), and open-label sildenafil treatment of serotonin reuptake inhibitor antidepressant-associated female sexual dysfunction (SRI-AAFSD).

Methods: 125 premenopausal women with SRI-AAFSD, no pre-existing SD, consistent SRI antidepressant treatment ≥ 8 weeks, and major depressive disorder in remission (MDD-R) received phosphodiesterase type 5 inhibitor (PDE5I) sildenafil (50-100 mg) or placebo for eight weeks, with the option for eight weeks of open-label extension. Plasma levels of prolactin, cortisol, progesterone, estradiol, FSH, LH, TSH, T_4 , total/free testosterone, and sex hormone-binding globulin (SHBG) were measured by radioimmunoassay at baseline and treatment endpoint. At endpoint, changes in SRI-FSD and hormone levels were evaluated.

Results: At endpoint, 76% of responders reporting improvement in SRI-AAFSD ($P=0.001$) were receiving sildenafil and remained with MDD-R on stable dose SRI antidepressant. Treatment responders were characterized by a profile of higher levels of estradiol, free testosterone, and FSH, and lower levels of cortisol and SHBG compared with nonresponders, which showed some quantitative changes between/within consistency of profile.

Conclusions: Sildenafil treatment improved SRI-AAFSD, allowing women to continue effective SRI treatment for MDD. Further study of hormone profiles and changes over the course of treatment may provide an endophenotype predictive of PDE5I treatment response in SRI-AAFSD.

References:

1. Fava M, Rankin M: Sexual functioning and SSRIs. *J Clin Psychiatry* 2002; 63 Supp 5:13-6.
2. Hensley PL, Nurnberg HG: SSRI sexual dysfunction: a female perspective. *J Sex Marital Ther.* 2002; 28 Supp 1: 143-53.

NR795 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Concomitant Lamotrigine and SSRIs in Bipolar I Disorder

Supported by GlaxoSmithKline

Angela M. Deveaugh-Geiss, M.S., *Department of Department of Neurosciences, GlaxoSmithKline, Five Moore Drive, Research*

Triangle Park, NC 27709; Charles Bowden, M.D., Ronald E. Stewart, M.S., Joseph R. Calabrese, M.D., Thomas R. Thompson, M.D., Mark A. Frye, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to have an understanding of the safety and efficacy of lamotrigine and concomitant use of lamotrigine and selective serotonin reuptake inhibitors.

Summary:

Objective: To retrospectively evaluate the clinical response and tolerability of concomitant lamotrigine and selective serotonin reuptake inhibitors (LTG+SSRIs) in bipolar I disorder.

Methods: During the eight- to 16-week, open-label preliminary phase (OLPP) of two maintenance trials (GW605/606) in bipolar I disorder, patients were administered lamotrigine as adjunctive or monotherapy. Adjunctive medication was discontinued a minimum of one week before randomization. Psychiatric rating scales and adverse events (AEs) were examined weekly for all patients enrolled in the OLPP.

Results: 21% of patients (273/1305) received LTG+SSRIs (paroxetine, sertraline, citalopram, fluoxetine, and fluvoxamine) (median duration=7.3 weeks). Approximately a 50% reduction was seen in mean HAM-D₁₇ score from study entry to the end of the OLPP for patients on LTG+SSRIs. Mean±SD observed CGI-S and GAS scores for patients on LTG+SSRIs were 4.3±0.7 and 50.3±9.6, respectively, at study entry and 2.7±1.3 and 67.9±15.9, respectively, at the end of the OLPP. AEs were similar in patients who received LTG+SSRIs vs. LTG-SSRIs; the most common AEs (>10%) were headache (18% vs. 25%), infection (4% vs. 12%), nausea (8% vs. 12%) and all nonserious rash (7% vs. 10%).

Conclusion: Concomitant lamotrigine and SSRIs appear to be effective and well tolerated in patients with bipolar I disorder.

References:

1. Calabrese J, Bowden C, Sachs G, Yatham L, et al. for the Lamictal 605 Study Group: Journal of Clinical Psychiatry 2003; 64:1013-1024.
2. Bowden C, Calabrese J, Sachs G, Yatham L et al. for the Lamictal 606 Study Group: Archives of General Psychiatry. 2003; 60:392-400.

NR796 Thursday, May 26, 12:00 p.m.-2:00 p.m.

The Interaction Between Lamotrigine and a Combined Oral Contraceptive

Supported by GlaxoSmithKline

Jagdev Sidhu, Ph.D., Department of CPDM, GlaxoSmithKline, Third Avenue, Harlow Essex CM19 5AW, United Kingdom; Sarah Job, M.S.C., Sunita Bulsara, B.S.C., Richard Philipson, B.S.C.

Educational Objectives:

At the conclusion of this session, the participant should be able to have an understanding of the pharmacokinetic interaction of lamotrigine and Combined Oral Contraceptive (COC).

Summary:

Objective: To investigate the pharmacokinetic (PK) interaction of lamotrigine and Combined Oral Contraceptive (COC).

Methods: LAM 10016 was an open-label study of 22 healthy females. Subjects took COC monotherapy (21 days active, seven days inactive), for one cycle, lamotrigine was added for three cycles followed by lamotrigine monotherapy for 21 days. PK profiling for the COC components was conducted at the end of the first and fourth cycles, and for lamotrigine at the end of the fourth cycle and the last day.

Results: Sixteen subjects completed the study and provided evaluable PK parameters. The COC had a clinically relevant effect on the PK of lamotrigine (AUC₍₀₋₂₄₎ decreased 52%, C_{max} decreased 39%). Lamotrigine had a minimal effect on the PK of ethinylestradiol (AUC₍₀₋₂₄₎ decreased 7%, C_{max} increased 2%), but had a modest effect on levonorgestrel (AUC₍₀₋₂₄₎ decreased 19%, C_{max} decreased 12%). In general, lamotrigine was well tolerated in healthy young females when co-administered with COC at doses up to 300mg/day. No subject showed hormonal evidence of ovulation.

Conclusions: The COC has a clinically relevant effect on the pharmacokinetics of lamotrigine; on average, systemic exposure to lamotrigine in the presence of the COC was approximately 50% of the exposure in the absence of the COC.

References:

1. Sabers A, Buchholt JM, Uldall P, Hansen EL: Lamotrigine plasma levels reduced by oral contraceptives. Epilepsy Res 2001; 47(1-2):151-4.
2. Sabers A, Öhman I, Christensen J, Tomson T: Oral contraceptives reduce lamotrigine plasma levels. Neurology 2003; 61(4):570-1.

NR797 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Aripiprazole Augmentation of SSRIs for Treatment-Resistant MDD

Supported by Bristol-Myers Squibb

George I. Papakostas, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114; Timothy J. Petersen, Ph.D., Gustavo Kinrys, M.D., Alana Burns, B.A., Jonathan E. Alpert, M.D., Maurizio Fava, M.D., Andrew A. Nierenberg, M.D.

Educational Objectives:

At the conclusion of this session, participants should be able to recognize the possible augmentation role for aripiprazole in treatment-resistant depression.

Summary:

Background: Aripiprazole, an atypical antipsychotic agent with partial dopaminergic- and serotonin 1A- receptor agonist activity, may be particularly useful when used in conjunction with standard antidepressants in treatment-resistant depression.

Methods: 12 patients (46.6 ± 11.3 years of age, eight women) with major depressive disorder (MDD), who had failed to experience a clinical response to an adequate trial of an SSRI were treated with open-label aripiprazole in addition to their SSRI for eight weeks. Clinical response was defined as a 50% or greater decrease in depressive symptoms during the course of the trial (baseline-endpoint), as measured by the 17-item Hamilton Depression Rating Scale (HAM-D-17) total score.

Results: 9/12 (75.0%) patients completed the trial. Using a completer analysis, five (55.5%) patients were classified as responders. An intent-to-treat (ITT) analysis resulted in seven (58.3%) responders. The overall proportion of remitters was 3/9 (33.3%) using a completer analysis and 5/12 (41.6%) using the ITT analysis. Aripiprazole administration appeared safe, with no severe adverse events observed in any of the study participants.

Conclusions: These results suggest a possible augmentation role for aripiprazole when used in conjunction with SSRIs in SSRI-resistant MDD.

References:

1. Fava M: Diagnosis and definition of treatment-resistant depression. Biol Psychiatry 2003; 53(8):649-59.

2. Fava M: Augmentation and combination strategies in treatment-resistant depression. *J Clin Psychiatry* 2001; 62 Suppl 18:4-11.

NR798 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Aripiprazole Augmentation of SSRIs for Treatment-Resistant MDD

George I. Papakostas, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114*; Timothy Petersen, Ph.D., John Worthington, M.D., Gustavo Kinrys, M.D., Jonathan Alpert, M.D., Maurizio Fava, M.D., Andrew Nierenberg, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the potential role of the atypical antipsychotic aripiprazole as an adjunctive treatment for major depressive disorder

Summary:

Background: Due to their favorable side-effect profile, atypical antipsychotic agents offer important therapeutic advantages in mood disorders. Aripiprazole, an atypical antipsychotic agent with partial dopaminergic- and serotonin 1A- receptor agonist activity, may be particularly useful when used in conjunction with standard antidepressants in treatment-resistant depression. The purpose of this study is to test this hypothesis in depressed outpatients who have not experienced significant clinical improvement following an adequate trial of a selective serotonin reuptake inhibitor (SSRI).

Methods: 12 patients (46.6 +/- 11.3 years of age, eight women) with major depressive disorder (MDD), who had failed to experience a clinical response to an adequate trial of an SSRI, were treated with open-label aripiprazole in addition to their SSRI for eight weeks. Clinical response was defined as a 50% or greater decrease in depressive symptoms during the course of the trial (baseline-endpoint), as measured by the 17-item Hamilton Depression Rating Scale (HAM-D-17) total score.

Results: 9/12 (75.0%) patients completed the trial. Using a completer analysis, 5 (55.5%) patients were classified as responders. An intent-to-treat (ITT) analysis resulted in seven (58.3%) responders. The overall proportion of remitters was 3/9 (33.3%) using a completer analysis and 5/12 (41.6%) using the ITT analysis. Aripiprazole administration appeared safe, with no severe adverse events observed in any of the study participants.

Conclusions: These results suggest a possible augmentation role for aripiprazole when used in conjunction with SSRIs in SSRI-resistant MDD.

Supported by an unrestricted grant Bristol Myers Squibb Pharmaceuticals (AAN).

References:

1. Papakostas GI, Petersen TJ, Nierenberg AA, Murakami JL, Alpert JE, Rosenbaum JF, Fava M: Ziprasidone augmentation of selective serotonin reuptake inhibitors (SSRIs) for SSRI-resistant major depressive disorder. *J Clin Psychiatry*. 2004 Feb; 65(2):217-21.
2. Worthington JW, Fava M, Hughes ME, Kinrys GD, Dording C, Reese H, Pollack M: Aripiprazole as an augmentor of SSRIs in mood and anxiety disorder patients. *American Psychiatric Association Annual Meeting, San Francisco, 2003.*

NR799 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Ziprasidone's Long-Term Efficacy in Treatment-Refractory Schizophrenia
Supported by Pfizer Inc.

John M. Kane, M.D., *Department of Psychiatry, Zucker Hillside Hospital, 75-59 263rd Street Kaufmann Boulevard, Glen Oaks,*

NY 11004-1150; Sumant Khanna, M.D., Earl Giller, Jr., M.D., Sunita Rajadhyaksha, M.D., Antony D. Loebel, M.D., Cynthia Siu, Ph.D.

Educational Objectives:

At the end of this presentation, participants should be able to recognize the long-term efficacy and safety of ziprasidone in patients with treatment-refractory schizophrenia.

Summary:

Objective: To evaluate ziprasidone's long-term efficacy and tolerability in treatment-refractory schizophrenia.

Methods: Treatment-refractory schizophrenic completers of a 12-week, double-blind (core) study comparing ziprasidone (n=66) and chlorpromazine (n=60) were continued on open-label ziprasidone for up to one year. Assessments included PANSS Total, movement disorder measures, and body weight.

Results: Long-term treatment benefits with ziprasidone (mean dosage 140 mg/d) were demonstrated. For ziprasidone→ziprasidone subjects, PANSS Total mean change from core baseline (86.9) to last extension visit was -22.4 ± 26.2 (SD) ($P < 0.0001$), showing sustained improvement over one year. For chlorpromazine subjects switched to ziprasidone, significant improvement was observed over the extension period (PANSS Total mean change -7.03 ± 27.01 ; $P < 0.05$). Of 54 extension-phase responders ($\geq 20\%$ PANSS Total improvement from core baseline to Week 12), 38 (70.4%) subjects did not experience symptom exacerbation ($\geq 20\%$ worsening of PANSS Total score and CGI-S score ≥ 3) over the one-year extension. Extension-phase discontinuation rate was $< 40\%$. Movement disorders were not exacerbated and remained infrequent with long-term ziprasidone. Median changes in body weight from baseline to last visit were negligible and not clinically significant.

Conclusions: Ziprasidone was effective in this long-term study of treatment-refractory schizophrenia and was notably well tolerated overall, with minimal weight gain.

References:

1. Khanna S, Kane J, Rajadhyaksha S, Giller E: Ziprasidone vs chlorpromazine in treatment-refractory schizophrenia. Presented at the 54th Institute on Psychiatric Services; October 9-13, 2002; Chicago, Illinois, USA.
2. Potkin SG, Keck PE Jr, Giller E, Ice K, Warrington L, Mandel FS: Ziprasidone in bipolar mania: efficacy across patient subgroups. Presented at the 157th Annual Meeting of the American Psychiatric Association, May 1-6, 2004; New York, NY USA.

NR800 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Categorical Weight and Lipid Improvements After Switch to Ziprasidone
Supported by Pfizer Inc.

John W. Newcomer, M.D., *Department of Psychiatry, Washington University School of Medicine, 660 South Euclid Avenue, Box 8134, St. Louis, MO 63110-1002*; Antony D. Loebel, M.D., Ruoyong Yang, Ph.D.

Educational Objectives:

At the conclusion of this session, the participants should be able to discuss the reported findings on the long-term benefits of switching schizophrenic patients who are overweight or obese or have an elevated lipid profile to ziprasidone from conventionals or other atypical antipsychotics.

Summary:

Objective: To evaluate long-term weight and lipid changes after switch to ziprasidone in schizophrenic patients who were obese or had at least borderline high (NCEP guidelines) lipid levels.

Methods: Subjects switched to ziprasidone from conventionals (n=71), olanzapine (n=71), or risperidone (n=43) in six-week trials and completing these studies entered one-year extensions. Patients with BMI \geq 30, TChol \geq 200 mg/dL, or triglycerides \geq 150mg/dL at core study baseline were analyzed to determine proportion experiencing categorical improvements: BMI \rightarrow $<$ 30; weight reduction \geq 7%; TChol \rightarrow $<$ 200 mg/dL; triglycerides \rightarrow $<$ 150 mg/dL. Analysis of observed cases at 58 weeks was used for all variables.

Results: Of patients with BMI \geq 30 switched from risperidone or olanzapine, 26% and 15%, respectively, had BMI $<$ 30 at 58 weeks; 59% and 35% had \geq 7% weight reduction. Patients switched from conventionals exhibited lesser improvements. Among patients switched from conventionals, olanzapine, or risperidone who had baseline TChol \geq 200 mg/dL, 50% had endpoint TChol $<$ 200 mg/dL. Of patients with triglycerides \geq 150 mg/dL, 42% of patients switched from risperidone, 33% switched from olanzapine, and 15% switched from conventionals had endpoint triglycerides $<$ 150 mg/dL.

Conclusions: Significant proportions of overweight or hyperlipidemic patients switched to ziprasidone demonstrated clinically relevant categorical long-term improvements in weight and lipids.

References:

1. American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity: consensus development conference on antipsychotic drugs and obesity and diabetes. *Diabetes Care* 2004; 27:596-601.
2. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001; 285:2486-2497.

NR801 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Pregabalin Efficaciously Treats Symptoms of Fibromyalgia Syndrome

Supported by Pfizer Inc.

Leslie J. Crofford, M.D., *University of Kentucky, 740 South Limestone, Lexington, KY 40536-0284*; Michael C. Rowbotham, M.D., Philip J. Mease, M.D., I. Jon Russell, M.D., Robert H. Dworkin, Ph.D., Susan A. Martin, Uma Sharma, Ph.D.

Educational Objectives:

At the conclusion of this session, the participants in this activity will gain a greater understanding of the constellation of symptoms associated with fibromyalgia syndrome and of the safety and efficacy of pregabalin used to treat symptoms associated with FMS.

Summary:

Objective: This trial evaluated efficacy and safety of pregabalin for reducing pain and associated symptoms in patients with fibromyalgia syndrome (FMS).

Methods: FMS patients (N=529) meeting American College of Rheumatology criteria completed a one-week baseline phase and were randomized to placebo, 150, 300, or 450 mg/d pregabalin during an eight-week, double-blind, fixed-dose treatment phase. Primary efficacy parameter was endpoint weekly mean pain score from patients daily pain diaries. Secondary efficacy measures included sleep-quality diary. Patient and Clinical Global Impressions of Change (PGIC/CGIC), Medical Outcomes Study (MOS)-Sleep Scale, and Multidimensional Assessment of Fatigue.

Results: Pregabalin-treated patients (450 mg/d) showed significant improvement in endpoint mean pain score and were significantly more likely to have 50% reduction in pain from baseline. Mean sleep quality, fatigue, PGIC, and CGIC scores at endpoint

were significantly improved for patients receiving 300 and 450 mg/d PGB. The MOS-Sleep Scale was significantly improved at endpoint for all doses. The most common AEs were dizziness and drowsiness; 9% of patients withdrew due to AEs. Most patients (78%) completed the trial and entered a follow-on safety trial.

Conclusion: Pregabalin 450 mg/d was effective and well tolerated as a treatment for pain and associated symptoms in patients with fibromyalgia.

References:

1. Wolfe F, Ross K, Anderson J, Russell I, Hebert L: The prevalence and characteristics of fibromyalgia in the general population. *Arthritis Rheum* 1995; 38:19-28.
2. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al: The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. *Arthritis Rheum* 1990; 33:160-172

NR802 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Quetiapine in Bipolar I Depression: Double-Blind, Placebo-Controlled Study

Supported by AstraZeneca Pharmaceuticals

Wayne Macfadden, M.D., *CNS Therapeutics, AstraZeneca, 1800 Concord Pike, PO Box 15437, Wilmington, DE 19850-5437*; Joseph R. Calabrese, M.D., Trisha Suppes, M.D., Robin McCoy, R.N., Margaret C. Minkwitz, Ph.D., Ellis Wilson, Jamie Mullen, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to (1) evaluate efficacy and tolerability data for quetiapine in patients with bipolar I depression; and (2) use the information in clinical practice for the management of bipolar I depression.

Summary:

Objective: To evaluate the efficacy and tolerability of quetiapine monotherapy for major depressive episodes in patients with bipolar I disorder.

Methods: Patients with bipolar I depression (N=360) were randomized to eight weeks of double-blind treatment with quetiapine (fixed dose 600 or 300 mg/d) or placebo. The primary endpoint was change from baseline to endpoint in Montgomery-Asberg Depression Rating Scale (MADRS) total score.

Results: Patients taking quetiapine 600 or 300 mg/d had a significantly ($P<0.001$) greater improvement in mean MADRS scores vs placebo at every assessment, starting with the first evaluation (Week 1) and sustained through endpoint (Week 8). Significantly ($P<0.05$) more quetiapine patients (both doses) vs placebo were considered responders from Week 2 through the end of the study (Week 8) (\geq 50% decrease from baseline MADRS score: 64% and 62% vs 33%). Treatment-emergent mania did not differ between quetiapine and placebo (3% vs 4%). Common quetiapine adverse events (\geq 10% and at least twice the placebo rate) were dry mouth (42%), somnolence (32%), sedation (24%), dizziness (19%), and constipation (11%).

Conclusions: Quetiapine monotherapy (600 or 300 mg/d) is significantly more effective than placebo and well tolerated for the treatment of depressive episodes in patients with bipolar I disorder.

References:

1. Post RM, Leverich GS, Altshuler LL, et al: An overview of recent findings of the Stanley Foundation Bipolar Network (Part I). *Bipolar Disord* 2003; 5:310-319.
2. American Psychiatric Association: Practice guideline for the treatment of patients with bipolar disorder (revision). *Am J Psychiatry* 2002; 159(4 Suppl):1-50.

NR803 Thursday, May 26, 12:00 p.m.-2:00 p.m.

The Use of Clorazepate SD Formulation in Preventing Rebound Anxiety Associated With Short Half-Life Benzodiazepine Treatment of Panic Disorder
Supported by Ovation Pharmaceuticals, Inc.

Eric Kaplan, M.D., 146-B Whitaker Road, Lutz, FL 33549-7611

Educational Objectives:

The participant should be able to understand that rebound anxiety may be associated with the use of benzodiazepines in the treatment of patients with panic disorder. The participant will learn about the use of Clorazepate SD formulation as an option of alleviating rebound anxiety symptoms, while maintaining therapeutic effectiveness.

Summary:

Objective: This study will evaluate the use of Clorazepate SD formulation to determine if this long half-life, slow-release formulation benzodiazepine will alleviate rebound anxiety symptoms associated with the use of short half-life benzodiazepines in the treatment of patients with panic disorder. This study will determine if Clorazepate SD alleviates rebound anxiety symptoms and if therapeutic effectiveness is maintained.

Method: This study evaluated five patients who were treated in a naturalistic setting (outpatient private psychiatric practice) who fulfilled DSM-4 criteria for panic disorder with and without agoraphobia. Four patients were female and one patient was male. All patients were Caucasian and ranged in age from 18 to 60. All patients had a reduction of anxiety symptoms with the use of a short half-life benzodiazepines, including alprazolam, clonazepam, and lorazepam as measured by the Sheehan Patient Rated Anxiety Scale. The first five patients to develop significant rebound anxiety symptoms were switched to Clorazepate SD formulation. All patients agreed to a trial of Clorazepate SD formulation.

Within four weeks of therapy with Clorazepate SD formulation (22.5 to 45 mg. daily), all five patients noticed a marked reduction in rebound anxiety symptoms. In addition, all five patients continued to respond to pharmacotherapy as monitored by low scores on the Sheehan Patient Rated Anxiety Scale.

Conclusions: This study provides clinicians with an effective treatment option for panic disorder patients who are treated with short half-life benzodiazepines and develop rebound anxiety. Switching these patients to a long half-life sustained release benzodiazepine (Clorazepate SD formulation) may alleviate rebound symptoms while maintaining therapeutic effectiveness.

References:

1. Fontaine, Chouinard, Annable: Rebound anxiety in anxious patients after abrupt withdrawal of benzodiazepine treatment. *Am J. Psychiatry* 1984, 141:848-852.
2. Nelson J, Chouinard G: Guidelines for the clinical use of benzodiazepines: Pharmacokinetics, dependency, rebound and withdrawal. *Can J Clin Pharmacol* 1999, 6:69-83.

NR804 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Neuropsychological Outcome and Antipsychotic Association Treatment

Oscar Pino, Ph.D., *Department of Psychiatry, Bellvitge Hospital, Felxa Llarga S/N, Barcelona 08907, Spain*; Jose E. Rojo, Ph.D., Georgina Guilera, Ph.D., Daniel Carmona, M.D.

Summary:

Objective: To assess changes in cognitive function in stable schizophrenia patients before and after conventional antipsychotic treatment administration of 80 mg. of ziprasidone.

Methods: Four cognitive domains (including working memory and attention, learning and verbal memory, executive functions, and speed of information processing), premorbid IQ and psychopathological symptomatology (PANSS scale), were explored during the basal visit. After four weeks of the treatment, it was performed the same exploration in order to compare ziprasidone effects into cognitive domains and results obtained by PANSS scale. In total, we assessed six patients with chronic schizophrenia.

Results: Working memory, long-delay recall learning, semantic fluency test, and the speed of information processing show a positive tendency after combination and antipsychotic association treatment. Moreover, similar improvement tendency can be observed in post-treatment PANSS scale results.

Conclusion: Our preliminary data show a positive effect in cognitive and psychopathological domains we explored with administration and antipsychotic association treatment.

References:

1. Kapur S, Remington G: Atypical antipsychotics: New directions and new challenges in the treatment of schizophrenia. *Annu Rev Med* 2001; 52:503-517.
2. Harvey PD, Meltzer H, Simpson GM, et al: Improvement in cognitive function following a switch to ziprasidone from conventional antipsychotics, olanzapine, or risperidone in outpatients with schizophrenia. *Sch Res* 2004; 66:101-13.

NR805 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Trends in Contacts With Mental Health Professionals and Cost Barriers to Mental Health Care Among Adults With Significant Psychological Distress in the U.S., 1997-2002

Ramin Mojtabai, M.D., *Department of Psychiatry, Beth Israel Medical Center, First Avenue At 16th Street, New York, NY 10003*

Educational Objectives:

At the conclusion of this session, the participants will be able to recognize recent changes in demand for mental health care in the U.S. community.

Summary:

Objectives: To assess recent trends in contacts with mental health professionals and cost barriers to mental health care among adults in need of such care.

Methods: Data from the National Health Interview Survey of 1997 to 2002 were analyzed. Among adults with significant psychological distress—ascertained by the K6 instrument—trends in contacts with mental health professionals in the past year and forgone use of mental health care or prescription medications due to cost were examined across years.

Results: Prevalence of any contact with mental health professionals increased across years—from 29.1% in 1997 to 35.5% in 2002 ($P<0.05$). Prevalence of forgone service use due to cost also increased—from 15.6% to 20.0% for mental health care ($P<0.05$) and from 27.7% to 34.1% for medication use ($P<0.001$). Age, racial/ethnic, income, and insurance disparities in receiving care and cost barriers persisted over time.

Conclusions: The number of individuals in need of mental health care who contacted mental health professionals grew in recent years, as did the number of individuals who experienced cost barriers to such care. Barring dramatic improvements in health insurance coverage, the number of individuals who face such barriers will likely continue to grow in coming years.

References:

1. Olfson M, Marcus SC, Druss B, et al: National trends in the outpatient treatment of depression. *JAMA* 2002; 287:203-209.

2. Zuvekas SH: Trends in mental health services use and spending, 1987-1996. *Health Aff* 2001; 20:214-224.

NR806 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Cost Effectiveness Evaluation of Long-Acting Risperidone

Supported by Janssen-Cilag Medical Affairs

Julie C. Locklear, M.B.A., *Department of Outcomes Research, Janssen Medical Affairs, 1125 Trenton Harborton Road, Titusville, NJ 08560*; Natalie Edwards, M.S.C., Marcia Rupnow, Ph.D., Ronald J. Diamond, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand the methods associated with this cost-effectiveness analysis and utilize this information for decision-making purposes in the treatment of patients with schizophrenia.

Summary:

Objective: To assess the cost-effectiveness of long-acting risperidone (LAI-RIS), oral risperidone (RIS), olanzapine (OLA), quetiapine (QUE), ziprasidone (ZIP), aripiprazole (ARI), and haloperidol decanoate (HAL-DEC) in patients with schizophrenia over one year from a health care system perspective.

Methods: Published medical literature, an unpublished consumer health database, and a clinical expert panel were utilized to populate a decision-tree model. The model captured rates of compliance and relapse, frequency and duration of relapse, adverse events, resource utilization, and unit costs. Outcomes included percentage, number and duration of relapses per patient per year, and direct medical costs.

Results: The mean days of relapse requiring hospitalization per patient per year were 28 HAL-DEC, 18 RIS, OLA, QUE, ZIP and ARI, 11 LAI-RIS, while the mean days of exacerbation not requiring hospitalization were 8 HAL-DEC, 5 RIS, OLA, QUE, ZIP and ARI, 3 LAI-RIS. Direct medical cost savings with LAI-RIS compared with RIS, OLA, QUE, ZIP, ARI, and HAL-DEC were \$161, \$1,425, \$508, \$259, \$1,068, and \$8,224, respectively.

Conclusions: Long-acting risperidone may lead to substantially lower rates and fewer days of symptom exacerbation and hospitalization compared with currently available treatments. These lower rates translate into direct medical cost savings with the use of long-acting risperidone.

References:

1. Edwards N, Rupnow M, Pashos C, et al: Cost-effectiveness model of long-acting risperidone in schizophrenia in the U.S. *Pharmacoeconomics*, in press.
2. Edwards N, Rupnow M, Locklear J, et al: Cost-effectiveness evaluation of long-acting risperidone. [Poster] Presented at ISPOR 9th Annual International Meeting. May 2004, Washington, D.C.

NR807 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Partial Sleep Deprivation in Patients With Major Depression: Gabaergic Mechanism
Supported by GlaxoSmithKline

Edith Holsboer-Trachsler, M.D., *Department of Depression Research, Psychiatric University Hospital, Wilhelm-Klein-Str. 27, Basel 4025, Switzerland*; Martin Hatzinger, M.D., Ulrich M. Hemmeter, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize sleep deprivation in depressed patients is a powerful antide-

pressive treatment and a valuable tool to investigate acute antidepressant mechanisms involved in regulation of mood and sleep.

Summary:

Background: Microsleep (MS) (short sleep-episodes) during sleep deprivation (SD) can prevent the antidepressant response of SD. The GABA-benzodiazepine receptor antagonist flumazenil was able to reduce NonREM sleep pressure in recovery sleep after SD in healthy subjects.

