1991

NEW RESEARCH PROGRAM AND ABSTRACTS

Our Children: Our Future

AMERICAN PSYCHIATRIC ASSOCIATION

144th ANNUAL MEETING

MAY 11-16, 1991

NEW ORLEANS, LOUISIANA

PROGRAM AND PAPERS ON NEW RESEARCH

IN SUMMARY FORM

THE ONE HUNDRED AND FORTY-FOURTH ANNUAL MEETING OF THE AMERICAN PSYCHIATRIC ASSOCIATION

NEW ORLEANS, LOUISIANA
May 11-16, 1991

Papers presented at New Research Sessions are not automatically the property of the *American Journal of Psychiatry*. Authors are free to submit them to the *American Journal of Psychiatry*, the *Journal of Hospital & Community Psychiatry*, or another publication of their choice.

American Psychiatric Association

1400 K Street, N.W.
Washington, D.C. 20005

May 11, 1991

Dear Fellow Research Practitioners and Consumers:

On behalf of the members and staff of the Scientific Program Committee, I would like to welcome you to the 1991 New Research Program.

This year's program reflects the increasing importance of basic and clinical neuroscience to psychiatry. The sessions are organized by topic and have been expanded to accommodate a myriad of excellent submissions. A second Young Investigators' Poster Session has been added on Monday afternoon, as well as two additional Poster Sessions on Tuesday and Wednesday afternoons.

The program begins Monday, May 13, at 9:00 a.m. with the first of two Young Investigators' Poster Sessions. It continues at 10:30 a.m. with "Research Advances in Psychiatry: An Update for the Clinician," with special emphasis on psychiatric disorders of children, OCD, schizophrenia, and sleep disorders.

The New Research Oral/Slide Sessions will be held Tuesday, May 14, through Thursday, May 16, from 9:00 a.m.-10:30 a.m. Sessions will focus on child and adolescent disorders and anxiety disorders (Tuesday); schizophrenia, organic mental syndrome, and deinstitutionalized populations (Wednesday); and mood, personality, substance abuse and eating disorders (Thursday). Poster Sessions will be held Tuesday and Wednesday from 12 noon-2:00 p.m. and 3:00 p.m.-5:00 p.m., and on Thursday from 12 noon-2:00 p.m. These sessions will be devoted to childhood and adolescent, alcohol and substance abuse, personality, eating and anxiety disorders; epidemiology; and economic and diagnostic issues (Tuesday); schizophrenic and other psychotic disorders; organic mental disorders; geriatrics; AIDS/HIV; consultation/liaison; emergency psychiatry; and sleep disorders (Wednesday); and affective disorders (Thursday).

The 36 oral/slide papers, 208 Young Investigators', and 416 poster presentations are a diverse and, we believe, a representative sampling of that which is new and significant in psychiatric research. We hope that you will find them informative, provocative and encouraging.

Sincerely,

Susan J. Fiester, M.D.
Chairperson
New Research Subcommittee of the
Scientific Program Committee

Outside Reviewers for the New Research Program

Nancy C. Andreasen, M.D.
Jamess C. Ballenger, M.D.
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Donald F. Klein, M.D.
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Andrew E. Skodol, M.D.
Robert L. Spitzer, M.D.
Michael J. Stanley, M.D.
Marvin Stein, M.D.
James J. Strain, M.D.
Trey Sunderland, M.D.
Kenneth J. Tardiff, M.D.
James W. Thompson, M.D.
Gary J. Tucker, M.D.
Joe P. Tupin, M.D.
Fred R. Volkmar, M.D.
B. Timothy Walsh, M.D.
Daniel R. Weinberger, M.D.
George E. Woody, M.D.

NEW RESEARCH

Monday, May 13, 1991, 9:00 a.m.-10:30 a.m.

New Research 1—Poster Session—Ballroom A, Level 1, Convention Center

YOUNG INVESTIGATORS' POSTER SESSION

Moderator: Harold Alan Pincus, M.D.

NR1 Gender Differences in Schizophrenia
Ana Maria Andia, M.D., Sidney Zisook, M.D., David L. Braff, M.D., John T. Moranville, M.D., Robert Heaton, Ph.D.

NR2 Glutamate Receptor Gene Expression in Kindling
Ma-Li Wong, M.D., Susan R.B. Weiss, M.D., Mark Smith, M.D., Phillip W. Gold, M.D.

NR3 Neurocognitive Components of Chronic Schizophrenia
Abraham Fiszbein, M.D., Lewis A. Opler, M.D., Stanley R. Kay, Ph.D., Carl E. Rosenkilde, M.D., Paul M. Ramirez, Ph.D., Julio Moizeszowicz, M.D., Amy S. Gorelick, M.D.

NR4 Schizophrenia Candidate Gene Association Study
Alan R. Sanders, B.S., Joseph D. Hamilton, II, M.D., William E. Fann, M.D., Pragna I. Patel, Ph.D.

NR5 Neuropathology in Schizophrenia: An MRI Study
Laura Marsh, M.D., Godfrey D. Pearlson, M.D., Stephanie Richards, B.A., Patrick E. Barta, M.D.

NR6 Eye Tracking, CPT and Schizotypal Traits in Relatives of Schizophrenics
Richard Keefe, Ph.D., Jeremy M. Silverman, Ph.D., Jackie Moskowitz, Ph.D., Philip D. Harvey, Ph.D., Lee Friedman, Ph.D., Larry J. Siever, M.D.

NR7 An Eight-Year Follow-up of DSM-III-R Major Psychoses
Debby W. Tsuang, M.D., William H. Coryell, M.D.

NR8 Clinical Study of Kraepelinian Schizophrenia
Ede Frecska, M.D., Richard Keefe, Ph.D., Seth Apter, M.A., Michael Davidson, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

NR9 Family History of Kraepelinian Schizophrenia
Jeremy M. Silverman, Ph.D., Ede Frecska, M.D., Richard Keefe, Ph.D., Michael Davidson, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

NR10 Identifying the Schizophrenia Related Phenotype
Jeremy M. Silverman, Ph.D., Larry J. Siever, M.D., Lynn Pinkham, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

NR11 Effects of Monoaminergic Agents in Schizophrenia
David G. Daniel, M.D., Nancy Breslin, M.D., James A. Clardy, A. Abi-Dargham, J. Linnoila, M.D., Daniel R. Weinberger, M.D.

NR12 Selegiline in the Treatment of Akathisia
William C. Wirshing, M.D., Donna Ames, M.D., Theodore Van Putten, M.D., Stephen R. Marder, M.D., George Bartzokis, M.D., Jeffrey L. Cummings, M.D.

NR13 Fluoxetine and Suicidality: A Consequence of Akathisia
William C. Wirshing, M.D., James Rosenberg, M.D., Theodore Van Putten, M.D., Stephen R. Marder, M.D.

NR14 Multidimensional Analysis of CSF Amines in Schizophrenia
Fuad Issa, M.D., Darrell G. Kirch, M.D., Greg A. Gerhardt, Ph.D., Richard L. Suddath, M.D., Robert Freedman, M.D., Richard Jed Wyatt, M.D.

NR15 Psychomotor/Psychosensory Symptoms in Psychiatric Patients
Nutan Atre-Vaidya, M.D., V. Chowdary Jampala, M.D., Chandra Vedak, M.D., Rukhsana Khan, M.D., Michael Alan Taylor, M.D.

NR16 Serotonin Dysfunction in Schizophrenia
Naveed Iqbal, M.D., Gregory Asnis, M.D., Scott Wetzler, Ph.D., R. S. Kahn, M.D., B. J. Schwartz, M.D., Herman M. van Praag, M.D.

NR17 Cardiolipin Antibodies in Schizophrenic Patients
Kadiamada N.R. Chengappa, M.D., A. Bettes Carpenter, Ph.D., Z.W. Yang, Ph.D., R.H. Kelly, Ph.D., B.S. Rabin, M.D., R. Ganguli, M.D.

NR18 Congenital Brain Anomalies in Psychosis Versus Controls
George J. Jurjus, M.D., Henry A. Nasrallah, M.D., Martha A. Brogan, M.D., Stephen C. Olson, M.D., Steve B. Schwarzkopf, M.D.

NR19 The Scale of Questions and Investigations of Restless Movements: A Scale for the Treatment of Akathisia
John Lauriello, M.D., Peter Weiden, M.D., Andrew Leon, Ph.D.

NR20 Assessment of Prosodic Deficits in Schizophrenia
Barbara G. Haskins, M.D., Michael S. Shutty, Jr., Ph.D.

NR21 Third Ventricle and P300 Findings in Schizophrenia
Louis W. Kraft, B.S., Steve B. Schwarzkopf, M.D., Michael W. Torello, Ph.D., Stephen C. Olson, M.D., Henry A. Nasrallah, M.D.

NR22 Subsequent Treatment in Dysthymia Unresponsive to TCA
Nina L. Miller, B.A., James H. Kocsis, M.D.

NR23 Autoantibodies to DNA in Multicase Families with Schizophrenia
Pinkhas Sirota, M.D., Klara Schild, M.D., Michael Firer, Ph.D., Amir Tanay, M.D., Elizur Avner, M.D., Dina Meytes, M.D.

NR24 Negative Symptoms and Dyskinesia in Schizophrenia
Elzbieta Wirkowski, M.D., Ravinder Reddy, M.D., Paolo Decina, M.D., David B. Schnur, M.D., Sukdeb Mukherjee, M.D.

NR25 Regional Brain Density: Schizophrenics Versus Controls
Charles L. Bowden, M.D., James L. Maas, M.D., Ermias Seleshi, M.D., Linda Funderburg, M.D., Salvador Contreas, M.D.

NR26 Expressed Emotion in Nonfamilial Relationships
Robert K. Heinssen, Ph.D., Steven B. Israel, M.D., Maureen E. Laferty, B.A., Wayne S. Fenton, M.D.

NR27 MRI Study of Caudate Nucleus in Major Depression
Patricio R. Escalona, M.D., William M. MacDonald, M.D., P. Murali Doraiswamy, M.D., Mustafa M. Hussain, M.D., Charles B. Nemeroff, M.D., K. Ranga Krishnan, M.D.

NR28 Dopamine Competes for 123 I-IBZM Binding In Vivo
Robert T. Malison, M.D., Mohammed Al-Tikriti, Ph.D., Elzbieta Sybirska, Ph.D., Sami S. Zoghbi, M.D., Ronald M. Baldwin, Ph.D., John Ellsworth, Ph.D., Robert H. Roth, Ph.D., Dennis S. Charney, M.D., George R. Heninger, M.D., Robert B. Innis, M.D., Paul B. Hoffer, M.D.

NR29 Quantitative Morphology of the Basal Ganglia
Jay N. Giedd, M.D., C. Edward Coffey, M.D., Ioanis Parashos, M.D., William Wilkenson, Ph.D.

NR30 Brain Imaging in Geropsychiatric Inpatients
Aseem Rawal, M.D., P. Murali Doraiswamy, M.D., William M. McDonald, M.D., Charles B. Nemeroff, M.D., K. Ranga Krishnan, M.D.

NR31 PET Studies of Brain Activation in Alzheimer's Disease
Susan R. Wisebrod, M.D., Howard Chertkow, M.D., Edith Hamel, Ph.D., Ernst Meyer, Ph.D., Albert Gjedde, M.D., Serge Gauthier, M.D.

NR32 Increased Sylvan Fissure Size in Schizophrenia
Joseph M. Schwartz, M.D., Elizabeth Aylward, Ph.D., Patrick E. Barta, M.D., Godfrey D. Pearlson, M.B.

NR33 D2 Receptor Activity in Tourette's Syndrome
Mark S. George, M.D., Mary M. Robertson, M.B., Durval C. Costa, M.D., Peter J. Ell, M.D.

NR34 HMPAO SPECT Scans of Comorbid OCD and Tourette's Syndrome Patients
Mark S. George, M.D., Mary M. Robertson, M.B., Durval C. Costa, M.D., Michael R. Trimble, M.B., Peter J. Ell, M.D.

NR35 A Demonstration of Parietal Lobe Activation with SPECT
Howard A. Ring, M.B., Mark S. George, M.D., Durval C. Costa, M.D., Kypros Kouris, Ph.D., Peter J. Ell, M.D.

NR36 Does Tardive Dyskinesia Cause Dysphagia?
Chandragupta S. Vedak, M.D., Kathy Yedor, M.A., Rukhsana Khan, M.D., Caryn Conlon, M.A., V. Chowdary Jampala, M.D.

NR37 Treatment of Tardive Dyskinesia with Vitamin E
Michael T. Egan, M.D., Thomas Hyde, M.D., Greg Albers, M.D., Ahmed Elkashef, M.D., Robert C. Alexander, M.D., Richard Jed Wyatt, M.D.

NR38 Early Antipsychotic Effect of Neuroleptics in Patients with Chronic Schizophrenia
Robert G. Stern, M.D., Rene S. Kahn, M.D., Michael Davidson, M.D., P.D. Harvey, Ph.D., R.T. McQueeney, M.D., Faroog Amin, M.D., K. Dumont, B.A., S. Apter, M.A., K.L. Davis, M.D.

NR39 Measuring Centrally Produced HVA in Plasma in Humans
Faroog Amin, M.D., Michael Davidson, M.D., Robert Stern, M.D., Rene S. Kahn, M.D., James Schmeidler, Ph.D., Peter Knott, Ph.D., Seth Apter, M.A., Kenneth L. Davis, M.D.

NR40 Perceived Criticism in Late Luteal Phase Dysphoric Disorder
Kimberly A. Yonkers, M.D., Jill Hooley, Ph.D., Paul Cneo, B.A., Annie Penn, B.S., Amy Vitale, B.A.

NR41 History and Biology Predict Late Luteal Phase Dysphoric Disorder Subtypes
Candace S. Brown, Pharm.D., Frank W. Ling, M.D., Carolyn M. Chesney, M.D., Richard G. Farmer, M.D.

NR42 The Cross-Cultural Examination of Women Utilizing the Premenstrual Assessment Form
Judith Marks, M.A., Ana Lucrecia Ramirez Restrepo, M.D., Javier Escobar, M.D., Catherine Hair, M.D., Susan Caruso-Klock, Ph.D.

NR43 Depressive Symptoms in Bereaved Children and Parents
Julie A. Guthrie, M.D., Ronald A. Weller, M.D., Mary A. Fristad, Ph.D., Elizabeth B. Weller, M.D.

NR44 Platelet Phospholipids: A New Tool to Study Mania
Alan S. Brown, M.D., Alan G. Mallinger, M.D.

NR45 The Diagnosis of Mania by Self-Report
Douglas B. Marlowe, M.A., Scott Wetzler, Ph.D.

NR46 Type of Psychotic Features and Outcome in Mania
Mauricio Tohen, M.D., Ming Tsuang, M.D.

NR47 Depression in Dementia Clinic Outpatients
William E. Reichman, M.D., Andrew C. Coyne, Ph.D., Hilary T. Hanchuk, M.D.

NR48 Depression in a Geriatric Medical Clinic
Linda C. Barr, M.D., James H. Kocsis, M.D.

NR49 Pregnancy Resolution and Depression in Adolescent and Young Women
John D. Mesaros, M.D., David B. Larson, M.D., John S. Lyons, Ph.D.

NR50 Onset Age Within Families with Bipolar I Disorder
Francis J. McMahon, M.D., Sylvia G. Simpson, M.D., O. Colin Stine, Ph.D., Deborah A. Meyers, Ph.D., J. Raymond DePaulo, M.D.

NR51 Hypersomnia in Bipolar Depression
Eric A. Nofzinger, M.D., M.E. Thase, M.D., C.F. Reynolds, III, M.D., J.M. Himmelhoch, M.D., A. Mallinger, M.D., D.J. Kupfer, M.D.

NR52 Risk of Discontinuation of Lithium in Bipolar Disorder
Trisha Suppes, M.D., Mauricio Tohen, M.D., Gianni Faedda, M.D., Ross J. Baldessarini, M.D.

NR53 Comorbidity in Bipolar Disorder at First Episode
Stephen M. Strakowski, M.D., Mauricio Tohen, M.D., Shelly F. Greenfield, M.D., Gianni L. Faedda, MD.

NR54 Erythrocyte Choline In Bipolar Disorder
Andrew Stoll, M.D., Bruce Cohen, M.D., Marjorie Snyder, M.D., Israel Hanin, Ph.D.

NR55 Sequence of Episodes Predicts Response to Lithium in Bipolar Disorders
Gianni L. Faedda, M.D., Ross J. Baldessarini, M.D., Mauricio Tohen, M.D., Stephen M. Strakowski, M.D., Christine Waternaux, Ph.D.

NR56 Outcome After Lithium Discontinuation in Mood Disorders: A Prospective Study
Gianni L. Faedda, M.D., L. Tondo, M.D., M. Tohen, M.D., G.F. Floris, M.D., R.J. Baldessarini, M.D.

NR57 ECT in Depressed Patients with Neurological Disease
Alexander S. Zwil, M.D., Thomas W. McAllister, M.D., Trevor R.P. Price, M.D.

NR58 Natural Killer Cells, Gender and Depression
John M. Petitto, M.D., James D. Folds, Ph.D., Howard Ozer, M.D., Susan G. Silva, M.S., Carol Murphy, R.N., Dwight L. Evans, M.D.

NR59 Altered Natural Killer Cells Diurnal Variation in Depression
John M. Petitto, M.D., James D. Folds, Ph.D., Howard Ozer, M.D., Dwight L. Evans, M.D.

NR60 Expression of G Protein-Coupled Receptors in Depressed Patients
Donatella Marazziti, M.D., Daniela Marazziti, Dr. Bio., Giovanni B. Cassano, M.D.

NR61 Distribution of Alexithymia in Depressive Subtypes
Larry V. Amsel, M.D., Mark J. Russ, M.D., Richard Hahn, M.D.

NR62 Stigma and the Use of Alternative Codes for Major Depression in the Primary Care Setting
Kathryn M. Rost, Ph.D., G. Richard Smith, M.D.

NR63 The Validation of an Outcomes Management System for the Treatment of Depressive Disorders
Kathryn M. Rost, Ph.D., G. Richard Smith, M.D.

NR64 DST Findings in Major Depression with Early Trauma
Kristin L. Lengowski, M.D., Mark H.N. Corrigan, M.D., Gregory M. Gillette, M.D., George A. Mason, Ph.D., J.C. Garbutt, M.D.

NR65 Fluoxetine Reduce CSF 5-HIAA and MHPG in Depression
Michael D. De Bellis, M.D., Thomas Geracioti, Jr., M.D., Margaret Altemus, M.D., Mark A. Demitrack, M.D., Philip W. Gold, M.D., Mitchel A. Kling, M.D.

NR66 Risk and Benefit Analysis of REM Latency in Depression
Douglas Mossman, M.D., Eugene C. Somoza, M.D.

NR67 Protein Phosphorylation in the Rat Anterior Pituitary
James C. Pryor, M.D., Fridolin Sulser, M.D.