Methods: A total of 27 patients with major depression received during a partial SD (PSD) in a double-blind, randomized design either flumazenil or placebo (orally) in two-hour intervals from 1:30 to 10:30 a.m. EEG was registered continuously for 60 hours ambulatory; and depression was assessed by the six-item Hamilton Depression Rating Scale (HDRS) before, during, and after PSD.

Results: Flumazenil significantly suppressed microsleep (MS) during SD compared with placebo. In the recovery night, slow-wave sleep was significantly increased in the flumazenil group. At day 2 after the recovery night, response rate was higher (HDRS) in the flumazenil group.

Conclusion: These findings show that flumazenil is able to suppress MS during PSD in patients with major depression. This effect is related to an intensification of NonREM sleep in the recovery night suggesting that GABAergic mechanisms are substantially involved in sleep-wake regulation during PSD in depressed patients. The improvement of the antidepressant efficacy of PSD after the recovery night is probably mediated by a secondary augmentation of GABAergic neurotransmission.

Funding Source: Swiss National Foundation No. 3200-056899.99

References:

1. Hemmeter U, Bischof R, Hatzinger M, Seifritz E, Holsboer-Trachsler E: Microsleep during partial sleep deprivation in depression. *Biol Psychiatry* 1998; 43:829-839.
2. Seifritz E, Hemmeter U, Trachsler L, Lauer CJ, Hatzinger M, Emrich HM, Holsboer F, Holsboer-Trachsler E: Effects of flumazenil on recovery sleep and hormonal secretion after sleep deprivation in male controls. *Psychopharmacology* 1995; 120:449-456.

NR808 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Ziprasidone for Behavioral and Psychological Symptoms of Dementia

Fabio L. Rocha, M.D., *Department of Psychiatry, IPSEMG, Rua Dos Ottoni-106, Belo-Horizonte 30150-270, Brazil*; Claudia Hara, M.S.C., Melissa Ramos, M.D., Milena A. Santos, M.D., Gustavo Guimaraes, Gleida Lanca, M.D., Francisca Scoranlick, M.D.

Educational Objectives:

At the conclusion of this session, the participant should know about the use of ziprasidone in the management of behavioral and psychological symptoms of dementia.

Summary:

Objective: The aim of this study was to evaluate the efficacy and tolerability of ziprasidone in the management of behavioral and psychological symptoms of dementia (BPSD).

Method: The authors conducted a seven-week, open-label, uncontrolled trial of ziprasidone in a flexible-dosage schedule (40-160 mg/day) in the treatment of BPSD.

Results: Twenty-five patients, mean age 80.6 years, with an average of 5.9 years of dementia, took part in the study. Of the 25 patients, 15 (60%) completed the study. The main reason for premature discontinuation was adverse events (60%). The mean

total NPI score fell significantly from 47.1 ± 17.1 at baseline to 25.8 ± 17.9 at day 49 ($p < 0.01$) demonstrating a reduction in frequency x severity of neuropsychiatric symptoms. The NPI caregiver burden showed a significant improvement from 22.6 ± 8.3 at baseline to 11.8 ± 7.3 after 49 days. Nineteen patients (76%) showed at least one adverse event. The most frequent adverse events were somnolence, gastrointestinal symptoms, and parkinsonism. In the population that completed the study, there was a nonsignificant increase in the QTc of 19 msec from baseline to day 49.

Conclusions: Ziprasidone was able to significantly improve distressing non-cognitive symptoms of demented patients. Additional large-scale, double-blind, well-controlled studies are necessary.

References:

1. Lee PE, Gill SS, Freedman M, Bronskill SE, Hillmer MP, Rochon PA: Atypical antipsychotic drugs in the treatment of behavioural and psychological symptoms of dementia: systematic review. *Bmj* 2004; 329(7457):75.
2. Tariot PN, Profenno LA, Ismail MS: Efficacy of atypical antipsychotics in elderly patients with dementia. *J Clin Psychiatry* 2004; 65 Suppl 11:11-5.

NR809 Thursday, May 26, 12:00 p.m.-2:00 p.m. SSRIs Are Associated With Earlier and Longer-Lasting Remissions

Burdette J. Wendt, *NASR Psychiatric, 2814 South Franklin Street, Michigan City, IN 46360*; Suhayl J. Nasr, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that paroxetine and sertraline were found to be more effective in achieving and maintaining remission in depressed outpatients than other antidepressants, including SNRIs.

Summary:

Objective: The SNRIs have been reported to induce a higher rate of remission than the SSRIs. This study examines the effectiveness of several antidepressants in achieving and maintaining remission in depressed outpatients.

Method: A chart review was performed on all patients currently being seen in a private, rural, outpatient psychiatric office who have a current clinical diagnosis of unipolar depression. Patients were deemed to be in remission if they had a Carroll Depression Rating Scale (CDRS) score of 7 or below. Data collected included patient demographics, CDRS scores, medication history, and length of treatment.

Results: A total of 297 unipolar depressed patients achieved remission at some point during their treatment, 121 on monotherapy, 134 on adjunctive therapy, and 42 without medication. Patients had an average CDRS at their initial visit of 17.7. Patients achieved remission in an average of 10 months and had an average of 1.8 relapses over an average observation period of 6.6 years. Patients on paroxetine and sertraline monotherapy achieved remission the fastest, in an average of 0.5 and 0.6 years, respectively. Patients also had the fewest relapses on sertraline and paroxetine monotherapy.

Conclusions: Two SSRIs were deemed superior to other antidepressants in achieving and maintaining remission in an outpatient psychiatric practice.

References:

1. Aberg-Wistedt A, Agren H, Ekselius L, Bengtsson F, Akerblad AC: Sertraline versus paroxetine in major depression: clinical outcome after six months of continuous therapy. *J Clin Psychopharmacol* 2000; 20:645-54.

2. Pintor L, Gasto C, Navarro V, Torres X, Fananas L: Relapse of major depression after complete and partial remission during a 2-year follow-up. *J Affect Disord* 2003; 73:237-44.

NR810 Thursday, May 26, 12:00 p.m.-2:00 p.m. Neuroactive Steroids and Suicidality in Schizophrenia and Schizoaffective Disorder

Marian I. Butterfield, M.D., *Department of Psychiatry, Durham VA Medical Center, 508 Fulton Street, 116A, Durham, NC 27705*; Jennifer Zervakis, Ph.D., Jennifer Strauss, Ph.D., Jeffrey Lieberman, M.D., Mark Massing, M.D., Christine Marx, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should understand (1) basic concepts in the neuroactive steroid area, and the potential relevance of neuroactive steroids to schizophrenia and schizoaffective disorder, and (2) potential relationships between neuroactive steroids and suicidality in schizophrenia and schizoaffective disorder.

Summary:

Objective: A number of investigations suggest that neuroactive steroids may be altered in schizophrenia. We recently reported that the neuroactive steroid DHEA is elevated in male veterans with PTSD who report a recent suicide attempt. We therefore investigated if neuroactive steroids are also altered in veterans with schizophrenia or schizoaffective disorder (SAD) who report suicidal ideation (SI) or a recent attempt.

Methods: Male veterans with schizophrenia or SAD ($n=143$) were assessed for suicidal ideation SI or a recent suicide attempt during the six months prior to study interview. Serum from morning blood draws was analyzed for the following steroids by radioimmunoassay: dehydroepiandrosterone (DHEA), androstenedione, testosterone, and estradiol. Bivariate associations between neuroactive steroids and suicidality were examined by Wilcoxon rank sum statistics. Logistic regression analyses were conducted, controlling for age.

Results: High rates of suicidality were observed: 48.3% had SI and 9.1% had attempted suicide. Patients who reported SI compared with those who did not demonstrated higher DHEA levels (14.95 ng/ml vs. 11.68 ng/ml, $p=0.07$). DHEA levels also tended to be higher in patients who reported a recent suicide attempt compared with those who did not (15.77 ng/ml vs. 12.93 ng/ml, $p=0.09$).

Conclusions: Patients with schizophrenia or SAD with SI demonstrated higher DHEA levels. DHEA levels also tended to be higher in patients who reported a recent suicide attempt. DHEA levels may be linked to suicidality in veterans with schizophrenia or SAD.

Funding Source: VA Research Career Development Award (MIB), NIMH K23 Career Development Award (CEM).

References:

1. Butterfield MI, Stechuchak KM, Davidson JRT, Wang C, Mackuen C, Pearlstein AM, Marx CE: Neuroactive steroids and suicidality in posttraumatic stress disorder. *The American Journal of Psychiatry*, in press.
2. Marx CE, VanDoren MJ, Duncan GE, Lieberman JA, Morrow AL: Olanzapine and clozapine increase the GABAergic neuroactive steroid allopregnanolone in rodents. *Neuropsychopharmacology* 2003; 28(1):1-13.

NR811 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Mirtazapine Fast Dissolving Tablets: A Global Preference Survey

Supported by NV Organon OSS, The Netherlands

Arjen PP. van Willigenburg, M.S.C., *Department of Marketing, NV Organon, P.O. Box 20, OSS 5340, Netherlands*; Dirk Rijmenams, M.S.C.

Educational Objectives:

At the conclusion of this session, the participant should be able to value better the use of new formulations such as a fast dissolving tablet.

Summary:

Objective: Today several psychotropic drugs are available as fast dissolving tablets (FDT). In general, patients regard FDT as very positive, and preferable to conventional tablets. The objective of this study was to obtain preference data on mirtazapine FDT on a large and global scale.

Method: Internet survey in 20 European, Asian, and Latin-American countries. Patients received a unique code that allowed them internet access to 11 questions on demographics, treatment response, and their impression of mirtazapine ODT. Participation in the survey was voluntary, anonymous, and no compensation was given.

Results: Almost 2,500 patients have completed the survey. Sample demographics and treatment characteristics were normal. 83% were positive about mirtazapine FDT. More than 62% preferred this new formulation over normal tablets. Reasons were ease of use (87%), pleasant taste (24%), and the possibility to take the tablet without water (32%). 48% responded improved compliance (correct dose/regularity) to their therapy. This proportion was higher in patients preferring the new formulation (66%).

Conclusions: In general, these data warrant the conclusion that mirtazapine FDT can be a valuable improvement to enhance the ease of use of antidepressant treatment, increase convenience, and improve compliance.

References:

1. Sastry SV et al: Recent technological advances in oral drug delivery. *Pharm Sci and Technol Today* 2000; 3(4):138-145.
2. Roose et al: Multi-site, open-label, observational study of the effectiveness and safety of mirtazapine orally disintegrating tablets in depressed patients who are at least 50 years of age. Presented at the 15th annual meeting of the American Association of Geriatric Psychiatry; February 24-27, 2002; Orlando, Florida.

NR812 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Mirtazapine in the Treatment of PTSD: A Short Review

Supported by NV Organon OSS, The Netherlands

Arjen PP. van Willigenburg, M.S.C., *Department of Marketing, NV Organon, P.O. Box 20, OSS 5340, Netherlands*; Roger M. Pinder, Ph.D.

Educational Objectives:

After the conclusion of this session, the participant should be able to value better the use of mirtazapine in the treatment of PTSD.

Summary:

Objective: Since its introduction in 1994, mirtazapine is increasingly being used in the treatment of PTSD, although this antidepressant lacks an indication for this. This development can be explained by the early antidepressant, anxiolytic, and sleep-improving properties of mirtazapine. A number of studies and case

reports show that mirtazapine might be effective in the treatment of PTSD. We here review and evaluate the data.

Method: Pubmed and Medline were screened (1994-2004). Publications on treatment of PTSD with mirtazapine were selected.

Results: We found six studies: four were open label of which one was controlled (sertraline). One had a randomized, placebo-controlled design. Mean treatment duration was 6.8 weeks. In total, 180 patients (40 females), mainly with chronic PTSD (150 combat-related) and with quite severe comorbidity were included. Assessments were: CGI (five studies), SPRINT (three studies) and CAPS (one study). Mean dose for mirtazapine ranged from 30-38 mg. Overall response rate at endpoint on main parameters was 50% to 88%. In all studies, differences to baseline or between mirtazapine and control were significant. Dropout rate was 7%.

Conclusion: Based upon the reviewed data, we conclude that mirtazapine is a promising treatment for chronic PTSD. Further research is highly recommended.

References:

1. Chung MY, Min KH, Jun YI et al: Efficacy and tolerability of mirtazapine and sertraline in Korean veterans with posttraumatic stress disorder: a randomized open label trial. *Hum Psychopharmacol* 2004; 19(7):489-94.
2. Davidson JR, Weisler RH, Butterfield MI et al: Mirtazapine vs. placebo in posttraumatic stress disorder: a pilot trial. *Biol Psychiatry* 2003; 53:188-91.

NR813 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Gabapentin Response in PTSD With Comorbid Alcohol Dependence: An Open-Label Trial of Adjunctive Therapy

Simon S. Chiu, M.D., *Addiction Rehabilitation Unit, Regional Mental Health Care, St. Thomas Site, 467 Sunset Drive, St. Thomas, ON N5P 3V9, Calendar*

Educational Objectives:

At the conclusion of this session, the participant should be able: (1) to evaluate critically the models linking traumatic stress, PTSD and substance abuse and (2) to assess the strength of evidence for the potential efficacy of anti-epileptic drugs, including GABApentin, in dual disorders: PTSD and Alcohol dependence.

Summary:

Introduction: PTSD exhibits only modest treatment response rate toward selective serotonin reuptake inhibitors (SSRIs) and is associated with high rate of substance use. No study has been conducted to investigate whether anti-epileptic drugs augment SSRI response in PTSD associated with alcohol dependence.

Objective: To evaluate the efficacy and tolerability of GABApentin in enhancing SSRI effects in civilian PTSD with comorbid alcohol dependence and to examine whether GABApentin reduces alcohol craving.

Method: The 12-week study was open label and naturalistic. Subjects with a DSM-IV diagnosis of PTSD and co-occurring alcohol dependence (in early sustained remission) showing marginal responses to optimal dosages of SSRI treatment for eight weeks entered the GABApentin augmentation protocol. Flexible dosage of GABApentin was used. Efficacy measures consisted of clinician-administered PTSD scale (CAP-S), HAM-D, HAM-A, CGI (Clinical Global Impression Scale for improvement), and Tiffany Craving Questionnaire (alcohol) at wk 0, wk 6, and wk 12. SSRI dosage was maintained through the period. Tolerability was monitored with treatment emergent adverse events.

Results: Twenty subjects participated in the study (female/male: 11/9). GABApentin was well tolerated at total daily dosage of 1200 mg. As compared with baseline, CAP-S, HAM-A, and CGI scores

improved significantly at wk 12 (ANOVA, $p < 0.01$). Tiffany Craving Questionnaire scores were significantly reduced at wk 6 and wk 12 ($p < 0.05$). Frequently reported side effects were over-sedation and mild dizzy spells. The dropout rate was 20% (4/20).

Conclusion: The promising results merit double-blinded, placebo-controlled studies of the efficacy of GABApentin in SSRI-resistant PTSD with alcohol dependence.

References:

1. Hamner MB, Brodrick PS, Laabbate LA: Gabapentin in PTSD: a retrospective, clinical series of adjunctive therapy. *Ann Clin Psychiatry* 2001; 13(3):141-6.
2. Jacobsen LK, Southwick SM, Kosten TR: Substance use disorder in patients with posttraumatic stress disorder: a review of literature. *Am J Psychiatry* 2001; 158: 1184-1190.

NR814 Thursday, May 26, 12:00 p.m.-2:00 p.m.

A Neuro-Biologically Informed Algorithm for Treating Resistant Depression

Supported by GlaxoSmithKline, HealthSmith Wellness Group

Kenneth Ocana, M.D., *Department of Family Medicine, University of British Columbia, 101 Cates Hill Corner Box 169, Bowen Island, BC V0N1G0, Canada*

Educational Objectives:

At the conclusion of this session participant should be (1) familiar with the neurobiology of treatment-resistant depression; (2) able to assess patient's neural circuit dysfunction and (3) able to choose treatments that selectively boost or block serotonergic, noradrenergic and/or dopaminergic neurotransmission to match patient's index symptoms and compensate for any residual symptoms.

Summary:

Recent advances in neuropharmacology are changing the way we look at mood disorders. Although most antidepressants are believed to act by selectively binding to the serotonin (5-HT) transporter, each SSRI has its own unique pharmacologic properties.

Objective: Can depression be better characterized and treated as a combination of malfunctioning circuits rather than as a distinct diagnostic entity?

Method: This Canadian study compared 625 primary care patients who presented with mood symptoms and were treated using a neurobiologically informed algorithm, with a control group of 300 similar patients treated with traditional DSM-IV driven care. The algorithm classifies each patient's neural circuit dysfunction according to their symptom complex as either hypo-serotonergic, hypo-adrenergic, hypo-dopaminergic, or a combination thereof, then matches each patient's characteristic dysfunction with the antidepressant most likely to address the index symptoms. Residual symptoms such as chronic fatigue, poor motivation, and executive dysfunction were treated by augmenting the index antidepressant with agents capable of boosting the remaining malfunctioning circuits including Bupropion SR, atypical antipsychotics, and extended-release psychostimulants. Patients' outcomes were followed over a minimum of 16 weeks and were classified as either no change (0% to 29% improvement), partial remission (30% to 69% improvement) or complete remission (>70% improvement).

Results: Using this approach, many fewer patients were lost to follow-up: 22 vs. 36% ($p < 0.01$), and more patients had complete remissions: 42 vs. 19% of controls ($p < 0.001$).

Conclusion: Treatment resistance was overcome and frequently residual symptoms could be targeted so that more patients could return to productive work, fully functioning families and communities, and the pleasures of life.

References:

1. Stahl SM et al: Brain circuits determine destiny in depression: a novel approach to the psychopharmacology of wakefulness, fatigue, and executive dysfunction in major depressive disorder. *J Clin Psychiatry* 2003; 64[suppl 14]:6-17.
2. Nemeroff CB, Owens MJ: Pharmacologic differences among the SSRIs: focus on monoamine transporters and the HPA axis. *CNS Spectr* 2004; 9(8 Suppl 4):23-31. Review.

NR815 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Outcome and Adverse Events for Escitalopram and Sertraline in a Real-World Setting

Supported by Pfizer Inc.

Kenneth Gersing, M.D., *Department of Psychiatry, Duke Medical Center, Box 3018, Durham, NC 27710*; Laura Taylor, M.S., Connie Mereadith, M.S.P.H.

Educational Objectives:

At the conclusion of this session, the participant should be able to educate readers on outcomes, duration, and side effects of selected antidepressants on major depression in a real-world setting in contrast to clinical trials results where the patient populations and confounding variables are controlled.

Summary:

Objective: Compare overall improvement, treatment duration, and adverse events rates among depressed patients receiving either escitalopram or sertraline alone in a real-world treatment setting.

Methods: Using a large-scale naturalistic anonymized database from an electronic medical record at Duke University Department of Psychiatry, percentages of patients achieving a clinical response of very much or much improved were compared as were percentages of side effects compared between either escitalopram or sertraline alone.

Results: Patients with major depressive disorders were selected. Of the 316 escitalopram and 802 sertraline patients, 68% were female and the average age was 41 years. Sixty-one percent of escitalopram patients reached a maximum total daily dose of > 10mgs, and 76% of sertraline patients reached 100 mgs or greater. The median duration on treatment was 103.5 and 146.4 days for escitalopram sertraline, respectively.

Across all dosages, 51% of escitalopram and 57% of sertraline patients achieved the CGI-I response. However, 41% of escitalopram and 29% of sertraline patients experienced any side effect, a difference was statistically significant. Specifically, a significantly greater percentage of escitalopram patients experienced sexual dysfunction, sedation, and anxiety/agitation in this real-world setting.

Conclusions: In a naturalistic, real-world setting, escitalopram is associated with a higher rate of adverse events, equivalent clinical outcome, and a shorter time on treatment as compared with sertraline.

References:

1. Einbinder JS, Scully K: Using a clinical data repository to estimate the frequency and costs of adverse drug events. *J Am Med Inform Assoc* 2002; 9(6 suppl):S34-S38.
2. Schubart JR, Einbinder JS: Evaluation of a data warehouse in an academic health sciences center. *Int J Med Inf* 2000; 60:319-333.

NR816 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Treatment Outcomes of Bipolar Disorder in a Real-World Setting

Supported by GlaxoSmithKline

Kenneth Gersing, M.D., *Department of Psychiatry, Duke Medical Center, Box 3018, Durham, NC 27710*; Bruce Burchett

Educational Objectives:

The objective is to educate readers on clinical outcomes of selected mood stabilizers in the treatment of bipolar disorder in a real-world setting in contrast to clinical trials results where the patient populations and confounding variables are controlled.

Summary:

Objectives: Our objective was to assess the overall effectiveness of lamotrigine and valproic acid and its derivatives in the real-world treatment of bipolar patients.

Methods: Using a large-scale naturalistic, anonymized database, from an electronic medical record at Duke University Department of Psychiatry, all bipolar patients except those with comorbid dementia were selected.

The Clinical Global Impression Improvement scale was used as the outcome measure. We compared the highest CGI-I scores prior to use of lamotrigine and valproic acid with those after its use by categorizing improvement as a highest CGI-I scores of very much improved or much improved.

Results: 1,707 bipolar patients were identified in this preliminary analysis 287 and 641 took lamotrigine and valproic acid, respectively. No significant demographic differences were found between the lamotrigine and valproic acid patients, with the average age being 39.6 years and 61% of the population being females. Of these groups, 64% of lamotrigine and 47% valproic acid patients experienced very much or much improvement in their CGI-I scores.

Conclusions: The analysis of outcomes in bipolar patients is inherently challenging because of comorbidity, chronicity, and fluctuating course. Duration of inter-episode remission and other treatment modalities are pending; nonetheless, this preliminary analysis showed significant superiority in the treatment of bipolar disorder.

References:

1. Einbinder JS, Scully K: Using a clinical data repository to estimate the frequency and costs of adverse drug events. *J Am Med Inform Assoc* 2002; 9(6 suppl):S34-S38.
2. Schubart JR, Einbinder JS: Evaluation of a data warehouse in an academic health sciences center. *Int J Med Inf* 2000; 60:319-335.

NR817 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Valproate Lowers Plasma Concentration of Olanzapine

Supported by AstraZeneca Pharmaceuticals

Niels Bergemann, M.D., *Department of Psychiatry, University of Heidelberg, Voss-Str. 4, D-69115 Heidelberg, Germany*; Kai R. Kress, M.D., Fatima Abu-Tair, M.D., Alex Frick, M.D., Juergen Kopitz, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to better understand new research findings in the field of psychopharmacology and apply an advanced treatment strategy using therapeutic drug monitoring.

Summary:

Olanzapine is an atypical antipsychotic that is metabolized mainly in the liver. After N-glucuronidation, it is catalyzed by oxidation

reactions via the cytochrome P450 isoenzyme CYP1A2, and, to a lesser degree, via CYP2D6. Whereas data on the interaction of olanzapine with a number of psychotropic drugs are available, little is known about the effect of valproate on the plasma concentrations of olanzapine, although a combination of these two drugs may be indicated in treating, for example, manic and mixed bipolar disorders. Therefore, we investigated whether valproate has a clinically relevant effect on the plasma concentration of olanzapine.

In four patients (three females, one male) between 32 and 42 years of age who had been treated with olanzapine, its plasma concentrations were determined by HPLC with electrochemical detection before and after receiving co-medication of valproate.

The patients received between 20 and 30 mg olanzapine daily. All patients demonstrated a significant decrease in dose-corrected olanzapine plasma concentration of between 32.3% and 78.8% after receiving valproate; the mean decrease was 53.6%.

These data suggest an induction of olanzapine-metabolizing enzyme systems by valproate. In contrast to this mechanism, a potential competitive inhibition of CYP1A2 by valproate does not seem to be clinically relevant. Further studies with increased numbers of patients are required to confirm these data.

References:

1. Bergemann N, Frick A, Parzer P, Kopitz J: Olanzapine plasma concentration, average daily dose, and interaction with co-medication in schizophrenic patients. *Pharmacopsychiatry* 2004; 37:63-68.
2. Perruca E: Pharmacological and therapeutic properties of valproate: a summary of 35 years of clinical experience. *CNS Drugs* 2002; 16:695-714.

NR818 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Effects in MDD on Sexual Functioning of Bupropion XL, Escitalopram, and Placebo in Depressed Patients
Supported by GlaxoSmithKline

Anita Clayton, M.D., *Department of Psychiatry, University of Virginia, 2955 Ivy Road, Northridge Suite 210, Charlottesville, VA 22903*; Donna Wightman, R.Ph., Jack G. Modell, M.D., Joseph Horrigan, M.D., Nathalie E. Richard, M.S.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that SSRIs such as escitalopram are associated with significantly more sexual dysfunction when compared with bupropion XL, and placebo, potentially resulting in medication non-adherence or reduction in quality of life.

Summary:

Objective: Antidepressant-induced sexual dysfunction may lead to medication noncompliance or diminished quality of life. Two identical studies compared the impact of two antidepressants, once-daily bupropion (bupropion XL) and the SSRI escitalopram, on sexual functioning.

Methods: 830 outpatients with moderate to severe major depressive episodes were treated with bupropion XL (300-450 mg/day), escitalopram (10-20 mg/day), or placebo for eight weeks in this randomized, double-blind, multicenter study. Patients' depression, sexual functioning, and safety were assessed at regular clinic visits.

Results: Based on investigator ratings, significantly more patients treated with escitalopram (30%) experienced orgasm dysfunction at week 8 compared with bupropion XL (15%) or placebo (9%). Differences were also evident at week 8 in the self-rated Changes in Sexual Functioning Questionnaire (CSFQ) total score. Otherwise, both active treatments were well tolerated. Bupropion XL and escitalopram were comparable in efficacy; the mean differ-

ence in change from baseline HAMD-17 was .38 (95% CI-0.82, 1.58).

Conclusions: Treatment with escitalopram was more often associated with sexual dysfunction than bupropion XL and placebo. Bupropion XL may offer tolerability advantages over escitalopram for the treatment of depression in sexually active patients.

References:

1. Clayton AH, Pradko JF, Croft HA, Montano B, Leadbetter RA, Bolden-Watson C, Bass KI, Donahue RMJ, Jamerson BD, Metz A: Prevalence of sexual dysfunction among newer antidepressants. *J Clin Psychiatry* 2002; 63:357-366.
2. Roose SP: Tolerability and patient compliance. *J Clin Psychiatry* 1999; 60 (suppl 17):14-17.

NR819 Thursday, May 26, 12:00 p.m.-2:00 p.m.

The Relative Performance of Newer Antidepressants in a Medicaid Population

Supported by Pfizer Inc.

Jeffery S. McCombs, Ph.D., *Pharm Economics, University of Southern California, 1540 E. Alcazar, Room CHP#140, Los Angeles, CA 90089-9004*; Jinhee Park, M.S., Morgan Bron, Pharm.D.

Educational Objectives:

At the conclusion of this session, the participant should understand if physicians treating depressed Medicaid patients in California target antidepressants to selected populations based on patient demographics and other factors.

Summary:

Objective: Assess the relative performance of new antidepressants in terms of compliance, drug switching, and cost.

Method: 246,116 episodes of antidepressant therapy were abstracted from the fee-for-service paid claims file of the California Medicaid program for years 1999-2002. Data for each episode cover six months prior and 12 months post-treatment.

Results: Initial analyses have focused on patients who restarted therapy using the same medication (n=130,905) or on a second antidepressant (n=46,515). Patients restarting on the same medication display better adherence to therapy and lower switching rates than patients who restart treatment on a second antidepressant. The average break in therapy for delayed switchers is three times that of restarters (>250 days). Unadjusted data suggest that patients treated with Zoloft, Prozac, or Effexor achieve better compliance than patients treated with Wellbutrin, Celexa, or Paxil, though differences are relatively minor.

Discussion: Unadjusted results indicate little difference in patient outcomes across alternative antidepressants. However, physicians may be selectively prescribing drugs to those subpopulations where each drug has a clinical advantage.

Future research: Propensity scoring methods will be used to investigate if clinicians have been successful in prescribing alternative medications for those subpopulations in which each product achieves superior outcomes.

References:

1. McCombs JS, Shi L, Croghan TW, Stimmel GL: Access to drug therapy and substitution between alternative antidepressants following an expansion of the California Medicaid formulary. *Health Policy* 2003; 65:301-311.
2. McCombs JS, Shi L, Stimmel GL, Croghan TW: A retrospective analysis of the revocation of prior authorization restrictions and the use of antidepressant medications for treating major depressive disorder. *Clinical Therapeutics* 2002; 24(11):1939-1959.

NR820 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Efficacy of Divalproex in Treating Residual Depression and/or Irritability

Supported by Abbott Laboratories

Robert Horne, M.D., *2915 West Charleston Boulevard #4, Las Vegas, NV 89102*; Cedric Cunanan, B.S., Michael Schwierts, M.S., Deborah Martz, R.N.

Educational Objectives:

At the conclusion of this session, the participants should be able to identify incomplete response to atypical antipsychotic medication on the basis of Patient Target Complaint and associated residual depression and irritability.

Summary:

Objective: Incomplete response to atypical antipsychotic medication is common. Management of residual depression and irritability is important for improved outcome.

Methods: This four-week study evaluated divalproex efficacy in reducing residual depression, irritability, or both after partial response to different atypical antipsychotics; for various DSM-IV diagnoses. CGI-I scores identified divalproex responders. Patients were divided into three residual symptom groups by Patient Target Complaint (PTC). Outcomes were evaluated by CGI-I, mean changes for total BPRS; BPRS depression, guilt, hostility; PTC depression, irritability; and CGI-S. Fisher's Exact Test and ANOVA analyses were used.

Results: Patients (n=49) stabilized (range, 1-10 months) on atypical antipsychotics (clozapine (n=11, mean: 536mg), risperidone (n=21, mean: 5.9mg), olanzapine (n=10, mean: 19.5mg), and quetiapine (n=7, mean: 529mg) were treated with adjunctive divalproex (mean serum level, 84 mcg/ml): 35 patients responded (CGI-I=1 or 2) Residual irritability (n=14), depression (n=12), or both (n=23) were identified by patients Fisher's Exact Test demonstrated a statistically significant difference between response and residual symptom group (P=.0447). Comparisons among groups demonstrated significant mean change for total BPRS (irritability both, P=.0008; depression/both, P=0.169) and BPRS hostility (depression and both, P=.0003).

Conclusion: Adjunctive divalproex reduces residual depression and irritability and may have greater efficacy in patients with both symptoms.

References:

1. Sachs GS, Grossman F, Ghaemi SN, Okamoto A, Bowden CL: Combination of a mood stabilizer with risperidone or haloperidol for treatment of acute mania: a double-blind, placebo-controlled comparison of efficacy and safety. *Am J Psychiatry* 2002; 159:1146-1154.
2. Gyulai L, Bowden CL, McElroy SL, et al: Maintenance efficacy of divalproex in the prevention of bipolar depression. *Neuropsychopharmacology* 2003; 28:1374-1382.

NR821 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Similarities and Changes in Antipsychotic Use at McLean Hospital From 1989 to 2004

Supported by Bristol-Myers Squibb, Pfizer, Bruce J. Anderson Foundation and the McLean Hospital Private Donors Fund for Neuropsychopharmacology Research

Franca Centorrino, M.D., *Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02478*; Alessandra Talamo, M.D., Guzzetta Francesca, M.D., Kate V. Fogarty, B.A., Mark Saadeh, B.S., Stephanie L. Cincotta, B.A., Ross J. Baldessarini, M.D.

Educational Objectives:

The objective of this presentation is to inform health care professionals of changes in the use of antipsychotic medications in an inpatient hospital setting.

Summary:

Background: In view of newer atypical antipsychotics available in the new millennium, we reexamined trends in inpatient antipsychotic use at McLean Hospital.

Method: Medical records of McLean Hospital inpatients prescribed antipsychotics from March-May 2004 were analyzed for DSM-IV discharge diagnosis, primary and adjunctive antipsychotics, other psychotropic prescriptions, and clinical changes.

Results: We evaluated 319 patients (60% female), age 43.5 ± 17.1 years, presenting with major affective (N=169, 53%) psychotic (N=101, 31.7%), or other disorders (N=49, 15.3%). Length of hospitalization (12.8 ± 15.1 days) declined from previous years. Psychotropics at discharge averaged 3.1 ± 1.4, including 1.2 ± 0.6 antipsychotics. Total chlorpromazine-equivalent discharge dose was 312 ± 323 mg/day, up 6.7% from 2002. Primary antipsychotic final dose was 260 ± 220 mg/day, slightly higher than 1989 but 18% lower than the 1998 peak and higher in psychotic disorders. Total discharge dose was much higher (69%) among patients on ≥ 2 antipsychotics (p < 0.0001). Mood stabilizer prescriptions rose by 47.2% from 1998-2002 (p < 0.0001) but fell slightly in 2004. At discharge, 63.3% of patients were prescribed ≥ 3 psychotropics, more often women (p = 0.007) and patients with a major affective disorder (p < 0.0001).

Second-generation agents represented 91% of primary antipsychotic prescriptions. While olanzapine was the most commonly prescribed antipsychotic in 1998 and 2002, quetiapine surpassed olanzapine in 2004, representing 28% of primary antipsychotics, quetiapine > risperidone > olanzapine >> aripiprazole > clozapine > haloperidol > perphenazine > ziprasidone > other conventional agents.

Conclusion: Use of second-generation antipsychotics dominates current inpatient practice. Inpatient length of stay continues to decrease while number of psychotropics prescribed at discharge and dose of combination antipsychotics rises.

References:

1. Baldessarini RJ, Kando JC, Centorrino F: Hospital use of antipsychotic agents in 1989 and 1993: Stable dosing with decreased length-of-stay. *Am J Psychiatry* 1995; 152: 1038-1044.
2. Centorrino F, Eakin M, Bahk W-M, Kelleher JP, Goren JL, Salvatore P, Egli S, Baldessarini RJ: Inpatient antipsychotic drug use in 1998: Comparisons to 1993 and 1989. *Am J Psychiatry* 2002; 159: 1932-1935.

NR822 Thursday, May 26, 12:00 p.m.-2:00 p.m. Time to All Cause Discontinuation of Atypical Versus Typical Antipsychotics in the Naturalistic Treatment of Schizophrenia

Marvin S. Swartz, M.D., *Department of Psychiatry, Duke University School of Medicine, Box 3173, Durham, NC 27710*; Baojin Zhu, Ph.D., Haya Ascher-Svanum, Ph.D., Douglas Faries, Ph.D., Sandra Tunis, Ph.D., Ronald Landbloom, M.D., Jeff Swanson, Ph.D.

Educational Objectives:

At the conclusion of this session the participant should be able to recognize that in the usual care of schizophrenia patients, atypical antipsychotics are not a homogeneous group. Some atypical agents, but not others, differentiate from typical antipsychotics (regardless of potency level) on time to all-cause medication discontinuation an important effectiveness measure.

Summary:

Objective: To prospectively compare atypical and typical antipsychotics on time to all-cause medication discontinuation, an important effectiveness measure in the usual care of schizophrenia.

Methods: Participants (N=1,704) were initiators on oral atypical or typical antipsychotics (low, medium, or high-potency) in a three-year, naturalistic study of schizophrenia. Medication groups were compared on time to all-cause medication discontinuation during the one year following medication initiation. Statistical analysis used Kaplan-Meier and Cox proportional hazard model.

Results: Patients treated with atypical antipsychotics had longer time to medication discontinuation compared with patients receiving low, medium, or high-potency typical antipsychotics (odds ratio=1.4, 1.5, 1.9; p=0.044, 0.004, <0.001, respectively). Among atypical antipsychotics, clozapine and olanzapine-treated patients had a significantly longer time to medication discontinuation than patients receiving low, medium, or high-potency typical agents. Risperidone and quetiapine-treated patients had longer time to medication discontinuation compared with only high-potency typicals. Ziprasidone did not significantly differ from low, medium, or high-potency typical agents. Further, only clozapine and olanzapine-treated patients had a significantly longer time to medication discontinuation compared to perphenazine, a medium-potency typical antipsychotic.

Conclusion: In usual care of schizophrenia patients, atypical antipsychotics appear to be superior to typical antipsychotics (regardless of potency level) and to significantly differ in treatment effectiveness.

References:

1. Stroup TS, McEvoy JP, Swartz MS, Byerly MJ, Glick ID, Canive JM, McGee MF, Simpson GM, Stevens MC, Lieberman JA: The National Institute of Mental Health Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) project: schizophrenia trial design and protocol development. *Schizophr Bull* 2003; 29:15-3
2. Hugenholtz GWK, Heerdink ER, Nolen WA, Egberts ACG: Less medication switching after initial start with atypical antipsychotics. *European neuropsychopharmacology* 2004; 14:1-5.

NR823 Thursday, May 26, 12:00 p.m. -2:00 p.m. Complicated Grief and Substance Use Treatment: A Pilot Study

Allan Zuckoff, Ph.D., *Department of Psychiatry, University of Pittsburgh School of Medicine, 3811 O'Hara Street, Pittsburgh, PA 15213*; M. Katherine Shear, M.D., Ellen Frank, Ph.D., Dennis C. Daley, Ph.D., Karen Seligman, M.Ed., Russell Silowhash, B.A.

Educational Objectives:

At the conclusion of this session, the participant should be able to demonstrate an understanding of the effects in an open prospective pilot study of a manual-guided, integrated psychotherapy for complicated grief and co-occurring substance abuse or dependence on grief symptoms, depression, and substance use.

Summary:

Objective: There are no empirically supported treatments for grief problems in persons with substance-use disorders (SUDs). We conducted an open pilot study of an outpatient, 24-session individual psychotherapy, Complicated Grief and Substance Use Treatment (CGSUT).

Methods: Nine women and seven men who were bereaved ≥ 6 months, scored ≥ 30 on the Inventory of Complicated Grief (ICG), and met DSM-IV criteria for an SUD (previous six months) were assessed pre- and posttreatment on ICG, BDI, and Timeline

Followback (TLFB). Participants were 42.3 years old (SD=9.8), 50% black/44% white. Mean time since the death was 9.8 years (SD=9.7).

Results: More men (N=5) than women (N=3) completed treatment. Mean ICG reductions were 30.9 (SD=15.4, $p=0.008$) for completers and 15.3 (SD=19.7, $p=0.011$) in the intent-to-treat (ITT) analysis, effect sizes 2.01 and 0.78. Mean BDI reductions were 15.5 (SD=5.5, $p=0.008$) for completers and 7.9 (SD=10.0, $p=0.009$) in ITT, effect sizes 2.82 and 0.79. TLFB Percent Days Abstinent increased 26.5 in completers (SD=29.8, $p=0.039$) and 20.4 in ITT (SD=43.4, $p=0.044$), effect sizes 0.89 and 0.47. Grief and depression outcomes were comparable to those obtained in a pilot study of patients without SUDs.

Conclusion: CGSUT is a promising intervention that merits further testing.

References:

1. Shear MK, Frank E, Foa E, Cherry C, Reynolds CF III, Vander Bilt J, Masters S: Traumatic grief treatment: a pilot study. *Am J Psychiatry* 2001; 158:1506-1508.
2. Prigerson HG, Maciejewski PK, Reynolds CF III, Bierhals AJ, Newsom JT, Fasiczka A, Frank E, Doman J, Miller M: Inventory of complicated grief: a scale to measure maladaptive symptoms of loss. *Psychiatry Res* 1995; 59:65-79.

NR824 Thursday, May 26, 12:00 p.m.-2:00 p.m. **Interventions Following the Pentagon Attack and Presence of Symptoms Two Years Later**

Douglas A. Waldrep, M.D., *Department of Psychiatry, Walter Reed Army Medical Hospital, 23222 Georgia Avenue, Brookville, MD 20833*; Thomas A. Grieger, M.D., Monica Louasz

Educational Objectives:

At the conclusion of this session, the participant should be able to: (1) recognize that acute interventions may not prevent trauma and (2) understand informal desensitization may increase the utilization of mental health resources over time compared with those victims that did not participate in the interventions.

Summary:

Introduction: Acute interventions following trauma are reported as having little or no value in prevention of trauma-related disorders.

Method: Pentagon survivors (N=129) were screened for PTSD and depression 25 months after the Pentagon attack using the PCL-17, PHQ-9, and other questions regarding exposure. Participation and value of each of the five types of interventions offered (supportive, psychoeducation, formal treatment, social support, and informal desensitization) were also surveyed.

Results: 87% participated in at least one intervention; 57% participated in any of the supportive interventions; 53% participated in any psychoeducational services, and 71% participated in any informal desensitization services. Of those that participated in any interventions, 76% found it helpful. Overall, 20% had PTSD, 7% met criteria for depression, and 6% had PTSD and depression. There was no relationship between participation or perceived benefit in any intervention and the presence of current PTSD or depression. Subjects who participated in the informal desensitization were more likely to be in mental health treatment than those who had current symptoms and were not seeking treatment (OR=4.44, 95 CI 1.40-14.03, Wald $\chi^2=4.06$, $df=1$, $p=0.044$).

Conclusion: Multiple interventions did not prevent trauma related disorders. Desensitization techniques may increase the likelihood of victims seeking mental health treatment.

References:

1. Schlenger WE, Caddell JM, Ebert L, Jordan BK, Rourke KM, Wilson D, Thalji L, Dennis JM, Fairbank JA, Kulka RA: Psychological reaction to terrorist attacks: findings from the national study of American's reactions to September 11, *Journal of the American Medical Association* 2002; 288:581-588.
2. Schuster MA, Stein BD, Jaycox LH, Collins RL, Marshall GN, Elliott MN, Zhou AJ, Kanouse DE, Morrison JL, Berry MA: A national survey of stress reactions after the September 11, 2001 terrorist attacks, *New England Journal of Medicine*, 2001; 345(20): 1507-1512.

NR825 Thursday, May 26, 12:00 p.m.-2:00 p.m. **Efficacy and Safety of Topiramate on Alcohol Withdrawal Symptoms**

Seon-Wam Ki, M.D., *Department of Psychiatry, Konyang University Hospital, 685, Gassowon-Dong, Seo-gu, Daejeon 302-718, Korea*; Eun-ae Choi, M.D., Sung-Eun Kim, M.D., Ji-Woong Kim, M.D., Jin-Kyun Park, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that topiramate may have a therapeutic efficacy and safety in treating alcohol withdrawal.

Summary:

Objective: Benzodiazepine are most often used for the treatment of alcohol withdrawal, but can be problematic due to sedation, cognitive impairment, disinhibition, and abuse potential. New anticonvulsant topiramate may have activity to treat effectively alcohol withdrawal. The purpose of this study is to compare effects of topiramate and benzodiazepine in the treatment of alcohol withdrawal.

Method: Fifty-two hospitalized patients with a diagnosis of DSM-IV alcohol dependence after providing written informed consent are randomized to either lorazepam (N=27) or topiramate (N=25) groups. Subjects were assessed with CIWA-Ar scores at the time of baseline, 1, 3, 5 day from the last alcohol drinking. Lorazepam was given 4mg divided by 4 on day 1, tapering to 2mg divided by 2, and topiramate was given fixed, single dose, 50mg. Subjects experiencing insomnia or severe withdrawal signs received additional medications including trazodone P.O. or lorazepam injection.

Results: There were no significant differences between two groups in demographic or clinical characteristics except marital state and s-ALT level. Two groups had similar ADS score and baseline withdrawal severity. There were no significant differences by treatment group in CIWA-Ar scores over time ($F=0.883$, $P>0.05$).

Conclusions: These preliminary results suggest that topiramate is a promising alternative to benzodiazepine for treating alcohol withdrawal.

References:

1. Bankole AJ: Progress in the development of Topiramate for treating alcohol dependence: From a hypotheses to a proof-of-concept study. *Alcohol Clin Exp Res* 2004; 28(8):1137-1144.
2. Elisabetta C, Kate JB, Richard WO: Topiramate attenuates withdrawal signs after chronic intermittent ethanol in rats: *Neuroreport* 2004; 15(1):207-210.

NR826 Thursday, May 26, 12:00 p.m.-2:00 p.m. **A Psychotherapy Training Module for Medical Students**

Jennifer S. Brasch, M.D., *Department of Psychiatry, McMaster University, 50 Charlton Avenue East, 3 Fontbonne, Hamilton, ON L8N 4A6, Canada*; Lawrence Mynors-Wallis, M.B.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the development and components of a six-week seminar series in psychotherapy training for medical students using Problem-Solving Therapy.

Summary:

Introduction: To offer learning opportunities that emphasize knowledge and skills of use to future non-psychiatrist physicians, a module on psychotherapy was introduced into the core clinical clerkship rotation in psychiatry.

Methods: The module was developed using Problem-Solving Therapy, a brief, structured intervention that can be easily learned and applied in a wide range of situations by health professionals inexperienced in psychotherapy. The module of six weekly two-hour seminars includes a variety of learning methods to reinforce key concepts.

Results: The module has been delivered regularly since June 2002 and is now an integral component of the psychiatry clerkship. (Results of the formal evaluation tools are presented in another poster.)

Discussion: Many students enjoy the opportunity to learn a practical, structured psychotherapy technique. The module is resource intensive, requiring a seminar leader and co-leader for large groups (over 10 students) as well as standardized patients. The caliber of the seminars depends on the motivation of the students.

References:

1. Mynors-Wallis L: Problem-solving treatment in general psychiatric practice. *Advances in Psychiatric Treatment* 2001;7, 417-425; <http://apt.rcpsych.org/cgi/reprint/7/6/417.pdf>.
2. Mynors-Wallis LM, Gath DH, Day A, Baker F: Randomised controlled trial of problem solving treatment antidepressant medication, and combined treatment for major depression in primary care. *BMJ* 2000; 320:26-30; <http://bmj.com/cgi/content/fall/320/7226/26>.

NR827 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Evaluation of a Psychotherapy Training Module for Medical Students

Jennifer S. Brasch, M.D., *Department of Psychiatry, McMaster University, 50 Charlton Avenue East, 3 Fontbonne, Hamilton, ON L8N 4A6, Canada*

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the effectiveness of a psychotherapy training module for medical students in teaching Problem-Solving Therapy; to determine students' interest in and enjoyment of a psychotherapy training module.

Summary:

Introduction: A six-week seminar series to teach Problem-Solving Therapy (PST), a brief, structured talk intervention, was introduced to the clerkship. The effectiveness of the module and students' interest in learning PST were assessed.

Method: Students completed a questionnaire assessing attitudes toward psychotherapy and ability to list the seven steps of PST before beginning the module and during the last of the six seminars. Students also complete an end-unit evaluation. Means and standard deviations were calculated for Likert-type questions. 1-tailed paired t-tests were used to compare pre- and post-module data.

Results: Between June 2002 and October 2004, the Psychotherapy Training Module was presented to 18 groups of clerks with 286 students. Paired pre- and post-questionnaires were com-

pleted by 121 students (42% of 251). The number of steps in PST listed correctly (max 7) rose from 2.1 to 5.7, t-test p value <0.001. Students ratings of being able to help patients with a problem increased from 5.1 to 6.2, t-test p-value <0.001. The end-module evaluation was distributed to 275 students and completed by 171 (62%). Results included scores for overall enjoyment of 4.76 (SD 1.57) and plans to use PST again of 5.81 (SD 1.31).

Discussion: The results demonstrate that students learned the steps of PST, developed increased confidence in helping patients with problems, and rated all components of the module positively.

References:

1. Mynors-Wallis L: Problem-solving treatment in general psychiatric practice. *Advances in Psychiatric Treatment* 2001;7, 417-425; <http://apt.rcpsych.org/cgi/reprint/7/6/417.pdf>.
2. Lofchy J: The Clerk Crisis Clinic: a novel educational program. *Academic Psychiatry* 2003;27(2), 82-7.

NR828 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Glucoregulation and Adiposity With Antipsychotic Therapy in Schizophrenia

Supported by Janssen Pharmaceutica and Research Foundation

Marilyn Ader, Ph.D., *Department of Physiology, University of Southern California, 1333 San Pablo Street, MMR 624, Los Angeles, CA 90033*, Richard N. Bergman, Ph.D., Timothy Garvey, M.D., Lawrence S. Phillips, M.D., Charles B. Nemeroff, M.D., Daniel R. Weinberger, M.D., Georges M. Gharabawi, M.D., Ramy A. Mahmoud, M.D., Andrew Greenspan, M.D., Jacqueline D. Morein, B.S., Young Zhu, Ph.D.

Educational Objectives:

At the conclusion of this presentation, participant should be able to recognize the differential impact of atypical antipsychotic agents on insulin resistance, insulin secretory dysfunction, and adiposity in patients with schizophrenia and schizoaffective disorder, and the relationships between these factors and the risk for diabetes.

Summary:

Background: Atypical antipsychotics induce weight gain and are linked to increased incidence of diabetes, but their relative impact on factors that elevate diabetes risk are unknown.

Methods: We performed a six-month randomized, double-blind study to evaluate effects of risperidone (RIS) or olanzapine (OLZ) on glucoregulatory function in patients with schizophrenia. At baseline and wks 6 and 24, we quantified insulin sensitivity (S) and pancreatic function (disposition index, DI) from the intravenous tolerance test, total adiposity by DEXA, and visceral adiposity by CT.

Results: Demographics: Groups (RIS: n=28, M/F 22/6; OLZ: n=31, M/F 18/13) were age-matched (RIS, 39.8±7.6 (S.D.): OLZ: 39.6±8.3 yrs), with race similarly represented. Anthropometry: Groups were matched for weight (RIS: 188.8±41.6, OLZ: 190.8±39.2 lbs) and both total and visceral adiposity. Metabolic Characteristics: Baseline S, (RIS: 2.13±1.40, OLZ: 2.42±1.97) and DI (RIS: 1529.7±1388.6, OLZ: 1406.5±1240.7) were similar between groups, as were all fasting plasma values except glucose (RIS: 97.6±10.7, OLZ: 92.6±7.6 mg/dl; p=0.042) and triglycerides (RIS: 145.6±102.3, OLZ: 99.2±49.6 mg/dl; p=0.039). Final six and 24-wk results will be presented.

Conclusions: This clinical study represents the first attempt to prospectively quantify effects of antipsychotics on metabolic processes that increase diabetes risk in the psychiatric population.

References:

1. Koro CE, Fedder DO, L'Italien GJ, Weiss SS, Magder LS, Kreyenbuhl J, Revicki DA, Buchanan RW: Assessment of inde-

pendent effect of olanzapine and risperidone on risk of diabetes among patients with schizophrenia: population based nested case-control study. *Br Med J* 2002; 325:243-247.

2. Nasrallah HA, Newcomer JW: Atypical antipsychotics and metabolic dysregulation: evaluating the risk/benefit equation and improving the standard of care. *J Clin Psychopharmacol* 2004; 24(5 Suppl 1):S7-14.

NR829 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Effect of Attitudes of Children With ADHD on Medication Compliance

Michelle Roby, *Center for Attention, 2129 Belcourt Avenue, Nashville, TN 37212*; Robert D. Hunt, M.D., Brandon S. Vestal, B.A.

Educational Objectives:

At the conclusion of this session, the participants will recognize the correlation between children's attitudes toward their medication and their compliance and response to treatment. These data suggests that physicians should ensure that children, not just parents, understand the reasons for and value of medication.

Summary:

Objective: This study assessed the relationship between children's understanding of their problems and medication in relation to their compliance and response to treatment.

Method: 30 children, ages 8-15, with a spectrum of DSM-IV diagnoses of ADHD or affective disorders completed a 14-item Medication Attitudes Scale for Children (MASC) developed at the Center for Attention to assess their awareness of their difficulties, diagnoses, reasons for treatment, and expectations of medication. Response on the MASC was analyzed in relation to their treatment compliance, therapeutic benefit, and tolerance of AEs.

Results: Children who demonstrated a high level of understanding of their problem and the purpose of their medication were more compliant with treatment. Those who knew what medication they were taking (85%) and the specific goals of their treatment (88%) were highly compliant over three months follow up. Patients with less understanding of their problems and treatment were less compliant ($p > 0.05$).

Conclusions: These findings clearly suggest that involving children in understanding the reasons for treatment and potential benefits from medication improves their attitude, compliance, and benefit from treatment. In fact, 91% of subjects said they would recommend medication to a friend who had similar problems.

References:

1. Efron D, Jarman FC, Barker MJ: Child and parent perceptions of stimulant medication treatment in attention deficit hyperactivity disorder. *Journal of Pediatrics & Child Health*, 1998; 34(3), 288-292.
2. All About ADD: Understanding Attention Deficit Disorder, Mark Selikowitz.

NR830 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Comparison of a Brief Prevention Program and Supportive Counseling for PTSD in Adult World Trade Center Survivors

JoAnn Difede, Ph.D., *Department of Psychiatry, Weill Medical College of Cornell University, 525 East 68th Street, Box 200, New York, NY 10021*; Jennifer Roberts, Ph.D., Meredith Singer, Ph.D., Amy Rubenstein, Ph.D., Cezar Giosan, Ph.D.

Summary:

The present study investigated the extent to which a brief prevention program (BP) led to greater symptom reduction and decreased diagnosis of chronic PTSD than supportive counseling (SC). The BP treatment combined cognitive restructuring (CR), prolonged exposure therapy (PE), and relaxation. A small sample of survivors with direct exposure to the World Trade Center (WTC) (N=15) were assessed using the Clinician Administered Posttraumatic Stress Scale (CAPS). Patients were diagnosed with PTSD or acute stress disorder and randomly allocated to SP (N=9) or SC (N=6) treatment conditions. Treatment involved weekly individual therapy sessions. Independent assessments were conducted pre-treatment and post-treatment. Findings revealed a significant improvement in initial (M=72.56, SD=20.58.) and final (M=36.00, SD=26.04) CAPS severity scores for patients in the BP condition ($t=3.39, p=.01$). Results also revealed an improvement that was not statistically significant in the initial (M=70.00, SD=35.54) and final (M=43.50, SD=20.40) CAPS severity scores in the SC condition. Results reinforce findings from previous research suggesting that a BP treatment may reduce PTSD symptoms more than providing SC alone.

References:

1. Foa EB, Dancu CV, Hembree EA, Jaycox LH, Meadows, Street GP: A comparison of exposure therapy, stress inoculation training, and their combination for reducing posttraumatic stress disorder in female assault victims. *Journal of Consulting and Clinical Psychology* 1999; 67: 194-200.
2. Bryant RA, Moulds ML, Guthrie RM, Dang ST, Nixon RDV: Imaginal exposure alone and imaginal exposure with cognitive restructuring in treatment of posttraumatic stress disorder. *Journal of Consulting and Clinical Psychology* 2003; 71, 706-712.

NR831 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Meta-Analysis of Randomized Clinical Trials Comparing Venlafaxine and SSRIs: The Evidence Revisited
Supported by Wyeth Pharmaceuticals

Michael E. Thase, M.D., *Department of Psychiatry, University of Pittsburgh Medical Center, 3811 O'Hara Street, Pittsburgh, PA 152132593*; A. Richard Entsuah, Ph.D., Saeed Ahmed, M.D., Diane Sloan, Pharm.D., Charles B. Nemeroff, M.D.

Educational Objectives:

At the conclusion of this session, the participant should know about the use of meta-analysis to compare the antidepressant effects of venlafaxine and SSRIs.

Summary:

Objective: Although there is evidence that venlafaxine has greater antidepressant efficacy than SSRIs, previous meta-analysis generally have not included studies by sponsors other than Wyeth. We now report a meta-analysis of all known studies from all funding sources.

Methods: Forty-six randomized, clinical trials (RCTs) comparing venlafaxine with citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, or sertraline were identified; 13 had not been included in our most recent meta-analysis. Odds ratios (OR) for remission (HAM-D₁₇ score ≥ 7 at week 8 or endpoint, whenever possible) were computed and funnel plot analysis was used to detect selection bias.

Results: The updated 46 study meta-analysis yielded an OR of 1.26 (95% CI 1.16-1.36), compared with an OR of 1.30 (95% CI 1.17-1.44) in the earlier meta-analysis based only on Wyeth-funded studies. Neither inspection of the funnel plots nor specific statistical tests revealed any evidence of study selection bias.

Conclusion: These findings extend prior meta-analyses suggesting that venlafaxine is more effective than SSRIs grouped as a class. The inclusion of all available studies, regardless of sponsor, did not substantially change results. It remains unclear, however, if the advantage for venlafaxine extends beyond eight weeks, and results may not be consistent across all individual SSRIs.

References:

1. Smith D, Dempster C, Glanville J, Freemantle N, Anderson I: Efficacy and tolerability of venlafaxine compared with selective serotonin reuptake inhibitors and other antidepressants: a meta-analysis. *Br J Psychiatry* 2002; 180(5):396-404.
2. Thase ME, Entsuah AR, Rudolph RL: Remission rates during treatment with venlafaxine or selective serotonin reuptake inhibitors. *Br. J. Psychiatry* 2001; 178(3):234-241.

NR832 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Effect of Long-Acting Injectable Naltrexone on Quality of Life

Henry R. Kranzler, M.A., *Department of Psychiatry, University of Connecticut Health Center, 263 Farmington Avenue, Farmington, CT 06030-2103*; Song Liou, M.S., John Loewy, Ph.D., Bernard Silverman, M.D., Elliot Ehrich, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that mental health-related quality of life is diminished in patients with alcohol dependence but can be significantly improved with a combination of psychosocial and pharmacological therapy.

Summary:

Objective: Assess the effect of long-acting injectable naltrexone (LA-NTX) on health-related quality of life (QoL) in patients with alcohol dependence.

Method: A 24-week, multicenter, double-blind, placebo-controlled study evaluated the safety and efficacy of LA-NTX, a polylactide microspheres intramuscular formulation of naltrexone given monthly. DSM-IV alcohol-dependent patients (N=624) were randomized to six monthly injections of LA-NTX 380 mg, LA-NTX 190mg, or placebo in combination with psychosocial support (BRENDA). QoL was assessed using SF-36v2.0.

Results: Baseline SF-36 Mental Component Scores (MCS) were 38.7, 40.3, and 40.6 for the 380mg, 190mg, and placebo groups, respectively (significantly lower than U.S. population norms [51-55]). Following treatment, MCS increased by 7.9, 6.2, 6.0, in the 380mg, 190mg, and placebo groups. The change from baseline was significant for all treatment groups (P<0.001) and was greater with 380mg vs. placebo (P<0.05). Improvements correlated positively with reduction in alcohol consumption. Physical Component Scores (normal at baseline for all groups) did not change with treatment.

Conclusion: A large sample of alcohol-dependent patients demonstrated deficits in mental health-related QoL, which improved significantly with treatment for alcohol dependence. LA-NTX plus psychosocial therapy showed improvements in QoL that were greater than treatment with psychosocial therapy alone.