NR68 Neuroimmunomodulation of Natural Killer Cells by Steroids
Irene E. Ortiz, M.D., Arthur D. Bankhurst, M.D., Raul N. Mandler, M.D.

NR69 Valproate and Lithium in Mania: A Chart Review
Abigail M. Stanton, M.D., Robert H. Gerner, M.D.

NR70 Growth Hormone Dynamics Following GHRH Challenge
Cheng-Jen Chen, M.D., Peter E. Stokes, M.D., Carolyn R. Sikes, Ph.D., Sobhan Mathew, M.D.

NR71 Disturbed Neuroendocrine Regulation in Depression
Robert L. Trestman, M.D., Martin Teicher, M.D., Emil F. Coccaro, M.D., David Harper, B.S., Theresa Mahon, S.A., Vivian Mitropoulou, M.A., Larry J. Siever, M.D.

NR72 Ultradian Cycles in Depression
Donald Hall, M.D., Helen Sing, M.S., Alan Romanoski, M.D.

NR73 Effect of Anticholinergics on Mood
William M. Kenny, M.D., John Lauriello, M.D., J. Christian Gillin, M.D.

NR74 Hypothalamic-Pituitary-Adrenal Dysfunction and Family Subtypes of Depression
Adrienne C. Lahti, M.D., Roger T. Haskett, M.D., Virginia Murphy-Weinberg, R.N., Elizabeth A. Young, M.D., Stanley J. Watson, M.D., Huda Akil, Ph.D.

NR75 Hypothesis to Explain the Nature of Responsiveness to Tricyclic Antidepressant Drugs
Atul Luthra, M.D.

NR76 Buprenorphine In Refractory Depression
Gwen L. Zornberg, M.D., J. Alexander Bodkin, M.D., Jonathan 0. Cole, M.D.

NR77 Depression Versus PTSD: Diagnosing via Neural Networks
Ibrahim Gunay, M.D., Eugene C. Somoza, M.D.

NR78 Levoprotiline Versus Amitriptyline in Depression
Raed R. Tamimi, M.D., Matig R. Mavissakalian, M.D.

NR79 Cyproheptadine in Major Depression
Enrico G. Camara, M.D.

NR80 Vitamin E in the Treatment of Tardive Dyskinesia
Christian L. Shriqui, M.D., Jacques Bradwejn, M.D., Barry D. Jones, M.D., Lawrence Annable, D.S.

NR81 A Test of Hopelessness in Depression and Suicide
Kim A. Heithoff, M.P.H.

NR82 Oculomotor Function in OCD
Allen Y. Tien, M.D., Steve Machlin, M.D., Godfrey D. Pearlson, M.B., Fred Bylsma, Ph.D.

NR83 Community Age/Gender Incidence of Hallucinations
Allen Y. Tien, M.D.

NR84 Mood Symptoms of Professional Cheerleaders
Joseph Henry, M.D., Paul Goodnick, M.D.

NR85 Tricyclic Antidepressant-Induced Seizures
Gary A. Fast, M.D., Sheldon H. Preskorn, M.D.

NR86 Antidepressant Effects on Melatonin Elimination
Helen L. Miller, M.D., Robert N. Golden, M.D., R. Bruce Lydiard, M.D., George Mason, Ph.D., David Ekstrom, M.P.H.

NR87 Benzodiazepines and Human Vision
Thomas E. Schlaepfer, M.D., Hans-U. Fisch, M.D.

NR88 Alprazolam Versus Behavioral Treatment Post-Rape
Kathleen A. Hughes, M.D., Dean G. Kilpatrick, Ph.D., James C. Ballenger, M.D., Heidi S. Resnick, Ph.D., Connie L. Best, M.D., Michelle Laraia, R.N.

NR89 Somatization and Conversion Disorders: A Comparison
Kristinn Tomasson, M.D., David A. Kent, M.D., William H. Coryell, M.D.

NR90 Body Dysmorphic Disorder: A Report of 20 Cases
Katharine A. Phillips, M.D., Susan L. Mc Elroy, M.D., Paul E. Keck, Jr., M.D., Harrison G. Pope, Jr., M.D., James I. Hudson, M.D.

NR91 A Comparison of Doxepin, Trazodone and Biofeedback Therapy in the Adjunctive Treatment of Chronic Back Pain
Edward A. Workman, M.D., Delmar D. Short, M.D., Frank F. Tellian, M.D.

NR92 Amitriptyline Myocardial Toxicity
Claudi Udina, M.D., Manuel Ballester, M.D., Ignasi Carrio, M.D., Vicens Marti, M.D.

NR93 Primate Behavioral Response to Lactate and Yohimbine
Jeremy D. Coplan, M.D., Leonard A. Rosenblum, Ph.D., Steven Friedman, Ph.D., Trina B. Bassoff, M.A., Jack M. Gorman, M.D.

NR94 Renal Side Effects of Long-Term Lithium Treatment
Hakan Coskunol, M.D., Simavi Vahip, M.D., Evert J.D. Mees, M.D., Ali Basci, M.D., Oya Bayindir, M.D., Isik Tuglular, M.D., Refet Saygili, M.D.

NR95 Dermatological Side Effects of Lithium
Isil Vahip, Tevhide Dincer, M.D., Simavi Vahip, M.D., Gunseli Ozturk, M.D., Isik Tuglular, M.D., Refet Saygili, M.D., Atilla Varol, M.D.

NR96 Subjective Versus Objective Memory Measures In ECT
Iannis Zervas, M.D., Max Fink, M.D., Lina Jandorf, M.A.

NR97 The Effect of ECT on EEG Coherence
Andrew D. Krystal, M.D., Richard D. Weiner, M.D., C. Edward Coffey, M.D., Pamela Smith, Rebekka Arias

NR98 Coding Interpersonal Processes in Family Therapy
Carol Tingle, M.D., Mark McLain, M.D., Dinesh Mittal, M.D., Nancy Krejmas, M.D., Jeanetta Rains, Ph.D., James L. Griffith, M.D., Melissa E. Griffith, M.S.N.

NR99 Personal Therapy for Psychiatry Residents
Anne I. Koplin, M.D., Mary Gutmann, Ph.D.

NR100 A Basic Computer Curriculum for Psychiatry
T. Bradley Tanner, M.D., Stuart Gitlow, M.D., Michael D. Rancurello, M.D.

NR101 Personality Ratings Predict Criminal Recidivism
Julie A. Tinklenberg, M.S., Jared R. Tinklenberg, M.D., Norman I. Dishotsky, M.D., Kristen Levitan, M.D., Hans Steiner, M.D.

NR102 Sex and Racial Bias on the Covers of the Journal of Hospital & Community Psychiatry
Gene A. Nakajima, M.D., Howard C. Rubin, M.D., Kewchang Lee, A.B.

NR103 Diagnosis in the Psychiatric Literature: 1948-1988
R. Andrew Schultz-Ross, M.D.

NEW RESEARCH

Monday, May 13, 1991, 3:00 p.m.-5:00 p.m.

New Research 2—Poster Session—Ballroom A, Level 1, Convention Center

YOUNG INVESTIGATORS' POSTER SESSION

Moderator: Susan J. Fiester, M.D.

NR104 HMPAO SPECT Abnormalities In Infantile Autism
Mark S. George, M.D., Durval C. Costa, M.D., Kypros Kouris, Ph.D., Howard A. Ring, M.B., Michael R. Trimble, M.B., Peter J. Ell, M.D.

NR105 Sexual Behavior Problems in Sexually Abused Girls
Glare E. Cosentino, Ph.D., Dr. Heino F.L. Meyer-Bahlburg, Richard Gaines, Ph.D.

NR106 The Increase of Multiple Television Sets and Rise in Youth Suicide
Michelle Sredy, Paul Kettl, M.D., Edward O. Bixler, Ph.D.

NR107 The Invisible Children: Are They Still Invisible?
James A. Van Haren, M.D.

NR108 Pictorial Instrument for Child Psychopathology
Monique Ernst, M.D., Raul R. Silva, M.D., Katherine A. Godfrey, M.D., Maria Solomou, Murray Alpert, Ph.D

NR109 Validity of Fluorescent Polarization Immunoassay of Plasma Cortisol for Use in the DST in Prepubertal Children
Shahnour Yaylayan, M.D., Elizabeth B. Weller, M.D., Ronald A. Weller, M.D., Mary A. Fristad, Ph.D.

NR110 Correlates of Violence Risk in Hospitalized Adolescents
Sophia Eldar, M.D., Graciela Finkelstein, M.D., Deborah Lipschitz, M.D., Daniel Grosz, M.D., Robert Plutchik, Ph.D.

NR111 Child Psychiatry Consultation in the Emergency Room: Presenting Problems and Disposition
Keith Cheng, M.D., William Gabriel, M.D., Terri Lee, M.D., Michel Mennesson, M.D., Melvin Lewis, M.D.

NR112 Rural Children's Reactions to Hurricane Hugo
Mitsuko Shannon, M.D., A.J. Finch, Ph.D., Charlotte Taylor, M.Ed., Pam Imm, M.A., F.R. Sallee, M.D.

NR113 Siblings in Foster Care: Factors Affecting Outcome
Marilyn B. Thorpe, M.D., GT Swart, M.D.

NR114 Predictive Value of 24-Hour LiCo3 Levels in Children
Rameshwari V. Tumuluru, M.D., Ronald A Weller, M.D., Mary A. Fristad, Ph.D., Elizabeth B. Weller, M.D.

NR115 Psychiatric Comorbidity in Communication Disorders
Charlotte A. Hobbs, M.Sc., I.B. Pless, M.D.

NR116 Classroom Academic Performance of ADHD Boys Improved by Stimulants
Josephine Elia, M.D., Patricia Welsh, M.Ed., Charles Gulotta, B.A., Judith H.L. Rapoport, M.D.

NR117 A Two-Year Prospective Follow-Up of Predictive Value of CSF 5-HIAA and Autonomic Measures in Children and Adolescents with Disruptive Behavior Disorders
Markus Kruesi, M.D., Euthymia D. Hibbs, Ph.D., Theodore Zahn, Ph.D., Judith H.L. Rapaport, M.D.

NR118 Difference in Caloric Utilization in Eating Disorder Adolescents
Afsaneh Nasserbakht, M.A., Sigrid Inthealer, M.D., Grace H. Shih, R.D., Hans Steiner, M.D.

NR119 Regional Cerebral Glucose Metabolism in Bulimia
Paul J. Andreason, M.D., Margaret Altemus, M.D., Alan Zametkin, M.D., Anna C. King, Julio Licinio, M.D., Robert M. Cohen, M.D.

NR120 Seasonal Subgroups In Bulimia Nervosa
Robert D. Levitan, M.D., Allan S. Kaplan, M.D., Russell T. Joffe, M.D., Anthony J. Levitt, M.D.

NR121 Impulsivity in Bulimia: A Serotonin Connection?
Barbara E. Walton, M.S.N., David C. Jimerson, M.D., Michael D. Lesem, M.D., Debra Franko, Ph.D., Jeffrey M. Levine, M.D., Nicholas A. Covino, Psy.D.

NR122 Two-Year Follow-Up of Family Function in Bulimia
D. Blake Woodside, M.D., Lorie Shekter Wolfson, M.S.W., Allan Kaplan, M.D., Marion Olmsted, Ph.D., Margus Heinmaa, B.S.

NR123 Promoting Condom Use Among College Students
Daniel P. Chapman, Ph.D.

NR124 Subtle, Early Cognitive Impairment in HIV Disease
Susan E. McManis, M.D., George R. Brown, M.D., James R. Rundell, M.D., Robert Zachary, Ph.D., Sarah Kendall, B.A.

NR125 Cognitive Impairment and CSF Values in HIV Disease
Susan E. McManis, M.D., George R. Brown, M.D., James R. Rundell, M.D., Robert Zachary, Ph.D.

NR126 Cognitive Impairment and Gender in HIV Positive Persons
Susan E. McManis, M.D., George R. Brown, M.D., Robert Zachary, Ph.D., Sarah Kendall, B.A., James R. Rundell, M.D.

NR127 Prospective Study of HIV-Associated Psychosis
Daniel D. Sewell, M.D., Dilip V. Jeste, M.D., J. Hampton Atkinson, M.D., James Chandler, M.D., Igor Grant, M.D., The HNRC Group

NR128 Mood and Neuropsychological Interactions in HIV
Robert A. Stern, Ph.D., Diana O. Perkins, M.D., Naomi G. Singer, B.A., Susan G. Silva, M.A., Dwight L. Evans, M.D.

NR129 SPECT Regional Cerebral Blood Flow in HIV Disease
Christopher H. van Dyck, M.D., Scott W. Woods, M.D., Stephanie O'Malley, Ph.D., Lawrence H. Price, M.D., Christopher J. McDougle, M.D., Thomas R. Kosten, M.D.

NR130 Early HIV Infection and Health Locus of Control
Irvin P. Brock III, M.D., George R. Brown, M.D., Richard Jenkins, Ph.D., James R. Rundell, M.D.

NR131 Affect and Health Locus of Control in HIV Disease
Irvin P. Brock III, M.D., George R. Brown, M.D., Richard Jenkins, Ph.D., James R. Rundell, M.D.

NR132 Primary Versus Secondary Depression in HIV
Snezana Cvejin, M.D., Diana O. Perkins, M.D., Carol Murphy, R.N., Bettina Knight, R.N., Dwight L. Evans, M.D.

NR133 Therapeutic Alliance and Distress After HIV Testing
Cheryl Card, M.A., Samuel Perry, M.D., Baruch Fishman, Ph.D., Robert Russell, Ph.D., Donald Rock, Ph.D.

NR134 Bereavement and Unresolved Grief in Seropositive Men and Men at High Risk for HIV
Jacquelyn Summers, M.S.W., Sidney Zisook, M.D., J.H. Atkinson, M.D., Tom Patterson, Ph.D., J. Chandler, M.D., J. Malone, M.D.

NR135 Suicide Attempts and AIDS Among Drug Addicts in Vienna, Austria
Peter Hofmann, M.D., Norbert Loimer, M.D., Elisabeth Werner, M.D.

NR136 Sexual Functioning in HIV Positive Women Without AIDS
Edwig K. Plotnick, M.D., George R. Brown, M.D.

NR137 Comparison of DSM-III-R and RDC Diagnostic Systems
Elizabeth Davidson, M.D., Diana O. Perkins, M.D., Carol Murphy, R.N., Bettina Knight, R.N., Duanping Liao, M.D., Dwight L. Evans, M.D.

NR138 A New DSM-III-R Based Questionnaire: The Behavior Emotions Questionnaire
Diana O. Perkins, M.D., Snezana Cvejn, M.D., Elizabeth Davidson, M.D., Carol Murphy, R.N., Lenn Murrelle, B.A., Dwight L. Evans, M.D.

NR139 Undetected Alcohol-Related Burn Trauma
Lawson F. Bernstein, M.D., Lawrence Jacobsberg, M.D., Theresa Ashman, M.A., Gloria Musagui, R.N., Cleon Goodwin, M.D., Samuel Perry, M.D.

NR140 Adolescent Alcohol Use and Psychological Symptoms
John F. Aruffo, M.D., John B. Jolly, Psy.D.

NR141 A Family Study: Bulimia Nervosa and Alcoholism
Barbara A. Johnson, M.D., Walter H. Kaye, M.D., Cynthia Bulik, Ph.D., Theodore Weltzin, M.D., L.K. George Hsu, M.D.

NR142 Alcohol and Sedative Use in Panic and OCD Patients
Joan R. Birnberg, B.A., Roger Cambor, M.D., Laura Portera, B.A., Andrew C. Leon, Ph.D., Robert B. Millman, M.D., M. Katherine Shear, M.D.

NR143 Phenomenology of Comorbid Anxiety and Alcoholism
Ihsan M. Salloum, M.D., Juan E. Mezzich, M.D., Joe Plial, M.A.

NR144 Aggression and Immunity in Inner-City Alcoholics
Angela Lignelli, B.S., Steven J. Schleifer, M.D., Steven E. Keller, Ph.D.

NR145 The North Carolina Family Study on the Genetics of Alcoholism
Lenn Murrelle, B.A., Diana O. Perkins, M.D., Jane Doody, M.S., David S. Janowsky, M.D.

NR146 Cocaine Withdrawal Locomotion and Mood State
Huan-Kwang Ferng, M.D., Martin P. Szuba, M.D., Lewis R. Baxter, M.D.

NR147 Time Limited Cocaine Treatment: Program Evaluation
Lisa Newell, Douglas Ziedonis, M.D.

NR148 Neuropsychiatric Effects of Anabolic Steroids
Tung-Ping T. Su, M.D., David R. Rubinow, M.D., Michael Pagliaro, R.N., Christine Ollo, Ph.D., David Pickar, M.D., Owen Wolkowitz, M.D.

NR149 Characterization of Buprenorphine Withdrawal
Haydn M. Thomas, M.D., Marc I. Rosen, M.D., Martin E. Waugh, D.O., Herbert R. Pearsall, M.D., Scott W. Woods, M.D., Thomas R. Kosten, M.D.

NR150 Substance Abuse in Chronic Schizophrenia
John R. DeQuardo, M.D., Christopher Carpenter, B.S.E., Rajiv Tandon, M.D.

NR151 A Controlled Study of Adolescent Gasoline Huffers
Dorothy Grice, M.D., Ann L. Taylor, M.D., Robert Malcolm, M.D.

NR152 Evaluation of Salivary Concentrations of Methadone for Monitoring Drug Therapy
Norbert Loimer, M.D., Rainer Schmid, Ph.D., Christian Wolf

NR153 Defining Substance Use in a Mentally Ill Population
Lisa Dixon, M.D., Erica Dibietz, L.C.S.W., Robert Conley, M.D., Timothy W. Santoni, M.A, Deborah Medoff, Ph.D.

NR154 Behavioral Syndrome of Alzheimer's Disease
Daniel S. Javier, M.D., Barry Reisberg, M.D., Steve Sclan, Ph.D., Emile Franssen, M.D., Carol Torossian, Ph.D., Steve Ferris, Ph.D.

NR155 Environments and Assessed Quality of Life
Jill S. Meyer, M.D., Robert L. Schalock, Ph.D.

NR156 Early Versus Late Dementia: Patient and Caregiver Issues
Hilary T. Hanchuk, M.D., Andrew C. Coyne, Ph.D., William E. Reichman, M.D.

NR157 Effect of Age on Psychiatric Patient Requests
Eve J. Wiseman, M.D., Gary W. Small, M.D.

NR158 Age-Related Effects of Lithium on the Phosphoinositide System
Krishna Dasgupta, M.D., Molly H. Weiler, Ph.D.

NR159 The Rate of Progression in Alzheimer's Dementia
Robert G. Stern, M.D., Richard C. Mohs, Ph.D., Michael Davidson, M.D., Terena Searcey, B.A., Kelly Ware, James Schmeidler, Ph.D., Kenneth L. Davis, M.D.