Supported by Alkermes, Inc. and NIAAA grant K24 AA13736.

References:

1. Volpicelli JR, Pettinati HM, McLellan AT, O'Brien CP: Combining medication and psychosocial treatments for addictions: the BRENDA approach. New York: The Guilford Press 2001.
2. Ware J, Kosinski M, Dewy J: How to score version 2 of the SF-36®. Lincoln, RI: QualityMetric Incorporated; 2000.

NR833 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Effect of Sertraline on Memory Function of Patients With PTSD

Moon Chung, M.D., *Department of Neuropsychiatry, Seoul Veterans Hospital, 632-6 yeoksamdong Kangnamku, Seoul 135-908, Korea*; Hae Jung, M.D., Jin Choi, M.D., Tae Kim, M.D.

Educational Objectives:

The study was done to evaluate effect of sertraline treatment on symptoms and memory function of posttraumatic stress disorder (PTSD). The study suggests that sertraline treatment improved symptoms and memory function of PTSD.

Summary:

Thirty veterans were recruited among whom 15 were PTSD patients and 15 were combat control subjects. Mississippi Scale for Combat-Related PTSD Combat Exposure Scale (CES), Hamilton Depression Rating Scale (HDRS) and Clinician-Administered PTSD Scale (CAPS) were used. Digit span, paired association learning test (PALT), and Rey Osterrieth complex figure (CFT) were assessed for memory function. HDRS, CAPS, and memory function test were evaluated at base line, two-week, and six-week intervals. There were significant differences between PTSD and non-PTSD veterans in Mississippi scale, CES, HDRS, and CAPS. Significant differences were found in memory function test between PTSD and non-PTSD veterans. PTSD veterans showed significant improvement in HDRS and CAPS at two-week and six-week and in memory function test at six-week of sertraline treatment. There was no significant correlation between symptoms and memory function.

Supported by Seoul Veterans Hospital.

References:

1. Hidalgo RB, Davidson JR: Selective serotonin reuptake inhibitor in posttraumatic stress disorder. *J psychopharmacol* 2000; 14:70-76.
2. Streckler T, Shagal A. The role of serotonergic-cholinergic interactions in the mediation of cognitive behavior. *Behav Brain Res* 1995; 67:165-199.

NR834 Thursday, May 26, 12:00 p.m.-2:00 p.m.

A Systematic Review of Research Findings on the Efficacy of Interpersonal Therapy for Depressive Disorders

Marcelo Mello, M.D., *Department of Psychiatry, Universidade Federal de Sao Paulo, Rua Prof. Alfredo Ashcar 430, Sao Paulo 05621010, Brazil*; Jair Mari, M.D., Josue Bacaltchuk, M.D., Helen Verdelli, Ph.D., Richard Neugebauer, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that the interpersonal psychotherapy is a efficient form of treatment for the depressive spectrum disorders, after a systematic review of literature and a meta-analysis.

Summary:

Interpersonal psychotherapy (IPT) is a time-limited psychotherapy for major depression. The aim of this study is to summarize findings from controlled trials of the efficacy of IPT in the treatment of depressive spectrum disorders using a meta-analytic approach.

Studies of randomized clinical trials of IPT efficacy were located by searching all available databases from 1974 to 2002. The efficacy outcomes were: remission, clinical improvement; the difference in depressive symptoms between the two arms of the trial at endpoint, and no recurrence. Dropout rates were used as an index of treatment acceptability.

Thirteen studies fulfilled inclusion criteria and four meta-analyses were performed. IPT was superior in efficacy to placebo in nine studies (Weight Mean Difference (WMD) – 3.57 [–5.9;–1.16]). The combination of IPT and medication did not show an adjunctive effect compared with medication alone for acute treatment (RR 0.78 [0.30;2.04]), for maintenance treatment (RR 1.01 [0.81; 1.25]), or for prophylactic treatment (RR 0.70 [0.30, 1.65]). IPT was significantly better than CBT (WMD –2.16 [–4.16;–0.15]).

The efficacy of IPT proved to be superior to placebo, similar to medication, and did not increase when combined with medication. Overall, IPT was more efficacious than CBT. Current evidence indicates that IPT is an efficacious psychotherapy for DSD and may be superior to some other manualized psychotherapies.

References:

1. Klerman GW, Rounsaville BJ: Interpersonal Psychotherapy of Depression. New York, Basic Books, 1984.
2. Weissman MM, JC; Klerman GL: Comprehensive Guide to Interpersonal Psychotherapy. New York, Basic Books, 2000.

NR835 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Starting Dose and Persistence for Ziprasidone Users in Medicaid

Supported by Pfizer, Inc.

C. Daniel Mullins, Ph.D., *PHSR, University of Maryland, 515 West Lombard Street - 2nd Floor, Baltimore, MD 21201*; Fadia T. Shaya, Ph.D., Julie Zito, Ph.D., James Gardner, M.S., Diane McNally, M.S., Fanlun Meng, M.S., David Harrison, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participants should comprehend the relationship between starting dose and persistence on ziprasidone therapy. Specifically, participants should recognize that doses in the medium to high range lead to longer persistence on therapy.

Summary:

Objective: To determine the relationship between ziprasidone starting dose and persistence among patients diagnosed with schizophrenia.

Method: Adult Medicaid recipients diagnosed with schizophrenia and having ziprasidone prescription claims between 7/1/01 and 9/30/03 were categorized by starting dosage: low (20-60mg) n=517; medium (61mg-119mg) n=339; and high (120-160 mg) n=341. Persistence was measured using refill patterns, allowing 15-day gaps between expected refill dates, and compared across starting doses using Chi-Square tests. Multivariate logistic analysis explored the simultaneous impact of age, gender, race, and year of treatment initiation in addition to starting dose.

Results: Discontinuation rates across the study period (maximum 30 months) were greater for patients initiated with low (p=0.001) and medium dose (p=0.02) than for high-dose patients. Discontinuation rates were not statistically different for low and medium doses. Discontinuation rates at 365, 180, and 90 days were higher for low dose than high dose (p<0.05) but not significantly different between low and medium or medium and high doses. These results were similar in the multivariate models.

Conclusions: Schizophrenia patients started on high doses of ziprasidone have greater persistence up to two and a half years than those who start on low doses.

References:

1. Sajatovic M, Davies M, Hrouda DR: Enhancement of treatment adherence among patients with bipolar disorder. *Psychiatr Serv* 2004; 55(3):264-9.
2. Kane J. Antipsychotic drug side effects: their relationship to dose. *J Clin Psychiatry* 1985; 46(5 Part 2):16-21.

NR836 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Impact of Medication Adherence on Healthcare Utilization in Bipolar Disorder

Supported by AstraZeneca LP

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Educational Objectives:

At the conclusion of this session, the participant should understand the economic impact of adherence to mood stabilizer medication on overall mental-health related health care costs for patients with bipolar disorder.

Summary:

Introduction: Annually, about 1% of American adults have bipolar (BD). This study examined the impact of patient adherence with a mood stabilizer (first-line treatment) for BD on health care utilization within a United States managed care organization (MCO).

Methods: A retrospective claims analysis of approximately 1.4 million MCO members identified adults with a BD diagnosis in 2002. Those continuously enrolled who received a mood stabilizer (lithium, valproate, carbamazepine, lamotrigine, or oxcarbazepine) during 2003, were stratified into two cohorts, based on percent of days during 2003 with filled supply of mood stabilizer: high adherence (≥80%) and low adherence (<80%). Mental health-related emergency room visits and inpatient hospitalizations were compared between cohorts, adjusting for age, gender, and comorbidity.

Results: Among 1,399 patients (mean age 42.9 years; 66.3% female) studied, mean adherence to mood stabilizer therapy in the high adherence group (n=550) was 94.8% (±6.3%) versus 42.8 (±23.7%) in the low adherence group (n=783). Patients with low adherence to mood stabilizer therapy were more likely to experience mental health-related, emergency room visits (OR=1.98; 95%CI=1.38–2.84) and inpatient hospitalizations (OR=1.71; 95%CI=1.27–2.32).

Conclusion: Better adherence with mood stabilizers was associated with significantly lower risk of mental health-related emergency room visits and hospitalizations in patients with BD.

References:

1. National Institute of Mental Health. Bipolar Disorder. Bethesda (MD): National Institute of Mental Health, National Institutes of Health, US Department of Health and Human Services; 2001. NIH Publication No. 002-3679.
2. American Psychiatric Association Practice Guideline for the Treatment of Patients with Bipolar Disorder (Revision). *Am J Psychiatry* 2002; 159(4Suppl):1-50.

NR837 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Duloxetine in Diabetic Peripheral Neuropathic Pain: Impact of Comorbid Conditions

Supported by Eli Lilly and Company

Michael J. Robinson, M.D., *Department of Neuroscience, Eli Lilly and Company, 12894 Brighton Circle, Carmel, IN 46032*; T. Hardy, M.D., A. Prakash, B.S., A. Rosen, M.S., S. Shen, Ph.D., J. Wernicke, M.D.

Educational Objectives:

At the conclusion of this presentation, the participants will learn that the safety and tolerability of duloxetine in the management of DPNP were not significantly affected by the presence of baseline comorbid conditions in this study.

Summary:

Background: To assess safety and tolerability for duloxetine in patients with diabetic peripheral neuropathic pain (DPNP) who also had comorbid conditions.

Methods: Data were pooled from two double-blind, placebo-controlled studies in which patients (age > 18 years) were randomized to duloxetine (20mg QD, 60mg QD, or 60mg BID; n=568), or placebo (n=223) for 12-13 weeks. Safety assessments: discontinuation rates, spontaneously reported treatment-emergent adverse events (AEs), and vital signs.

Results: Entry demographics (mean) across all patients: age, 60.4 years (SD=10.8); diabetes duration, 10.8 years (SD=9.6); and diabetic neuropathy duration, 3.8 years (SD=4.1). Common comorbid conditions were hypertension, hyperlipidemia/hypercholesterolemia, gastroesophageal reflux disease, and erectile dysfunction. The AE discontinuation rate was similar between duloxetine-treated patients with and without baseline hypertensive disorders (13.5% vs. 14.5%). AE incidence was similar between patients with and without baseline comorbid conditions. Mean baseline-to-endpoint changes in sitting systolic and diastolic blood pressure (BP) were similar between patients with and without baseline elevated BP (sitting systolic BP, elevated: duloxetine -9.3mm Hg vs. placebo -8.4mm Hg, p=.639; normal: duloxetine 3.6mm Hg vs. placebo 2.0mm Hg, p=.255).

Conclusions: In this study, the safety and tolerability of duloxetine in the management of DPNP were not significantly affected by the presence of baseline comorbid conditions.

References:

1. Sowers JR, Epstein M, Frohlich ED: Diabetes, hypertension, and cardiovascular disease: an update. *Hypertension* 2001; 37:1053-1059.
2. Wernicke J, Lu Y, D'Souza D, Waninger A, Tran P: Antidepressants: duloxetine at doses of 60 mg QD and 60 mg BID is effective in the treatment of diabetic neuropathic pain (DNP). *J Pain* 2004; 5(Suppl 1):S48.

NR838 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Effects of Rivastigmine on Attention in Patients With Dementia Associated With Parkinson's Disease Supported by Novartis Pharma AG, Basel, Switzerland

Keith Wesnes, Ph.D., *Cognitive Drug Research Ltd, Gatehampton Road, Goring-on-Thames RG8 0EN, United Kingdom*; Chris Edgar, B.S.C., Roger Lane, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to identify attentional deficits and fluctuations in dementia associated with PD, and consider the potential effects of cholinesterase inhibitor treatment on these symptoms.

Summary:

Objective: To investigate the effects of rivastigmine, an inhibitor of acetylcholinesterase and butyrylcholinesterase, on attentional deficits and fluctuations in dementia associated with Parkinson's disease (PD). These key symptoms of dementia associated with PD are believed to be caused by cholinergic deficits.

Methods: This was a 24-week, multicenter, double-blind, placebo-controlled study of rivastigmine. Patients had a diagnosis of dementia associated with PD and Mini-Mental State Examination scores of 10-24. Attention was assessed using three tests from the Cognitive Drug Research computerized cognitive assessment system: simple reaction time, choice reaction time, and digit vigilance. The study enrolled 541 patients, of whom 487 provided CDR data.

Results: Four composite scores from the three tests that utilized every individual measure were derived and analyzed. Highly sig-

nificant benefits of rivastigmine over placebo were seen on Power-of-Attention (a measure of ability to focus attention), Continuity-of-Attention (a measure of sustained attention), Response Variability (a measure of fluctuating attention), and Cognitive-Reaction Time (a measure of central processing).

Conclusions: Rivastigmine produced a widespread and marked improvement, the patients reaching up to 68% of normal functioning on the four measures. The attentional deficits in this dementia respond very well to cholinergic therapy.

References:

1. Simpson PM, Surmon DJ, Wesnes KA, Wilcock GK: The cognitive drug research computerized system for demented patients: a validation study. *Int J Geriatr Psychiatry* 1991; 6:95-102.
2. Emre M, Aarsland D, Albanese A et al: Rivastigmine in Parkinson's disease patients with dementia: a randomized, double-blind, placebo-controlled study. *NEJM* 2004, in press.

NR839 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Association Between Serotonin Transporter Polymorphism and the Effect of Atypical Antipsychotics on the Serum Glucose and Lipid Supported by GlaxoSmithKline

Park Se Hyeon, M.D., *Neuropsychiatry Department, College of Medicine, Inje University, 633-165 Gaegeum-dong, Busanjin-gu, Busan 614-735, Korea*; Park Se Hyeon, M.D., Kim Young Hoon, M.D., Yoon Seong Hwan, M.D., Kong Bo Geum, M.D., Lee Sang Kyeong, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should understand the effect of atypical antipsychotics on the serum glucose and lipid in schizophrenic patients and the association with the genotype distribution of 5-HTTLPR.

Summary:

Objectives: The author investigated the association between the genotype distribution of 5-HTTLPR and the effect of atypical antipsychotics on the serum glucose and lipid in schizophrenic patients.

Methods: Study subjects were 66 schizophrenic patients taking atypical antipsychotics (risperidone, olanzapine, clozapine, quetiapine, zotepine) and control subjects were 82 schizophrenic patients taking typical antipsychotics (haloperidol) for at least 12 weeks. The author examined serum fasting blood sugar (FBS), HbA1c, total cholesterol, triglyceride, and the genotype distribution of 5-HTTLPR in all subjects, using polymerase chain reaction of genomic DNA with primers flanking the promoter regions of the 5-HTT gene. Between group comparisons of the genotype distribution and the effect of antipsychotics on the serum glucose and lipid level were performed by using score test for t-test, one way ANOVA and chi-square test.

Results: There was a significant increase in FBS level in patients taking atypical antipsychotics except for risperidone. But there was no statistical difference in 5-HTTLPR genotype distribution and the effect of atypical antipsychotics on FBS, HbA1c, total cholesterol and triglyceride serum level in schizophrenic patients.

Conclusions: These results suggest that 5-HTTLPR polymorphism had no significant association with the effect of atypical antipsychotics on the serum glucose and lipid in Korean schizophrenic patients.

References:

1. Lindenmayer JP, Czobor P, Volavka J, Citrome P, Sheitman B, Joseph PM et al: Changes in glucose and cholesterol levels in patients with schizophrenia treated with typical or atypical antipsychotics. *Am J Psychiatry* 2003; 160:290-6.

- Masellis M, Basile V, Meltzer HY, Liberman JA, Sevy S, Macciardi FM et al: Serotonin subtype 2 receptor genes and clinical response to clozapine in schizophrenia patients. *Neuropsychopharmacology* 1998; 19:123-32.

NR840 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Impact of Atypical Agents on Outcomes of Care in Schizophrenia Patients
Supported by Pfizer Inc.

Amie T. Joyce, M.P.H., *Pharmetrics, 206 Lake Avenue, Trumbull, CT 06611*; David J. Harrison, Ph.D., Daniel A. Ollendorf, M.P.H.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the therapeutic and economic disparities between ziprasidone, risperidone, and olanzapine in the treatment of patients with schizophrenia.

Summary:

Objective: To compare persistence, compliance, and psychiatric treatment costs in patients initiating atypical therapies.

Methods: Medical and pharmacy claims data were used to compare persistence (days of therapy between first and last prescription, allowing therapy gaps <90 days); compliance (days of medication supplied with total days on therapy); and treatment costs in schizophrenic adults with claims for atypicals from 3/2001-8/2003 and enrollment for ≥ 6 months before and ≥ 12 months after therapy initiation. One-year psychiatric treatment costs were examined before and after therapy initiation. Differences in cost fluctuations were tested by univariate techniques.

Results: Persistence was approximately 30 days longer for patients receiving ziprasidone (n=217; 228 days) than risperidone (n=831; 193 days) or olanzapine (n=762; 201 days). Compliance was significantly ($P<0.01$) higher among patients receiving ziprasidone (87%) compared with other treatments (78%-80%). Ziprasidone patients had significantly larger decreases (-\$6,866) in mean annual psychiatric-related costs following therapy initiation than those on risperidone (-\$3,353; $P=0.0116$) or olanzapine (-\$4,764; $P=0.0021$). The primary driver of cost savings was reduced hospitalization after treatment initiation.

Conclusion: Patients initiated on ziprasidone had longer persistence, better compliance, and greater decreases in psychiatric-related costs than those initiated on other atypicals.

References:

- Arato M, O'Connor R, Meltzer, HY on behalf of the ZEUS Study Group: A 1-year, double-blind, placebo-controlled trial of ziprasidone 40,80, 160 mg/day in chronic schizophrenia: the Ziprasidone Extended Use in Schizophrenia (ZEUS) study. *Int Clin Psychopharmacol* 2002; 17:207-215.
- Loebel A, Siu CO, Romano SJ: Overview of ziprasidone tolerability in patients 55 years of age and older. Presented at the 156th Annual Meeting of the American Psychiatric Association; May 17-22, 2003; San Francisco, California, USA.

NR841 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Interaction of 5-HT_{2A} Receptor (T102C Polymorphism) and 5HT Transporter Genes (5-HTTLPR Insertion/Deletion Polymorphism) for the Development of Schizophrenia and Antipsychotic Response

Chi-Un Pae, M.D., *Department of Psychiatry, The Catholic University of Korea, 505 Bapo-Dong, Seocho-Gu, Seoul 137-701, South Korea*; Wang-Yeoun Won, M.D., Alessandro Serretti, M.D., Paola Artioli, M.D., Jung-Jin Kim, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the method and interpretation of interactive gene polymorphism for the development of schizophrenia as well as to antipsychotic response.

Summary:

Objectives: The pathogenesis of schizophrenia may lie on multiple genetic and environmental etiologies, so that it is more rational to think several genetic factors could interact synergistically, needing interaction studies. We have investigated the potential interaction of the 5-HT_{2A} and 5-HTTLPR polymorphisms in the development of schizophrenia, as well as the interaction of the two polymorphisms in relation with symptomatology, family history, onset age, and antipsychotic response.

Methods: Genomic DNA analysis with polymerase chain reaction (PCR) was used for 5-HTTLPR and 5-HT_{2A} polymorphisms genotyping. Patients with schizophrenia and healthy individuals participated in this study. A possible interaction between the two polymorphisms was analyzed by regression and analysis of variance (ANOVA) methods.

Results: Neither 5-HTTLPR variants nor 5HT-2A variants were associated with response as a categorical variable (response/no response: Chi sq.= 3.83, p=0.14 for 5-HTTLPR genotypes and Chi sq.=0.42, p=0.81 for 5HT-2A genotypes). There was no difference between genotypes either in familiarity for the disease or in antipsychotic treatment used. Neither 5-HTTLPR nor 5HT-2A polymorphisms were associated with response as a continuous variable (MANOVA: F=0.20 df 2, 108 p=0.82 for SERTPR and MANOVA: F=0.53 df 2, 108 p=0.58 for 5HT-2A); the negative results did not change even considering *I or *s carriers and *C or *T carriers versus other genotypes, respectively. MANOVAs also gave negative results. The same negative results were confirmed by Factorial ANOVA (F=0.40 df 4 p= 0.80).

Conclusion: These results suggest that the interaction between 5-HTTLPR and 5HT-2A polymorphism may not contribute to susceptibility to antipsychotic response as well as schizophrenia development itself, at least in the Korean population.

This study was supported by a grant (KRF-2004-003-E00145) from Korea Research Foundation.

References:

- Pae et al: Polymorphism of the serotonin transporter gene and symptomatic dimensions of schizophrenia in the Korean population. *Neuropsychobiology* 2003; 47:182-186.
- Minov et al: Serotonin-2A-receptor and -transporter polymorphisms: lack of association in patients with major depression. *Neurosci Lett.* 2001; 303:119-122.

NR842 Thursday, May 26, 12:00 p.m.-2:00 p.m.

A Novel, Point of Care Test for Lithium Levels
Supported by Akers Biosciences Inc. ReliaLAB Inc

William M. Glazer, M.D., *Massachusetts General Hospital, Harvard Medical School, 100 Beach Plum Lane, P.O. Box 121, Menemsha, MA 02552*; John Sonnenberg, Ph.D., Michael Reinstein, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the reliability of an instant, office-based test for blood lithium levels and discuss its utility in the clinical setting.

Summary:

Background: In a previous publication we reported high reliability for the measurement of blood lithium levels with a new instant (two-minute) test as compared with standard laboratory measures. This study replicates these findings.

Design: 56 bipolar psychiatric patients on oral lithium contributed 88 matched data points, for which blood lithium levels were estimated by the instant test, and two different laboratories that employed atomic absorption (AA) spectrophotometry. As part of the comparative testing, masked aliquots of control solutions were tested in order to generate comparative precision data. The 88 comparative points (New test vs Labs 1 and 2, and Lab 1 vs Lab 2) were analyzed by four statistical tests: (1) descriptive statistics including means, standard deviations, and range (min-max), (2) matched pairs t-tests (two-tail), (3) orthogonal regressions, and (4) bias (difference) plots.

Results: The data showed excellent agreement between the instant method and the AA reference methods. This study design also showed some lack of consistency between the two AA methods, which was expected.

Conclusions: This study shows that the same clinical information is obtained regardless if testing by the novel test or routine laboratory, and the added benefits of immediate feedback from the new test will help improve monitoring rates.

References:

1. Glazer WM, Sonnenberg JG, Reinstein MJ, and Akers RF: A novel, point-of-care test for lithium levels: description and Reliability. *J Clin Psych* 2004; 65(5):652-656.
2. Marcus SC, Olfson M, Pincus HA, et al: Therapeutic drug Monitoring of Mood Stabilizers in Medicaid Patients with Bipolar disorder. *AM J Psychiatry* 1999; 156:1014-1018.

NR843 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Suicide Risk/Efficacy of Antidepressants in Youth (N > 1,800): Six Years of Data

Daniel A. Deutschman, M.D., *Department of Psychiatry, Southwest General, 18051 Jefferson Park Road, Suite 106, Cleveland (Middleburg Heights), OH 44130*; Douglas Deutschman, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate knowledge of the safety and efficacy of antidepressants in youth from a large population of patients seen in typical clinical practice.

Summary:

Objective: We present a rigorous statistical review of our data on the safety and efficacy of antidepressants in 2000 individual trials in youth from our real-world clinical practice in an effort to contribute to the data on this important issue.

Methods: We tracked clinician-rated youth suicidal thoughts, impulses, gestures, attempts and completions as well as efficacy, GAF scores, and symptom severity. We scrutinized reasons for discontinuation, side effects, and tolerability.

Results: Age range was 3 to 17 years; mean 14.4 years. 95% were Caucasian, 50% were male. Antidepressants were Celexa/Lexapro (38%), Wellbutrin (33%), and Zoloft (23%), followed by Prozac (16%), Effexor (13%), and Paxil (12%). Mean doses were mid to upper range of FDA "label". Robust efficacy was observed across all agents. We saw no signal of suicidal thinking, impulses, gestures or attempts (no completions).

Discussion: The divergence between these data and the FDA data raises many questions. Among them are: (1) is there a suicide risk signal in complex real-world patients, (2) are the "n's" for both groups too small and (3) are the two populations' (registration study vs. "real" patients) different?

Conclusion: In our clinical population of youth, antidepressants appear safe and effective.

References:

1. FDA Proposed Medication Guide: About Using Antidepressants in Children or Teenagers.
2. US Food and Drug Administration, Center for Drug Eval. and Research, posted 11/3/04.
3. Wegner L: Advice for treating children with antidepressants *AAP News* 2004; 25:146.

NR844 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Metabolic and EKG Monitoring of Patients Treated With Ziprasidone

Thomas E. Hansen, M.D., *Department of Psychiatry, Veterans Administration Medical Center, 3710 SW US Veterans Hospital Road, Portland, OR 97239*; Daniel Casey, M.D., William Hoffman, M.D., Laura Ross, B.A.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize and manage the metabolic and cardiac side effects that occur in a naturalistic, clinical setting with use of ziprasidone.

Summary:

Objective: Our objective was to carefully monitor metabolic effects and QTc in a clinical population treated with ziprasidone, hypothesizing that patients would improve in weight, fasting glucose and lipid levels (lowering cardiac risk), but that QTc would not change.

Method: Sample of convenience with only entry criterion ziprasidone treatment. Weight, EKG, fasting glucose, hemoglobin A1c, and lipids recorded pretreatment, 1 week, and 1, 3, 6, and 12 months.

Results: 44 patients enrolled (prior medication olanzapine in 30) with mean BMI 34. Twenty-three patients completed three months and 15 went 12 months. Metabolic measures (12 months) indicated improved health: cholesterol 212 to 179 ($p=.02$), fasting glucose 132 to 104 ($p=.12$), triglycerides 192 to 168 (NS). Weight, HDL, HgbA1c did not change. Initially 61% met criteria for metabolic syndrome, improving to 40% (12 months). QTc did not change at any point (420 ± 4 msec).

Conclusion: Measures of patient health improved over time, despite no mean decline in weight. Changes support monitoring patients early after changing medication. The lack of mean weight loss suggests that avoidance of weight gain should be a priority. For uncomplicated patients, EKG monitoring does not seem necessary.

Funding: Portland VA Research Foundation.

References:

1. Gunasekara NS, Spencer CM, Keating GM: Ziprasidone—A review of its use in schizophrenia and schizoaffective disorder. *Drugs* 2002; 62:1217-1251.
2. Marder SR, Essock SM, Miller AL et al: Physical health monitoring of patients with schizophrenia. *Am J Psychiatry* 2004; 161: 1334-1349.

NR845 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Evaluation of LTC Residents Converted to Divalproex Sodium Extended Release Supported by Abbott Laboratories

George G. Demos, R.Ph., *Consulting, Omnicare of Northern Illinois, 2313 S. Mount Prospect Rd, DesPlaines, IL 600181849*; Vicki Burton, Pharm.D., Viral Mehta, Pharm.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the importance of medication compliance in the elderly population and that use of extended release divalproex sodium maintains or improves behavior outcomes and is well tolerated in this population.

Summary:

Introduction: Omnicare of Northern Illinois (ONI) supports 160 LTC facilities representing over 20,000 residents. In 2003, over 2700 of these residents received some form of valproate. In that year, we adopted an initiative to convert these patients, as appropriate, to once daily divalproex sodium extended release (DVPX ER) in an effort to improve patient compliance and reduce nursing time. Medication compliance has been identified as a serious issue in the elderly as co-morbidities and complex dosage regimens abound. Agitated LTC residents are more likely to refuse medications that require multiple daily doses. This study retrospectively evaluated the efficacy, safety, and pharmaco-economic benefits of converting LTC residents from various forms of valproate to DVPX ER.

Methods: This chart review included 286 patients converted from valproic acid (VPA) or divalproex sodium (DVPX) to DVPX ER. Consultant pharmacists collected data on VPA levels and behavioral symptoms as noted in the Behavior Monitoring Tool pre and post conversion. The Behavior Monitoring Tool is an accepted industry standard in determining efficacy of drug therapies aimed at achieving optimal doses and in reducing distressing symptoms to patients and others.

Conclusion: This study demonstrated that residents with behavior problems stabilized on the valproex sodium extended release dosage form. In addition, a low fluctuation in VPA levels was noted and the once daily dosing was well tolerated.

References:

1. Fulmer TT, et al: An Intervention Study to Enhance Medication Compliance in Community-Dwelling Elderly Individuals. *Journal Geront Nurs* 1999; 25(8):6-14.
2. Zlotnick S. et al: Cost analysis of immediate versus controlled-release medication administrations in long-term care. *Consult Pharm.* 1996; 11:689-692.

NR846 Thursday, May 26, 12:00 p.m.-2:00 p.m. Are SSRI Responders More Likely to Report Discontinuation Symptoms? Supported by GlaxoSmithKline

David J. Carpenter, Pharm. D., *Department of Psychiatry—Department of Neurosciences MDC, GlaxoSmithKline, 2301 Renaissance Blvd, King of Prussia, PA 19406*; Karen Hewett, Ph.D., David Duff, Ph.D., Jacquie Christie, M.S., Regan Fong, Ph.D., John Davies, M.S.

Educational Objectives:

At the conclusion of the presentation, the participant should recognize that discontinuation symptoms can occur upon SSRI treatment cessation, and that the probability of experiencing discontinuations may be influenced by whether the patient responded to treatment or not.