NR160 Cortisol Response to CRF in Alzheimer's Disease
Peter M. Aupperle, M.D., Brian A. Lawlor, M.D., Richard C. Mohs, Ph.D., Gabriel Tsubuyama, M.D., Bonnie M. Davis, M.D., Steven Gabriel, Ph.D., Michael Davidson, M.D., Kenneth L. Davis, M.D.

NR161 Risk Factors for Alzheimer's Disease: A Case Control Study from China
Ge Li, M.D., Yu-Cun Shen, M.D., Cuang-Hui Chen, M.D., Yong-Tong Li, M.D.

NR162 Medial Temporal Lobe Size P300 and Subjects At-Risk for Alzheimer's Disease
Bradley S. Jacobs, B.S., Michael Torello, Ph.D., Robert Bornstein, Ph.D., Elizabeth Burns, Ph.D., Henry A. Nasrallah, M.D.

NR163 CSF HVA in Schizotypal and Other Personality Disorders
Farooq Amin, M.D., Emil F. Coccaro, M.D., Robert L. Trestman, M.D., Peter Knott, Ph.D., Theresa Mahon, B.A., Michael Davidson, M.D., Kenneth L. Davis, M.D., Larry J. Siever, M.D.

NR164 A Test of the Tridimensional Personality Theory
Robert G. Ruegg, M.D., John Gilmore, M.D., Mark Corrigan, M.D., David Ekstrom, M.P.H., Bettina Knight, R.N., Robert N. Golden, M.D.

NR165 Enlarged Ventricle to Brain Ratio in Schizotypal Personality Disorder
Merrill Rotter, M.D., Oren Kalus, M.D., Miklos Losonczy, M.D., Ling Guo, M.D., Robert Trestman, M.D., Emil F. Coccaro, M.D., Michael Davidson, M.D., Ken Davis, M.D., Larry J. Siever, M.D.

NR166 Traumatic Brain Injury in Patients with BPD
Chris A. Conway, Robert Van Reekum, M.D., David Bachman, M.D.

NR167 Impulsivity and 5HT in Personality Disorders
Robert L. Trestman, M.D., Timothy L. Lawrence, M.D., Emil F. Coccaro, M.D., Vivian Mitropoulou, M.A., Susan Weston, M.D., James Weisberg, M.S., Steven Gabriel, Ph.D., Larry J. Siever, M.D.

NR168 Noradrenergic Activity in Impulsivity/Aggression
Timothy Lawrence, M.D., Emil F. Coccaro, M.D., Robert Trestman, M.D., David Bernstein, Ph.D., Vivian Mitropoulou, M.A., Larry J. Siever, M.D.

NR169 Assessing Axis II Disorders by Informant Interview
David P. Bernstein, Ph.D., Chrysoula Kasapis, M.A., Thomas B. Horvath, M.D., Howard Klar, M.D., James Schmeidler, Ph.D., Larry J. Siever, M.D.

NR170 Event Related Potentials in Schizotypal Personality Disorder
Oren Kalus, M.D., Thomas B. Horvath, M.D., Ann Peterson, M.A., Emil F. Coccaro, M.D., Vivian Mitropoulou, M.A., Michael Davidson, M.D., Kenneth L. Davis, M.D., Larry J. Siever, M.D.

NR171 Generalized Anxiety Disorder: Long-Term Outcome
Mark H. Townsend, M.D., Donna M. Mancuso, M.D., James G. Barbee, M.D., Donald E. Mercante, Ph.D.

NR172 Classification of Anxiety Disorders: The Controversy
Michael Bach, M.D., Detlev O. Nutzinger, M.D., Martina de Zwaan, M.D.

NR173 Serotonin Function in Generalized Anxiety Disorder
Mark Germine, M.D., Andrew W. Goddard, M.D., George R. Heninger, M.D., Dennis S. Charney, M.D., Scott W. Woods, M.D.

NR174 CSF Diazepam-Binding Inhibitor Concentrations in Panic Patients
Richard Payeur, M.D., R. Bruce Lydiard, M.D., James C. Ballenger, M.D., Michele T. Laraia, M.S.N., Mark D. Fossey, M.D., Joseph Zealberg, M.D.

NR175 Long-Term Fate of Specific Agoraphobic Fears in Panic Disorder
Michaela Amering, M.D., Heinz Katschnig, M.D.

NR176 Immune Function in Panic Disorder with Agoraphobia
John S. McDaniel, M.D., Emile D. Risby, M.D., Rita D. Jewart, Ph.D., Mary B. Eccard, R.N., June Caudle, M.LN., Mark Stipetic, B.S., Donald E. Manning, M.D., Samuel C. Risch, M.D.

NR177 Feeling of Unreality as a Panic Disorder Symptom
James Cancienne, M.S., M. Katherine Shear, M.D., Laura Portera, B.A., Andrew C. Leon, Ph.D., Marylene Cloitre, Ph.D.

NR178 Personality in Early Dropout From Clinical Trials
Dane K. Wingerson, M.D., Peter P. Roy-Byrne, M.D., Mark D. Sullivan, M.D., Deborah Cowley, M.D., Stephen R. Dager, M.D., David L. Dunner, M.D.

NR179 Caffeine in Panic Disorder
William J. Apfeldorf, M.D., Joan R. Birnberg, B.A., Andrew C. Leon, Ph.D., Jack M. Gorman, M.D., M. Katherine Shear, M.D.

NR180 A Comparison of Limited Symptom Episodes and Full-Blown Panic Attacks
Laura Portera, M.A., M. Katherine Shear, M.D., James Cancienne, M.S., Andrew C. Leon, Ph.D., Marylene Cloitre, Ph.D.

NR181 Personality Disorders in Patients with Panic
Naresh P. Emmanuel, M.D., R. Bruce Lydiard, M.D., J. Allen Melvin, M.D., Virginia Villeponteaux, M.D., James C. Ballenger, M.D.

NR182 Familial Relationship Between Panic and PTSD
Linda M. Nagy, M.D., Kathleen R. Merikangas, Ph.D., Steven M. Southwick, M.D., Nancy Docherty, M.A., Elisheva Dan, M.A., Laurie Harkness, Ph.D., Dennis S. Charney, M.D.

NR183 PTSD and Re-Injury Behavior
Cheryl Cottrol, M.D., Jacob Lindenthal, Ph.D.

NR184 Efficacy of Clomipramine in PTSD
Ramanujam Mohan, M.D., Daniel M. Samonsky, M.D., Bruce I. Diamond, Ph.D.

NR185 PTSD and Dissociation in Vietnam Combat Veterans
J. Douglas Bremner, M.D., Steven Southwick, M.D., Elizabeth Brett, Ph.D., Alan Fontana, Ph.D., Robert Rosenheck, M.D., Dennis S. Charney, M.D.

NR186 Dissociation and Trauma in Psychiatric Inpatients
Glenn N. Saxe, M.D., Bessel A. van der Kolk, M.D., Robert Berkowitz, M.D., Gary Chinman, M.D., Kathryn Hall, M.D., Gabriel Leiberg, M.D., Jane Schwartz, M.D.

NR187 Predictors of Psychological Distress after Burn Injury
JoAnn Difede, M.A., Samuel W. Perry, M.D., Lawrence B. Jacobsberg, M.D., Ellen Halpern, M.A.

NR188 An Open Trial of Fluoxetine For Hypochondriasis
Brian A. Fallon, M.D., Michael R. Liebowitz, M.D., Franklin Schneier, M.D., Raphael Campeas, M.D., Ester Salman, B.S., Sharon O. Davies, R.N.

NR189 Are You Benzo or Buspirone Prone?
Christine Reynaert, M.D., Pierre Janne Pascal, Ph.D., Leon Cassiers, M.D., Jean Kinable, Ph.D.

NR190 A Family Study of Obsessive-Compulsive Disorder
Margaret A. Richter, M.D., Richard P. Swinson, M.D., Russell T. Joffe, M.D.

NR191 Personality Disorders in Trichotillomania
Gary A. Christenson, M.D., Elizabeth Chernoff, B.A.

NR192 Treatment of Trichotillomania with Fluoxetine
Gary A. Christenson, M.D., Thomas B. Mackenzie, M.D., James E. Mitchell, M.D., Alan Callies, B.A.

NR193 Effects of Fenfluramine on HVA in OCD and Controls
Dan J. Stein, M.B., Eric Hollander, M.D., Jihad B. Saoud, M.S., Concetta M. Decaria, M.S., Michael Stanley, Ph.D., Michael R. Liebowitz, M.D.

NR194 Obsessional Severity in Tourette's Syndrome
Dan J. Stein, M.B., Ruth Bruun, M.D., Stephen Josephson, Ph.D., Concetta M. Decaria, M.S., Sari Trungold, B.A., Eric Hollander, M.D.

NR195 Nocturnal Penile Tumescence is Diminished in Diabetic Men
Eric A. Nofzinger, M.D., C.F. Reynolds III, M.D., J.R. Jennings, Ph.D., M.E. Thase, M.D., Ellen Frank, Ph.D., D.J. Kupfer, M.D.

NR196 Length of Stay Determinants on an Inpatient Unit
Joseph V. Pace, M.D., George Brown, M.D.

NR197 Repeat Users of Psychiatric Emergency Services
Patrick F. Sullivan, M.D., Steven D. Forman, M.D., Cynthia M. Bulik, Ph.D., Juan E. Mezzich, M.D.

NR198 Psychiatric Morbidity in Liver Transplant Patients
Andrea F. DiMartini, M.D., Kathleen A. Pajer, M.D., John Fung, M.D., Thomas Starzl, M.D., Paula T. Trzepacz, M.D., Ronald Tringali, M.S.M.

NR199 Popular Remedies for a Society's Debilities: Medicines for Neurasthenia in Victorian America
John B. Stea, M.D., William K. Fried, Ph.D.

NR200 A Rehabilitation Program for Chronic Fatigue Syndrome
Andrew John Wilson, M.M., Ian Hickle, M.D., Catherine Hickle, M.B., Andrew Lloyd, M.D., Denis Wakefield, M.D.

NR201 Clinical Correlates of Nonsuicidal Self-Injury
Douglas R. Langbehn, M.D., Bruce Pfohl, M.D.

NR202 Crisis Intervention and Suicide: A Follow-Up Study
Anelise Muhlebach, Ph.D., Antonio Andreoli, M.D., Maryvonne Gognalons, Ph.D., Jeanne Abensur, M.D.

NR203 Aftercare Compliance Among Drug Overdose Patients
Jessica Hellings, M.D., George A.D. Hart, Ph.D., Elizabeth Penick, Ph.D.

NR204 Mental Health Risk Factors In Vietnamese Amerasians
Robert S. McKelvey, M.D., Alice R. Mao, John A. Webb, Ph.D.

NR205 Race and Haloperidol-Induced Side Effects
James C-Y Chou, M.D., Richard Douyon, M.D., Pal Czobor, Ph.D., Jan Volavka, M.D.

NR206 Motor Vehicle Fatalities and Mental Illness
Carole Menard-Buteau, M.D., Richard Boyer, Ph.D., Alain D. Lesage, M.D., Frederic Grundberg, M.D.

NR207 WITHDRAWN

NR208 Psychiatric Disorders in Patients with Epilepsy
M. Caroline Burton, M.D., Teresa A. Rummans, M.D., Max R. Trenerry, Ph.D., Gregory D. Cascino, M.D., Frank W. Sharbrough, M.D., Robert J. Ivnik, Ph.D.

Tuesday, May 14, 1991, 9:00 a.m.-10:30 a.m.

New Research 3—Oral/Slide Session—Room 7, Level 2, Convention Center

CHILD AND ADOLESCENT DISORDERS

Chp.: Joseph T. Coyle, M.D.

NR209 Meiotic Origin of Nondisjunction in Down's Syndrome — 9:00 a.m.
Melvin G. McInnis, M.D., Michael B. Petersen, M.D., Patricia Adalsberger, B.Sc., Stylianos Antonarakis, M.D.

NR210 Nocturnal Endocrine Profiles of Depressed Teens — 9:15 a.m.
Stanley P. Kutcher, Dina Malkin, M.D., Jay Silverberg, M.D., Peter Marton, Ph.D., Peter Williamson, M.D., Aaron Malkin, M.D.

NR211 Locomotor Activity and the Diagnosis of ADHD — 9:30 a.m.
Martin H. Teicher, M.D., Carol A. Glod, M.S., Kambiz Pahlavan, M.D., David Harper, B.S., Eleanor Magnus, B.S., Frances Wren, M.D.

NR212 Family Genetic Risk Factors in ADHD — 9:45 a.m.
Joseph Biederman, M.D., Stephen V. Faraone, Ph.D., Ming T. Tsuang, M.D., Belinda R. Krifcher, B.A., Kate Keenan, B.A.

NR213 Adult Outcome of Childhood Hyperactivity — 10:00 a.m.
Salvatore Mannuzza, Ph.D., Rachel G. Klein, Ph.D., Abrah W. Bessler, B.A.

NR214 Psychopathology in Male Prostitutes: Implications — 10:15 a.m.
Richard R. Pleak, M.D., Heino F.L. Meyer-Bahlburg, Ph.D.

Tuesday, May 14, 1991, 9:00 a.m.-10:30 a.m.

New Research 4—Oral/Slide Session—Room 9, Level 2, Convention Center

ANXIETY DISORDERS

Chp.: Jeffrey A. Lieberman, M.D.

NR215 A Family Study of Social Phobia and Panic Disorder — 9:00 a.m.
Abby J. Fyer, M.D., Salvatore Mannuzza, Ph.D., Tim Chapman, M.S., Michael R. Liebowitz, M.D., Jack M. Gorman, M.D., Donald Klein, M.D.

NR216 A New Primate Model for Panic Disorder — 9:15 a.m.
Frank R. Ervin, M.D., Roberta M. Palmour, Ph.D., Jacques Bradwejn, M.D.

NR217 Comparison of Cholecystokinin-tetrapeptid-4e-4 and Oxygen in Normal Controls — 9:30 a.m.
Diana Kozycki, M.A., Jacques Bradwejn, M.D., Michel Bourin, M.D.

NR218 Cognitive Mediation of Lactate-Induced Panic — 9:45 a.m.
David M. Clark, D.Phil., Michael Gelder, M.D., Paul M. Salkovskis, Ph.D., Pavlos Anastasiades, M.A.

NR219 The Use of Alpidem in Generalized Anxiety Disorder — 10:00 a.m.
Bruce I. Diamond, Ph.D., Emelia O'Neal, M.E.D., Richard L. Borison, M.D., Mark Kaffeman, M.S., Rachel Ochs, M.D.

NR220 Social Phobia: Morbidity in a Community Sample — 10:15 a.m.
Franklin R. Schneier, M.D., Jim Johnson, Ph.D., Christopher Hornig, B.A., Michael R. Liebowitz, M.D., Myrna M. Weissman, Ph.D.

Tuesday, May 14, 1991, 12 noon-2:00 p.m.

New Research 5—Poster Session—Ballroom A, Level 1, Convention Center

CHILDHOOD AND ADOLESCENT, ALCOHOL AND SUBSTANCE ABUSE, PERSONALITY, AND EATING DISORDERS

Moderator: Charles B. Nemeroff, M.D.

NR221 Impact of Support Network on Bereaved Children
Mary A. Fristad, Ph.D., Natalie K. Wolfe, B.A., Elizabeth B. Weller, M.D., Ronald A. Weller, M.D.

NR222 A Positive and Negative Scale for Children and Adolescent: A Study of Criterion Validity and Interrater Reliability
Joel H. Fields, M.D., Stanley R. Kay, Ph.D. (Posthumously), Gail Alexander, M.D., Sandra Grochowski, B.A., Daniel Grosz, M.D., Jean Pierre Lindenmayer, M.D., Gary Pawl, M.D., Amoro Reyes, M.D., Len Leven, M.D.

NR223 Depressive Disorders in Maltreated Children
Joan Kaufman, Ph.D.

NR224 Suicidal Ideation in Children with ADHD
Catherine A. Martin, M.D., Kaye L. McGinty, M.D., Jeanetta F. Smith

NR225 Fluoxetine Treatment of Patients with Autism and Mental Retardation
Edwin H. Cook, M.D., Randall Rowlett, M.D., Catherine Jaselskis, D.O., Bennett L. Leventhal, M.D.

NR226 Fenfluramine Effects on Cerebral Metabolism
Edwin H. Cook, M.D., John Metz, Ph.D., Malcolm Cooper, M.D., Jin Shin Chou, Bennett L. Leventhal, M.D.

NR227 Psychosocial Impact of Pediatric Rheumatic Disease
Sharon Silber, Ph.D., Cathy Pacyna, M.S.W., Lynn Parker, Ph.D., Theresa Constans, M.S.

NR228 Comorbidity and Methylphenidate Response in ADHD
Richard L. Livingston, M.D., Roscoe A. Dykman, M.D., Peggy A. Ackerman, M.A.

NR229 Cost of Child Day Treatment Program Versus Inpatient Treatment Program
Natalie Grizenko, M.D., Danielle Papineau, M.Sc.

NR230 Effectiveness of Family Therapy in Day Treatment
Natalie Grizenko, M.D., Danielle Papineau, M.Sc.

NR231 Effects of Nicotine Haloperidol Versus Nicotine in Tourette's Syndrome
Brian J. McConville, M.D., Harold M. Fogelson, M.D., Paul R. Sanberg, Ph.D., Paul Cirino, B.A., Judy King, B.A., Andrew B. Norman, Ph.D.

NR232 Specific Symptoms and Cognitive Deficit in Tourette's Syndrome
Chris N. Larson, M.D., Robert A. Bornstein, Ph.D.

NR233 Childhood Sexual Abuse and Adult Personality
Bruce Pfohl, M.D., Nancee Blum, M.S.W.

NR234 Cross-Gender Ratings of Boy Outpatients: New Data
Richard R. Pleak, M.D., Glenn S. Hirsch, M.D., Dennis A. Anderson, M.D., David E. Sandberg, Ph.D.

NR235 Neuroleptics and Adolescent Borderline Pathology
Arthur H. Schwartz, M.D., Harriet E. Hollander, Ph.D., George T. Pavlidis, Ph.D., Michael A. Gara, Ph.D.

NR236 Unmet Service Demands in Child Disruptive Behaviors
Christopher R. Thomas, M.D., Rolf Loeber, Ph.D., Magda S-Loeber, Ph.D.

NR237 Fluoxetine in Adolescent Psychiatric Inpatients
Lee S. Cohen, M.D., Gwen Schneider, M.D., A. Lawrence Rubin, M.D., Dipak Nandi, M.D., Dane Bonn, B.S.

NR238 Family History in Adolescent Suicide Attempters
Lee S. Cohen, M.D., Owen Schneider, M.D., A. Lawrence Rubin, M.D., Jane Salvowitz, R.N., Barbara Sprung, R.N.