Summary:

Objective: Examine whether responders to the SSRI paroxetine (PAR) have a different probability of experiencing discontinuation symptoms (DS, i.e., predefined AEs emergent upon stopping treatment) than do non-responders.

Methods: All acute, placebo (PBO)-controlled PAR studies in adults that systematically collected AEs emergent during taper/follow-up phases were included in these analyses. Twelve such

studies (in MDD, PMDD, GAD, PTSD, and SAD [social anxiety disorder]) were identified (N=4,686 patients; 2,794 for PAR and 1,892 for PBO). Patients reporting DS were classified according to treatment response, based on the CGI-Improvement scale.

Results: For PTSD, SAD, and PMDD, the probability of reporting DS was significantly higher in patients who responded to treatment. This effect existed in both the PAR and PBO groups. Additionally, in SAD, there was some evidence that the odds ratio (OR) of having DS based on response differed depending on treatment (i.e., OR greater for PAR than that for PBO). For MDD and GAD, there was no evidence of a relationship between treatment response and DS for either treatment.

Conclusions: Treatment responders may be more likely to experience DS than non-responders. Differences in response rates may account for some of the differences between treatments with respect to the incidence of DS.

References:

1. Haddad P: The SSRI discontinuation syndrome. *J Psychopharmacology* 1998; 12(3):305-313.
2. Black K, et al: Selective serotonin reuptake inhibitor discontinuation syndrome: Proposed diagnostic criteria. *J Psychiatry Neuroscience* 2000; 25(3):25-261.

NR847 Thursday, May 26, 12:00 p.m.-2:00 p.m. Bupropion SR Improves Sexual Functioning in Depressed Minority Women Supported by GlaxoSmithKline

Roseanne DeFronzo Dobkin, Ph.D., *Department of Psychiatry, Robert Wood Johnson Medical School, 675 Hoes Lane, Room D-317, Piscataway, NJ 08854*; Matthew Menza, M.D., Humberto Marin, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to: (1) diagnose and treat sexual dysfunction in depressed minority women, (2) recognize the impact of switching antidepressants on both depression and sexual function in minority women.

Summary:

Introduction: Minority women introduce a unique set of cultural factors into the treatment setting of depression. Yet, there is a dearth of research that addresses how depressed minority women respond to prescribed interventions for sexual concerns. This was the first study to examine the impact of a medication switch, from an SSRI to Bupropion SR, on the sexual functioning of depressed minority women.

Methods: A total of 18 minority women (five Hispanic, 10 African American, two Asian American, one Native American), who experienced poor tolerability or lack of efficacy in response to an adequate trial of an SSRI for depression and were experiencing low sexual desire were enrolled. The SSRI and Bupropion SR were cross-tapered with a target dose of 150-300mg of Bupropion SR. The patients were followed for 10 weeks and measures of sexual functioning (CSFQ) and depression (HAM-D) were administered bi-weekly in an academic medical setting.

Results: A single-group, repeated measures pretest-posttest design ($\alpha=.01$) was employed. In the group as a whole, there were significant improvements in desire $F(1, 17)=32.32, p<.001$, arousal $F(1, 17)=22.47, p<.001$, and orgasm $F(1, 17)=20.01, p<.001$. Additionally, African-American women demonstrated the largest improvement in depression (HAM-D) following the switch $F(1, 17)=7.78, p=.01$.

Conclusion/Discussion: This intervention effectively treated sexual concerns in this diverse, understudied group of depressed women.

References:

1. Miranda J, Chung JY, Green, BL et al: Treating depression in predominantly low-income young minority women: A randomized controlled trial. *JAMA* 2003; 290:57-65.
2. Clayton AH, McGarvey EL, Abouesh AL, Pinkerton RC: Substitution of an SSRI with bupropion sustained release following SSRI induced sexual dysfunction. *Journal of Clinical Psychiatry*, 2001; 62:185-190.

NR848 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Lipid Screening in a Cohort of Antipsychotic Medication Users

Supported by Bristol-Myers Squibb

Susan A. Oliveria, Sc.D., *Galt Associates, Inc., 160 East 53rd Street, 2nd floor, New York, NY 10022*; Marianne Ulcickas Yood, D.Sc., Karen E. Wells, B.S., Gil L'Italien, Ph.D.

Educational Objectives:

After reading the poster, the participant should have a better understanding of lipid screening practices among users of antipsychotic medications.

Summary:

Objective: The recent consensus conference of the American Diabetes Association has recommended active monitoring of lipid levels among antipsychotic users and more research to better understand the association between antipsychotics and dyslipidemia. Studies among treated schizophrenia patients suggest that the overall prevalence of dyslipidemias exceeds 40%. As a prelude to this research, it is important to understand the frequency of lipid screening among patients treated with antipsychotic therapy in current practice. The purpose of this study is to quantify the proportion of antipsychotic users that receive lipid screening in a real world setting.

Method: A retrospective cohort analysis was conducted in a large, Midwestern United States health care delivery system. Using computerized encounter, pharmacy, and laboratory result data, all patients who filled at least one prescription (index prescription) for an antipsychotic during 12/01/2002 through 06/10/2003 were identified. We obtained information on laboratory tests for low density lipoprotein (LDL), high density lipoprotein (HDL), and triglycerides (TG) for one year after the index prescription.

Results: We identified 1,200 antipsychotic users. Overall, 38.3% of antipsychotic users had laboratory measurements for LDL, HDL, or TG after the index prescription. The mean number of tests per patient was 1.6 (standard deviation=2.4). Overall, 21.5% of patients had an abnormal test result (defined as: TG >200; HDL<40; LDL>100 if coronary heart disease (CHD) or CHD risk equivalents; LDL>130 if 2 or more CHD risk factors; LDL>160 if 0 or 1 risk factor).

Conclusion: Almost 62% of patients exposed to antipsychotics did not receive testing for dyslipidemia. Given the high prevalence of dyslipidemias in these populations, increased screening is needed to avoid clinical outcomes associated with dyslipidemias.

References:

1. American Diabetes Association: Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. *Diabetes Care*, 2004; 27(2):p. 596-601.
2. Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults-Adult Treatment Panel III. National Institutes of Health, No. 01-3670, May 2001.

NR849 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Clinical Impact and Cost-Benefit Analysis of Switching From Other Atypical Antipsychotic Agents to Ziprasidone in Patients With Metabolic Dysfunction and/or Poor Clinical Response to Other Atypical Agents

Supported by Pfizer Pharmaceuticals

Judith Hyatt, Pharm.D., *Behavioral Health, VAWNY Healthcare System, 3495 Bailey Avenue, Buffalo, NY 14215*; Fern Beavers, M.S.N., Alicia Saldana, M.D., Josie Olympia, M.D., Sudha Krishnaswamy, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the risks and benefits of switching antipsychotic agents in patients experiencing metabolic dysfunction and/or poor response to current therapy.

Summary:

Introduction: A consensus panel scrutinized peer-reviewed studies examining risks for metabolic dysfunction in patients receiving atypical antipsychotic agents and determined a three-tier risk: clozapine, olanzapine>risperidone, quetiapine>ziprasidone, aripiprazole. The current study examines the effect of switching patients experiencing poor clinical response, dyslipidemia, and/or diabetes with currently used atypical agent to ziprasidone.

Methods: Patients with poor clinical response, dyslipidemia, and/or diabetes participated in this six-month prospective study. Positive and Negative Syndrome Scale (PANSS), lipid panels, and A1c were used to evaluate outcomes at baseline and at scheduled intervals.

Results: 34 patients consented and 20 patients completed this ongoing study. 16 patients enrolled for poor clinical response, six for diabetes, and 15 for dyslipidemia. Patients with poor clinical response had a significant reduction in total, positive, and negative PANNS ($p<0.01$). Patients with diabetes had a mean reduction in A1c of 0.98% ($P=NS$). Patients with dyslipidemia had a significant reduction in total cholesterol and triglycerides ($p<0.05$). Drug acquisition costs were significantly reduced ($p<0.01$) in these 20 patients (mean annual reduction >\$25,000).

Conclusions: Patients switched from other atypical antipsychotic agents to ziprasidone had significant improvement in clinical response, total cholesterol, and triglycerides. An improvement was seen in A1c, but this did not achieve statistical significance.

References:

1. Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. *Journal of Clinical Psychiatry* 2004; 65(2):267-272.
2. Stratton IM, Alder AI, Neil HA, Matthews DR, Manley SE, Cull CA, Hadden D, Turner RC, Holman RR: Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *British Medical Journal* 2000; 321(7258):405-412.

NR850 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Risks for Medication Nonadherence in Veterans With Severe Mental Illness

Jennifer L. Strauss, Ph.D., *HSRD, Durham VA Medical Center, Box 152, 508 Fulton Street, Durham, NC 27705*; Karen M. Stechuchak, M.S., Jennifer B. Zervakis, M.S., Maren K. Olsen, Ph.D., Eugene Z. Oddone, M.D., Marian I. Butterfield, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to: (1) recognize several risks for nonadherence to psychotropic medications in persons with severe mental illnesses and

(2) identify commonly reported patient reasons that contribute to medication nonadherence.

Summary:

Objective: Medication nonadherence is a leading cause of relapse among persons with severe mental illnesses (SMI). This study examines risks for nonadherence in veterans with SMI.

Methods: A research interview was administered to psychiatrically hospitalized veterans with SMI (N = 122). We assessed medication adherence and patient risk variables including alcohol/drug use, working alliance, treatment motivation, social support and insight into illness, and other potential reasons for nonadherence. Bivariate and logistic regression analyses were conducted.

Results: Over one-third (36%) reported medication nonadherence. Adherent and nonadherent participants did not statistically differ on demographics, diagnosis, alcohol use, alliance, treatment motivation, or social support. In the adjusted model, those with drug-use disorders (OR = 0.43, CI = 0.19-0.98, p = 0.04) and poor insight into illness (OR = 0.28, CI = 0.10-0.81, p = 0.02) were less likely to report medication adherence. Among nonadherent participants, patient-related factors were common reasons for nonadherence, specifically forgetting to take medications (21%) and side effects (9%).

Conclusion: High rates of psychotropic medication nonadherence are seen in hospitalized veterans with SMI. Illicit drug use and poor insight are risks for nonadherence. Common reasons for nonadherence are forgetting to take medication and side effects.

References:

1. Gray R, Wykes T, Gournay K: (2002). From compliance to concordance: a review of the literature on interventions to enhance compliance and antipsychotic medication 2002; 9: 277-284.
2. Oehl M, Hummer M, Fleischhacker WW: Compliance with anti-psychotic treatment. Acta Psychiatrica Scandinavica 2000; 102 (Suppl407), 83-86.

**NR851 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Hospitalization and Emergency Room Visits Before and After Treatment With Atypical
Supported by AstraZeneca LP**

Krithika Rajagopalan, Ph.D., *Health Economics, AstraZeneca LP, 1800 Concord Pike, Wilmington, DE 19850*; Maureen Lage, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that patients treated with different atypical antipsychotics may experience different outcomes. In the case of this analysis, differences in hospitalizations and emergency room visits were seen with quetiapine treatment, which may be reflective of improved medication compliance, overall effectiveness, or tolerability.

Summary:

Objective: Examine differences in hospitalization and emergency room visit rates pre- and post-initiation on olanzapine, quetiapine, or risperidone.

Methods: Retrospective analysis of a commercial claims database capturing inpatient, outpatient, and prescription drug services. Individuals with a mental illness diagnosis, and initiated with olanzapine (N=8,730), quetiapine (N=5,709) or risperidone (N=9,339) between 7/1/98 and 7/2/02 were identified. Mean differences in the hospitalization and ER visit rates between the pre- and post-six month periods across the treatments were examined using ANCOVA, controlling for age, gender, region, and type of mental illness diagnosis.

Results: Individuals initiated with olanzapine or risperidone were found to have a significantly higher difference in hospitalization rates (2.19%, p<0.0001; 1.72%, p<0.0001) and ER visit rates (3.80%, p<0.0001; 4.60%, p<0.0001) post initiation of medication compared with the six months prior to initiation of medication. In contrast, individuals who were initiated on quetiapine had a significantly lower difference in hospitalization rates (-4.37%, p<0.0001) and ER visit rates (-2.89%, p<0.0001) post initiation of quetiapine compared with the six months prior to quetiapine initiation.

Conclusion: Quetiapine, unlike olanzapine or risperidone, may be associated with fewer hospitalizations and ER visits following medication initiation. These results may suggest a more favorable side-effect profile and/or better compliance with quetiapine, and needs further investigation.

References:

1. Weiden PJ et al: Schizophr Bulletin 1995; 21(3):419-429.
2. Glazer WM et al: J Clin Psych 1996; 57:337-345.

NR852 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Estimating the Budget Impact of Quetiapine Treatment of Acute Mania Among Hospitalized Patients

Supported by AstraZeneca LP

Krithika Rajagopalan, Ph.D., *Health Economics, AstraZeneca LP, 1800 Concord Pike, Wilmington, DE 19850*; Jaime Caro, M.D., Karen Lee, Krista Huybrechts

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the economic and clinical benefit to managed care payers of increased use of quetiapine for the treatment of acute mania in their respective plans.

Summary:

Objective: Estimate the budget impact of treatments for acute mania in bipolar I disorder from a U.S. health care payer perspective.

Methods: Individual patient treatment course was simulated beginning with hospitalization. Young Mania Rating Scale score determined discharge, which changed according to equations relating it to treatment derived from clinical trial data and decision rules (clinical experts). Outcomes included time to response and symptom resolution, proportion of subjects reaching each outcome, and number of adverse events. Medical care costs were obtained from hospital discharge databases, the National Medicare Physician Fee Schedule and RedBook®. Different treatment scenarios were examined.

Results: Scenarios with a greater proportion of quetiapine users (5% vs. 40% and 100%) resulted in less impact on the health care budget (\$6,912, \$6,277, and \$5,525 per patient, respectively) and improvements in patient outcomes (e.g., 43%, 47%, and 54% responding at day 21; 74%, 77%, and 80% remitting by day 84). Quetiapine was found to be cost saving compared with olanzapine (about \$250 per patient), mainly due to fewer side effects. Sensitivity analyses found drug prices, discharge criteria, and side-effect management as influencing budget impact.

Conclusions: Increased use of quetiapine for mania in the U.S. is economically sound and may improve health outcomes.

References:

1. Woods SW: The economic burden of bipolar disease. Journal of Clinical Psychiatry 2000; 6:38-41.
2. Simon GE, Unützer J: Health care utilization and costs among patients treated for bipolar disorder in an insured population. Psychiatric Services 1999;50:1303-1308.

NR853 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Effectiveness and Safety of Topiramate in Bipolar Disorder

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Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that the combination of risperidone and topiramate, a new antiepileptic drug, may be a valuable option for short- and long-term treatment of bipolar disorder.

Summary:

Objectives: Topiramate (Topamax), a new antiepileptic agent, is a candidate drug for bipolar disorder. We evaluated topiramate as adjunctive treatment for bipolar patients. The safety and efficacy of the combination of risperidone and topiramate in the treatment of mania were assessed.

Method: Subjects (N=17) who met DSM-IV criteria for bipolar disorder and for a manic episode received both risperidone and topiramate for the treatment of their manic symptoms.

The patients were initiated on topiramate, 25mg/day, increasing by 25-50mg every three to seven days to a target dose between 100 and 300 mg/day, as other medications were held constant for five weeks. The Young Mania Rating Scale (Y-MRS), Clinical Global Impression-Bipolar Version Scale (CGI-BP), and Hamilton Rating Scale for Depression (HAM-D) were used to rate subjects weekly.

Results: By five weeks, 12 patients were responders, 50% reduction in the Y-MRS scores and a CGI of much or very much improved. Two patients were minimally improved, two showed no change. In all cases, side effects were transient. The most common adverse effect was paresthesia (n=3).

All patients lost weight with a mean of 4.13kg in five weeks, and significant reduction in body mass index (BMI) occurred. The mean topiramate dose at endpoint was 150mg/day.

Conclusion: Topiramate appears to have efficacy for the manic phase of bipolar illness. Among obese bipolar disorder patients, the weight loss potential of topiramate may be beneficial.

References:

1. Vieta E, Goikolea JM, Olivares JM, Gonzalez-Pinto A, Rodriguez A, Colom F, Comes M, Torrent C, Sanchez-Moreno J: 1-year follow-up of patients treated with risperidone and topiramate for a manic episode. *J Clin Psychiatry* 2003; 64(7):834-839.
2. Letmaier M, Schreinzer D, Wolf R, Kasper S: Topiramate as a mood stabilizer. *Int Clin Psychopharmacol* 2001;16(5): 295-298.

NR854 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Income of Individuals With Schizophrenia Supported by Eli Lilly and Company

Daniel Ball, M.B.A., *Outcomes Research, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Haya Ascher-Svanum, Ph.D., Baojin Zhu, Ph.D., Walter Deberdt, M.D.

Educational Objectives:

At the conclusion of this session, the participant should have a better understanding of the income of individuals with schizophrenia in the United States. Participants should also be able to place the income of schizophrenia patients in the context of income levels according to 2000 Federal poverty guidelines.

Summary:

Objectives: This study assessed the annual income of individuals with schizophrenia in the United States and made comparisons to the 2000 Federal poverty guidelines.

Methods: Data were from a naturalistic, prospective study of 2,327 actively treated schizophrenia patients conducted between 1997 and 2003. Self-reported monthly income in the prior six months was collected at an initial interview and annualized.

Results: Income was reported by 2,084 individuals. Medicaid (non-dual) was the payer for 45% of recipients, 17% Medicare only, 19% were dually eligible for Medicare and Medicaid, 6% CHAMPUS (Department of Defense), 5% private insurance, and 8% uninsured. Mean annual income was \$8,360, with 66% reporting incomes below the Federal poverty guidelines (\$8,350 for a family unit comprised of one individual). Income of Medicaid (non-dual) recipients was \$6,824; Medicare only \$10,629; dual eligibles \$7,750; CHAMPUS \$17,911; private insurance \$9,148; and, uninsured \$5,967. Over two-thirds of Medicaid only, dual eligible, or uninsured reported incomes below Federal poverty guidelines compared with approximately 50% of Medicare only or privately insured recipients and less than one-fourth of CHAMPUS recipients.

Conclusions: The majority of individuals with schizophrenia have incomes below poverty, which limits resources available to cover prescription drug and other medical cost sharing.

References:

1. Federal Register 2000; 65(31):7555-7557.

NR855 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Comparison of the Formal Published Human Clinical Trials for the Six 5HT SSRIs Supported by Pfizer Pharmaceuticals

Mohamed I. Ramadan, M.D., *Department of Psychiatry, University of Kansas-Wichita, 1010 North Kansas, Wichita, KS 67214*; Jane Griffith, M.S., Ahsan Khan, M.D., Sheldon Preskorn, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the magnitude and the quality of published clinical trial data of the safety, tolerability, and efficacy of citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline.

Summary:

Background: Confidence in the predictability of the safety, tolerability, and efficacy of a medication is directly proportional to the magnitude and quality of its published clinical trials. The goal is to provide an assessment of the amount of information from well-controlled, systematic clinical trials. There will be a difference in the extent of clinical trials amongst the six serotonin selective reuptake inhibitors (SSRIs) in terms of number of therapeutic areas studied, study quality, formal drug-drug interaction studies, number and diversity of subjects in each category.

Methods: Search PubMed (Medline) from 1966 to February 2003 for articles reporting randomized controlled trials of citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, or sertraline in humans. Use Reference Manager database software to manage retrieval. Analyze citations and abstracts for trial information. Create a Microsoft Excel spreadsheet for data manipulation. Query the database and spreadsheet to compile information about the extent and quality of studies.

Results: The search retrieved 1,475 citations. Analysis indicates that articles represent 723 studies. There were more efficacy studies than safety studies. Drugs marketed for a longer period had more studies. The total number of safety studies was 419. There

were 65 drug-drug interaction studies and 354 other safety studies. The total number of efficacy studies was 632. Efficacy studies were categorized by indication for each medication. Depression was the most studied indication, although SSRIs were also studied for generalized anxiety disorder, obsessive-compulsive disorder, posttraumatic stress disorder, social phobia, panic disorder, premenstrual dysphoric disorder, premature ejaculation, eating disorders, and substance abuse/dependence. For both efficacy and safety, the rank order from most to least studied was: fluoxetine, paroxetine, sertraline, fluvoxamine, citalopram, and escitalopram.

Conclusion For SSRIs, published data efficacy studies outnumbered safety studies. Depression was the most studied indication for SSRIs. SSRIs were also studied for other indications. Safety studies were divided into DDI studies and other safety studies. There were fewer DDI studies than other safety studies and significantly fewer subjects. It is important to study the safety and efficacy of SSRIs to help clinicians understand research behind a frequently used class of medications. The study found that SSRIs have the magnitude and the quality of data to support the class as an effective and safe group of medications, especially for the SSRIs, which have been in the market for a longer period of time.

References:

1. Geddes JR, Freemantle N, Mason J, Eccles MP, Boynton J: Selective serotonin reuptake inhibitors (SSRIs) versus other antidepressants for depression. The Cochrane Database of systematic Reviews 1999; (4): Art No.:CD001851.-DOI:10.1002/14651858.CD00185116.
2. Friedman LM; Furberg CD; DeMets DL: Fundamentals of Clinical Trials, 3rd ed. New York: Springer-Verlag; 1998.

NR856 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Cost of Antipsychotic Polypharmacy in the Treatment of Schizophrenia

Supported by Eli Lilly and Company

Baojin Zhu, Ph.D., *Outcomes Research, Eli Lilly and Company, Lilly Research Laboratories, Indianapolis, IN 46285*; Haya Ascher-Svanum, Ph.C., Douglas Faries, Ph.D., Christoph U. Correll, M.D., John M. Kane, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that antipsychotic polypharmacy is highly prevalent in the treatment of schizophrenia and that it adds substantial cost to the treatment of schizophrenia. A clearer understanding of the concomitant antipsychotic costs provides a more accurate portrayal of medication cost.

Summary:

Objective: To compare the cost of antipsychotic polypharmacy during the treatment of schizophrenia patients with risperidone, olanzapine, or quetiapine.

Methods: Data were drawn from a large prospective, naturalistic study of treatment for schizophrenia in the United States, conducted between 7/1997 and 9/2003. Participants who initiated on risperidone (N=276), olanzapine (N=405), or quetiapine (N=115) were followed for one year post initiation and compared on annual cost of all antipsychotic medications, and on daily cost of concomitant antipsychotic medication. Statistical analysis used propensity score adjusted bootstrap re-sampling methods.

Results: Quetiapine-treated patients accrued significantly higher annual cost of all antipsychotic medications compared with olanzapine or risperidone ($p < .01$). The daily cost of concomitant antipsychotic medications was significantly higher for quetiapine (\$8.70) compared with olanzapine (\$3.82, $p < .01$) or risperidone-treated patients (\$4.30, $p < .01$). The total daily cost of antipsychotics, including index antipsychotic cost, was \$15.33, \$13.90, and

\$11.04 for quetiapine, olanzapine, and risperidone, respectively. Each dollar spent on quetiapine-treated patient was accompanied by additional \$1.31 on concomitant antipsychotic medication, compared with \$0.64 for risperidone, and \$0.38 for olanzapine-treated patients.

Conclusions: Prevalent antipsychotic polypharmacy adds substantial cost to the treatment of schizophrenia. A clearer understanding of the concomitant antipsychotic costs provides a more accurate portrayal of medication cost.

References:

1. Miller AL, Craig CS: Combination antipsychotics: pros, cons, and questions. *Schizophr Bull* 2002; 28:105-109.
2. Centorrino F, Goren JL, Hennen J, salavatore P, Kelleher JP, Baldessarini RJ: Multiple versus single antipsychotic agents for hospitalized psychiatric patients: Case-control study of risks versus benefits. *Am J Psychiatry* 2004; 161:700-706.

NR857 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Outcomes in Patients With Schizophrenia Treated Adjunctively With Divalproex

Supported by Abbott Laboratories, Inc.

Erica Duncan, M.D., *Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine; Atlanta VA; 116A, 1670 Clairmont Rd., Decatur, GA 30033*; Maya Sternberg, Ph.D., William Boshoven, B.S.

Educational Objectives:

At the conclusion of the presentation, the participant should be more aware of the potential clinical benefits of adjunctive divalproex treatment for schizophrenia.

Summary:

Divalproex has proven efficacy in the treatment of bipolar disorder. This medication is being used increasingly as adjunctive treatment for schizophrenia, although the long-term effects on clinical course are not well known. We conducted a retrospective outcomes study in VA patients with schizophrenia receiving divalproex augmentation treatment. Patients diagnosed with schizophrenia were studied using a database of clinical information from our VA region. 416 patients received adjunctive divalproex at an average dose of 1126 ± 507 mg/day for some portion of their treatment (mean \pm SD = 388 ± 457 days on divalproex). The rate of hospitalizations and emergency psychiatric visits while taking divalproex was compared with rates while not taking divalproex using generalized estimating equations to account for the longitudinal nature of the data. Divalproex treatment resulted in decreased psychiatric hospitalizations (on divalproex: 2.7 admissions per month per 100 people, 96%CI(2.1, 3.5); off divalproex: 4.9 admissions per month per 100 people, 96%CI(3.7, 6.7); $p < 0.01$) and decreased emergency psychiatric outpatient visits (on divalproex: 2.6 visits per month per 100 people, 96%CI(2.1, 3.4); off divalproex: 6.1 visits per month per 100 people, 96%CI(4.9, 7.6); $p < 0.01$). These results suggests that divalproex as an adjunct treatment for schizophrenia can improve clinical course in patients with schizophrenia.

References:

1. Citrome L, Levine J, Allingham B: Changes in use of valproate and other mood stabilizers for patients with schizophrenia from 1994 to 1998. *Psychiatric Services* 2000; 51:634-8.
2. Casey DE, Daniel DG, Wassef A, Tracy KA, Wozniak P: Effect of divalproex combined with olanzapine or risperidone in patients with an acute exacerbation of schizophrenia. *Neuropsychopharmacology* 2003; 28:182-92.

NR858 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Risk of Glucose Elevation With Antipsychotics in a VA Population

Supported by Janssen Pharmaceutica, Inc.

Erica Duncan, M.D., *Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine; Atlanta VA; 116A, 1670 Clairmont Rd., Decatur, GA 30033*; Boadie Dunlop, M.D., William Boshoven, B.S., Sandra Woolson, M.S., Robert Hamer, Ph.D., Lawrence Phillips, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should have a greater appreciation of the effects of atypical antipsychotics on glucose metabolism in a clinical population.

Summary:

Schizophrenia may confer an increased risk of diabetes compared with the general population. Accumulating evidence indicates that the atypical antipsychotics are more diabetogenic than older typical agents. It is unclear whether all atypicals have equivalent effects on glucose metabolism. We conducted a retrospective, nonrandomized cohort analysis of 18,674 VA patients receiving outpatient prescriptions for olanzapine, risperidone, or typical antipsychotics from 10/1/98-6/30/03. Plasma glucoses collected over this period were classified regarding whether they were drawn before or during medication exposure. Maximum random glucoses during treatment did not reveal a significant effect of medication after covariates (age, sex, race, and diagnosis of schizophrenia) were included. In subjects without any glucose measurement \geq 160 mg/dl before index medication ($n=1,394$), olanzapine exposure was associated with a greater rate of developing at least one glucose \geq 200 mg/dl than risperidone (Odds Ratio=2.14, $p=0.003$). In subjects with fasting glucoses, olanzapine was associated with a greater rate of developing one or more fasting glucoses \geq 126 mg/dl than risperidone (Odds Ratio=4.74, $p=0.05$). Typical antipsychotics were associated with risk intermediate between the two atypicals. Thus, in this VA clinical population, olanzapine was associated with a greater risk of developing new onset of elevated glucose than risperidone.

References:

1. Ryan MC, Collins P, Thakore JH: Impaired fasting glucose tolerance in first-episode, drug-naive patients with schizophrenia. *Am J Psychiatry* 2003; 160:284-289.
2. Sernyak M, Leslie DL, Alarcon RD, Losonczy MF, Rosenheck R: Association of diabetes mellitus with use of atypical neuroleptics in the treatment of schizophrenia *Am J Psychiatry* 2002; 159:561-6.

NR859 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Donepezil for Cognitive Decline After Coronary Artery Bypass Grafting: A Randomized, Controlled Trial

Supported by Pfizer, Inc.

P. Murali Doraiswamy, M.D., *Department of Psychiatry, Duke University, 3350 Hospital South, Box 3018, Durham, NC 27710*; Michael Babyak, Ph.D., Therese Hennig, PA-C, Ranak Trivedi, M.S., Joseph Matthew, M.D., Mark Newman, M.D., James Blumenthal, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to discuss the use of cholinesterase inhibitors for treating post-surgical cognitive decline.

Summary:

Interventions to treat cognitive decline following coronary artery bypass grafting (CABG) are needed. We conducted a randomized, double-blind, 12-week, placebo-controlled trial of donepezil for post-CABG cognitive decline in subjects aged 50-85 with post-CABG decline (relative to pre-CABG). Donepezil was started at 5 mg qod, raised to 5 mg qd at week 2, and raised to 10 mg qd at week 6. Memory, attention, speed, and language were tested at baseline, week 6, and endpoint. 44 subjects were randomized to donepezil or placebo, of which 39 completed. The two groups did not differ significantly in mean age (70 years), gender, mean MMSE (26.3), or mean education level (10 years) ($p>0.05$). Diarrhea occurred more frequently in donepezil patients ($p<0.05$) and insomnia tended to occur more often in placebo group ($p<0.1$). These were the only AEs that differed significantly between groups. There were three serious adverse events (two on placebo and one on donepezil). Efficacy and safety analyses will be discussed with implications for further studies and treatment of post-CABG decline.

References:

1. Newman MF, Kirchner JL, Phillips-Bute B, et al: Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery. *N Eng J Med* 2001; 344:395-402.
2. Raja PV, Blumenthal JA, Doraiswamy PM: Cognitive deficits following coronary artery bypass grafting: Prevalence, prognosis, and therapeutic strategies. *CNS Spectrums* 2004; 9(10):763-772.

NR860 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Duloxetine in the Treatment of Fibromyalgia

Supported by Eli Lilly and Company

Deborah D'Souza, M.B.A., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Joachim Wernicke, M.D., Amy Rosen, M.S., Yili Lu-Pritchett, Ph.D., Donna Westell, B.S., Lesley Arnold, M.D.

Educational Objectives:

Audience participants will better understand the effects of duloxetine in the treatment of pain and other symptoms associated with fibromyalgia in female patients with or without major depressive disorder.

Summary:

Objective: To assess the efficacy of duloxetine, a balanced and potent dual-reuptake inhibitor of serotonin and norepinephrine, on the reduction of pain severity in female patients with primary fibromyalgia, with or without current major depressive disorder (MDD).

Method: This was a 12-week (followed by a one-week discontinuation phase), double-blind, randomized study comparing duloxetine 60 mg once daily (DLX60QD; $n=118$) and 60 mg twice daily (DLX60BID; $n=116$) with placebo (PBO; $n=120$), for efficacy and safety in treating female patients with fibromyalgia. The primary outcome measure was the Brief Pain Inventory (BPI) 24-hour average pain severity score (score range: 0 [no pain]-10 [pain as bad as you can imagine]). Response to treatment was defined as a 30% reduction in the BPI 24-hour average pain score. Secondary outcome measures included remaining BPI pain and interference scores, Fibromyalgia Impact Questionnaire (FIQ), the tender point pain threshold and tender point number, Clinical Global Impression of Severity (CGI-Severity), Patient Global Impression of Improvement (PGI-Improvement), and 17-item Hamilton Rating Scale for Depression. Health outcome measures were also assessed.

Results: Duloxetine-treated patients improved significantly compared with placebo-treated patients, on the BPI 24-hour average

pain score ($p < 0.001$, each dose vs. PBO; DLX60QD vs. PBO: difference = -1.23 [95% CI: $-1.82, -0.64$]; DLX 60 BID vs. PBO: difference = -1.24 [95% CI: $-1.83, -0.65$]). A greater number of duloxetine-treated patients compared with placebo-treated subjects achieved response at endpoint (DLX60QD: 55%, $p < 0.001$ vs. PBO, DLX60BID: 54%, $p = 0.002$ vs. PBO [33%]). The treatment effect of both doses of duloxetine on significant pain reduction was independent of the effect on mood and the presence of MDD. DLX60BID showed superiority over placebo in improvement in mean tender point threshold ($p = 0.003$) and reduction in number of tender points with low threshold ($p = 0.046$). In addition, both duloxetine doses compared with placebo significantly improved the CGI-Severity ($p = 0.005$) and PGI-Improvement ($p < 0.006$) scores. Duloxetine (both doses) compared with placebo significantly improved other secondary measures (BPI 24-hour average pain Area Under the Curve, FIQ total score, all other BPI pain and interference scores), with no significant differences between the duloxetine doses. Both doses of duloxetine were numerically superior to placebo on most health outcome measures. Significantly more duloxetine-treated patients reported treatment-emergent adverse events (PBO 79.2%, DLX60QD 92.4%, DLX60BID 90.5%). The rates of serious adverse events in both duloxetine treatment groups did not differ significantly from placebo (PBO 0%, DLX60QD 0.8%, DLX60BID 0.9%).

Conclusion: This study confirms previous findings that duloxetine is an efficacious and safe treatment for symptoms associated with fibromyalgia in female patients with or without MDD.

References:

1. Wolfe F, Ross K, Anderson J, et al: The prevalence and characteristics of fibromyalgia in the general population. *Arthritis Rheum* 1995; 38(1):19-28.
2. Arnold LM, Lu Y, Crofford LJ, et al: A double-blind, multicenter trial comparing duloxetine to placebo in the treatment of fibromyalgia patients with or without major depressive disorder. *Arthritis Rheum* 2004; 50(9):2974-2984.

NR861 Thursday, May 26, 12:00 p.m.-2:00 p.m. **Duloxetine in the Treatment of Diabetic Peripheral Neuropathic Pain: Results From Three Clinical**

Joel Raskin, M.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Yili Pritchett, Ph.D., Amy Chappell, M.D., Deborah D'Souza, M.B.A., Cheng Kar Wong, Ph.D., Joachim Wernicke, M.D.

Educational Objectives:

Audience participants will better understand the effects of duloxetine in the treatment of patients with diabetic peripheral neuropathic pain.

Summary:

The efficacy and safety of duloxetine, a dual-reuptake inhibitor of serotonin and norepinephrine, on the treatment of diabetic peripheral neuropathic pain (DPNP) was assessed in three studies. Patients with DPNP of at least six months duration, and without depression as diagnosed by DSM-IV were enrolled in the 12-week, acute-therapy studies. Study 1 (N=457) had treatment groups of duloxetine 20-mg once daily (QD), 60-mg QD, 60-mg twice daily (BID), and placebo; Studies 2 (N=334) and 3 (N=348) compared duloxetine 60-mg QD and 60-mg BID with placebo. The primary outcome measure was the weekly mean score for 24-hour average pain severity based on an 11-point Likert scale. Across all three studies, duloxetine 60-mg QD and duloxetine 60-mg BID demonstrated significant treatment effect on DPNP and showed rapid onset of action, with separation from placebo occurring at week one on the 24-hour average pain severity score ($p < 0.001$). This finding was confirmed in most secondary measures for pain. Du-

looxetine 60-mg QD and 60-mg BID achieved similar efficacy results on most measures, with duloxetine 60-mg BID showing significantly more improvement on some McGill pain descriptors. The evaluation of Clinical Global Impression of Severity and Patient Global Impression of Improvement also demonstrated superiority of duloxetine 60-mg QD and 60-mg BID over placebo. A significant treatment effect for duloxetine was observed for most health outcome measures. Duloxetine showed no adverse effects on diabetic control or complications, and was safely administered and well tolerated. In these clinical trials, duloxetine (only FDA-approved drug for DPNP) was an efficacious and safe treatment for patients suffering from DPNP.

Supported by Eli Lilly and Company.

References:

1. Clark CM, Lee DA: Prevention and treatment of the complications of diabetes mellitus. *N Engl J Med* 332:1210-1217, 1995.
2. Iyengar S, Webster AA, Hemrick-Luecke SK, Xu JY, and Simmons RMA: Efficacy of duloxetine, a potent and balanced serotonin-norepinephrine inhibitor in persistent pain models in rats. *J Pharmacol Exp Ther* 311:576-584, 2004.

NR862 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Quality of Life and Functionality in Panic Disorder: Long-Term Relapse Prevention Study of Venlafaxine Supported by Wyeth

Huabin Zhang, M.D., *Wyeth Research, 500 Arcola Road, Collegeville, PA 19426*; Rezaul Khandker, Ph.D., Bo Gao, Ph.D.

Educational Objectives:

At the conclusion of the presentation, participants will: (1) understand functional disability and quality-of-life implications from long-term use of antidepressants for patients with panic disorder, (2) be able to discuss standard measures for assessing disability and quality of life.

Summary:

Objectives: This study compared the efficacy of venlafaxine ER and placebo in the prevention of long-term quality of life and functionality relapses in panic disorder patients.

Method: DSM-IV panic disorder patients who responded to venlafaxine ER (75-225mg/day) in the 12-week, open-label phase of a multicenter trial were randomly assigned during the double-blind phase to either venlafaxine extended release (ER) or placebo for six months. Secondary analyses focused on functional impairment as measured by the Sheehan Disability Index (SDI) and quality of life as measured by the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q). Treatment-related improvements at final-on-therapy (FOT) and week 26 were analyzed for four SDI and 10 Q-LES-Q components.

Results: Venlafaxine ER was superior to placebo on all SDI subscales (work, social life and leisure activities, family life and home responsibilities, and work and social disability) at both FOT ($P < 0.001$) and week 26 ($P < 0.005$). At FOT, venlafaxine ER was superior to placebo on all Q-LES-Q subscales except school/course work. At week 26, venlafaxine ER was superior on all Q-LES-Q subscales except school/course work and leisure activities.

Conclusion: Venlafaxine ER was associated with significant improvement in functionality and quality of life in patients with panic disorder.

References:

1. Leon AC, Klerman GL, Weissman MM, Fyer AJ, Johnson J: Assessing impairment in patients with panic disorder: the Sheehan Disability Scale. *Soc Psychiatry Psychiatr Epidemiol* 1992; 27:78-82.

2. Endicott J, Nee J, Harrison W, Blumenthal R: Quality of Life Enjoyment and Satisfaction Questionnaire: a new measure. *Psychopharmacol Bull* 1993; 29:321-326.

NR863 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Health-Related Work Productivity in Panic Disorder: Venlafaxine, Paroxetine, and Placebo
Supported by Wyeth

Huabin Zhang, M.D., *Wyeth Research, 500 Arcola Road, Collegeville, PA 19426*; Rezaul Khandker, Ph.D.

Educational Objectives:

At the conclusion of the presentation, participants should be able to: (1) to understand the impact of antidepressants on health related work productivity among panic disorder patients, (2) discuss different scales and efficacy measures used to assess work impairment and limitations in MDD patients.

Summary:

Objectives: This study assessed the effect of treatments with venlafaxine ER, paroxetine, and placebo on health-related work productivity among panic disorder patients.

Methods: In a multicenter, double-blind trial, patients with DSM-IV panic disorder were randomly assigned to fixed-dose (75 mg or 225 mg) venlafaxine extended release (ER), paroxetine 40mg, or placebo for a maximum of 12 weeks. Secondary analyses focused on health-related work productivity impairments as measured by the Work Limitations Questionnaire (WLQ). WLQ has 25 items in four limitation dimensions (time, physical, mental-interpersonal, and output demands). Treatment-related improvements at final-on-therapy (FOT) and week 12 were compared using analysis of covariance adjusting for baseline impairment score and center.

Results: Venlafaxine ER 225 mg was associated with significantly greater improvement from baseline, relative to placebo, on all subscales of WLQ ($P < 0.005$) except physical demands. At the FOT assessment, venlafaxine ER 75 mg showed significant improvement compared with placebo in time management ($P < 0.05$), marginally significant improvement in mental/interpersonal demands ($P = 0.059$) and output demands ($P = 0.054$), and no significance for physical demands. Paroxetine failed to show significant improvement relative to placebo on all WLQ subscales in the FOT assessment.

Conclusion: Venlafaxine reduced work impairment compared with placebo. Paroxetine did not separate from placebo.

References:

1. Lerner D, Amick BC 3rd, Rogers WH, Malspeis S, Bungay K, Cynn D: The work limitations questionnaire. *Medical Care* 2001; 39:72-85.
2. Lerner D, Amick BC 3rd, Lee JC, Rooney T, Rogers WH, Chang H, Berndt ER: Relationship of employee-reported work limitations to work productivity. *Medical Care* 2003; 41:649-659.

NR864 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Quality of Life and Functionality in Panic Disorder: Venlafaxine, Paroxetine, and Placebo
Supported by Wyeth

Huabin Zhang, M.D., *Wyeth Research, 500 Arcola Road, Collegeville, PA 19426*; Rezaul Khandker, Ph.D., Bo Gao, Ph.D.

Educational Objectives:

At the conclusion of the presentation, participants should be able to: (1) to understand functional disability and quality-of-life

implications from the use of antidepressants for panic patients, (2) discuss different scales and efficacy measures used to assess quality of life and functionality in MDD patients.

Summary:

Objectives: This study compared the efficacy of venlafaxine ER, paroxetine treatments, and placebo on the quality of life and functionality in panic disorder patients.

Methods: In a randomized, double-blind trial, patients with DSM-IV panic disorder were treated with fixed-dose venlafaxine extended release (ER), paroxetine 40mg, or placebo for a maximum of 12 weeks. Secondary analyses focused on functional impairment as measured by the Sheehan Disability Index (SDI) and quality of life as measured by the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q). Treatment-related improvements at final-on-therapy (FOT) and week 12 were analyzed for each of the four SDI and 10 Q-LES-Q components adjusting for baseline impairment score and center.

Results: At the FOT assessment, venlafaxine ER (75mg and 225mg) was superior to placebo on all SDI subscales (work, social life and leisure activities, family life and home responsibilities, and work and social disability) ($P < 0.01$). Venlafaxine ER was superior to placebo on most Q-LES-Q subscales. Paroxetine was also better than placebo on SDI and Q-LES-Q measures.

Conclusion: Venlafaxine ER and paroxetine were both associated with significant improvement in functionality. Quality of life also improved in most subscales for these two therapies, although less so for venlafaxine at its lower dose.

References:

1. Leon AC, Klerman GL, Weissman MM, Fyer AJ, Johnson J: Assessing impairment in patients with panic disorder: the Sheehan Disability Scale. *Soc Psychiatry Psychiatr Epidemiol* 1992; 27:78-82.
2. Endicott J, Nee J, Harrison W, Blumenthal R: Quality of Life Enjoyment and Satisfaction Questionnaire: a new measure. *Psychopharmacol Bull* 1993; 29:321-326.

NR865 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Improvement of Anxiety Symptoms Among Outpatients With Major Depression Treated With Venlafaxine, Sertraline, or Placebo
Supported by Wyeth Research

Huabin Zhang, M.D., *Wyeth Research, 500 Arcola Road, Collegeville, PA 19426*; Rezaul Khandker, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to: (1) recognize the association between anxiety symptoms and treatment outcomes, (2) discuss the effects of treatment with venlafaxine XR and sertraline on anxiety symptoms in outpatients with major depressive disorder.

Summary:

Objective: To estimate amelioration of anxiety symptoms among depressed outpatients treated with venlafaxine extended release (ER), sertraline, or placebo.

Methods: Data were pooled from two identical 10-week, multicenter, randomized, double-blind, placebo-controlled studies of flexible-dose venlafaxine ER (37.5-300 mg/day) and sertraline (50-200 mg/day) in the treatment of DSM-IV MDD ($N = 1352$). Anxiety symptoms were assessed using the anxiety subscale of the Hospital Anxiety and Depression Scale. Improvement was evaluated as reduction from baseline score at week 10 using ANCOVA analysis controlling study center and baseline value. Chi-square test was used to compare the percentage of patients recovering with normal (anxiety subscale score ≤ 7) The overall trend of

weekly scores was evaluated using repeated measures mixed model.

Results: The mean baseline anxiety subscale score was 12.4 for venlafaxine and 12.3 for placebo. At week 10, venlafaxine ER was associated with significantly greater score reduction from baseline versus placebo (5.0 vs. 3.49, $P < 0.0001$) and a significantly larger proportion of patients with normal anxiety level versus placebo (51.0% vs. 35.9%, $P = 0.0003$). The overall trend of weekly scores was also significantly better for venlafaxine ER ($P < 0.0001$). Sertraline/placebo differences were also statistically significant.

Conclusion: Venlafaxine ER and sertraline treatment were associated with significant improvement on anxiety symptoms.

References:

1. Snaith RP: The Hospital Anxiety and Depression Scale. *Health and Quality of Life Outcomes*. 2003; 1:29-32.
2. Janssens AC: Anxiety and depression influence the relation between disability status and quality of life in multiple sclerosis. *Mult Scler* 2003; 9:397-403.

NR866 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Genetic Variations in the 5HT Receptor 5A Gene and Short-Term Treatment Response to Citalopram and Microarray Analysis

Choi Myoung-Jin, M.S., *Department of Psychiatry, Korea University College of Medicine, Anam-Dong 5Ga, Sungbuk-Ku, Seoul 135-705, Korea*; Kang Rhee-Heon, M.D., Jeong Han-Yong, M.D., Lee Min-Soo, M.D.

Summary:

Objective: The purpose of this study is to find the relationship between serotonin receptor 5A variants (-19G/C and 12A/T) and citalopram response in Korean major depressive disorder (MDD) patients, and furthermore investigating identification of the genes changed in blood with cDNA microarray after administering citalopram.

Methods: The sample was composed of 71 patients. We diagnosed according to DSM-11 criteria and evaluated severity of the symptoms with 21-item Hamilton Depression Rating Scale (HAM-D) during the follow-up and to determine clinical response and remission condition of the patients at first, second, and 4th week, respectively. Therapeutic response was evaluated by the percentage score reduction in total and subcategory HAM-D scores ((baseline score - 4 week score) / 100/baseline score). To analyze genetic polymorphisms, a polymerase-chain-reaction based method was used. The differences of the genotypes distribution and carrier frequency were analyzed by using chi square analysis. And the comparison of HAM-D scores in the genotype group was performed using ANOVA analysis.

To analyze cDNA microarray, this study included 10 patients with major depression (six in response group with citalopram treatment, four in non-response group with citalopram treatment), and eight healthy controls. To examine the difference of gene expression profile in depression patients, total RNA samples were purified from blood, at 0, 4, and 8 wks treatment, respectively. Radioactive complementary DNA microarrays were used to evaluate changes in the expression of 1,152 genes in a total. Using 33P-labeled probes, this method provided highly sensitive gene expression profiles including brain receptors, drug metabolism, and cellular signaling.

Results: Genotypes for MDD and control group were all in Hardy-Weinberg equilibrium.

For the -19G/C polymorphism, significant differences were not observed in the genotype, allele frequencies and allele carriers between MDD and control group. GG, GC and CC frequencies were about 32, 53, and 15% both MDD and control group. G allele was about 58-59%, and C allele was 41-42% both MDD and

control group. Also, there was no significant difference between citalopram response at 4 weeks after treatment and -19G/C variation in 5HT5A receptor gene. For the 12A/T polymorphism, also significant differences were not observed in the genotype, allele frequencies and allele carriers between MDD and control group.

AA, AT, and TT frequencies were about 14-16, 50-53, and 33% both MDD and control group. A allele was about 40-41%, and T allele was 59-60% both MDD and control group. Also, there was no significant difference between citalopram response at four weeks after treatment and 12A/T variation in 5HT5A receptor gene. To cDNA analysis, gene transcription profiles were classified into several categories in accordance with the antidepressant gene-regulation. The gene profiles were significantly up-(18 genes) and down-(45 genes) regulated in the response group when compared to the control group. Also, in the non-response group, 13 genes were up-regulated and 48 genes were down-regulated when compared to the control group.

Conclusion: Our results suggest that two polymorphisms (-19G/C and 12A/T) in the 5HT5A receptor gene do not play major role in the pathogenesis of MDD and therapeutic response to citalopram in the MDD patients. As a result of cDNA analysis, there were differences in the genes changed in blood after administering citalopram between response and non-response groups compared the control group.

References:

1. Dubertret C, Hanoun N, Ades J, Hamon M, Gorwood P: Family-based association studies between 5-HT5A receptor gene and schizophrenia. *J Psychiatr Res* 2004; 38(4):371-6.
2. Birkett JT, Arranz MJ, Munro J, Osbourn S, Kerwin RW, Collier DA: Association analysis of the 5-HT5A gene in depression, psychosis and antipsychotic response, *Neuroreport* 2000; 26; 11(9):2017-20.

NR867 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Age Differences in Response to Citalopram and Symptomatology According to 5HT Receptor 2A Genetic Variation (-1438A/G)

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Summary:

Objective: The purpose of this study is to find age differences in citalopram response related to the serotonin 2A receptor genetic variation(-1438A/G), and the association between -1438A/G variation and improvement for specific cluster symptoms by age in the Korean major depressive disorder(MDD) patients.

Methods: The sample was composed of 71 Korean patients. We diagnosed according to DSM-IV criteria and evaluated severity of the symptoms with a 21-item Hamilton Depression Rating Scale (HAM-D) during the follow-up and to determine clinical response and remission condition of the patients at 1, 2, and 4 weeks, respectively. To evaluate specific cluster depressive symptoms, the HAM-D items were grouped according to the following factors: core (Items 1, 2, 7, 8, 10, 13), sleep (Items 4, 5, 6), activity (Items 7, 8), psychic anxiety (Items 9, 10), somatic anxiety (Items 11, 12, 13), and delusion (Items 2, 15, 20). Both the total and subcategory HAM-D scores were subjected to statistical analysis. Therapeutic response was evaluated by the percentage score reduction in total and subcategory HAM-D scores ((baseline score - 4 week score) / 100/baseline score). To analyze genetic polymorphisms, A polymerase-chain-reaction based method was used. The differences of the genotype distributions and allele frequencies were analyzed by using chi square analysis. And the comparison of HAM-D scores in the genotype group was performed using AN-

OVA analysis. Comparison of HAM-D scores in the genotype group was performed using ANOVA analysis.

Results: There were significant differences clinical response to citalopram according to the genetic variant, -1438A/G of serotonin receptor 2A gene and age. At 4th week, in the group of under 60 yr of age, Percentage change of HAM-D score was higher in the group with GG allele (AA: 44.5%, AG: 51.3%, GG: 72.0%; $p=0.037$), but in the group of over 60 yr of age there were no differences.

Distribution of GG genotype was higher than it of AA or AG allele in both response ($p=0.014$) and remission ($p=0.004$) group compared to non-response and non-remission group only the group under 60 yr of age.

The improvement for specific cluster symptoms was different by -1438A/G variation and age. In the under 60 yr of age, there were differences in core and sleep. Percentages of the HAM-D score changes were high in the group with GG allele otherwise, the group with AA allele showed lowest percentage both core and sleep symptoms. In the over 60 yr of age, though there were no significant differences between -1438A/G variation and cluster symptoms, as a result of LSD multiple comparison testing, AA or AG allele was associated with better improvement than GG allele (AA: 100%, AG: 86.8%, GG: 53.5%) in symptom of sleep.

Conclusion: There was differential citalopram response with regard to age, and 5HTR2A genetic variation. The citalopram response according to -1438A/G variation was associated with only the group of 60 yr of age. In addition, improvement for specific cluster symptoms by the age differences related to the -1438A/G variation was different. These results may help understanding the differences in the antidepressant response according to age, particularly in relation to genetic variation and suggest new guidelines to therapy in MDD patients.

References:

1. Serretti A, Artoli P: From molecular biology to pharmacogenetics: a review of the literature on antidepressant treatment and suggestions of possible candidate genes. *Psychopharmacology* 2004; 174(4):490-503.
2. Sato K, Yoshida K, Takahashi H, Ito K, Kamata M, Higuchi H, Shimizu T, Itoh K, Inoue K, Tezuka T, Suzuki T, Ohkubo T, Sugawara K, Otani K: Association between -1438G/A promoter polymorphism in the 5-HT(2A) receptor gene and fluvoxamine response in Japanese patients with major depressive disorder. *Neuropsychobiology* 2002;46(3):136-40.

NR868 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Just-in-Time Management Philosophy in Community Treatment Services: A 16-Week Pilot Study *Supported by Eli Lilly*

Marios Adamou, M.D., *KIHMS, University of Kent, Research and Development Building, Canterbury CT2 7PD, United Kingdom*; Tanushree Sharma, M.D., Karen White, M.D., Anthony Hale, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to evaluate a new model of community treatment delivery for patients with chronic enduring mental illness and familiarize with the just-in-time management philosophy.

Summary:

Crisis resolution teams for the treatment of patients with mental illness are a recent advent in the British National Health Service. The data relating to readmission, length of stay, general functioning, and mental state of patients treated by these teams are inconclusive. We trained a community team in the principles of Just in Time Philosophy and changed its operational mode from case

management to Just in Time Management aiming to increase the efficiency of the team. We collected data for the number of admissions and length of patient hospital stay for 16 weeks with Just-in-Time Management and compared these with 116 weeks of case management before the intervention. Cox proportional hazards regression analysis showed that patients receiving the intervention were 1.65 times (95% CI: 1.08-2.51, $p=0.020$) more likely to be rapidly discharged from hospital compared to the case management group. The introduction of Just-in-Time Philosophy in the operational mode of community teams may help to reduce hospital stay and resolve crises quicker than case management.

References:

1. Joy C, Adams C, Rice K: Crisis intervention for people with severe mental illnesses. *Cochrane Database Syst Rev* 2004(4): CD001087.
2. Amasaka K, "New JIT": A new management technology principle at Toyota. *International Journal of Production Economics* 2002. 80(2): 135-144.

NR869 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Perospirone in the Treatment of Patients With Delirium

Takashi Takeuchi, M.D., *Department of Psychiatry and Behavioral Medicine, Tokyo Medical and Dental Univ. Graduate School, 1-5-45, Yushima, Bunkyo-KU, Tokyo 1138519, Japan*; Ko Huruta, M.D., Toshiyuki Hirasawa, M.D., Tomoaki Yukizane, M.D., Hidenori Atsuta, M.D., Hiroshi Arakaki, M.D., Toru Nishikawa, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the efficacy of perospirone in patients with delirium.

Summary:

Introduction: Perospirone is a recently developed atypical antipsychotic with a potent serotonin 5-HT₂ and dopamine D₂ antagonist (SDA) activity. Other atypical antipsychotics including risperidone, quetiapine, and olanzapine have widely been used for treatment of not only schizophrenic symptoms but delirium because of their low potential to induce extrapyramidal disturbances. In the present study, to extend clinical application of perospirone, we have examined the therapeutic efficacy of this atypical in patients with delirium.

Method: Thirty-eight patients with DSM-IV delirium were treated with open-label perospirone. To evaluate the usefulness of perospirone, scores from 13 severity items of the Delirium Rating Scale-Revised-98, Japanese version, were assessed. Date were gathered from October 2003 to September 2004.

Results: Perospirone was effective in 86.8% (33/38) of patients, and the effect appeared within several days (5.1 ± 4.9 days). The initial dose was 6.5 ± 3.7 mg/day and maximal dose of perospirone was 10.0 ± 5.3 mg/day. Eight patients experienced adverse events, but none showed extrapyramidal symptoms.

Conclusions: It is proposed that perospirone may be another safe and effective atypical antipsychotic drug in the treatment of delirium symptoms in medically hospitalized patients. This is a preliminary open trial, and further randomized, double-blind, placebo-controlled studies are needed.

Grant-in-aid of Ministry of Education, Science, Sports and Culture in Japan.

References:

1. Mittal D, Jimerson NA, Neely EP, et al: Risperidone in the treatment of delirium. *J Clin Psychiatry* 2004; 65(5):662-667.

2. de Paulis T: Perospirone(Sumitome Pharmaceuticals). *Curr Opin Investig Drugs* 2002; 3(1):121-129.

NR870 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Frontal EEG at One Week Predicts Clinical Response to SSRIs in MDD

Dan V. Iosifescu, M.D., *Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, Suite #401, Boston, MA 02114*; Scott Greenwald, Ph.D., Philip Devlin, M.Eng., Jonathan Alpert, M.D., Sarah Hamil, B.A., Maurizio Fava, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the role of automated EEG analysis as a clinically useful predictor of treatment efficacy in major depressive disorder.

Summary:

Objective: To investigate the role of frontal EEG as predictor of clinical response to SSRIs in major depressive disorder (MDD).

Method: 60 subjects (mean age 36.1 + 12.5; 43.3% female) meeting DSM-IV criteria for MDD entered an eight-week prospective treatment with open-label, flexible dose SSRIs. At each study visit (baseline, week 1, 4, and 8) we assessed MDD severity with the 17-item Hamilton Depression Rating Scale (HAM-D) and we recorded serial, 4-channel EEGs (F7-Fpz, F8-Fpz, A1-Fpz, A2-Fpz).

Results: 34 subjects (56.7%) were treatment responders (HAM-D reduction > 50%). Frontal relative theta power (i.e., 4-8Hz power/2-20Hz power) decreased from baseline (21%) to week 1 (20%) in treatment responders, but remained constant (24%) in non-responders. At one week, relative theta power was significantly lower in treatment responders versus non-responders ($p = 0.003$), predicting response with 67% accuracy (71% sensitivity, 61% specificity) and 0.71 Area Under the Receiver Operating Curve (AUC). Relative theta power at one week also correlated with percent improvement in HAM-D ($R = -0.337$, $p = 0.009$). In retrospective analysis, a three-parameter model yielded improved performance (0.78 AUC).

Conclusion: It may be possible to develop an easy-to-use tool using automated analysis of frontal EEG to predict treatment efficacy after one week of antidepressant treatment.

This research was supported by Aspect Medical Systems, Inc.

References:

1. Cook IA, Leuchter AF, Witte EA, Stubbeman WF, Abrams M, Rosenberg S: Early changes in prefrontal activity characterize clinical responders to antidepressants. *Neuropsychopharmacology* 2002; 27:130-131.
2. Marie-Mitchell A, Leuchter AF, Chou CP, et al: Predictors of improved mood over time in clinical trials for major depression. *Psychiatry Res* 2004; 127(1-2):73-84.