NR239 Length of Stay on Latency-Ages Psychiatric Units: A Comparative Study
Richard F. Dalton, M.D., Kent M. Ward, M.D.

NR240 Cornell Friendship and Peer Interview
Paulina T. Kernberg, M.D., Audrey J. Clarkin, Ph.D., Edward Greenblatt, Ph.D., Jonathan C. Cohen, Ph.D.

NR241 Conduct Disorder and Personality Characteristics in Hospitalized Adolescents
Wade C. Myers, M.D., Roger C. Burket, M.D., Terry Otto, M.D.

NR242 Low Dopamine Beta Hydroxylase: A Biological Sequela of Abuse and Neglect?
Matthew Galvin, M.D., Anantha Shekhar, M.D., Jay Simon, Ph.D., Barbara Stilwell, M.D., Robert Ten Eyck, Ph.D., Gina Laite, M.D., George Karwisch, M.D., Susanne Blix, M.D.

NR243 Activity and Antidepressant Response in Children
Carol A. Glod, M.S., Martin H. Teicher, M.D., Kambiz Pahlavan, M.D., David Harper, B.S., Eleanor Magnus, B.S., Elyse Duboe, M.D.

NR244 Altered Immunity in Childhood Major Depressive Disorder
Jacqueline Bartlett, M.D., Steven E. Keller, Ph.D., Steven J. Schleifer, M.D.

NR245 Alcohol and Depressive Cognitions in Adolescents
John B. Jolly, Psy.D., John F. Aruffo, M.D., Richard L. Livingston, M.D.

NR246 Cortisol Abnormalities in Sexually Abused Girls
Frank W. Putnam, M.D., Penelope K. Trickett, Ph.D., Karen Helmers, R.N., Elizabeth J. Susman, Ph.D., Lorah Dorn, Ph.D., Barbara Everett, Ph.D.

NR247 Measuring Therapy Outcome in an Urban Child Clinic
Kathleen P. Longeway, Ph.D., Kathleen P. Longeway, Ph.D., Lucille B. Glicklich, M.D.

NR248 Marital Change After the Birth of an At-Risk Child
Mary Klinnert, Ph.D., Leslie A. Gavin, Ph.D., Frederick S. Wamboldt, M.D., David Mrazek, M.D.

NR249 DSM-III-R Pathological Gambling in Young Adults
Glenn C. Davis, M.D., Naomi Breslau, Ph.D., Patricia Andreski, M.A.

NR250 Childhood Abuse and Types of Adult Anger
Nicholas G. Ward, M.D., Albert S. Carlin, Ph.D., Heather Sowell, B.S., Belinda Gustafson, B.S.

NR251 Adolescent Suicidality in an Inner-City Population
Beverly Delaney, M.D., Jacqueline Bartlett, M.D., Steven J. Schleifer, M.D., Haftan Eckholdt, M.A., Steven E. Keller, Ph.D.

NR252 Rurality and Early Adolescent Alcohol Use
Kelly J. Kelleher, M.D., Vaughn Rickert, Ph.D., Brian Hardin, M.D., Sandra Pope, M.P.H.

NR253 Carbamazepine Reduces Childhood Rage Symptoms
Sidney Werkman, M.D., Gordon Farley, M.D., Jeanne Van Der Zanden, Ph.D.

NR254 Suicidal Youth: The Decision to Hospitalize
Richard Morrissey, Ph.D., Robert Dicker, M.D., Howard Abikoff, Ph.D., Harold S. Koplewicz, M.D., Amelia DeMarco, M.S.

NR255 Rapid Meclizine-Induced Cerebellar-Vestibular Improvement in Adult Learning Disabled
Harold Levinson, M.D.

NR256 MRI of the Posterior Fossa in Autistic Adults
H. Jordan Garber, M.D., Edward R. Ritvo, M.D.

NR257 SPECT in Lithium: Responsive Conduct Disorder
H. Jordan Garber, M.D., Gregory T. Slomka, Ph.D., Craig A. Taylor, M.D., Eric P. Fishman, Ph.D., Kishor M. Patel, Ph.D., Mustafa H. Adatepe, M.D.

NR258 Psychopharmacology of Conduct Disorder
Emily S. Klass, Ph.D., Rachel G. Klein, Ph.D., Howard Abikoff, Ph.D.

NR259 A Cartoon-Like Questionnaire to Assess Children 6-12 Years of Age
Jean-Pierre Valla, M.D., Huguette Berube, Ph.D., Lise Bergeron, M.Sc.

NR260 Family and Individual Adjustment in Cystic Fibrosis Children
Andres J. Pumariega, M.D., Deborah Pearson, Ph.D., Daniel Seilheimer, M.D.

NR261 Exclusion of Close Linkage of Tourette's Syndrome to D1 Dopamine Receptor
Joel Gelernter, M.D., James L. Kennedy, M.D., David Grandy, Ph.D., Olivier Civelli, Ph.D., David L. Pauls, Ph.D., Andrew J. Pakstis, Ph.D., Roger Kurlan, M.D., R.K. Sunahara, Hyman B. Niznik, Brian O'Dowd, P. Seeman, Kenneth K. Kidd, Ph.D.

NR262 Are Parkinson's Disease and ADHD Related?
Amy J. Holland, B.S., John M. Diamond, M.D., Stephen L. McNeil, M.D.

NR263 Predictive Value of Brief Alcoholism Screening Tests in a Sample of Hospitalized Adults
Frederic Blow, Ph.D., Kirk Brower, M.D., James Young, M.S., Elizabeth Hill, Ph.D., Kathleen Singer, R.N., Thomas Beresford, M.D.

NR264 Alcohol Dependence Among Hospitalized Eating Disorder Patients
Frederic Blow, Ph.D., Dean Krahn, M.D., Thomas Beresford, M.D.

NR265 Long-Term Antidepressant Treatment of Alcoholism
Barbara J. Mason, Ph.D., James H. Kocsis, M.D.

NR266 Psychiatric, Alcoholic and Antisocial Characteristics in Adult Offspring of Alcoholics Versus Non-Alcoholics
Veronica Moore, M.S.W., Gerald L. Brown, M.D., Irene Culver, B.A., Markku Linnoila, M.D.

NR267 Comparative Validity of Eleven Alcoholism Topologies
Elizabeth C. Penick, Ph.D., Barbara J. Powell, Ph.D., Elizabeth Nickel, M.A., Barry L. Liskow, M.D., Jan Campbell, M.D., Ruth Hassanein, Ph.D.

NR268 The Platelet Benzodiazepine Receptor in Alcoholics
Domenic A. Ciraulo, M.D., Jamie G. Barnhill, Ph.D., Steve Epstein, M.D., Ann Marie Ciraulo, R.N., Maura A. Faggart, B.S., Richard I. Shader, M.D., David J. Greenblatt, M.D.

NR269 Naltrexone in the Treatment of Alcohol Dependence
Joseph R. Volpicelli, M.D., Bruce J. Berg, M.D., Arthur I. Alterman, Ph.D., Charles P. O'Brien, M.D.

NR270 Controlled Trial of Buspirone in Alcoholism Relapse
Robert J. Malcolm, M.D., Raymond Anton, M.D., Kathleen J. Brady, M.D., Carrie L. Randall, Ph.D., Amanda Johnston, Ph.D., R. Eric. Jones, M.D.

NR271 Neuroendocrine Correlates of Alcohol Expectancy
Rachel Yehuda, Ph.D., Earl L. Giller, M.D., Lance Bauer, Ph.D., Roger E. Meyer, M.D.

NR272 WITHDRAWN

NR273 Hypomania in Post-Acute Alcohol Withdrawal
Ellen M. Cawthra, R.N., Kim Nagel, M.D., Lawrence E. Adler, M.D., Merilyne C. Waldo, Ph.D., Robert Freedman, M.D.

NR274 A General Population Survey of Drinking Patterns
Michael J. Marchese, M.D., Colleen Rand, Ph.D., John M. Kuldau, M.D.

NR275 Platelet MAO Activity and Alcohol Dependence: A Study of Patients and Their Healthy First-Degree Relatives
Mario Guazzelli, M.D., Pietro Pietrini, M.D., Antonio Ciapparelli, M.D., Federica Loprieno, M.D., Ilaria Bianchi, M.D., Pietro Sarteschi, M.D.

NR276 Predictive Validity of Two Screen Tests for Alcoholism
Thomas P. Beresford, M.D., Frederic Blow, Ph.D., James Young, M.S., Kathleen Singer, R.N., Elizabeth Hill, Ph.D.

NR277 Young Adult Children of Alcoholic Parents: Protective Effects of Positive Family Relationships
Elizabeth Hill, Ph.D., Janet Nord, Ph.D., Frederic Blow, Ph.D.

NR278 Immunity in Inner-City Alcoholics
Steven J. Schleifer, M.D., Steven E. Keller, Ph.D., Stephanie LaFarge, Ph.D., Angela Lignelli, B.S., Hong-Lin Nui, M.B.

NR279 Acute and Chronic Ethanol Effects on Lymphocytes
Martha M. Sarasua, M.D., Mariano V. Tolentino, M.D., Ray Hill, B.S., Debra Wentworth, B.S., Robert Smith, Ph.D., Jonathan Dunn, M.D.

NR280 Effects of Steroids on Immune Cells
Martha M. Sarasua, M.D., Mariano V. Tolentino, M.D., Ray Hill, B.S., Pat Warnaka, B.S.

NR281 Imipramine Treatment of Depressed Drug Abusers
Edward V. Nunes, M.D., Frederic M. Quitkin, M.D., Ronald Brady, M.D., Jonathan Stewart, M.D., Theresa Post, R.N.

NR282 Depression Predicts Improved Response to the Use of Medication in Cocaine Treatment
Douglas Ziedonis, M.D., Thomas Kosten, M.D.

NR283 Relapse Prevention Group Therapy is Effective in the Treatment of the Mentally Ill Substance Abuser
Douglas Ziedonis, M.D., Adam Jaffe, Ph.D., Ellen Davis, Ismene Petrakis, M.D., Izola Hogan, R.N.

NR284 Psychosocial Factors in Adolescent Drug Use: Older Sibling Influence on Younger Sibling Drug Use in the Context of Parent-Child Relations
David W. Brook, M.D., Judith S. Brook, Ed.D.

NR285 Dual Diagnoses and Recovery From Addictions
Robert C. Ness, Ph.D., Lois Cecil, M.A., Lionel Solursh, M.D., William Nolan, Ph.D.

NR286 Activation of Locus Coeruleus in Opiate Withdrawal
Gary Aston-Jones, Ph.D., Hideo Akaoka, Ph.D.

NR287 Noradrenergic Function and Ethanol Intoxication
Christopher J. McDougle, M.D., John H. Krystal, M.D., Lawrence H. Price, M.D., George R. Heninger, M.D., Dennis S. Charney, M.D.

NR288 Alcohol Screening in Acute Psychiatric Inpatients
Cynthia A. Pristach, M.D., Cedric M. Smith, M.D., Cathy Perkins, M.D.

NR289 Mentally Ill Chemical Abusers in the VA Psychiatric Programs: 1976-1988
Robert Rosenheck, M.D., Louis Massari, M.P.H.

NR290 Caffeine Dependence Among Cola Drinkers
John R. Hughes, M.D., Alison H. Oliveto, Ph.D., William Valliere, B.A., Warren K. Bickel, Ph.D., Stephen T. Higgins, Ph.D.

NR291 Substance Dependence in Psychiatric Patients
Norman S. Miller, M.D., Richard K. Ries, M.D.

NR292 Substance Abuse in HIV Infected Males
Patricia Rosenberger, Ph.D., Robert A. Bornstein, Ph.D., Henry A. Nasrallah, M.D., Michael F. Para, M.D., Robert J. Fass, M.D., Robert R. Rice, Jr., Ph.D.

NR293 Medical Student Substance Use/Parental Alcohol Use
Lon R. Hays, M.D., David W. Metzler, M.D.

NR294 Subpopulations of Substance Abusers: A New Concept
Nathaniel T. Marvel, M.D., Van R. Silka, M.D., Thor Tangvald, IV, M.D., James B. Shackson, M.D., Ibrahim Gunay, M.D.

NR295 Geriatric Substance Abusers: Erroneous Assumptions
Nathaniel T. Marvel, M.D., James B. Shackson, M.D., Thor Tangvald, IV, M.D., Van R. Silka, M.D., Ibrahim Gunay, M.D.

NR296 Acetorphan Blocks Opiate Withdrawal Symptoms
Francois Hartmann, M.D., Marie F. Poirier, M.D., Marie C. Bourdel, Ph.D., Henri Loo, M.D., Jeanne-Marie Le Comte, Ph.D., Jean-Charles Schwartz, Ph.D.

NR297 Risk for Alcoholism in Relatives of Drug Addicts
Leonard Handelsman, M.D., Marc Branchey, M.D., Jeremy Silverman, Ph.D., Laure Buydens-Branchy, M.D., Karen Holloway, M.D., David P. Bernstein, Ph.D.

NR298 Waiting for Drug Treatment: A Naturalistic Study
Leonard Handelsman, M.D., Karen Holloway, M.D., Marvin Aronson, Ph.D., John Chiaramonte, C.S.W., Robert Ness, Ph.D.

NR299 ADHD in Adult Opiate Dependent Outpatients
Christian Y. Herrera, M.D., Juan M. Segui, M.D., Andres Cascio, Ph.D., Carmen Aragon, Ph.D., Viviana C. Torresi, Ph.D.

NR300 Nasal Naloxone: A New Approach to Detect Opiate Dependence
Norbert Loimer, M.D., Peter Hofmann, M.D., Haroon Choudhry, Rainer Schmid, Ph.D.

NR301 Short-Term Hospital Course of Personality Disorder
Steven D. Roth, M.D., Mark J. Russ, M.D., William H. Berman, Ph.D., Kay Harrison, R.N.

NR302 Lack of Efficacy of Buspirone in Borderline Personality Disorder
Michael Wolf, M.D., Dan Carreon, M.D., Donald Summers, M.D., Ron Leino, M.D., Thomas Grayden, M.D., Martin Cosgrow, M.A., Jay Goldstein, M.D., Yi Jin, M.D., Steven G. Potkin, M.D.

NR303 Multiple Regression of Outcome in BPD and Narcissistic Personality Disorder
Jonathan R. Aronoff, Ph.D., Eric Plakun, M.D.

NR304 Personality Disorder Overlap in a Community Survey
David P. Bernstein, Ph.D., Patricia Cohen, Ph.D., Mary Sohwab-Stone, M.D., C. Noemi Velez, Ph.D., Larry J. Siever, M.D., Lillian T. Shinsato, B.A.

NR305 Characteristics of Autistic Children
Brian J. Cuffel, Ph.D.

NR306 PET and Personality Disorders
Peter F. Goyer, M.D., Paul J. Andreason, M.D., William E. Semple, Ph.D., Anita H. Clayton, M.D., Anna C. King, B.S., S. Charles Schulz, M.D.

NR307 Reliability Study of the Munich Diagnostic Checklists for the DSM-III-R Personality Disorders
Thomas Bronisch, M.D., Diego Garcia-Borreguero, M.D., Susan Flett, M.D., Reinert Wolf, M.D., Wolfgang Hiller, Ph.D.

NR308 Axis II Features and Social Impairment
Elizabeth Squires-Wheeler, Ph.D., Andrew E. Skodol, M.D., L. Erlenmeyer-Kimling, Ph.D.

NR309 Borderline Patients on Maintenance Fluoxetine
Michael J. Norden, M.D.

NR310 Elevation in Pain Thresholds in Bulimia Nervosa
Nancy C. Raymond, M.D., Martina deZwann, M.D., Patricia L. Faris, Ph.D., Elke D. Eckert, M.D., James E. Mitchell III, M.D.

NR311 Long-Term Outcome in Bulimia Nervosa
Richard L. Pyle, M.D., James E. Mitchell, M.D., Elke D. Eckert, M.D., Martina de Zwaan, M.D.

NR312 Disordered Eating in Girls with Insulin Dependent Diabetes Mellitus
Ruth H. Striegel-Moore, Ph.D., Timothy Nicholson, B.S., William Tamborlane, M.D.

NR313 Resting Metabolic Rate in Bulimia Nervosa
Margaret Altemus, M.D., Marion Hetherington, D.Phil, Tana Grady, M.D., Julio Licinio, M.D., Aviva Bernat, B.A., P.W. Gold, M.D.

NR314 Four Treatments of Bulimia Nervosa
L.K. George Hsu, M.D., Betty Chesler, M.Ed., Robin Santhouse, M.S.W., Lisa McDermitt, R.D., Walter Kaye, M.D.

NR315 Bulimia Nervosa: Fluoxetine and Psychological Change
David S. Goldbloom, M.D., Marion P. Olmsted, Ph.D.

NR316 Continued Open Trial of Fluoxetine in Anorexia
Theodore E. Weltzin, M.D., L.K. George Hsu, M.D., Walter H. Kaye, M.D.

NR317 Prevalence of Mental Disorders in the Morbidly Obese
Donald W. Black, M.D., Rise B. Goldstein, M.P.H., Sue E. Bell, M.S., Edward Mason, M.D.

NR318 Alexithymia and Neuroticism in Anorexia Nervosa
Graeme J. Taylor, M.D., Michael P. Bourke, M.D., James D. Parker, M.A., Michael R. Bagby, Ph.D.

NR319 Treatment Response in Obese Binge-Eaters
Detlev O. Nutzinger, M.D., Martina de Zwaan, M.D.

NR320 Eating Disorders in Women Who Misuse Alcohol
Robert C. Peveler, M.D., Amanda Taylor, M.D.

NR321 Prevalence of Eating Disorders in Diabetics
Robert C. Peveler, M.D., Christopher Fairburn, M.D.

NR322 Eating Disorder Pathology in Middle School Pupils
Ann C. Childress, M.D., Timothy D. Brewerton, M.D., Elizabeth L. Hodges, M.S.W.

NR323 Markers Linked to Eating Symptoms in School Girls
Howard Steiger, Ph.D., Freedom Leung, M.A., Guadalupe Puentes-Newman, M.A., L. Houle, B.A., J. Gulko, M.A.

NEW RESEARCH

Tuesday, May 14, 1991, 3:00 p.m.-5:00 p.m.

New Research 6—Poster Session—Ballroom A, Level 1, Convention Center

ANXIETY AND STRESS DISORDERS, EPIDEMIOLOGY, AND ECONOMIC AND DIAGNOSTIC ISSUES

Moderator: James W. Thompson, M.D.

NR324 The Low Dose DST in PTSD
Rachel Yehuda, Ph.D., Earl L. Giller, M.D., David Boisoneau, B.S., Martin T. Lowy, Ph.D., Steven M. Southwick, M.D., John W. Mason, M.D.

NR325 Fluvoxamine, Fluoxetine and Frontal Lobe Function
Rudolf Hoehn-Saric, M.D., Godfrey D. Pearlson, M.B., Christiane Cox, M.S., Gordon J. Harris, Ph.D., Edwaldo E. Camargo, M.D., Jeffrey Petra, M.D.

NR326 Sex Differences in CSF Levels of CRF and TRH
Mark D. Fossey, M.D., R. Bruce Lydiard, M.D., Michele T. Laraia, M.S.N., Garth Bissette, Ph.D., Charles B. Nemeroff, M.D., James C. Ballenger, M.D.

NR327 Disruption of Sensory Gating by Yohimbine in NC's
Lee D. Hoffer, B.A., Larry E. Adler, M.D., Merilyne Waldo, Ph.D., Herb Nagamoto, M.D., Robert Freedman, M.D.

NR328 Buspirone Addition in Fluvoxamine-Refractory OCD
Christopher J. McDougle, M.D., Wayne K. Goodman, M.D., Lawrence H. Price, M.D., Jacob C. Holzer, M.D., Elinore F. McCance-Katz, M.D., George R. Heninger, M.D.

NR329 Oral Idazoxan Versus Yohimbine in Healthy Subjects
Christopher J. McDougle, M.D., John H. Krystal, M.D., Scott W. Woods, M.D., Lawrence H. Price, M.D., Deborah A. Herbst, B.S., George R. Heninger, M.D., Dennis S. Charney, M.D.

NR330 Yohimbine Potentiates Startle Reflex in Humans
Charles A. Morgan, M.D., Steve Southwick, M.D., Christian Grillon, Ph.D., M. Davis, Ph.D., V. Ouillette, R.N., Dennis S. Charney, M.D.

NR331 Alprazolam Discontinuation in Panic Disorder
John C. Pecknold, M.D., Dennis Munjack, M.D., Paul Alexander, M.D., Lorenz Luthe, M.S.C.

NR332 Gepirone in Panic Disorder
John C. Pecknold, M.D., Lorenz Luthe, M.S.C., Stephen Jenkins, M.D.

NR333 Low Iron Levels and Tricyclic-Induced Jitterness
Vikram K. Yeragani, M.D., Robert Pohl, M.D., Richard Balon, M.D., C. Ramesh, M.D., Paula Weinberg, M.S.N.

NR334 Clinician-Accompanied Exposure and Self-Exposure in Phobia Reduction: A Controlled Study
Tarik Fahal J. Al-Kubaisy, M.D., Isaac M. Marks, M.D.

NR335 Benzodiazepines Compared Using Three Mice Models
Michel Bourin, M.D., Bouzekri Mansouri, M.A., Martine Hascoet, M.A., Jacques Bradwejn, M.D.

NR336 Social Phobia: Behavioral Versus Drug Therapies
Cheryl Shea Gelernter, Ph.D., T. Uhde, M.D., P. Cimbolic, Ph.D., D. Arnkoff, Ph.D., B.J. Vittone, M.D., M.E. Tancer, M.D., J.J. Bartko, Ph.D.

NR337 Auditory Sensory Gating in PTSD and Depression
Lawrence E. Adler, M.D., Herbert T. Nagamoto, M.D., Carla Drebing, B.S., Jonette Bronson, Ph.D.

NR338 Progressive Withdrawal of Chronic Lorazepam Users
Marc M. Ansseau, M.D., Remy Von Frenckell, Ph.D.

NR339 Withdrawal Phenomena of Suriclone and Diazepam
Marc M. Ansseau, M.D., Remy Von Frenckell, Ph.D., Philippe Guillet, M.D.

NR340 Trichotillomania: CSF Values and Treatment Response
Philip T. Ninan, M.D., Mary Eccard, M.S., R.D. Jewart, Ph.D., Mark Stipetic, B.S., Richard J. Lewine, Ph.D., Craig S. Risch, M.D.

NR341 Effect of Imipramine Treatment on Lactate Anxiety
Robert Pohl, M.D., Richard Balon, M.D., Vikram K. Yeragani, M.D., Debra Glitz, M.D., C. Ramesh, M.D., Paula Weinberg, M.S.N.

NR342 Buspirone Versus Diazepam in Reducing Anxiety
M.W. van Laar, M.D., E.R. Volkerts, A.P.P. von Willigenburg, T.A. Plomp, R.A.A. Maes

NR343 Polydiagnostic Issues in Anxiety Disorders
Michael Bach, M.D., Detlev O. Nutzinger, M.D., Martina de Zwaan, M.D., Lydia Hartl, M.D.

NR344 Risk Assessment by Patients with Anxiety Disorders
Randolph M. Nesse, M.D., Richard Klaus, B.A.

NR345 Somatization and Anxiety: Is There an Overlap?
Donna M. Mancuso, M.D., James G. Barbee, M.D., Andrew R. Kuczmierczyk, Ph.D., Alexandre A. Todorov, M.Ed.

NR346 Non-Habituation of the Startle Response in PTSD
Arieh Y. Shalev, M.D., Scott P. Orr, Ph.D., Tuvia Peri, M.A., Shaul Schreiber, M.D., Roger K. Pitman, M.D.

NR347 Psychophysiology of PTSD in Korean and WWII Veterans
Scott P. Orr, Ph.D., Roger K. Pitman, M.D., Lawrence R. Herz, M.D., Natasha B. Lasko, Ph.D.

NR348 Yohimbine and M-chloro-phenyl-piperazine in PTSD
Steven M. Southwick, M.D., John H. Krystal, M.D., Andrew Morgan, M.D., Linda M. Nagy, M.D., Ellie Dan, P.A., David Johnson, M.D., Douglas Bremner, M.D., Dennis S. Charney, M.D.

NR349 Comorbidity of Anxiety Disorders and PTSD
Eugene J. Fierman, M.D., Molly F. Hunt, B.A., Molly F. Hunt, B.A., Lisa A. Pratt, B.S., Meredith G. Warsaw, M.S.S., K.A. Yonkers, M.D., L.G. Peterson, M.D., J. Reich, M.D., Tamar Epstein-Kay, B.A., Hilary F. Norton, M.Ed.

NR350 5HT Function and Neurology of Social Phobia
Eric Hollander, M.D., Concetta M. Decaria, M.S., Sari Trungold, B.A., Franklin Schneier, M.D., Brian Fallon, M.D., Larry Welkowitz, Ph.D., Michael R. Liebowitz, M.D.

NR351 M-chloro-phenyl-piperazine Activated Regional Cerebral Blood Flow in OCD
Eric Hollander, M.D., Isak Prohovnik, Ph.D., Concetta M. Decaria, M.S., Jihad B. Saoud, M.S., Sari Trungold, B.A., Dan J. Stein, M.D., Michael R. Liebowitz, M.D.

NR352 Predictors of Treatment Outcome in OCD
Eric Hollander, M.D., Concetta M. Decaria, M.S., Jihad B. Saoud, M.S., Sari Trungold, B.A., Maxim Frenkel, M.D., Dan J. Stein, M.D., Michael R. Liebowitz, M.D.

NR353 Effect of the 5HT Agonist M-chloro-phenyl-piperazine on Brain Metabolism
Chawki Benkelfat, Paul Andreassen, M.D., Dennis L. Murphy, M.D., W. Semple, Ph.D, T.N. Nordahl, M.D., R.M. Cohen, M.D.

NR354 Behavioral Responses to Methylphenidate in OCD
Delbert G. Robinson, M.D., Carmen Z. Lemus, M.D., Michael H. Kronig, M.D., Gail Lerner, M.S.

NR355 A Time-Limited Behavioral Group Treatment for OCD
Barbara Van Noppen, A.C.S.W., Steven A. Rasmussen, M.D., Jane L. Eisen, M.D.

NR356 WITHDRAWN

NR357 OCD and Compulsive Traits: Phenomenology and Outcome
Jane Eisen, M.D., Steven A. Rasmussen, M.D., Brandon Krupp, M.D.

NR358 Symptoms in OCD With and Without Tic Disorder
Jacob C. Holzer, M.D., Lawrence H. Price, M.D., Christopher J. McDougle, M.D., Beth K. Boyarsky, M.S.N., Wayne K. Goodman, M.D.

NR359 Family Study of OCD
Donald W. Black, M.D., Russell Noyes, M.D., Rise Goldstein, M.P.H., Nancee Blum, M.S.W.

NR360 Tetrapetide and Octapeptid Concentrations in Panic Disorder and Normal Controls
R. Bruce Lydiard, M.D., James C. Ballenger, M.D., Michele T. Laraia, R.N., Mark D. Fossey, M.D., Margerie C. Beinfeld, Ph.D.

NR361 Psychoeducation/Reflective Listening Compared to Cognitive-Behavioral Treatment in Panic Disorder
M. Katherine Shear, M.D., Andrew C. Leon, Ph.D., Laura Portera, B.A., Janet Klosko, Ph.D., Marylene Cloitre, Ph.D.

NR362 Comorbidity of Social and Simple Phobia in Generalized Anxiety Disorder and Panic Disorder
Andrzej R. Kuczmierczyk, Ph.D., James G. Barbee, M.D., Donna M. Mancuso, M.D., Richard Maddock, M.D., Cameron Carter, M.B., Barbara Kennedy, M.D.

NR363 Doxapram: A Novel Panicogenic Probe
Yue-Joe Lee, M.D., George C. Curtis, M.D., John G. Weg, M.D., James L. Abelson, M.D., Jack Modell, M.D.

NR364 Panic in Balance Disorder Patients
Duncan B. Clark, M.D., Rolf G. Jacob, M.D., Martha Leslie

NR365 Long-Term Alprazolam Therapy in Panic Disorder
Richard C. Shelton, M.D., Phyleen Stewart, Shawn Harvey, Peter T. Loosen, M.D.

NR366 Effects of Intravenous Diazepam on Lactate-Induced Panic
Michael R. Liebowitz, M.D., Jeremy D. Coplan, M.D., Jack M. Gorman, M.D., Abby J. Fyer, M.D., Jose Martinez, M.A., Donald F. Klein, M.D.

NR367 Replication of Action of Cholecystokinin-tetrapeptide-4 in Panic Disordered Patients
Jacques Bradwejn, M.D., Diana Koszycki, M.A., Richard Payeur, M.D., Heather Borthwick, M.D.

NR368 Fluoxetine Augments Tricyclics in Panic Disorder
Indu M. Varia, M.D., Craig L. Donnelly, M.D.

NR369 Follow-Up Study of Alprazolam Treated Panic Disorder
James L. Abelson, M.D., George C. Curtis, M.D., Oliver G. Cameron, M.D., Pamela B. Schweitzer, B.S.N.

NR370 Thyroid Activity in Depression with Panic Symptoms
Gary M. Hasey, M.D., Robert G. Cooke, M.D., Jerry J. Warsh, M.D., David Koczerginski, M.D., A. Bonello, B.A., T. Jorna, B.Sc.

NR371 Explaining Impairment in Panic Patients
Andrew C. Leon, Ph.D., M. Katherine Shear, M.D., Laura Portera, M.A.

NR372 Child Abuse in Panic Disorder: Hypnotic Findings
Ambrogio Pennati, M.D., Emilio Sacchetti, M.D.

NR373 Panic Disorder in an Inner-City Psychiatric Outpatient Department: Results of a Structured Interview
Cheryl M. Paradis, Psy.D., Steven Friedman, Ph.D., Ronald M. Lazar, Ph.D., John Grubea, M.D., Martin Kesselman, M.D.

NR374 HLA and Panic Disorder
Jose L. Ayuso-Gutierrez, M.D., Leopoldo J. Llorente Perez, M.D., Carmen Ponce De Leon, M.D., Jose L. Ayuso-Mateos, M.D.

NR375 Mental Health Intervention Programs in Primary Care: Their Scientific Basis
Wim van den Brink, M.D., Johan Ormel, Ph.D.

NR376 Effects of Aging on Somatization in Panic Disorder
Javaid I. Sheikh, M.D., Gregory R. Bail, B.A., Gregory C. Sazima, M.D., Roy J. King, M.D.

NR377 Panic Disorder and Chest Pain in the Coronary Care Unit
Cameron S. Carter, M.D., Richard M. Maddock, M.D., Steven McCormick, Ph.D., C. Waters, M.D., J. Billett, M.D., E. Amsterdam, M.D.

NR378 Co-Segregation of Alcoholism, Anxiety and Depression
Wolfgang Maier, M.D., Dirk Lichtermann

NR379 The Effects of Single-Dose Anxiolytics Upon Memory
James G. Barbee, M.D., William F. Black, Ph.D., Catherine E. Kehoe, M.Ed., Alexandre A. Todorov, M.Ed.

NR380 Discontinuation of Fluoxetine in Trichotillomania
Cesar L. Benarroche, M.D.

NR381 Comparison of Two Flexible Drug Schedules for Panic
Sergio Gloger, M.D., Francisco O'Ryan, M.D., Alexei Franulic, M.D., Fernando Pizarro, M.T., Mario Barahona, R.N.

NR382 Social Phobia in Panic Patients
Jean-Michel Chignon, M.D., Mardjane Teherani, R.A., Elie Hantouche, M.D., J. Pierre Lepine, M.D.

NR383 Panic Disorder: Which Diagnostic Criteria?
Jean-Pierre Lepine, M.D., Joseph Lellouch, Ph.D.

NR384 PTSD in Combat Veterans of WWII, Korea and Vietnam
Robert Rosenheck, M.D., Alan Fontana, Ph.D.

NR385 Diagnosis Related Group Based-Budgeting and the VA Psychiatric Care
Robert Rosenheck, M.D., Louis Massari, M.P.H.

NR386 The Multidimensionality of Grief: A New Measure
Susan D. Cunningham, M.D.

NR387 Stress and Coping Within Couples Forced to Relocate
Frederick S. Wamboldt, M.D., Peter Steinglass, M.D., Atara Kaplan-Denour, M.D.

NR388 1988 Spitak Earthquake: Child PTSD Reactions
Robert S. Pynoos, M.D., Armen K. Goenjian, M.D., Meline Karakashyan, Ed.S., Raffi Manjikian, C.A.S., Madlene S. Tashjian, R.N., Setrak Setryian, Ph.D.

NR389 Course of Psychological Symptoms After Lawsuits
Renee L. Binder, M.D., Michael R. Trimble, M.B., Dale E. McNiel, Ph.D.

NR390 Dopamine in Acute and Chronic Stress
Mark B. Hamner, M.D., John I. Entrekin, B.S., Bruce I. Diamond, Ph.D.

NR391 Perceived Stress, Sleep and Natural Killer Function in Medical School
Steven E. Keller, Ph.D., David F. Dinges, Ph.D., Emily Carota-Orne, Nancy Bauer-Manley, M.S.S., Wayne G. Whitehouse, Ph.D., Martin T. Orne, Ph.D.

NR392 Physician Pregnancy: Colleagues' Attitudes
Marijo B. Tamburrino, M.D., Cynthia L. Evans, M.D., Kathleen Franco, M.D., Nancy Campbell, M.D.

NR393 Effects of Disasters on Emergency Workers
J. Lachenmeyer, Ph.D., M. Gibbs, Ph.D., A. Dillonma, L. Lodico, M.D., R. Deucher, M.D., T. Vandersall, M.D.

NR394 Psychiatric Predictors of Length of Hospital Stay in Hip Fracture Patients
John S. Lyons, Ph.D., James J. Strain, M.D., Marianne Fahs, Ph.D., Jeffrey S. Hammer, M.D.

NR395 Psychopathology and Treatment of 30344 Swedish Twins
Christer T. Allgulander, M.D., John P. Rice, Ph.D., Justyna Nowak, M.Sc.

NR396 Heatwave Deaths in Psychiatric Patients
Nigel M. Bark, M.D., Anne Brebbia, M.A.

NR397 PTSD Symptoms in a Community Sample of WWII Veterans
Bruce A. Kaup, M.D., Joseph Liberto, M.D., Paul E. Ruskin, M.D.

NR398 Establishing Reliability and Validity for Axis IV
Carolyn M. Mazure

NR399 Admission Decisions Using Artificial Neural Nets
Eugene C. Somoza, M.D., John Somoza, B.A.

NEW RESEARCH

Wednesday, May 15, 1991, 9:00 a.m.-10:30 a.m.

New Research 7—Oral/Slide Session—Room 7, Level 2, Convention Center

SCHIZOPHRENIA

Chp.: Raymond Cohen, M.D.

NR400 Sequelae of Birth Problems: The Vancouver Study — 9:00 a.m.
G. William MacEwan, M.D., Geoffrey N. Smith, Ph.D., Raymond J. Ancill, M.B., Henry G. Dunn, M.B.

NR401 MRI in Schizophrenics and Their Siblings — 9:15 a.m.
Stephen C. Olson, M.D., Henry A. Nasrallah, M.D., Steven B. Schwarzkopf, M.D., Mary B. Lynn, M.S.

NR402 Follow-Up MRI Study in First Episode Schizophrenia — 9:30 a.m.
Gustav Degreef, M.D., Manzar Ashtari, Ph.D., Howard Wu, B.M.D., Michael Borenstein, Ph.D., Stephen Geisler, M.D., Jeffrey A. Lieberman, M.D.

NR403 Changes in Plasma HVA Concentrations and Neuroleptic Treatment Response — 9:45 a.m.
Rene S. Kahn, M.D., Michael Davidson, M.D., Robert G. Stern, M.D., Peter Knott, M.D., Farooq Amin, M.D., Kim Dumont, B.A., Seth Apter, M.A., Kenneth Davis, M.D., Michelle Duffelmeyer, B.S.

NR404 Catecholamine Metabolites and Clozapine Response — 10:00 a.m.
Alan I. Green, M.D., Mohammed Y. Alam, M.D., Kathleen M. Pappalardo, B.S., Carl Salzman, M.D., Alan F. Schatzberg, M.D., Joseph J. Schildkraut, M.D.

NR405 Dementia in Elderly Schizophrenics: Clinical Features — 10:15 a.m.
Michael Davidson, M.D., Peter Powchik, M.D., Miklos F. Losonczy, M.D., Shlomit Katz, M.D., Michael Parrella, Ph.D., Marvin Goldstein, Ph.D., Janice McCrystal, R.N., Kenneth L. Davis, M.D., Danya Vardi, M.A.

NEW RESEARCH

Wednesday, May 15, 1991, 9:00 a.m.-10:30 a.m.

New Research 8—Oral/Slide Session—Room 9, Level 2, Convention Center

ORGANIC MENTAL SYNDROME AND DEINSTITUTIONALIZED POPULATIONS

Chp.: Craig N. Karson, M.D.

NR406 Limbic Plaque/Tangles in Patients with Alzheimer's Disease and Psychosis — 9:00 a.m.
Alan J. Waldman, M.D., William Ballinger, M.D.

NR407 Velnacrine Raises Brain Metabolism in Alzheimer's Disease — 9:15 a.m.
Richard A. Margolin, M.D., Lon S. Schneider, M.D., Yaorong Ge, M.S.