NR871 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Impact of Painful Physical Symptoms on Antidepressant Response and Quality of Life
Supported by Eli Lilly

Hector J. Duenas, M.D., *Avenida Durango 290, Sanatorio Durango, Avenida Durango 290-409 Roma, Mexico City 06700, Mexico*; Alan J.M. Brnabic, M.S.C., Hernán Bobadilla, M.D., Alberto Monchablón, M.D., Sandra Ruschel, M.D., Adriana Acuña, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will appreciate the relationship between painful physical symptoms and response to treatment, remission rate, and quality of life in patients with MDD. These results reflect naturalistic clinical practice and complement existing findings from randomized controlled clinical trials.

Summary:

Introduction: Relationships between painful physical symptoms, treatment response, and changes in quality of life are examined for Latin American patients with major depressive disorder (MDD).

Method: Patients ($n=989$) enrolled in this 12-month, multi-center observational study (H6U-BC-LRAG/BL-LRAH) were categorized at baseline using the Somatic Symptom Inventory (SSI) into those experiencing painful physical symptoms (SS+) and those without pain (SS-). Clinical status was determined using HAMD17 and CGI-S, while QLDS quantified subjective wellbeing.

Results: Most patients (77.6%) completed the study, 88.5% responded to treatment (>50% reduction from baseline HAMD17), and 67.9% achieved sustained remission (HAMD17 ≤ 7 for ³4 weeks). The 72.6% (95% CI: 69.8, 75.4) of patients who were SS+ were compared with SS- patients in all subsequent analyses. During the study, SS+ patients had greater improvement in HAMD17 ($p=0.0081$) and QLDS ($p=0.027$), but remission rate ($p=0.018$) was significantly lower (65.8%) when compared with SS- patients (74.6%). Of the patients prescribed a combination of serotonin and norepinephrine reuptake inhibitors at baseline ($n=106$), the improvement in HAMD17 was 3.7 points (CI: -1.21, 8.53; $p=0.1387$) greater for SS+ patients.

Conclusions: Painful physical symptoms are prevalent in MDD and adversely affect the possibility of remission. Effective treatment should address both physical and emotional symptoms of depression.

References:

1. Muñoz R, McBride M, Brnabic A, López C, Hetem L, Secin R, Dueñas H: Major depressive disorder in Latin America: The relationship between depression severity, painful somatic symptoms and quality of life. *J Affective Disorders*, accepted.
2. Greco T, Eckert G, Kroenke K: The outcome of physical symptoms with treatment of depression. *J Gen Intern Med* 2004; 19(8): 813-818.

NR872 Thursday, May 26, 12:00 p.m.-2:00 p.m.
Comparing Age and Gender Responses to Treatments With Venlafaxine and SSRIs
Supported by Wyeth Research

Lee S. Cohen, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, Boston, MA 02114*; Susan G. Kornstein, M.D., Richard Entsuah, Ph.D., Wilfrido Ortega-Leon, M.Eng., Raj Tummala, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to: (1) discuss the efficacy of venlafaxine and SSRIs in the treatment of depressed women and men (2) describe age- and gender-related differences in the response to antidepressant treatment with venlafaxine or SSRIs.

Summary:

Introduction/Hypothesis: Comparing antidepressant treatment effects across age and gender subgroups.

Method: Meta-analysis of individual patient data from 31 double-blind RCTs comparing venlafaxine/venlafaxine XR ($n=3273$), SSRIs (fluoxetine, paroxetine, sertraline, citalopram, or fluvoxamine; $n=3217$), or placebo (9 studies; $n=932$) in depressed pa-

tients. Remission (week 8 HAM-D17 score ≤ 7) was computed separately for women and men; women aged >50 and ≤ 50 , and men aged >50 and ≤ 50 .

Results: Women comprised 66% (4889/7420) of the patient population; 71% of the total population (5,327/7,409) were aged ≤ 50 years. Age and gender distributions were similar across treatment groups.

Remission rates for women were 41%, 34%, and 26% for venlafaxine/venlafaxine XR, SSRIs, and placebo, respectively ($P < 0.0001$ venlafaxine/venlafaxine XR vs SSRI and placebo; $P = 0.0002$ SSRI vs placebo). Results were similar for men and younger women. Older women treated with venlafaxine/venlafaxine XR responded similarly to younger women; among older women, remission with SSRIs (30%) was not significantly different from placebo (27%; $P = 0.4698$). Younger men showed similar remission rates; remission rates among older men were lower in all 3 groups.

Conclusion/Discussion: Venlafaxine/venlafaxine XR efficacy was consistent across most gender and age subgroups except older men. Younger women responded better to the studied SSRI comparators than older women.

References:

1. Entsuah AR, Huang H, Thase ME: Response and remission rates in different subpopulations with major depressive disorder administered venlafaxine, selective serotonin reuptake inhibitors, or placebo. *J Clin Psychiatry* 2001; 62:869-877.
2. Thase ME, Entsuah AR, Rudolph RL: Remission rates during treatment with venlafaxine or selective serotonin reuptake inhibitors. *Br J Psychiatry* 2001; 178:234-241.

NR873 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Short-Term Efficacy of Escitalopram Treatment of MDD: A Pooled Analysis Versus SSRIs and Venlafaxine

Supported by Lundbeck

Sidney H. Kennedy, M.D., *Department of Psychiatry, UHN, 200 Elizabeth Street, EN8-222, Toronto M5G 2C4, Canada;* Elisabeth Wreford Andersen, M.S.C.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to critically appraise the efficacy of escitalopram in the treatment of major depressive disorder compared to other antidepressants using a meta-analytical approach.

Summary:

Introduction: The hypothesis that escitalopram has at least as good efficacy in the acute treatment of major depressive disorder (MDD) as other available antidepressants was tested. In this analysis, studies comparing escitalopram with the following antidepressant compounds: citalopram, fluoxetine, paroxetine, sertraline, and venlafaxine XR were used.

Methods: A total of 2,743 patients were in the ten studies in patients with MDD; 2,687 (98.0%) were included in the ITT analysis of the efficacy of escitalopram ($n=1,345$), SSRIs ($n=1,102$). And venlafaxine XR ($n=240$). The meta-analysis was done by ANCOVA on the MADRS total score adjusting for baseline value, centre and treatment.

Results: Pooling data from all currently available studies reveals that escitalopram carries an advantage of about 1.1 MADRS points over other antidepressants. The majority of comparisons were with SSRIs, where the effect is consistently larger than that observed in the comparison versus venlafaxine XR. The effect size increased to 2.3 MADRS points when only severe patients (MADRS ≥ 30) were included in the analysis. Escitalopram also demonstrated

superior rates of response and remission compared to SSRI treatment.

Conclusion: These results suggest that some heterogeneity exists within the class of SSRIs in terms of magnitude of antidepressant effect.

References:

1. MacGillivray S, Arroll B, Hatcher S, Ogston S, Reid I, Sullivan F, Williams B, Crombie I: Efficacy and tolerability of selective serotonin reuptake inhibitors compared with tricyclic antidepressants in depression treated in primary care: systematic review and meta-analysis. *BMJ* 2003; 326:1014.
2. Vaswani M, Linda FK, Ramesh S: Role of selective serotonin reuptake inhibitors in psychiatric disorders: a comprehensive review. *Prog Neuropsychopharmacol Biol Psychiatry* 2003; 27:85-102.

NR874 Thursday, May 26, 12:00 p.m.-2:00 p.m.

A Comparison of Sexual Function in Remitted-Depressed Patients Following Agomelatine or Venlafaxine XR Treatment

Sidney H. Kennedy, M.D., *Department of Psychiatry, UHN, 200 Elizabeth Street, EN8-222, Toronto M5G 2C4, Canada;* Michel Lejoyeux, M.D., Chris Hawley, M.B., Antoine Hebert, M.D., Christian Debodinat, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be aware of methods to evaluate sexual dysfunction during antidepressant treatment and appreciate differences in various aspects of sexual dysfunction during treatment with agomelatine and venlafaxine.

Summary:

The purpose of the study was to compare global and component aspects of sexual function in depressed patients who demonstrated sustained remission following treatment for 12 weeks with agomelatine 50 mg or venlafaxine 150 mg. Sexual function was evaluated using the clinician-administered Sex Effects (Sex FX) scale in which lower scores reflect higher levels of sexual function. Of 277 randomized patients, 78 of 137 (57%) agomelatine and 83 of 140 (59%) venlafaxine-treated patients achieved remission (MADRS score < 12). At baseline the mean Sex FX score was higher in women 27.6 (+ 8.9) compared with men 21.3 (+ 10.3). Male patients on agomelatine showed a greater decrease in Sex FX scores (8.2+ 11.3) compared to male patients in the venlafaxine group (0.6 + 7.3). No treatment differences over time were observed for women.

In the agomelatine group 103/137 (75%) and 90/140 (64%) in the venlafaxine group reported sexual activity at baseline. Among these sexually active patients (men and women combined) there was a greater reduction in Sex FX scores in the agomelatine (3.4 + 5.3) compared with the venlafaxine (0.5 + 10.2) group. Similarly for the orgasm subscale, significantly fewer patients in the agomelatine group (20%) than in the venlafaxine group (47%) reported orgasm dysfunction ($p < .002$). Both groups demonstrated comparable antidepressant benefit based on MADRS and CGI-I&S between 0 and 12 weeks.

References:

1. Loo H, Hale A, D'haenen H: Determination of the dose of agomelatine, a melatoninergic agonist and selective 5-HT_{2C} antagonist, in the treatment of major depressive disorder: A placebo-controlled dose range study. *Int Clin Psychopharmacol* 2002; 17:239-247.
2. Kennedy SH, Eisfeld BE, Dickens SE, Bacchiochi JR, Bagby RM: Antidepressant induced sexual dysfunction during treat-

ment with moclobemide, paroxetine, sertraline and venlafaxine
J Clin Psychiatry 2000; 61:276-281.

NR875 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Health Care Utilization Among Cardiac Patients Treated for Depression With Zoloft Versus No Antidepressant

Supported by Pfizer Inc.

Tami L. Mark, Ph.D., *Outcomes Research and Econometrics, Medstat, 4301 Connecticut Avenue, NW Suite 330, Washington, DC 20008*; Morgan Bron, Pharm.D., Lucinda Orsini, M.P.H.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to describe the association between Zoloft usage and health care utilization in patients with cardiac conditions.

Summary:

Objective: To compare the health care utilization of patients hospitalized with acute myocardial infarction or unstable angina with a depression diagnosis who were or were not treated with Zoloft.

Methods: Patients 45 or older, with a hospitalization for either acute myocardial infarction or unstable angina, and evidence of depression treatment (diagnosis or Zoloft) were identified in Medstat's MarketScan® claims databases. Claims incurred between January 1, 1999, and December 31, 2003, were utilized. Patients without any antidepressant use 30 days prior or 60 days after their cardiac event and receiving a diagnosis of depression in the 180 days before or after their cardiac event comprised the diagnosis only group. Patients with a 30-day clean period of any antidepressant prior to their cardiac event and incurring a script for Zoloft in the 60 days after their cardiac event comprised the Zoloft group. The two groups were matched using propensity score methods.

Results: In the 24 weeks following discharge for the index cardiac event, the diagnosis-only group was more often admitted to the hospital overall as well as for AMI, was more likely to visit the ER, and had significantly higher utilization of psychiatric-related outpatient services.

References:

1. Glassman AH, O'Connor CM, Califf RM, Swedberg K, Schwartz P, Bigger JT Jr, Krishnan KR, van Zyl LT, Swenson JR, Finkel MS, Landau C, Shapiro PA, Pepine CJ, Mardekian J, Harrison WM, Barton D, McIvor M, Sertraline Antidepressant Heart Attack Randomized Trial (SADHEART) Group: Sertraline treatment of major depression in patients with acute MI or unstable angina. *JAMA* 2002; 288(6):701-9.
2. Serebruany VL, Glassman AH, Malinin AI, Nemeroff CB, Muselman DL, van Zyl LT, Finkel MS, Krishnan KR, Gaffney M, Harrison W, Califf RM, O'Connor CM, Sertraline AntiDepressant Heart Attack Randomized Trial Study Group: Platelet/endothelial biomarkers in depressed patients treated with the selective serotonin reuptake inhibitor sertraline after acute coronary events: the Sertraline AntiDepressant Heart Attack Randomized Trial (SADHART) Platelet Substudy. *Circulation* 2003; 108(8):939-44.

NR876 Thursday, May 26, 12:00 p.m.-2:00 p.m.

The Effect of Raising Three-Tier Copayments on SSRI Compliance Rates

Supported by Pfizer, Inc.

Tami L. Mark, Ph.D., *Outcomes Research and Econometrics, Medstat, 4301 Connecticut Avenue, NW Suite 330, Washington, DC 20008*; Morgan Bron, Pharm.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the potential effect of raising copayments on SSRI compliance.

Summary:

Objectives: To determine the effect of raising copayments on compliance rates with SSRI antidepressants.

Methods: Data comprised benefit information and claims from Medstat's MarketScan database. Any patient who filled a prescription for an SSRI antidepressant in 2000 and was continuously enrolled through 2001 was identified. A difference in difference approach was used to examine the change in the days supplied and number of claims filled for an employer's plan that raised their three tiered copayments as compared with an employer's plan that kept constant one tier copayment rates. The employer's plan that raised copayments went from offering a \$5, \$10, \$25 three-tier plan to a \$5, \$15, \$35 copayment plan.

Results: From year 2000 to year 2001, the employer that raised copayments by 50% experienced a 25% decline in the number of prescriptions per person filled (from 5.2 to 3.9 prescriptions), while the other employer plan demonstrated a 20% decline (from 6.0 to 4.8). Days supplied fell by 41.3 days or 24% in the employer's plan that raised copayments and by 36.3 days or 17% in the control plan.

Conclusions: Increasing copayments may have a negative effect on compliance and possibly outcomes.

References:

1. Goldman DP, Joyce GF, Escarce JJ, Pace JE, Solomon MD, Laouri M, Landsman PB, Teutsch SM: Pharmacy benefits and the use of drugs by the chronically ill. *JAMA* 2004; 291(19):2344-50.
2. Huskamp HA, Deverka PA, Epstein AM, Epstein RS, McGuigan KA, Frank RG: The effect of incentive-based formularies on prescription-drug utilization and spending. *N Engl J Med* 2003; Dec 4; 349(23):2224-32.

NR877 Thursday, May 26, 12:00 p.m.-2:00 p.m.

The Effect of Escitalopram Versus Sertraline Versus Duloxetine on CYP 2D6 Function

Supported by Pfizer, Inc.

Sheldon H. Preskorn, M.D., *Department of Psych, UKSM-W, 1010 N Kansas St, Wichita, KS 67214-3124, U.S.S.R.*; Alisa Klick-Davis, R.N., Laurie Coyner, M.D., Mohamed Ramadan, M.D., David Flockhart, M.D., Bryan Baker, R.N., Kelli Omo, R.N.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to learn the differential effects of three antidepressants on the functional activity of the cytochrome P450 enzyme 2D6 as reflect by changes in the metabolism and clearance of metoprolol.

Summary:

Hypothesis: Sertraline will have less in vivo effect on the functional activity of the cytochrome P450 (CYP) drug metabolizing enzyme 2D6 than does either duloxetine or escitalopram.

Methods: Single-dose pharmacokinetics of metoprolol, a model CYP 2D6 substrate-drug, was measured before and after 17 days of treatment with duloxetine 60 mg/day, escitalopram 20 mg/day, or sertraline 100 mg/day in young healthy male and female volunteers (15 ~ 20 individuals in each treatment condition). The metoprolol outcome measures were change in peak plasma levels (C_{max}), area under the plasma concentration — time curve (AUC), and clearance. These results were tested using analysis of covari-

ance (two-tailed) taking into account the following patient data as indicated: height, weight, and body mass index.

Results: Escitalopram in comparison to sertraline produced a greater increase in C_{max} (1.945 versus 1.277, respectively, $p < 0.01$) and AUC (1.995 versus 1.428, respectively, $p, 0.05$). The reduction in clearance trended in the same direction but was not statistically significant. The duloxetine samples are being assayed now.

Conclusion: Under steady-state dosing conditions, escitalopram 20 mg/day produced a greater in vivo inhibition of CYP 2D6 than did sertraline 100 mg/day. The results for duloxetine 60 mg/day are pending.

References:

1. Preskorn SH: Reproducibility of the in vivo effect of the selective serotonin reuptake inhibitors on the in vivo function of cytochrome P450 2D6: an update (part I). *Journal of Psychiatric Practice* 2003; 9(2):150-158.
2. Heneryck A, Lefebvre RA, De Vriendt C, Belpaire FM, Belpaire E: Paroxetine affects metoprolol pharmacokinetics and pharmacodynamics in healthy volunteers. *Clin Pharm Ther* 2000; 67(3):283-291.

NR878 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Pharmacotherapy of Personality Disorders: A Preliminary Report on Atypical Antipsychotics in Cluster A Personality Disorders

Roberta Bassetti, M.D., *Department of Psychiatry—Department Clinical Sciences “L. Sacco, University of Milan, via G.B. Grassi 74, Milan 20157, Italy*, Emanuela Mundo, M.D., Elisabetta Cattaneo, M.D., Serena Vismara, M.D., A. Carlo Altamura, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the potential use of atypical antipsychotics in the treatment of Cluster A personality disorders.

Summary:

Objectives: This study aimed to evaluate the efficacy of atypical antipsychotics on a sample of patients with Cluster A personality disorders.

Methods: Ten outpatients with schizoid (N=3) or schizotypal personality (N=7) disorders, who gave their informed consent to participate into the study, were assessed by trained psychiatrists with semi-structured interviews based on DSM-IV criteria for Axis I and Axis II diagnosis. All patients were treated with flexible doses of olanzapine (mean dose: 7.7+8.2 mg die) or quetiapine (mean dose: 158.4 + 90.4 mg die) for six months according with an open design. Patients with Axis I diagnoses were excluded. Brief Psychiatric Rating Scale (BPRS) scores were recorded at baseline and monthly for six months. Data were analyzed using ANOVA with repeated measures.

Results: A significant improvement was found on the BPRS total scores ($F=83.3$; $p<0.002$)

Conclusions: The results from this preliminary study suggest that in cluster A personality disorders, the treatment with an atypical compound could be beneficial.

Further studies on larger samples and analyses considering the effects of drug therapy on specific psychopathological dimensions associated with cluster A personality disorders are warranted.

References:

1. Kapfhammer HP, Hippus H: Special feature: pharmacotherapy in personality disorders. *J Personal Disord* 1998; 12(3):277-88.
2. Markovitz PJ: Recent trends in the pharmacotherapy of personality disorders. *J Personal Disord* 2004; 18(1):90-101.

NR879 Thursday, May 26, 12:00 p.m.-2:00 p.m.

IM Risperidone: Modeling Blood Levels to Manage Real-World Dosing Dilemmas

William H. Wilson, M.D., *Department of Psychiatry, Oregon Health & Science Univ, UHN-80, 3181 SW Sam Jackson Park Rd, Portland, OR 97239*

Educational Objectives:

At the end of the presentation, the participant should be able to recognize expected antipsychotic blood level changes with varying doses and timing of long-acting injectable risperidone and plan appropriate clinical management based on these levels.

Summary:

Background: Risperidone is the only second-generation antipsychotic medication available as a long-acting injectable. In clinical trials steady blood levels are obtained by giving a fixed dose of the medication every two weeks. In real-world clinical practice, such uniformity of timing and dose is often difficult to achieve due to vacations, pharmacy issues, staffing variations, etc. As the pharmacokinetics of long-acting injectable risperidone is unique, physicians may have difficulty predicting the effects of variations in dosing. Thus, clinical dilemmas arise when real-world factors introduce variability in the dose or timing of injections.

Method: Published empirical data were used to model expected antipsychotic levels in clinical situations that result in dosing and timing variation. The model was validated by comparing modeled results to published long-term empirical data.

Results: Graphs are displayed of expected of blood levels during nine examples of dosing variability that might occur in practice, such as missing a dose, receiving medication early or late, etc. Clinical vignettes illustrate the practical application of the model. Suggestions for clinical management are made based on the mathematically modeled blood levels.

Conclusions: Mathematical modeling is a useful aid in dosing long-acting risperidone when real-world factors cause variability in doses and timing of injections.

References:

1. Ereshefsky L and Mascarenas CA: Comparison of the effects of different routes of antipsychotic administration on pharmacokinetics and pharmacodynamics. *J Clin Psychiatry* 2003; 64[suppl 16]:18-23.
2. Wilson WH: A visual guide to expected blood levels of long-acting injectable risperidone in clinical practice. *J Practical Psychiatry*, in press.

NR880 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Changing Clinical Practice: Patient-Centered Care in Inpatient Psychiatry

William H. Wilson, M.D., *Department of Psychiatry, Oregon Health & Science Univ, UHN-80, 3181 SW Sam Jackson Park Rd, Portland, OR 97239*; William Nunley, M.D., Kimber Pezzoni, M.D., Dan Costa, M.D., Dianne Wheeling, R.N., Leigh Hedrick, M.S.W.

Educational Objectives:

By the end of the presentation, participants will be able to discuss patient-centered care as an overriding value for acute inpatient care and describe practical ways to implement patient centered care in acute inpatient settings as a means of improving clinical care, psychiatric education, and interdisciplinary cooperation.

Summary:

Background: The acute inpatient psychiatric service at Oregon Health & Science University adopted the value of patient-centered care several years ago.

Methods: Participation in the Creating Violence Free and Coercion Free Mental Health Treatment Environments Project, sponsored by the National Association of State Mental Health Program Directors, has given additional impetus to change the unit culture and practice, resulting in further reductions, and near elimination, of seclusion and restraint. Decision making on the unit has become increasingly collaborative. Treatment decisions have become increasingly patient directed. This poster outlines the theory and implementation of Patient Centered Care as applied to inpatient psychiatric care.

Results: Quantitative outcome measures are presented, including data showing the marked reductions in seclusion and the near elimination of the use of restraint. A case presentation by psychiatric residents and a medical student illustrate the successful implementation of patient-centered, interdisciplinary care factors in a clinical situation. The case illustrates techniques to avoid coercive care, and demonstrates how patient-centered values and techniques are modeled and learned during clinical training.

Conclusion: Patient-centered values and techniques are applicable to busy general inpatient psychiatric units, residency training, and medical student clinical education, resulting in better clinical care.

References:

1. Bloom S: Creating Sanctuary. New York: Routledge, 1997.
2. NASMHPD Medical Directors Council: Reducing the use of seclusion and restraint. Alexandria VA: National Association of State Mental Health Program Directors, 1999.

NR881 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Buprenorphine/Naloxone Treatment of Opioid-Dependent Chronic Pain Patients

Supported by Purdue Pharmaceuticals

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Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize the combination tablet of buprenorphine and naloxone as a treatment for opioid dependent patients who require chronic opioid pain management.

Summary:

Objective: Chronic pain patients treated with prescription opioid medications (POMs) may develop aberrant drug-use behavior meeting DSM-IV criteria for dependence. Buprenorphine and naloxone (BUP/NX) administered as a sublingual combination tablet is evaluated for treatment of POM dependence where ongoing opioid-based pain therapy is also required.

Methods: Case analysis and literature review. We reviewed six outpatients with chronic non-malignant pain with opioid dependence (DSM-IV). All were inducted (switched) to BUP/NX therapy with daily doses titrated and stabilized to achieve a Visual Analog Scale (VAS) pain rating of < 4. Urine drug screens were administered 30 days after induction of BUP/NX.

Results: Six patients, dependent on hydromorphone, oxycodone, and acetaminophen, sustained release oxycodone, hydrocodone, and acetaminophen or combinations of the above, were successfully inducted and stabilized as outpatients to stable doses of BUP/NX over 14 days. All achieved good pain control (VAS <4) by day 14 and required no ancillary pain medication. Thirty

days after beginning BUP/NX, VAS scores remained <4 and urine drug screens were negative.

Conclusion: BUP/NX offered a safe and effective means of treating chronic pain in patients who are also diagnosed as opioid dependent. These preliminary findings support the need for a larger randomized study.

Supported by Purdue Pharmaceuticals.

References:

1. Johnson RE, Strain EC, Amass L: Buprenorphine: how to use it right. *Drug and Alcohol Dependence* 2003; 70: 59-77.
2. Savage SR: Addition in the treatment of pain: significance, recognition and management. *J Pain Symptom Management* 1993; 8: 265-278.

NR882 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Quetiapine Treatment of Agitation in Patients With Alzheimer's Disease

Supported by AstraZeneca

Jacobo E. Mintzer, M.D., *Alzheimer's Research, Medical University of South Carolina, 5900 Core Road, Suite 203, N. Charleston, SC 29404*; Kate Zhong, M.D., Pierre Tariot, M.D., Margaret C. Minkwitz, Ph.D., Nancy A. Devine, M.S.

Educational Objectives:

At the conclusion of this presentation, the participant should understand that quetiapine is effective in reducing agitation in patients with Alzheimer's disease. Quetiapine is also well-tolerated in this patient population.

Summary:

Objective: Evaluation of efficacy and tolerability of quetiapine for agitation in patients with Alzheimer's disease (AD).

Methods: Pre-planned secondary analysis of patients with probable AD (n=260) who took part in a 10-week, double-blind, placebo-controlled study of quetiapine (100 mg/day and 200 mg/day) in patients with dementia and agitation (n=333). Key efficacy measures: PANSS-Excitement Component (EC); CGI-C; response rates (>=40% reduction PANSS-EC; much or very much improved CGI-C). Tolerability was also assessed.

Results: Compared with placebo, PANSS-EC, CGI-C and PANSS-EC response rates were significantly improved with quetiapine 200 mg/day, but not 100 mg/day (ITT, LOCF). Mean (SE) changes in PANSS-EC scores were -6.49 (0.758) for quetiapine 200 mg/day versus -3.47 (0.846) for placebo (p<0.01). Mean (SE) CGI-C scores were 3.08 (0.17) versus 3.76 (0.19), respectively (p<0.01). CGI-C response rates were significantly higher with both doses of quetiapine versus placebo (p<0.05). In patients with vascular dementia, quetiapine did not differentiate from placebo on the efficacy measures. Incidences of AEs (74-78%), serious AEs (5-10%), withdrawals for AEs (6-10%), postural hypotension, and falls was comparable among groups. No CVAEs were reported with quetiapine.

Conclusion: Quetiapine 200 mg/day was effective in reducing agitation in patients with AD and was generally well tolerated.

References:

1. Lawlor BA: Behavioral and psychological symptoms in dementia: the role of atypical antipsychotics. *J Clin Psychiatry* 2004; 65(Suppl 11): 5-10.
2. Zhong K, Tariot P, Minkwitz MC, Devine NA, Mintzer J: Quetiapine for the treatment of agitation in elderly institutionalized patients with dementia: a randomized, double-blind trial. Poster presented at the 9th International Conference on Alzheimer's Disease and Related Disorders, Philadelphia, PA, USA, July 17-22, 2004.

NR883 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Differential Effects of Novel Second Generation Antipsychotic Drugs on Insulin Resistance and Secretion: Clamp and HOMA Studies

Supported by Janssen-Cilag, Eli Lilly, Sanofi-Aventis

Daniel Kopf, M.D., *Internal Medicine Consult Service, Central Institute of Mental Health, J5, Mannheim 68159, Germany*, Maria Gilles, M.D., Florian Lederbogen, M.D., Fritz A. Henn, M.D., Johannes Thome, M.D., Hendrik Lehnert, M.D., Michael Deuschle, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the differential effects of antipsychotic drugs on insulin resistance and insulin secretion and their significance for antipsychotic related diabetes.

Summary:

The role of insulin sensitivity (IS), insulin secretion, and antipsychotic receptor profile in antipsychotic-related diabetes was studied.

Methods: (1) Patients with schizophrenic psychosis underwent HOMA testing for IS and insulin secretion prior to and after three weeks of treatment with olanzapine (n=8) or risperidone (n=7). (2) 10 healthy subjects underwent clamp studies after acute administration of olanzapine 10 mg or amisulpride 400 mg vs. placebo and after acute administration of the selective 5HT_{2A} antagonist ketanserin 40 mg vs. placebo in a double-blind, cross-over design.

Results: (1) HOMA IS was significantly reduced after treatment with olanzapine (80+/-28% of baseline), but unaffected after risperidone (120 +/-29%, interaction time*treatment p=0.034). (2) C-peptide*) secretion during hyperglycemic clamp was stimulated by amisulpride compared with olanzapine or placebo (ANOVA p=0.043), while IS (euglycemic clamp) was unchanged. IS was impaired after ketanserin compared with placebo (euglycemic clamp glucose disposal rate 7.7 ± 2.4 vs. 9.4 ± 3.6 mg/kgBW/min; p=0.030).

Conclusion: IS is impaired after chronic treatment with olanzapine compared with risperidone. Acute administration of olanzapine, in contrast, does not affect IS. Amisulpride, but not olanzapine, acutely improves insulin secretion. In addition to weight gain, antagonism at 5HT_{2A} receptor may be one mechanism of impaired IS.

References:

1. Pfutzner et al. Clin 2003; 49:227-232.

NR884 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Atomoxetine Alleviates Executive Function Impairment Associated With ADHD

Supported by Eli Lilly and Company

Thomas E. Brown, Ph.D., *Department of Psychiatry, Yale Medical School, 1188 Whitney Avenue, P.O. Box 6694, Hamden, CT 06517*; Virginia Sutton, Ph.D., Ann Rogers, Ph.D., Calvin Sumner, M.D.

Educational Objectives:

At the conclusion of this presentation, attendees will be able to describe the efficacy of atomoxetine in reducing core symptoms and deficits in executive function for patients with ADHD.