NR408	Bright Light Treatment of Sleep Disturbances in Alzheimer's Disease Andrew Satlin, M.D., Ladislav Volicer, M.D., Virginia Ross, Ph.D., Lawrence Herz, M.D., Scott Campbell, Ph.D.	9:30 a.m.
NR409	Aging, Sleep Disorders and Sexual Function Raul C. Schiavi, M.D., John Mandeli, Ph.D., Patricia Schreiner-Engel, Ph.D., Anthony Chambers, B.S.	9:45 a.m.
NR410	Psychiatric Epidemiology and the Homeless Louise Fournier, Ph.D., Vivianne Kovess, Ph.D., Cecile Rousseau, M.D.	10:00 a.m.
NR411	Psychopathology Among Homeless Female Veterans Catherine A. Leda, M.P.H., Robert Rosenheck, M.D., Peggy Gallup, Ph.D.	10:15 a.m.

NEW RESEARCH

Wednesday, May 15, 1991, 12 noon-2:00 p.m.

New Research 9—Poster Session—Ballroom A, Level 1, Convention Center

SCHIZOPHRENIA AND OTHER PSYCHOTIC DISORDERS

Moderator: William Z. Potter, M.D.

NR412 Third Ventricle and Cognitive Deficit in Schizophrenia
Robert A. Bornstein, Ph.D., Henry A. Nasrallah, M.D., Stephen C. Olson, M.D., Steven B. Schwarzkopf, M.D.

NR413 Asymmetric Frontal Horns in Kraepelinian Psychosis
Miklos F. Losonczy, M.D., Ede Frecska, M.D., Michael Davidson, M.D., Richard Keefe, Ph.D., Kenneth L. Davis, M.D.

NR414 Hemispheric Activation Treatment for Schizophrenia
Bruce E. Wexler, M.D., Erika Navarro, M.D., Keith Hawkins, Ph.D., Terry Halwes, Ph.D.

NR415 Comparison of the Positive and Negative Syndrome Scale with the Brief Psychiatric Rating Scale
Morris Bell, Ph.D., Robert Milstein, M.D., Joseph L. Goulet, M.S., Paul H. Lysaker, Ph.D., Dominic V. Cicchetti, Ph.D.

NR416 Schizophrenic Premorbid Adjustment
James J. Levitt, M.D., Martha E. Shenton, Ph.D., Robert W. McCarley, M.D., Amy S. Ludwig, B.A., Robert S. Smith, B.A.

NR417 Systematic Reduction of High-Dose Neuroleptics in Chronic Treatment Refractory Schizophrenia
Linda Bowen, Ph.D., B.D. Marshall, Jr., M.D., R.P. Liberman, M.D., Timothy G. Kuehnel, Ph.D., Joel Kelsch, L.C.S.W., Jeffery Hayden, B.S.

NR418 Trazodone as Adjunctive Treatment of Negative Symptoms in Chronic Schizophrenia
Paolo Decina, M.D., Sukdeb Mukherjee, M.D., Pierluigi Scapicchio, M.D., Ferdinando Saraceni, M.D., Christos Hadjichristos, M.D.

NR419 Genetic Linkage Studies in Schizophrenia Using the (CA)n Repeat Polymorphisms
Mihael H. Polymeropoulos, M.D., Hong Xiao, Denise S. Rath, Angela Boccio, Timothy Crow, James L. Weber, Lynn Delisi, Carl R. Merril

NR420 Continued Medication Trials in Borderline Personality
Jack R. Cornelius, M.D., Paul H. Soloff, M.D., Anselm W. George, M.D., James M. Perel, Ph.D., Marie D. Cornelius, Ph.D., Richard F. Ulrich, M.S.

NR421 Predictors of Subjective Stress in Schizophrenic Patients
Ross M.G. Norman, Ph.D., Ashok K. Malla, M.D.

NR422 A Prospective Study of Stress and Schizophrenia
Ross M.G. Norman, Ph.D., Ashok K. Malla, M.D.

NR423 Schizophrenics' Views of Relatives Predict Outcome
Malca B. Lebell, Ph.D., Stephen R. Marder, M.D., Jim Mintz, Ph.D., Lois Mintz, Ph.D., Martha Tompson, M.A.

NR424 Schizophrenia: P3 Asymmetries Vary with Handedness
Dorothy P. Holinger, Ph.D., Nicholas S. Sokol, Robert W. McCarley, M.D., Steven F. Faux, Ph.D.

NR425 Mazindol in Negative Symptoms Schizophrenics
John P. Seibyl, M.D., John H. Krystal, M.D., Robin Johnson, M.D., Dennis S. Charney, M.D.

NR426 Rat Entorhinal Neuron Physiology and Morphology
David M. Finch, Ph.D., Thomas D. White, Ph.D., Kurt Lingenhohl, B.A., Aiko M. Tan, B.S.

NR427 Cyproheptadine Treatment for Tardive Dyskinesia
Larry D. Alphs, M.D.

NR428 Reliability of a Depression Scale for Schizophrenia
Donald E. Addington, M.D., Jean M. Addington, Ph.D., Eleanor Matickatyndale, Ph.D., Joan Joyce, M.D.

NR429 Blood-Brain Barrier Permeability in Schizophrenia
Robert C. Alexander, M.D., Darrell G. Kirch, M.D., Richard L. Suddath, M.D., Nicholas M. Papadopolous, Ph.D., Charles A. Kaufmann, M.D., Richard Jed Wyatt, M.D.

NR430 Central Interleukin-2 in Unmedicated Schizophrenics
Julio Licinio, M.D., John Seibyl, M.D., Margaret Altemus, M.D., Dennis S. Charney, M.D., John Krystal, M.D.

NR431 Alterations in Interleukins in Schizophrenics
Rohan Ganguli, M.D., Cathy G. McAllister, Ph.D., B.S. Rabin, M.D., W. Solomon, J.S. Brar, M.D., T. Rehn, M.S.

NR432 Cognitive Deficits in Sporadic Schizophrenia
Frederic J. Sautter, Ph.D., Barbara E. McDermott, Ph.D., F. William Black, Ph.D., Patrick O'Neill, M.D.

NR433 Cognitive Deficits and Loss of Role Functioning
Frederic J. Sautter, Ph.D., Barbara E. McDermott, Ph.D., F. William Black, Ph.D., Tammy Sobrapena, M.A.

NR434 Natural Auto-Antibodies in Schizophrenia
A. Galinowski, M.D., P. Levy-Soussan, R. Barbouche, H.F. Poirier, F. Hartmann, H. Loo, S. Avrameas

NR435 Postpartum Psychosis and Neuroleptic Dosage
John A. Baker, M.D., Dale D'Mello, M.D., Melpomeni Kavadella, M.D.

NR436 Hyponatremia in a State Hospital: 31 New Cases
Pritesh J. Shah, M.D., William M. Greenberg, M.D.

NR437 Structural Abnormalities in Schizophrenic Patients with Hyponatremia
William B. Lawson, M.D., Darrell Kirch, M.D., Richard Shelton, M.D., David Daniels, M.D., Andrei Lager, M.D., Gary Robertson, M.D., Larry Welch, Ed.D.

NR438 Depot Neuroleptics and Negative Symptoms
Susanne Steinberg, M.D., Lawrence Annable, D.S.

NR439 Plasma HVA in Psychotic and Nonpsychotic Disorders
Giovanni Muscettola, M.D., Andrea de Bartolomeis, M.D., Giuseppe Barbato, M.D., Dina Nerozzi, M.D.

NR440 Clozapine Treatment of Borderline Patients
Frances R. Frankenburg, M.D., Mary C. Zanarini, Ed.D., Joan H. Glutting, B.A.

NR441 The Heterogeneity of Schizophrenia: Season of Birth
Ann E. Pulver, Sc.D., John J. McGrath, M.D., Paula S. Wolyniec, M.A., Doreen Tam, B.S.

NR442 Premorbid Functioning and Outcome in Schizophrenia
Jean M. Addington, Ph.D., Donald E. Addington, M.D.

NR443 Gender Differences and Schizophrenic Symptoms
Jean M. Addington, Ph.D., Donald E. Addington, M.D.

NR444 CSF Diazepam-Binding Inhibitor in Schizophrenia On and Off Haloperidol
Daniel P. van Kammen, M.D., Alessandro Guidotti, Ph.D., John A. Gurklis, Jr., M.D., Mark W. Gilbertson, Ph.D., Jeffrey Yao, Ph.D., Erminio Costa, M.D.

NR445 Schizophrenia: Gender and Familial Risk
Paula S. Wolyniec, M.A., Ann E. Pulver, Sc.D., John J. McGrath, M.A., Doreen Tam, B.S.

NR446 Treatment of Schizophrenia in the Mentally Retarded
Michael B. Sheikman, M.D.

NR447 Cognition and Social Functioning in Schizophrenia
Patrick W. Corrigan, Psy.D., Charles J. Wallace, Ph.D., Michael F. Green, Ph.D., Mark L. Schade, M.A.

NR448 Impact of Clozapine on Chronically State Hospitalized Treatment of Refractory Schizophrenic Patients
Jeffery Grace, M.D., Marvin Herz, M.D., John Treanor, M.D., Kerry Donnelly, Ph.D., Stephen B. Bellus, Ph.D., Patricia Smith, R.N., Susan Gunn, R.N., Thomas Hays, M.D., Margaret Paroski, M.D.

NR449 P3 and Thought Disorder Index Scores in Families of Schizophrenics
Brian F. O'Donnell, Ph.D., Martha E. Shenton, Ph.D., Robert W. McCarley, M.D., Seth D. Pollak, M.E.D., Steven F. Faux, Ph.D., Robert S. Smith, B.A.

NR450 M-chloro-phenyl-piperazine in Schizophrenia: Typical Versus Atypical Neuroleptic Effects
John H. Krystal, M.D., John Seibyl, M.D., Lawrence H. Price, M.D., Scott W. Woods, M.D., George R. Heninger, M.D., Dennis S. Charney, M.D.

NR451 Factor Analysis of MRI Volumes in Schizophrenia
Allen Y. Tien, M.D., Godfrey D. Pearlson, M.B., Pat Barta, M.D., Richard Powers, M.D., Gary Chase, Ph.D.

NR452 Hallucinations in a State Hospital Population
Kenneth N. Sokolski, M.D., Edward M. Demet, Ph.D., Bruce I. Abrams, M.D., Jerome F. Costa, M.D., Christopher Reist, M.D., Jeffrey L. Cummings, M.D.

NR453 Family Intervention for Schizophrenia Among Hispanics
Cynthia Telles, Ph.D., Marvin Karno, M.D., George Paz, M.D., Miguel Arias, M.D., Douglas Tucker, M.D., Jim Mintz, Ph.D.

NR454 A Carbamazepine Augmentation Trial in Chronic Schizophrenics
Kurt Meszaros, M.D., Christian Simhandl, M.D., Elisabeth Denk, M.D., A. Liechtenstein, M.D., A. Topitz, M.D., K. Thau, M.D.

NR455 Role of Serum Serotonin Assay in Schizophrenia
Anand K. Pandurangi, M.D., Anthony L. Pelonero, M.D., Nedathur Narasimhachari, Ph.D.

NR456 Cessation of Polydipsia in Schizophrenia Following Clozapine Administration
John C. Kluznik, M.D.

NR457 Indicators of Vulnerability to Schizophrenia
Wolfgang Maier, M.D., Christoph Hain, Peter Franke, Thomas Klingler, Dirk Lichtermann

NR458 Patterns of Substance Use in New Onset Psychosis
Beatrice Kovasznay, M.D., Ranganatha Ram, M.D., Joseph E. Schwartz, Ph.D., Evelyn Bromet, Ph.D.

NR459 The DST and Psychosis: An Eight-Year Follow-Up
William H. Coryell, M.D., Debby Tsuang, M.D.

NR460 Symptoms and Work Performance in Patients with Schizophrenia
Robert Milstein, M.D., Morris Bell, Ph.D., Paul Lysaker, Ph.D., Gary Bryson, B.S., Joseph L. Goulet, M.S.

NR461 Relationship Between Depression/Anxiety and Positive and Negative Symptoms in Schizophrenia
Ashok K. Malla, Ross M.G. Norman, Ph.D.

NR462 Third and Lateral Ventricular Volumes in Schizophrenia
Steven B. Schwarzkopf, M.D., Henry A. Nasrallah, M.D., Stephen C. Olson, M.D., Mary B. Lynn, M.S., Tanmoy Mitra, M.S.

NR463 Symptom Profile in First Episode Schizophrenia
Derri Shtasel, M.D., Raquel E. Gur, M.D., Carolyn Heimberg, M.D., David Mozley, M.D., Fiona Gallacher, B.A., Jeff Richards, B.A., Ruben C. Gur, M.D.

NR464 WITHDRAWN

NR465 Can Clinical Response to Clozapine Be Predicted?
Wayne S. Fenton, M.D., Beth Lee, R.N.

NR466 Self-Appraisal Deficits in Schizophrenia
Xavier F. Amador, Ph.D., D.H. Strauss, M.D., S. Yale, M.S.W., K. Gimmestad, O.T.R., A.E. Rundquist, R.N., H. Deutsch, R.N., P. Stern, M.A., C. Kaufmann, M.D., J.M. Gorman, M.D.

NR467 Are Neurological Soft Signs a Marker of Perinatal Brain Damage?
Michael Linden, M.D., Albert Diefenbacher, M.D.

NR468 Delusions of Parasitosis: An Entomologist's View
Donald J. Kushon, M.D., Jean Helz, M.D., Kendrick Lau, Michael Williams, Ph.D.

NR469 The Use of ECT in Neuroleptic Malignant Syndrome
John M. Davis, M.D., Philip Janicak, M.D., Cindy K. Gilmore, Psy.D., Paul Sakas, M.D., Zhengu Wang

NR470 Early Response to Neuroleptic Treatment by Schizophrenics
David B. Glovinsky, M.D., Richard Jed Wyatt, M.D., Darrell G. Kirch, M.D.

NR471 Outpatients Assess Treatment Involvement and Satisfaction
Kishor Sangani, M.D., Charles Sheppard, M.D.

NR472 Effects of a Smoking Ban on a Psychiatry Unit
Noel E. Taylor, M.D., Richard N. Rosenthal, M.D., Brent Chabus, M.D., Stewart Levine, M.D., Amy Hoffman, M.D.

NR473 The Incidence of Tardive Dyskinesia in Chronic Outpatients
William M. Glazer, M.D., Hal Morgenstern, Ph.D.

NR474 Laterality of Tardive Dyskinesia and Parkinsonism
Thomas E. Hansen, M.D., George A. Keepers, M.D., William F. Hoffman, M.D., Melinda K. Lowe, B.S., Daniel E. Casey, M.D.

NR475 Does the N-methyl-d-aspartate Receptor Mediate the Effects of PCP?
Andrew B. Norman, Ph.D., Lindy M. Wyatt, B.A., Eugene C. Somoza, M.D.

NR476 Reliability of Rating Extrapyramidal Side Effects
Darien S. Fenn, Ph.D., William F. Hoffman, M.D., George A. Keepers, M.D., Thomas E. Hansen, M.D., Daniel E. Casey, M.D.

NR477 Neuroleptics Obscure the Correlation of Tardive Dyskinesia and Ventricular Brain Ratio
William F. Hoffman, M.D., Linda C. Ballard, M.N., George A. Keepers, M.D., Thomas E. Hansen, M.D., Daniel E. Casey, M.D.

NR478 Endocrine Effects of Antipsychotic Drugs in Patients
Fabrice Duval, M.D., M-Claude Mokrani, Ph.D., Juarez Oliveira-Castro, M.D., Marc-Antoine Crocq, M.D., Jean-Paul Macher, M.D.

NR479 Adrenocorticotropic and Ovine Corticotropin Releasing Hormone Effects on Dopamine Activity in Man
Joel A. Posener, M.D., Alan F. Schatzberg, M.D., Joseph J. Schildkraut, M.D.

NR480 Fetal Alcohol Exposure, Schizophrenia and Pervasive Developmental Disorders
Richard L. Livingston, M.D., H. Stefan Bracha, M.D.

NR481 Controlled Study of Intravenous Amobarbital in Relieving Catatonic Mutism
William V. McCall, M.D., Frank E. Shelp, M.D., William M. McDonald, M.D., Martha S. Wingfield, M.D.

NR482 Imaging of Extrastriatal Dopamine Receptors in Man
Robert M. Kessler, M.D., William O. Whetsell, M.D., Mohammad S. Ansari, M.S., John R. Votaw, Ph.D., Tomas dePaulis, Ph.D., Robert Bell, M.D., Dennis Schmidt, Ph.D., N. Scott Mason, Ph.D., Ronald G. Manning, Ph.D., Michael H. Ebert, M.D.

NR483 MRI Volume in Late-Life Onset Schizophrenia
Godfrey D. Pearlson, M.B., Richard E. Powers, M.D., Patrick E. Barta, M.D., Elizabeth H. Aylward, Ph.D., Peter V. Rabins, M.D., Lisa D. Raimundo, Gary A. Chase, Ph.D., Larry E. Tune, M.D.

NR484 Computer Automated Magnetic Resonance Brain Volume Measures in Schizophrenics
Martha E. Shenton, Ph.D., Ron Kikinis, M.D., Robert W. McCarley, M.D., M. Anderson, B.S., Ferenc A. Jolesz, M.D.

NR485 Fractal Dimension of Schizophrenic Brains
Patrick E. Barta, M.D.

NR486 Basal Ganglia MRI Volumes in Schizophrenia
Rajendra Persaud, M.D., Godfrey D. Pearlson, M.B., Patrick E. Barta, M.D., Steven R. Machlin, M.D., Larry E. Tune, M.D.

NR487 Brain Iron and Oxidative Stress Increase Extrapyramidal System Risk
George Bartzokis, M.D., Stephen R. Marder, M.D., William H. Oldendorf, M.D., F. Chang, M.D., J. Mintz, Ph.D., C.K. Phelan, M.D.

NR488 Support Program Influence on Daily Activity Pattern
Raymond Tempier, M.D., Celine Mercier, Ph.D.

NEW RESEARCH

Wednesday, May 15, 1991, 3:00 p.m.-5:00 p.m.

New Research 10—Poster Session—Ballroom A, Level 1, Convention Center

ORGANIC MENTAL DISORDERS, GERIATRICS, AIDS/HIV, CONSULTATION/LIAISON, EMERGENCY PSYCHIATRY, AND SLEEP DISORDERS

Moderator: Frederic M. Quitkin, M.D.

NR489 Impaired Perception of Emotion in Neuropsychiatry
Christopher Starratt, Ph.D., H. Jordan Garber, M.D., Kirshor M. Patel, Ph.D., Mustafa H. Adatepe, M.D., Gilbert H. Isaacs, M.D.

NR490 Risk Factors for Delirium in Psychiatric Inpatients
Warren Steiner, M.D., Janet Ritchie, M.D., Michal Abrahamowicz, Ph.D.

NR491 Distinguishing the Organic Psychoses
Jack R. Cornelius, M.D., Juan Mezzich, M.D., Horacio Fabrega, M.D., Marie D. Cornelius, Ph.D., Nancy L. Day, Ph.D., Joyce Myers, M.D.

NR492 The Effects of Nicotinic Blockade on Cognition
Paul A. Newhouse, M.D., Kathryn Pedersen, M.S., Robert Lenox, M.D.

NR493 Memory and Serotonergic/Cholinergic Interactions
Vahram Haroutunian, Ph.D., Anthony C. Santucci, Ph.D., Kenneth L. Davis, M.D.

NR494 MRI High Intensity Signals in Alzheimer's Disease
Anand Kumar, M.D., David Yousem, M.D., Elaine Souder, Ph.D., David Miller, M.D., Gary Gottlieb, M.D., Abass Alavi, M.D.

NR495 The Relationship of Apathy and Depression
Robert S. Marin, M.D., Ruth C. Biedrzycki, M.E.D., I. Firinciogullar, M.S.

NR496 Diagnostic Markers in Alzheimer's Disease
Larry D. Altstiel, M.D., Brian A. Lawlor, M.D.

NR497 Optic Nerve in Alzheimer's Disease Patients
Michael Davidson, M.D., Jacqueline Lustgarten, M.D., Pamela Rizzuto, M.A., Robert Massini, M.S., James Schmeidler, Ph.D., Brian A. Lawlor, M.D.

NR498 Correlation Between rCBF and Cognitive Tests
Philippe H. Robert, M.D., Octave Migneco, M.D., Valerie Aubin, M.D., J. Darcourt, M.D., O. Ricq, M.D., G. Darcourt, M.D.

NR499 Mini Mental State Examination: A Discrimination of Alzheimer's Disease?
Jane C. Wells, M.D., Penelope M. Keyl, Ph.D., Gary A. Chase, Ph.D., Ahmed Aboraya, M.D., Marshal F. Folstein, M.D., James C. Anthony, Ph.D.

NR500 Variable HLA Association in Alzheimer's Disease
Gary W. Small, M.D., Steven S. Matsuyama, Ph.D., Albert Heyman, M.D., Emily G. Reisner, Ph.D., Edward B. Renvoize, M.D., Raimo Sulkava, M.D.

NR501 Course of Major Depression in the Elderly
Gregory A. Hinrichsen, Ph.D.

NR502 Psychogeriatric Delirium
Raymond J. Ancill, M.B., Leslie J. Sheldon, M.B., Nelson Collins, M.D., William Carlyle, M.D., Nagi Youssef, M.D.

NR503 Physical Restraints in Dementia with Agitation
Elisse Kramer, Ph.D., Blaine S. Greenwald, M.D., Susan Abraham, M.D., Jacob Reingold, M.S., Helene Grossman, M.S.

NR504 Increased Synthesis and Accumulation of Heat Shock 70 Proteins in Alzheimer's Disease Brain
William Wallace, Ph.D., Nancy Perez, B.A., Carl Merril, M.D., J. Sugar, B.S., L. Bierer, M.D., V. Haroutunian, Ph.D.

NR505 Dyskinesia and Neuroleptic Use in Elderly Inpatients
Robert A. Sweet, M.D., Benoit H. Mulsant, M.D., Aicha H. Rifai, M.D., George S. Zubenko, M.D.

NR506 Suicide and Aging: Psychological Autopsy Findings
Yeates Conwell, M.D., Eric D. Caine, M.D., Robin E. Henderson, Ph.D., Catherine J. Flannery, M.D., Nicholas T. Forbes, M.D.

NR507 Mortality and Psychotropics in Long-Term Care of Elderly Patients
Ira R. Katz, M.D., Paul Thuras, Ph.D., Patricia Parmelee, Ph.D., Patricia Beaston-Wimmer, Ph.D.

NR508 Predictors of Mild Postoperative Psychopathology
Marion Zucker Goldstein, M.D., Barry Fogel, M.D.

NR509 Major Depression in Severe Dementia
Blaine S. Greenwald, M.D., Elisse Kramer, Ph.D.

NR510 Appropriate Terminal Care for End-Stage Dementia
Daniel J. Luchins, M.D., Patricia Hanrahan, Ph.D.

NR511 Alz50 Binding in the Brains of Demented Elderly Psychiatric Patients is Identical to That of Nondemented Nonpsychiatric Controls
Peter Powchik, M.D., D. Purohit, Charles B. Nemeroff, M.D., M. Davidson, M.D., V. Haroutunian, Ph.D., D. Perl, M.D., K.L. Davis, M.D.

NR512 Efficacy and Side Effects of Nortriptyline Versus Desipramine in Geriatric Inpatients with Major Depression
Lawrence W. Lazarus, M.D., David Winemiller, B.S., Lesley Blake, M.D., Carolyn Hartman, M.D., Mehrdad Abbassian, M.D., Usha Kartan, M.D., Pauline Langsley, M.D., Andrew Ripeckyj, M.D., Virginia Markvart, R.N., Jan Fawcett, M.D.

NR513 Efficacy and Side Effects of Methylphenidate (Ritalin) for Post-Stroke Depression
Lawrence W. Lazarus, M.D., David Winemiller, B.S., Venkata Lingam, M.D., Carolyn Hartman, M.D., Ida Neyman, M.D., Mehrdad Abbassian, M.D., Usha Kartan, M.D., Pauline Langsley, M.D., Virginia Markvart, R.N., Jan Fawcett, M.D.

NR514 Learning and Memory Impairment in Elderly Detoxified Benzodiazepine Dependent Patients
Teresa A. Rummans, M.D., Leo J. Davis, Ph.D., Robert M. Morse, M.D.

NR515 Anticholinergic Effects of Common Medications
Larry E. Tune, M.D.

NR516 10-OH-Nortriptyline and Hypotension in the Elderly
Robert C. Young, M.D., George S. Alexopoulos, M.D., Barnett S. Meyers, M.D., Richard Shindledecker, M.A., Gabriel Tsuboyama, M.D., Amiya K. Dhar, D.S.C.

NR517 Hospitalization of the Elderly: Canadian Trends
Alex Richman, M.D., Rod Riley, B.Sc.

NR518 Low-Dose Neuroleptic Treatment for AIDS Delirium
William Breitbart, M.D., Meredith Platt, Ph.D., Rocco Marotta, M.D., Kathy Corbera, M.D., Carmen Grau, M.D., Susan Raymond, B.S., Henry Weisman, M.D., Maria Derevenco, Psy.D.

NR519 Methylphenidate's Antidepressant Effect in HIV
Francisco Fernandez, M.D., Joel K. Levy, Ph.D., Francis Pirozzolo, Ph.D., Becky Viscuso, R.N.

NR520 HIV Infection, Psychiatric Symptoms and Risk Taking
David S. Metzger, Ph.D., George E. Woody, M.D., A.T. McLellan, Ph.D., Charles P. O'Brien, M.D.

NR521 Peptide T for Cognitively Impaired HIV Positive Patients
Marc I. Rosen, M.D., Mikel Thomas, M.D., H. Rowland Pearsall, M.D., Christopher H. van Dyck, M.D., Scott W. Woods, M.D., Thomas R. Kosten, M.D.

NR522 Suicidal Ideation After HIV Testing
Samuel W. Perry III,, M.D., Lawrence B. Jacobsberg, M.D., Baruch F. Fishman, Ph.D.

NR523 Health Attributions Mediate Distress in HIV Seropositives
Baruch F. Fishman, Ph.D., Samuel W. Perry III,, M.D., Lawrence B. Jacobsberg, M.D.

NR524 Denial in Self-Report of Cognitive Function in HIV
Robert A. Stern, Ph.D., Naomi G. Singer, B.A., Jane Leserman, Ph.D., Susan G. Silva, M.A., Dwight L. Evans, M.D.

NR525 Psychosocial Predictors of HIV High-Risk Behavior
Diana O. Perkins, M.D., Jane Leserman, Ph.D., Duanping Liao, M.D., John Boucvalt, B.S., Dwight L. Evans, M.D.

NR526 HIV Seroprevalence in Psychiatric Inpatients
Michael H. Sacks, M.D., Helen Dermatis, Ph.D., Salome Looser-Ott, M.A., William Burton, M.A., Samuel W. Perry III, M.D.

NR527 Two Clinical Service Delivery Models for HIV Patients
Marianne C. Fahs, Ph.D., George Fulop, M.D., James J. Strain, M.D., Henry S. Sacks, Ph.D., Charlotte Muller, Ph.D., Paul D. Cleary, Ph.D., James Schmeidler, Ph.D., Barbara Turner, M.D.

NR528 Early Neuropsychiatric Morbidity in HIV Disease
Rifaat S. El-Mallakh, M.D., David J. Ligay, M.S.W.

NR529 Psychiatric Disorders in 100 HIV-Infected IV Drug Users
Steven L. Batki, M.D., Julie A. London, Ph.D., Stephen Ferrando, M.D., Jerry Pattillo, Ph.D., Craig J. Abbott, B.A., Rochelle Hartwig, B.A.

NR530 Depression in HIV Infected Men
Patricia Rosenberger, Ph.D., Robert A. Borenstein, Ph.D., Henry A. Nasrallah, M.D., Michael F. Para, M.D., Robert J. Fass, M.D., Robert R. Rice, Jr., Ph.D.

NR531 The Use of Fluoxetine in Patients on Hemodialysis
Michael Blumenfield, M.D., Norman B. Levy, M.D., Anjani Dubey, M.D., Richard Solomon, M.D., Alvin Goodman, M.D.

NR532 Nonpsychiatric Physicians Frequently Misdiagnose Delirium and Other Conditions as Major Depression
Russell L. Margolis, M.D.

NR533 Somatization and Recognition of Psychiatric Distress
Laurence J. Kirmayer, M.D., J. Robbins, Ph.D., M. Dworkind, M.D., M. Yaffe, M.D.

NR534 Chronic Fatigue Syndrome and Psychiatric Illness
Grant E. Mitchell, M.D., Steven B. Friedenthal, M.D., Michael Blumenfield, M.D., Barbara Orlowski, Ph.D., Louis Raimondo, M.D.

NR535 Cognitive and Emotional Findings in Intensive Care Unit Ventilator Patients
Kathleen Franco, M.D., Laurie Verbosky, M.B.A., John McSweeney, Ph.D., Keith Freeman, M.S., James Tita, D.O.

NR536 Interictal Psychiatric Morbidity and Focus of Epilepsy in Treatment Refractory Subjects
Dr. Rahul Manchanda, Betsy Schaefer, Dr. Richard S. McLachlan, Warren T. Blume

NR537 Chronic Pain and Suicide Death
David A. Fishbain, M.D., Myron Goldberg, Ph.D., Hubert Rosomoff, M.D., R. Steele-Rosomoff, R.N., M. Jorge, M.A., E. Abdel-Moty, Ph.D.

NR538 Clonazepam Open Clinical Trial for Chronic Pain of Myofascial Pain Syndrome Origin Refractory to Pain Unit Treatment
David A. Fishbain, M.D., Myron Goldberg, Ph.D., Hubert Rosomoff, M.D., R. Steele-Rosomoff, R.N., M. Jorge, M.A., E. Abdel-Moty, Ph.D.

NR539 Magnesium Levels in Chronic Pain Patients
David A. Fishbain, M.D., Myron Goldberg, Ph.D., Hubert Rosomoff, M.D., R. Steele-Rosomoff, R.N., M. Jorge, M.A., E. Abdel-Moty, Ph.D.

NR540 Screening for Psychiatric Disorders in the General Hospital: A Validation and Calibration Study
David M. Clarke, M.D., Graeme Smith, M.D., Dean McKenzie, B.A.

NR541 Psychophysiologic Correlates in Asthmatics
David A. Baron, D.O., William Samuel, M.D.

NR542 Religiosity and Psychosocial Adjustment in Cancer
Basawaraj M. Karajgi, M.D., Arthur Rifkin, M.D., Seshagiri Doddi, M.D., Luz Alvarez, M.D., Zully M. Mateus, M.D., Pedro Polanco, M.D.

NR543 Death-Mindedness in General Surgery Patients
Caryl E. Boehnert, Ph.D., Lynn Trochel, B.A., Allan Callies, B.A.

NR544 Fear of Recurrence and Breast Conserving Surgery
Richard G. Margolese, M.D., Jean-Claude Lasry, Ph.D., Robert A. Stern, M.D., Julie Beckwith, M.S.N., Claire E. Morey, B.S., George Mason, Ph.D., Arthur J. Prange, Jr., M.D.

NR545 Psychiatric Effects of Subclinical Hypothyroidism
John J. Haggerty, Jr., M.D.

NR546 Quantitative MRI Findings in HIV-1 Infected Males
Elizabeth H. Aylward, Ph.D., Julie McArthur, B.S.N., Justin McArthur, M.D., Brian Shi, Gerald Dalpan, M.D., Patrick E. Barta, M.D., Godfrey D. Pearlson, M.B.

NR547 Quantitative SPECT and MRI in Mild Huntington's Disease
Gordon J. Harris, Ph.D., Godfrey D. Pearlson, M.B., Elizabeth Aylward, Ph.D., Joy Roberts, B.S., Patrick E. Barta, M.D., Edwaldo E. Camargo, M.D., Susan E. Folstein, M.D.

NR548 Trends of a Unique VA Consultation/Liaison Service
Samuel O. Okpaku, M.D., Peter Loosen, M.D., Norman Stephenson, Ph.D.

NR549 Longitudinal Validity of DSM-III-R Alcohol Dependence
Thomas P. Beresford, M.D., Frederic Blow, Ph.D., James Young, M.S., Kathleen Singer, R.N., Elizabeth Hill, Ph.D.

NR550 Pain Disorders: A Proposed Classification for DSM-IV
Steven A. King, M.D., James J. Strain, M.D.

NR551 Subsyndromal Somatization and Hypochondriacal Worry
James M. Robbins, Laurence L. Kirmayer, M.D.

NR552 Quality of Life and Breast Cancer Surgery
Jean-Claude M. Lasry, Ph.D., Richard G. Margolese, M.D.

NR553 Premorbid Psychopathology in Somatoform Pain Syndrome
Peter B. Polatin, M.D., Regina K. Kinney, B.A., Robert J. Gatchel, Ph.D.

NR554 Type A Hypothesis: Identification of Toxic Complex
Tomas de Flores Formenti, M.D., Miguel Bernardo, M.D., Carlos Ballus, M.D.

NR555 Triazolam: Intermittent Administration
Anthony Kales, M.D., Rocco L. Manfredi, M.D., Alexandros Vgontzas, M.D., E. O. Bixler, Ph.D., Antonio Vela-Bueno, M.D., Kathy Tyson, B.S.

NR556 Low Energy Emission Therapy Treatment for Insomnia
Milton K. Erman, M.D., Roza Hajdukovic, M.D., Boris Pasche, M.D., Alexandre Barbault, Merrill M. Mitler, Ph.D.

NR557 Sleep Disturbances and Episodic Mental Symptoms
M. Eileen McNamara, M.D., Richard P. Millman, M.D., Barry S. Fogel, M.D.

NR558 Sleep Abnormalities in Chronic Fatigue Syndrome
M. Eileen McNamara, M.D., Steven Sepe, M.D., Richard P. Millman, M.D., John J. Campbell, M.D., Barry S. Fogel, M.D.

NR559 Sleep Apnea: Hypoxia and Neuropsychologic Deficits
Alexandros N. Vgontzas, M.D., Ralph A.W. Lehman, M.D., Edward O. Bixler, Ph.D., Lynne D. Curran, B.A., Raymond P. Zarlengo, M.D.

NR560 Therapeutic Alliance and Psychiatric Emergency Room
Ronald C. Rosenberg, M.D., Martin Kesselman, M.D.

NR561 Measurements of Day Treatment Center Effectiveness
Mary Lou Edgington, RN.C., Eugene C. Somoza, M.D.

NR562 Effect of Crisis Intervention in Acute Psychiatry
Nageswara Rao Punukollu, M.B.

NR563 Mental Health Service Use Among Homeless Veterans
Peggy Gallup, Ph.D., Robert Rosenheck, M.D., Catherine Leda, M.S.N.

NR564 Gender and Homeless Mentally Ill
Paula N. Goering, Ph.D., Donald Wasylenki, M.D., Myreille St. Onge, M.Sc., Darianna Paduchak, B.A., William Lancee, M.Sc.

NR565 Use of Nationwide Registers in Predicting Admission After Childbirth
Marianne C. Kastrup, M.D.

NR566 Homeless Suburban State Hospital Admissions
Miklos F. Losonczy, M.D., Martin Darcy, M.S.W., Douglas Carbonara, Ph.D.

NR567 Deinstitutionalization by Law: Psychiatric Patients in Italy Before and After the Psychiatric Reform Act
Carlo A. Altamura, M.D., Gianluigi Tacchini, M.D., Santina Maggi, M.D., Anna M. Moroni, Ph.D., Antonio Musazzi, M.D.

NR568 DSM-III-R Disorders in Vietnamese Refugees
Joseph Chen, M.D., Walter Hinton, M.D., Nang Du, M.D., Carolee G. Tran, B.A., Francis Lu, M.D., Jeanne Miranda, Ph.D.

NR569 Medical Student's Attitudes on Public Psychiatry
Anthony L. Pelonero, M.D., William T. Ferriss, M.S.W.

Thursday, May 16, 1991, 9:00 a.m.-10:30 a.m.

New Research 11—Oral/Slide Session—Room 7, Level 2, Convention Center

MOOD DISORDERS

Chp.: Raymond Cohen, M.D.

NR570 Non-REM Sleep in Depression Studied with PET — 9:00 a.m.
Monte S. Buchsbaum, M.D., Andrew P. Ho, B.S., Christian J. Gillin, M.D., Joseph Wu, M.D., Stephen Lottenberg, M.D., William E. Bunney, M.D.

NR571 Opiate Receptors in Depression Measured with PET — 9:15 a.m.
Helen S. Mayberg, Robert F. Dannals, M.D., Chris A. Ross, M.D., Alan A. Wilson, Ph.D., Hayden T. Havert, Ph.D., J. James Frost, M.D.

NR572 G Proteins in Postmortem Brain in Bipolar Disorder — 9:30 a.m.
L. Trevor Young, M.D., Peter P. Li, Ph.D., Stephen J. Kish, Ph.D., Jerry J. Warsh, M.D.

NR573 Treatment of Hypertriglyceridemia and Depression — 9:45 a.m.
Robert L. Kunkel, M.D., Murray Tieger, Ph.D., Charles J. Glueck, M.D., Trent Tracy, P.A., James Speirs, B.A., Patricia Stricker, R.D.

NR574 Disorientation and Bilateral Suprathreshold-Dose ECT Treatment — 10:00 a.m.
Avraham Calev, Ph.D., Baruch Shapira, M.D., Bernard Lerer, M.D.