Summary:

Objective: Usually effectiveness of medications for attention-deficit/hyperactivity disorder (ADHD) is assessed only with measures of DSM-IV symptoms. Effects of atomoxetine on executive function impairments in children and adults with ADHD were as-

sessed using a parent report/self-report measure that captures a wider range of executive functions often impaired in individuals with ADHD.

Methods: The Brown ADD Scale, a normed measure of executive function impairments, was used in three trials of atomoxetine involving 744 patients aged 6 to 50 years old with DSM-IV-defined ADHD. The two child trials were placebo-controlled; the adult trial was not. The primary objective of these trials was to assess core ADHD symptoms using the ADHD Rating Scale and Conners' Adult Attention-deficit/Hyperactivity Rating Scale. In each study, separately analyzed, changes from baseline were compared across treatments using ANCOVA repeated measures. Student's t-test was used to test for non-zero improvement from baseline.

Results: In both child/adolescent trials, mean Brown scores improved significantly on atomoxetine compared with placebo (p<.05). In the adult trial, mean Brown ADD scores improved significantly from baseline (p<.001).

Conclusions: In addition to previously demonstrated effectiveness for ADHD core symptoms, atomoxetine treatment also improves a wide range of ADHD-related executive function impairments in children and adults.

References:

1. Brown, TE (Ed.): Attention-deficit disorders and comorbidities in children, adolescents and adults. Washington, DC: American Psychiatric Press, 2000.
2. Michelson D, Allen A, Busner J, et al: Once-daily atomoxetine treatment for children and adolescents with attention deficit hyperactivity disorder: a randomized, placebo-controlled study. *Am J Psychiatry* 2002; 159(11):1896-901.

NR885 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Expression Pattern of Bcl-xL by Chronic Treatment of Fluoxetine in Rat C6 Glioma Cells

Supported by AstraZeneca Inc.

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Educational Objectives:

At the conclusion of the presentation, the participant should understand the actions of some SSRI antidepressants.

Summary:

When depressive patients take the selective serotonin reuptake inhibitor (SSRI) fluoxetine serotonin reuptake inhibitory action occurs immediately. However, the antidepressant effect of fluoxetine appears 2-3 weeks later. Though fluoxetine increases level of serotonin and/or norepinephrine, many studies have proved that therapeutic effects are achieved by gene expression regulation through more complicated processes, such as intracellular signal transduction cascade in connection with nerve cell survival.

This research tried to analyze gene expression pattern of rat C6 glioma cells treated with 10 uM fluoxetine, and cultured for 24 and 72 hrs using cDNA microarray. By the results, we intended to identify the genes regulated by the antidepressants, and to provide informations about action mechanism of SSRI-antidepressants. cDNA microarray revealed that seven of 5,000 genes were down-regulated and 33 genes including Bcl-xL, antiapoptotic gene, were up-regulated in the fluoxetine-treated C6 cells for 24 hrs. In the fluoxetine-treated C6 cells for 72 hrs, 77 genes were down-regulated and 53 genes were up-regulated. One of the up-regulated genes by fluoxetine, Bcl-xL, was confirmed by real-time RT-PCR.

References:

1. Ananthan J, Goldberg AL, Voelmy R: Abnormal proteins serve as eukaryotic stress signals and trigger the activation of heat shock genes. *Science*, 1986; 232:522-524.
2. Rudolf R, Entsuah R, Derivan A: Early clinical response in depression to venlafaxine hydrochloride. *Biol Psychiatry* 1991; 29:630-635.

NR886 **Thursday, May 26, 12:00 p.m.-2:00 p.m.** **A Randomized, Controlled Trial of Paroxetine CR in Irritable Bowel Syndrome** *Supported by GlaxoSmithKline*

Prakash S. Masand, M.D., *Department of Psychiatry, Duke University Medical Center, 110 Swift Avenue Suite 1, Durham, NC 27705*; Kathleen Peindi, Ph.D., Stan Krulewicz, M.A., Paolo Mannelli, M.D., Indira Varia, M.D., Ashwin Patkar, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the role of selective serotonin uptake inhibitors in the treatment of irritable bowel syndrome.

Summary:

Objective: In the first double-blind, controlled trial of SSRIs, we examined the efficacy and safety of paroxetine, controlled release (CR) in IBS.

Method: 72 subjects were randomized to paroxetine CR (12.5-50 mg/ day) or placebo for 12 weeks. Efficacy was measured by composite pain scores (primary outcome) and Patient Global Impression (PGI) on the interactive voice response system (IVRS), CGI-I and CGI-S ratings.

Results: The dropout rate was 16%. There were no significant differences in reduction in composite pain scores between the drug (-2.79 diff, 95% C.I. = 1.05-4.50) and placebo (-1.85 diff, C.I. = 18-3.68) ($F=0.84$, $p=.49$). 70% in the drug group responded on the CGI-I versus 15% in placebo ($\chi^2 = 18.3$, $p < .001$). The CGI-S showed a 66% response in the drug group versus 25% in placebo ($\chi^2 = 9.42$, $p < .01$). On the PGI there was a trend favoring the drug (62%) over placebo (39%) ($\chi^2=6.50$, $p=.07$). The mean paroxetine CR dose was 30 mg/ day.

Conclusions: The inability to detect a difference on the primary outcome may be related to inadequate power. Overall paroxetine CR seems to improve global well-being in IBS. Studies with adequate samples may clarify the role of SSRI in IBS.

References:

1. Masand PS, Gupta S, Schwartz TL, Virk S, Lockwood K, Hameed A, King M, Kaplan DS: Paroxetine in patients with irritable bowel syndrome: a pilot open-label study. *Prim Care Companion J Clin Psychiatry* 2002; 4(1):12-16.
2. Creed F, Fernandes L, Guthrie E, Palmer S, Ratcliffe J, Read N, Rigby C, Thompson D, Tomenson B, North of England IBS Research Group: The cost-effectiveness of psychotherapy and paroxetine for severe irritable bowel syndrome. *Gastroenterology* 2003; 124(2):303-17.

NR887 **Thursday, May 26, 12:00 p.m.-2:00 p.m.** **Results of an Open-Label Study Evaluating the Safety and Efficacy of Rivastigmine in Patients Not Responding Adequately to Donepezil** *Supported by Employees of Novartis Pharmaceuticals*

Dario F. Mirski, M.D., *15 Bonnell Lane, Randolph, NJ 07869*; Gary Figiel, M.D., Barbara Koumaras, B.A., Ibrahim Gunay, M.D., Michael Chen, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that switching patients from donepezil to rivastigmine is well-tolerated.

Summary:

Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative disorder. Previous data have suggested that switching patients from one ChEI to another represents a viable option for patients not responding to current therapy. This study evaluated a treatment switch to rivastigmine in patients not responding to (or declining on) treatment with donepezil.

Methods: Analysis of 26-week switch data from a study assessing the safety/efficacy of rivastigmine 3-12 mg/day in patients with mild-to-moderate AD not responding to donepezil. Safety and tolerability were measured by the occurrence of adverse events (AEs) and patient disposition. Treatment effects on global functioning were assessed using the CGIC.

Results: Two-hundred seventy patients with a mean age of 78.5 (SD=7.64) and mean duration of dementia of 3.5 (SD=2.06) years are included; 61.5% (n=166) were female. 81% of patients reported at least one AE, with the most frequently occurring AEs in the GI system (52%). 69% of patients completed the study with < 20% discontinuing due to adverse events. 70% of patients experienced improvement/no decline on the CGIC at Week 26.

Conclusion: Switching patients from donepezil to rivastigmine is well tolerated. Additionally, these results suggest that patients previously not responding adequately to donepezil either improved or stabilized after switching to rivastigmine.

References:

1. Auriacombe S, Pere J-J, Loria-Kanza Y, et al: Efficacy and safety of rivastigmine in patients with Alzheimer's disease who failed to benefit from treatment with donepezil. *Cur Med Res Opin* 2002; 18(3), 129-138.
2. Shua-Haim J, Smith JM, Amin S: Crossover results from donepezil (Aricept) to rivastigmine (Exelon) in Alzheimer's disease patients: an overall analysis of 3 prospective studies. Poster presented at: American Geriatrics Society Annual Meeting; May 9-13, 2001; Chicago, Ill. S115. P330.

NR888 **Thursday, May 26, 12:00 p.m.-2:00 p.m.** **Adding Memantine to Therapy With Rivastigmine in Patients With Mild to Moderate Alzheimer's Disease: Results of a 12-Week Study** *Supported by Employee of Novartis Pharmaceuticals*

Dario F. Mirski, M.D., *15 Bonnell Lane, Randolph, NJ 07869*; Matthias Riepe, M.D., Georg Adler, M.D., Bernd Ibach, M.D., Birgit Weinkauf, M.D., Ferenc Tracik, M.D., Ibrahim Gunay, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that the addition of memantine to treatment with rivastigmine may result in cognitive benefit and is well tolerated in patients with mild to moderate AD.

Summary:

Introduction: Cholinesterase inhibition and glutamate antagonism are two therapeutic approaches successfully improving cognition in patients with Alzheimer's disease (AD). The dual cholinesterase inhibitor rivastigmine is indicated for mild-to-moderate AD, and the NMDA antagonist memantine is indicated for moderate-to-severe disease. This study investigated the efficacy and tolerability of rivastigmine and add-on memantine in patients with mild-to-moderate AD.

Methods: This was a 12-week, open-label, pilot study where memantine 10-20 mg/day, was added to rivastigmine 6-12 mg/day in patients with probable AD. There were 90 patients in the ITT population (measuring ADAS-cog), and 95 patients in the safety population.

Results: After 12 weeks of treatment, there was a mean 1.7-point improvement in ADAS-cog score ($p < 0.005$). Significant improvements in MMSE (1.2 points; $p < 0.01$), Digit-Span Test (0.5 points; $p < 0.05$) and Verbal Fluency Test (0.8 points; $p < 0.01$) scores were also observed. Overall <10% of patients had adverse events (AEs) suspected to be related to treatment. Four patients (4.2%) withdrew due to AEs, and there were two serious AEs. Vital signs remained stable during combination therapy.

Conclusion: Addition of memantine to treatment with rivastigmine suggests additional cognitive benefit and is well tolerated in patients with mild-to-moderate AD.

References:

1. Darreh-Shori T, Almkvist O, Guan ZZ, et al: Sustained cholinesterase inhibition in AD patients receiving rivastigmine for 12 months. *Neurology* 2002; 59:563-572.
2. Doody R, Wirth Y, Schmitt F, et al: Specific functional effects of memantine treatment in patients with moderate to severe Alzheimer's disease. *Dement Geriatr Cogn Disord* 2004; 18:227-232.

NR889 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Effects of Rivastigmine in Patients With Traumatic Brain Injury With Cognitive Deficits: Results of a 12-Week, Double-Blind Study

Supported by Employees of Novartis Pharmaceuticals

Dario F. Mirski, M.D., 15 Bonnell Lane, Randolph, NJ 07869; Jonathan Silver, M.D., Adrian Rabinowicz, M.D., Barbara Koumaras, B.A., Michael Chen, Ph.D., Steven Potkin, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that using rivastigmine is safe and well tolerated, and may improve some cerebral deficits secondary to TBI.

Summary:

Introduction: Traumatic brain injury (TBI) is common in the U.S. Many individuals with non-penetrating TBI have cognitive deficits and/or other neuropsychiatric disorders, with no currently approved treatment. This study hypothesizes that enhancement of central cholinergic activity using rivastigmine improves cognitive, memory, attention, and behavioral deficits secondary to TBI.

Methods: This 12-week, double-blind, placebo-controlled, multi-center study assessed the safety and efficacy of rivastigmine 3-6mg/day in patients with TBI. Primary objectives compared rivastigmine versus placebo on measures of attention or memory, and safety and tolerability. Results reported here describe the study population. Other results will be reported.

Results: There are 157 patients in the demographics analysis (106 males/51 females). Mean age was 37; 89% were Caucasian; 86% had known loss of consciousness (LOC). 48% had a Glasgow Coma Scale (GCS) score (mean 6.5), collected within 24 hours of injury. 85% reported memory loss; 92% experienced altered mental state.

Conclusion: These results present a sample of non-penetrating TBI patients with persistent cognitive or attention deficits for ≥ 12 months following injury. The population represents individuals with moderate-to-severe TBI: predominantly men (2:1 ratio), many with history of LOC and GCS in the severe range.

References:

1. Griffin SL, van Reekum R, Masanic C: A review of cholinergic agents in the treatment of neurobehavioral deficits following

traumatic brain injury. *J Neuropsychiatry Clin Neurosci* 2003; 15:17-26.

2. Chen Y, Shohami E, Constantini S, et al: Rivastigmine, a brain-selective acetylcholinesterase inhibitor, ameliorates cognitive and motor deficits induced by closed-head injury in the mouse. *J Neurotrauma* 1998; 15:231-237.

NR890 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Effects of Aripiprazole on Pharmacokinetics of Lithium in Healthy Subjects

Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd.

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Educational Objectives:

At the conclusion of the presentation, the participant should be able to assess effects of aripiprazole on the pharmacokinetics of lithium.

Summary:

Objective: To assess the effects of 30 mg/day oral doses of aripiprazole on the steady-state pharmacokinetics of lithium in healthy subjects.

Methods: In this open-label, sequential study, 32 subjects received 450 mg lithium carbonate (controlled release) every 12 hours (q12h) on Days 1-6 and once on Day 7 (morning). Following a two-day washout, aripiprazole was administered once daily until Day 26, titrating from 10 mg to 30 mg from Days 14 onwards. Lithium carbonate was co-administered on Days 20-26 (450 mg q12h). Serial blood samples were collected for 12h on Days 7 and 26.

Results: Based on serum trough concentrations on Days 5-6, steady-state for lithium was attained by Day 7. PK parameters for lithium alone were: $C_{max} = 0.68$ mM; $AUC(TAU) = 7.16$ mM-h (geometric means); and for lithium administered with aripiprazole: $C_{max} = 0.75$ mM; $AUC(TAU) = 7.62$ mM-h (geometric means). Point estimates for lithium + aripiprazole/lithium were: $C_{max} = 1.10$ (90%CI: 1.06, 1.14); $AUC(TAU) = 1.06$ (90%CI: 1.02, 1.10). Since 90% confidence intervals with and without aripiprazole were between 80% and 125% for both C_{max} and $AUC(TAU)$ of lithium, it was concluded aripiprazole did not affect these steady-state pharmacokinetics of lithium.

Conclusions: Aripiprazole appears to have no effect on the pharmacokinetics of steady-state lithium when administered at 30 mg/day to healthy subjects.

References:

1. Keck PE Jr, McElroy SL: Clinical pharmacodynamics and pharmacokinetics of antimanic and mood-stabilizing medications. *J Clin Psychiatry* 2002; 63(Suppl 4):3-11.
2. Mallikarjun S, Salazar DE, Bramer SL: Pharmacokinetics, tolerability, and safety of aripiprazole following multiple oral dosing in normal healthy volunteers. *J Clin Pharmacol* 2004; 44:179-187.

NR891 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Risks for Cerebrovascular Adverse Events: Use of Quetiapine in Patients With Dementia

Supported by AstraZeneca

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Southern California, 1510 San Pablo Street, HCC-600, Los Angeles, CA 90033; Lon S. Schneider, M.D., Pierre Tariot, M.D., Jacobo Mintzer, M.D., Margaret C. Minkwitz, Ph.D., Kate Zhong, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be knowledgeable about the extent of the evidence for potential risks for cerebrovascular adverse events with quetiapine, risperidone, and olanzapine in nursing home patients with dementia.

Summary:

Objective: In clinical trials of nursing home patients with dementia, risperidone and olanzapine were associated with increased risks of cerebrovascular adverse events (CVAEs). We assessed the evidence for whether this risk extends to quetiapine, another frequently used atypical antipsychotic.

Methods: Pooled data (n=684) from the only two 10-week, multicenter, double-blind, placebo-controlled, randomized nursing home trials, using either flexible (25-500 mg/d) or fixed (100 or 200 mg/d) doses of quetiapine, or a flexible dose of haloperidol (0.5-6.0 mg/d), were analyzed for CVAEs (i.e., strokes or transient ischemic episodes) and treatment exposures from which hazard ratios (HRs) were calculated.

Results: CVAEs per trial were 0.3% (1/355), 0.9% (1/116), and 1.9% (4/213) for quetiapine, haloperidol, and placebo, respectively. Exposure was greater for quetiapine (54.7 patient/yrs) than for haloperidol (17.5) or placebo (32.7). CVAE incidences were lower with quetiapine (1.8/100 pt*yrs) than with haloperidol (5.7) or placebo (12.2). HRs for quetiapine and haloperidol compared with placebo were 0.15 (95% CI 0.02-1.34) and 0.47 (95% CI 0.05-4.19), respectively.

Conclusion: The small sample, limited exposure, and broad CIs restrict conclusions, but the analysis does not provide evidence for increased risk of CVAEs with quetiapine and risk may be lower than with other atypicals in similar populations; however, more studies are needed.

References:

1. Wooltorton E: Risperidone (Risperdal): increased rate of cerebrovascular events in dementia trials. *CMAJ* 2002; 167:1269-1270.
2. Wooltorton E: Olanzapine (Zyprexa): increased incidence of cerebrovascular events in dementia trials. *CMAJ* 2004; 170:1395.

NR892 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Real-World Usage of Weight Gain Drugs in Patients on Second-Generation Antipsychotics

Supported by Bristol-Myers Squibb

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Educational Objectives:

The results of this study provide evidence to primary care physicians that along with the consideration of weight gain as a side effect in patients on SGAs, concomitant therapies, which also may cause weight gain, should be considered in treatment strategies.

Summary:

Introduction: Second-generation antipsychotics (SGAs) class of medications has been associated with weight gain. This adverse event can be of particular concern in patients taking concomitant medications that also have weight gain as a potential side effect.

Methods: From January 1995 to March 2004, 25,396 patients on SGAs were identified in the Logician national electronic medical record (EMR) research database and assessed for utilization of concomitant drugs known to cause weight gain.

Results: Of 25,396 patients who were on SGAs, 14,122 (55.6%) unique patients were on drugs with weight gaining potential (5-15 kg over 3-12 months) according to the literature. Of the 14,122, 53.5% (7,751) were on antidepressants, 33% (4,704) were on anticonvulsants, 22% (3,093) were on diabetic agents (including insulin and sulfonylureas), 20% (2,784) were on corticosteroids, 19% (2,622) were on estrogen therapy, 14% (1,989) were on oral contraceptives, and 1.7% (239) were on cancer agents (including antineoplastics and alkylating agents). Many patients were on several of these drugs simultaneously.

Conclusion: A large portion of patients on SGAs are also on concomitant medications that can affect weight. These effects need to be considered when optimizing SGA therapy outcomes for patients in a primary care setting.

References:

1. Pijl H, Meinders AE: Bodyweight change as an adverse effect of drug treatment. Mechanisms and management. *Drug Saf* 1996; 14(5):329-42.

NR893 Thursday, May 26, 12:00 p.m.-2:00 p.m.

A Two-Year Longitudinal Study of Adjunctive VNS for Patients With Treatment-Resistant

Supported by Cyberonics Inc.

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Educational Objectives:

To determine whether long-term adjunctive VNS is an effective therapy for patients with TRD.

Summary:

Objective/Background: A recent naturalistic, long-term study suggested that patients with TRD who received adjunctive vagus nerve stimulation (VNS) showed continued improvement in depression symptoms over the timeframe of one year. We now report the two-year results.

Methods: Patients were randomized initially to either active or sham VNS during a 12-week acute trial, and then elected to receive active VNS in the long-term open, naturalistic study. Patients were assessed on a monthly basis. Changes were allowed in concomitant medications as well as VNS parameters.

Results: At two years, 157 of 205 evaluable patients provided efficacy data. Response was defined as $\geq 50\%$ reduction in scores compared with their pre-stimulation baseline. HRSD24 response rates increased from 29.8% at one year to 32.5% at two years, and IDS-SR30 from 21.7% to 27.4%. Sustained response was defined as having a $\geq 50\%$ reduction in HRSD24 scores at the three-month or one-year visit, and $\geq 40\%$ reduction at the two-year visit. Two-year sustained response rates for three-month and one-year responders were 70% and 69%. The incidence of adverse events beyond one year of stimulation either decreased or was unchanged over time. At two years the patient continuation rate was 82%.

Conclusions: These data suggest that treatment-resistant depressed patients who receive adjunctive VNS in addition to their usual antidepressant medications show improving response and remission rates over a two-year time frame. This suggests that VNS, when combined with antidepressant medications, may provide long-lasting antidepressant effects.

References:

1. Rush AJ, Marangell LB, George MS, Sackeim HA: A one-year longitudinal study of VNS therapy in patients with treatment-resistant depression [Poster]. Presented at the 44th Annual NCDEU Annual Meeting Phoenix, Arizona, 2004.
2. Marangell LB, Rush AJ, George MS, Sackeim HA, Johnson CR, Husain MM et al: Vagus nerve stimulation (VNS) for major depressive episodes: one year outcomes. *Biol Psychiatry* 2002; 51:280-287.

NR894 Thursday, May 26, 12:00 p.m.-2:00 p.m. **Curing OCD**

James Hooper IV, M.D., *Department of Psychiatry, Al Department of Mental Health, 1301 Jack Warner Parkway, Tuscaloosa, AL 35404*

Educational Objectives:

At the conclusion of the presentation, the participant should be able to diagnose and cure OCD.

Summary:

OCD is a very destructive mental illness. New treatments have led to what is essentially a cure for this disease. Three persons in the U.S. have had deep brain stimulus treatment, with resulting cures. I will bring one of these patients to discuss the course of his illness and his successful recovery.

References:

1. Anderson D, Ahmed A: *J Neurosurg.* 2003; 98(5):1104-8.
2. Nuttin BJ et al: *Neurosurgery* 2003; 52(6):1263-72.

NR895 Thursday, May 26, 12:00 p.m.-2:00 p.m. **Efficacy of Olanzapine in Antisocial Opioid Addicts**

Mohamad R. Eskandari, M.D., *Department of Psychiatry, Zanjan University of Medical Sciences, Arq Square Beheshti Hospital, Zanjan 45136, Iran; Soghra Karami, M.Psy.*

Educational Objectives:

At the conclusion of the presentation, the participant should know that olanzapine may be useful in treatment of patients with opioids dependency afflicted with antisocial personality disorder.

Summary:

Background: Antinociceptive activity of olanzapine was demonstrated in animals and is a useful drug in controlling of aggression. This study evaluated the efficacy of this drug in treatment of patients that were dependant to opioid substances and had apd.

Methods: During six-month (2004) study, 36 cases with opioid substances dependency evaluated and 24 of them introduced as main study group with apd. Clinical interview and mmpi-2 test has been used in this process, all patients received clonidine and analgesics and 12 of them received olanzapine 10-30 mg/day. Patients evaluated after one month of treatment.

Results: compliance for treatment was better (10 of 12 cases = %83.3) in cases that have been received olanzapine than versus group (4 of 12 cases = % 33.3) $P < 0.05$. Frequently-reported symptoms in second group were irritability (% 100), verbal and physical hostility (% 100, % 84), and restlessness (100%).

Conclusion: In patients with opioid substance dependency and concomitant apd usefulness of olanzapine may be in focus of attention in new researches. This drug improves the compliance of treatment especially in acute withdrawal phase.

References:

1. Khojainova N, Santiago-Palma J, Gonzales GR: Pain reduction in cognitively impaired cancer patients treated with olanzapine. *Pain Med* 2001; 2(3):243-4.
2. Sattar SP, Grant K, Bhatia S, Petty F: Potential use of olanzapine in treatment of substance dependence disorders. *J Clinical Psychopharmacology* 2003; 23(4):413-5.

NR896 Thursday, May 26, 12:00 p.m.-2:00 p.m. **The Effectiveness and Tolerability of Long-Acting Risperidone Microsphere: A 12-Week, Multicenter, Switching Study in Korea**

Suk Hoon Jung, M.D., *Department of Psychiatry, Asan Medical Center, Pungnap-Dong, Seoul, SD 11, Korea; Chang-Yoon Kim, Ph.D., Jun-Soo Kwon, Ph.D., Chan-Hyung Kim, Ph.D., Won-Myong Bahk, Ph.D., Jin-Sang Yoon, Ph.D., Young-Hoon Kim, Ph.D.*

Educational Objectives:

To evaluate maintained efficacy and tolerability when treated with long-acting risperidone microsphere compared with the previous antipsychotic medication in patients with schizophrenia or other psychotic disorders and to compare maintained efficacy between oral risperidone and non-risperidone subgroups based on their previous medication.

Summary:

Purpose: To evaluate maintained efficacy and tolerability when treated with long-acting risperidone microsphere compared with the previous antipsychotic medication in patients with schizophrenia or other psychotic disorders and to compare maintained efficacy between oral risperidone and non-risperidone subgroups based on their previous medication.

Methods: Subjects aged at least 18 years who required long-term antipsychotic therapy and who have been symptomatically stable on a stable dose of antipsychotics during the last month were enrolled in the non-randomized, single-arm, multi-center, 12 duration with optional six months extension study where antipsychotic medications were switched from oral antipsychotics to long-acting risperidone microsphere injection every two weeks. Most patients were started on 25 mg long-acting risperidone injection or 37.5mg in some patients. The dosages were adjusted according the patients' symptoms and responses to treatment at the discretion of investigators. Oral antipsychotics were continued at the same dose as before for two weeks and then were stopped or tapered off within next seven days.

Results: A total of 198 patients with schizophrenia (N=178) and schizoaffective disorder (N=18) from 20 sites in Korea were enrolled in this switching study. The percentage of drop-out was 25.5% at 12 weeks. Observed case analysis has been performed excluding these dropped out cases.

At 12 weeks after switching from oral antipsychotics to long-acting risperidone microsphere injection, statistically significant improvement was observed from baseline across all symptom domains including PANSS total, positive, negative, general subscale, CGI-S(Clinical Global Impression-Severity) scores, and GAF(Global Assessment of Functioning) scores. The proportion of responders was 98.7% where response was defined a ??20 % reduction from baseline PANSS total score. The proportion of symptom worsening at 12 weeks was 9.32% (N=15) where symptom worsening was defined as more than 20% increase from baseline in PANSS total score or drop-out due to insufficient response or any two points change on any of four PANSS psychotic items(delusion, conceptual disorganization, hallucinatory behavior, suspiciousness/persecution), excluding changes in which the ratings remained at nonpsychotic levels.

Significant improvement from baseline was also observed in the measure of parkinsonism assessed using Extrapyramidal Symptom Rating Scale (ESRS).

In addition, overall, patients were satisfied with long-acting risperidone injection on a single-item measure of satisfaction.

When subgroup analysis was performed on the basis of previous antipsychotics before switching to long-acting risperidone, no statistically significant differences were detected between oral risperidone (N=136) and non-risperidone subgroup(N=60) on all measures of efficacy and tolerability including baseline demographic and clinical characteristics, symptom improvements, proportion of symptom improvement or worsening, and ESRS score changes.

Conclusion: Our study results demonstrated maintained efficacy and tolerability of long-acting risperidone microsphere and also could confirm successful switching from not only oral risperidone but also non-risperidone to long-acting risperidone injection.

This study was supported by a grant from the Janssen Korea Ltd.

References:

1. J Clin Psychiatry 2004; 65; 1084-1089.
2. J Clin Psychiatry 2003; 64; 1250-1257.

NR897 Thursday, May 26, 12:00 p.m.-2:00 p.m.

Recent Improvement in Access to ADHD Pharmacotherapy: Evidence From a Large, National Health Plan

Supported by Eli Lilly and Company

Peter Sun, Ph.D., *Lilly Research Laboratories, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285;*
Joseph Johnston, M.D., David Van Brunt, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize that realized access to ADHD medications has improved from 2002 to 2003, but documented pharmacotherapy rates continue to lag behind national prevalence estimates, suggesting many patients remain untreated with pharmacotherapy.

Summary:

Objective: To examine recent trends in realized access to medications for treating attention-deficit/hyperactivity disorder (ADHD) in a managed care setting.

Methods: Assuming similar prevalence rates of ADHD among health plan members in 2002 and 2003, we defined the realized access to ADHD medications as the percent of members who had at least one prescription for an ADHD medication in 2002 or 2003. Using claims data from a national health plan covering 7-8 million lives, we compared the realized access, stratified by age and gender, between 2002 and 2003.

Results: The percent of patients who had a prescription for an ADHD medication increased 14% from 2002 to 2003 (1.35% vs. 1.54%). While overall a higher percentage of children (5.6%) and adolescents (5.4%) used ADHD medications than adults (0.85%), the increase was greater in females (+19%) than males (+11%), and in adults (+25%) than children (+6%) or adolescents (+12%). The greatest increase (+27%) occurred in females at age between 18 and 64.

Conclusions: In our cohort, realized access improved from 2002 to 2003. While the improvement was more pronounced among females and adults, documented pharmacotherapy rates continue to lag behind national prevalence estimates, suggesting that many patients remain untreated with pharmacotherapy.

References:

1. Group TMC: A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. The MTA Cooperative Group. Multimodal Treatment Study of Children with ADHD. Arch Gen Psychiatry 1999; 56(12):1073-1086.
2. Montano B: Diagnosis and treatment of ADHD in adults in primary care. J Clin Psychiatry 2004; 65 Suppl 3:18-21.

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