NR575 A New Flexible Method to Target Tricyclic Doses — 10:15 a.m.
William A. Kehoe, Pharm.D., Joseph A. Kwentus, M.D., Arthur F. Harralson, Pharm.D., John J. Jacisin, M.D., M.J. Hetnal, M.D., William B. Sheffel, M.A.

Thursday, May 16, 1991, 9:00 a.m.-10:30 a.m.

New Research 12—Oral/Slide Session—Room 9, Level 2, Convention Center

PERSONALITY, SUBSTANCE ABUSE, AND EATING DISORDERS

Chp.: Philip Muskin, M.D.

NR576 No Association Between DRD2 Allele and Alcoholism — 9:00 a.m.
Joel Gelernter, M.D., S. O'Malley, Ph.D., N. Risch, Ph.D., H. Kranzler, Ph.D., D. Grandy, Ph.D., O. Civelli, Ph.D., J. Krystal, M.D., K. Merikangas, Ph.D., J. Kennedy, M.D., K. Kidd, Ph.D.

NR577 Phenotypic Markers in Familial Alcoholism — 9:15 a.m.
Roberta M. Palmour, Ph.D., Andrew J.K. Smith, B.Sc., Jillian P. Parboosingh, B.Sc., Jordan Peterson, B.Sc., Robert O. Pihl, Ph.D.

NR578 Imipramine Treatment of Depressed Alcoholics — 9:30 a.m.
Patirck J. McGrath, M.D., Deberah Goldman, Ph.D., Edward N. Nunes, M.D., Frederic M. Quitkin, M.D., Jonathan W. Stewart, M.D., Ron Goldman, M.D.

NR579 Buprenorphine in Heroin Dependence Treatment — 9:45 a.m.
Richard B. Resnick, M.D., Marc Galanter, M.D., Noel Flood, R.N., Alise Cohen, M.S.W.

NR580 Phenelzine Versus Haloperidol in Borderline Personality — 10:00 a.m.
Jack R. Cornelius, M.D., Paul H. Soloff, M.D., Anselm W. George, M.D., James M. Perel, Ph.D., Richard F. Ulrich, M.S., Douglas Fitzgerald, M.S.

NR581 Tryptophan Depletion Alters Feeding in Bulimia — 10:15 a.m.
Theodore E. Weltzin, M.D., John D. Fernstrom, Ph.D., Walter H. Kaye, M.D.

NEW RESEARCH

Thursday, May 16, 1991, 12 noon-2:00 p.m.

New Research 13—Poster Session—Ballroom A, Level 1, Convention Center

AFFECTIVE DISORDERS

Moderator: Donald F. Klein, M.D.

NR582 Phenelzine Treatment of Melancholia
Michael H. Kronig, M.D., Patrick J. McGrath, M.D., John M. Kane, M.D., Frederic M. Quitkin, M.D., Karyl G. Cole, M.D., Jonathan W. Stewart, M.D., Delbert G. Robinson, M.D., Alfreda H. Howard, M.A., Sabina Meyer, B.S., Carmen Z. Lemus, M.D.

NR583 A Linkage Study of Bipolar Disorder and Distal 5q
Arvin L. Mirow, M.D., Paul Shilling, B.A., Sharon Hirsch, M.D., Helgi Kristbjnarson, M.D., Tomas Helgason, M.D., Janice Egeland, Ph.D., J. Christian Gillin, M.D., John R. Kelsoe, M.D.

NR584 Cerebral Volume is Reduced in Bipolar Disorder
Henry A. Nasrallah, M.D., Stephen C. Olson, M.D., Steve B. Schwarzkopf, M.D.

NR585 DST, TRH and Clonidine Tests in Psychiatry
Fabrice Duval, M.D., M-Claude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Juarez Oviveira Castro, M.D., Sergio Valdivieso, M.D., Jean-Paul Macher, M.D.

NR586 TRH-TSH Tests and Antidepressant Treatment Outcome
Fabrice Duval, M.D., M-Claude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Gabrielle Wagner, Sergio Valdivieso, M.D., Jean-Paul Macher, M.D.

NR587 WITHDRAWN

NR588 Verapamil Compared to Lithium in Acute Mania
Enrique S. Garza-Trevino, M.D., John E. Overall, Ph.D., Leo E. Hollister, M.D., William F. Alexander, M.D.

NR589 Seasons and Platelet 5HT Uptake: A Cohort Study
Jan L. Campbell, M.D., Thomas A. Kent, M.D., Barry I. Liskow, M.D., Barbara J. Powell, Ph.D.

NR590 The Cerebral Neurobiology of Hope and Hopelessness
Louis A. Gottschalk, M.D., Janny Fronczek, M.S., Lennart Abel, M.S., Monte Buschsbaum, M.D.

NR591 Phenylacetic Acid in Panic Disorder and Depression
Joseph J. Zealberg, M.D., R. Bruce Lydiard, M.D., James C. Ballenger, M.D., Michele T. Laraia, R.N., Hossein Ghanbari, Ph.D.

NR592 Interhemispheric Serotonergic Asymmetry in the Human Brain
Mihaly Arato, M.D., Kornelia Tekes, Ph.D., Laszlo Tothfalusi, Ph.D., Ede Frecska, M.D., Rick Guscott, M.D., J. Duncan Maccrimmon, M.D.

NR593 Therapeutic Efficacy of L-Thyroxine in PMS
Peter J. Schmidt, M.D., Gay N. Grover, M.S.N., Margaret F. Jensvold, M.D., David R. Rubinow, M.D.

NR594 WITHDRAWN

NR595 Alprazolam Treatment of Premenstrual Dysphoria
Rebecca Potter, M.D., Martha P. Fankhauser, M.S., Lynda Bologna, R.N., Judith Steward, R.N., Stephen Scheiber, M.D., Betty Jo Tricou, M.D.

NR596 Depression in Women After an Adverse Birth Outcome
Martha A. Teitelbaum, Ph.D., Karen Bouden, M.A., Ben Z. Locke, M.S.P.

NR597 Cross-Cultural Meaning of Somatic Symptoms in Depression
Albert Diefenbacher, M.D., Gerhard Heim, Ph.D., Martina Heiche

NR598 Depression, Compulsive Personality and Serotonin
Marc M. Ansseau, M.D., Benoit J. Troisfontaines, M.D., Patrick G. Papart, M.D., Remy Von Frenckell, Ph.D.

NR599 Flesinoxan, A 5-HT1A Agonist in Major Depression
Marc M. Ansseau, M.D., William R. Pitchot, M.D., Antonio M. Gonzalez Moreno, M.D., H. Hansennemichel, B.Sc., Patrick G. Papart, M.D., R. Van Der Hoop Gerritsen, M.D., L. Dianne Bradford, M.D.

NR600 Life-Events and Biological Markers of Depression
Marc M. Ansseau, M.D., Caroline Lamberty, B.Sc., Remy Von Frenckell, Ph.D., Patrick G. Papart, M.D., Marie-Anne Gerard, M.D., Jacques Wautry, B.Sc., Georges Franck, M.D.

NR601 Major Depression, Family Functioning and Recovery
Gabor I. Keitner, M.D., Christine E. Ryan, Ph.D., Ivan W. Miller, Ph.D., Nathan B. Epstein, M.D., Duane S. Bishop, M.D., Robert Kohn, M.D.

NR602 Major Depression and 12-Month Outcome
Gabor I. Keitner, M.D., Christine E. Ryan, Ph.D., Ivan W. Miller, Ph.D., William H. Norman, Ph.D.

NR603 Concurrent Panic Disorder and Major Depression
Leon J. Grunhaus, M.D., Atul C. Pande, M.D., Roger F. Haskett, M.D.

NR604 The Diagnosis of Major Depression by Self-Report
Scott Wetzler, Ph.D., Douglas B. Marlowe, M.A.

NR605 A Multicentre, Double-Blind, Randomized Study Comparing Paroxetine and Amitriptyline in Patients with Major Depression
V. Rapisarda

NR606 Echocardiographic Measures of the Safety of ECT
Anthony Messina, M.D., Mary Paranicas, B.A., Barri L. Katz, M.D., (presenter) John M. Markowitz, M.D., Richard Devereux, M.D.

NR607 ECT-Induced Cortisol Release in Melancholia
Conrad Swartz, M.D.

NR608 Prediction of Lithium and Other Drug Doses
Conrad Swartz, M.D.

NR609 Linkage Studies of the D2 Gene in Bipolar Families
John R. Kelsoe, M.D., Paul Shilling, B.A., Arvin Mirow, M.D., Sharon Hirsch, M.D., Helgi Kristbjnarson, M.D., Tomas Helgason, M.D., J. Christian Gillin, M.D., Janice Egeland, Ph.D.

NR610 Lithium and Sexual Function in Bipolar Patients
A. Missagh Ghadirian, M.D., Lawrence Annable, D.S., Guy Chouinard, M.D., Marie-Claire Belanger, R.N.

NR611 Abnormal Speech Articulation in Major Depression
Alastair J. Flint, M.D., Sandra E. Black, M.D., Irene Campbell-Taylor, Ph.D., Gillian F. Gailey, M.HSc., Carey Levinton, B.Sc.

NR612 Antidepressant Treatment of Double Depression
David J. Hellerstein, M.D., Phillip Yanowitch, M.D., Jesse Rosenthal, M.D., Camille Hemlock, M.D., Karen Kasch, B.A.

NR613 Reduced Seizure Potential in Animals and Reduced Incidence of Seizures in Depressed Patients During Treatment with the Selective Serotonin Re-Uptake Inhibitor Paroxetine
J.G.C. Rasmussen

NR614 The Potential Role of Antidepressants in the Precipitation of Mania
J.G.C. Rasmussen

NR615 Comparative Effects of Selective Serotonin Uptake Inhibitors Paroxetine and Fluoxetine on Food Intake in Rats and Effect of Paroxetine on Body Weight in Depressed Patients
J.G.C. Rasmussen

NR616 Paroxetine in the Treatment of Severe Melancholic Depression
G.C. Dunbar

NR617 Wellbutrin Blood Levels and Clinical Response
Paul J. Goodnick, M.D., Richardo Sandoval, M.D.

NR618 Light for SAD: How it is Used and Who Responds
Dan Oren, M.D., Frederick Jacobsen, M.D., Constance Carpenter, M.A., Christine L. Cameron, B.S., Thomas A. Wehr, M.D., Norman E. Rosenthal, M.D.

NR619 Fluoxetine Associated Sexual Dysfunction: Open and Placebo Controlled Trials of Treatment with Yohimbine
Frederick M. Jacobsen, M.D.

NR620 Effect of Phototherapy on 5-HT Metabolism in SAD
Attila Nemeth, M.D., Mihaly Arato, M.D., Erika Szadoczky, M.D., Annamaria Falus, Ph.D., Laszlo Tothfalusi, Ph.D., Rick Guscott, M.D.

NR621 Primary Care Depression: Psychotherapy or Drugs?
Christopher P. Freeman, M.B., Allan I. Scott, M.D.

NR622 A Study to Investigate the Efficacy, Adverse Events, Safety and Pharmacokinetic Effects of Co-Administration of Paroxetine and Lithium
G. Stellamans

NR623 A Double-Blind Multicentre Study Comparing Paroxetine with Fluoxetine in Depressed Patients
J. De Wilde

NR624 Methylphenidate Test in Depression: A Qualitative Study
Philippe Baruch, M.D., Roch H. Bouchard, M.D., Emmanuelle Pourcher, M.D., Alain Dion, M.D., Marie-Josee Filteau, M.D., Pierre Vincent, M.D.

NR625 Dysthymia: Response to Fluoxetine and Trazodone
Jesse S. Rosenthal, M.D., Camille Hemlock, M.D., David Hellerstein, M.D., Phillip Yanowitch, M.D.

NR626 The Prevalence of Post-Stroke Depression
Wayne A. Gordon, Ph.D., Mary R. Hibbard, Ph.D., Patricia L. Paddison, M.D., Paula N. Stein, Ph.D., Susan Grober, Ph.D., Martin Sliwinski

NR627 The Effect of Enalapril on Serum Lithium Levels
Krishna Dasgupta, M.D., James W. Jefferson, M.D., Kenneth A. Kobak, M.S.W., John H. Greist, M.D.

NR628 Sleep Deprivation May Alter Dopamine Activity
Kenneth N. Sokolski, M.D., Chris Reist, M.D., Evagelos Coskinas, M.D., Chen-Chung Chen, M.D., Edward M. Demet, Ph.D.

NR629 Platelet Imipramine Binding and Clinical Symptoms
David L. Knight, B.S., William McDonald, M.D., K. Ranga K. Krishnan, M.D., Charles B. Nemeroff, M.D.

NR630 Acceleration of Nortriptyline by Sleep Deprivation
Richard C. Shelton, M.D., Peter T. Loosen, M.D.

NR631 Serotonin Function and Antidepressant Action
Pedro L. Delgado, M.D., Dennis S. Charney, M.D., Helen Miller, M.D., Julio Licinio, M.D., Ronald Salomon, M.D., George Heninger, M.D.

NR632 Comorbidity of OCD and Bipolar Affective Disorder
Linda S. Austin, M.D., R. Bruce Lydiard, M.D., James C. Ballenger, M.D., Mark D. Fossey, M.D., Joseph J. Zealberg, M.D., Michele Laraia, M.S.N.

NR633 Self-Report of Mood in Post-Stroke Depression
Robert B. Fields, Ph.D., H. Jordan Garber, M.D., Ben Zimmer, M.D.

NR634 Comorbidity of Substance Abuse and Psychiatric Disorders
Kathleen R. Merikangas, Ph.D., Bruce Rounsaville, M.D.

NR635 Sex Difference in the Course of Depression
Kathleen R. Merikangas, Ph.D., Jules Angst, M.D.

NR636 Information Processing Deficits in Mania
Kirsten Fleming, Ph.D., Michael Green, Ph.D.

NR637 Clinical Utility of Subtyping Psychotic Depression
Raymond F. Anton, M.D., William Carson, M.D., Earl Burch, M.D.

NR638 Circadian Performance and Depressive Disorders
Lawrence J. Whalley, M.D., Patricia A. Shering, B.Sc., John Bennie, B.Sc.

NR639 The Evolution of Reactive Depression in the USSR
Flavio A. Poldrugo, M.D., Serge J.G. Obukhov, M.D.

NR640 Primary Care Depression: Personality and Outcome
Allan I. Scott, M.D., Christopher Freeman, M.B.

NR641 New Clinician-Administered Rating Scale for Mania
Edward G. Altman, Psy.D., Philip G. Janicak, M.D., James L. Peterson, B.S., Donald Hedeker, Ph.D., John M. Davis, M.D.

NR642 Cognitive Dysfunction in Late-Onset Depression
George S. Alexopoulos, M.D., Steven Mattis, M.D., Barnett S. Meyers, M.D., Robert C. Young, M.D., Janis Chester, M.D.

NR643 Disability and Environment in Late-Onset Depression
George S. Alexopoulos, M.D., Barnett S. Meyers, M.D., Robert C. Young, M.D., Janis Chester, M.D.

NR644 Neuroleptic-Induced Psychosis in Affective Disorders
John M. Downs, M.D., Hagop S. Akiskal, M.D., Anna D. Downs, Ph.D.

NR645 Seasonal Variation of Symptoms at 41 Degrees North Latitude
David S. Schlager, M.D., Joseph E. Schwartz, Ph.D., Lisa Brandon, B.S., Evelyn J. Bromet, Ph.D.

NR646 Auditory Dysfunction and Late-Onset Depression
Balu Kalayam, M.D., Tatsu Kakuma, Ph.D., Robert Young, M.D., Gabriel Tsuboyama, M.D.

NR647 Suicidal Thoughts and Behavior with Paroxetine
S. Mewett

NR648 Neurobiology of Early-Life Trauma in Depression
Christopher J. McDougle, M.D., Lisa Calvocoressi, John P. Seibyl, M.D., John H. Krystal, M.D., George R. Heninger, M.D., Lawrence H. Price, M.D.

NR649 Fluoxetine in Major Depressives With or Without History of Suicidality
Emilio Sacchetti, M.D., Alessandra Alciati, M.D., Alessandro Calzeroni, M.D., A. Pennati, M.D., A. Terzi, M.D., L. Guarneri, M.D., P. Bartoli, M.D.

NR650 A Dose-Response Curve for ECT Outcome Prediction
Stephen I. Kramer, M.D.

NR651 Serotonergic Function in Lithium Augmentation
Elinore McCance-Katz, M.D., Lawrence H. Price, M.D., Dennis S. Charney, M.D., George R. Heninger, M.D.

NR652 Folate and B12 Concentration in Manic Depressive Outpatients Treated with Lithium
Pablo Cervantes, M.D., A. Missagh Ghadirian, M.D., Stephan Vida, M.D., Michel Paradis, M.D., Irena Straszak, M.D.

NR653 Trimipramine Versus Doxepin Cardiac Safety in Elderly Depressives
N. P. Vasavan Nair, M.D., Mohamed Amin, M.D., Ramzy Yassa, M.D., George Schwartz, M.Sc., Joseph Thavundayil, M.D., Carolyn McDonald, B.Sc.

NR654 SAD: Circadian Effects of Midday Light Exposure
Janis L. Anderson, Ph.D., Anna Wirz-Justice, Ph.D., Edith Holsboer-Trachsler, M.D., Hans-Joachim Haug, M.D., Thomas Bruehl, M.D., Kurt Kraeuchi, Dr. Peter Van Der Velde, Gabi Moll, Charles A. Czeisler, M.D.

NR655 Depression Severity Predicts Medical Disability
Mark D. Sullivan, M.D., Wayne J. Katon, M.D., Robert A. Dobie, M.D., Joan Russo, Ph.D., Connie S. Sakai, M.S.

NR656 Nicotine Use High in Dysthymia or Major Depression
Cynthia M. Churchill, M.D., Chris N. Larson, M.D., Stephen F. Pariser, M.D., Steven C. Dilsaver, M.D.

NR657 Light Exposure at Birth and Later Suicide Risk
Paul A. Kettl, M.D., Tracey Collins, M.D., Michelle Sredy, B.S., Edward O. Bixler, Ph.D.

NR658 Ethnic Differences in Nortriptyline Metabolism
Lon Schneider, M.D., Sonia Pawluczyk, M.D., Julie Dopheide, Pharm.D., Scott A. Lyness, M.A., Raymond F. Suckow, Ph.D., Thomas B. Cooper, M.A.

NR659 Delusional Thinking and Suicide Attempts in Major Affective Disorders
Alessandra Alciati, M.D., Emilio Sacchetti, M.D., Alessandro Calzeroni, M.D., A. Pennati, M.D., A. Terzi, M.D., L. Guarneri, M.D.

NR660 Urinary Catecholamines and Cortisol in Suicide
Gregory Brown, M.D., Catherine Mancini, M.D.

NR1 Monday May 13, 9:00 a.m.-10:30 a.m.

Gender Differences in Schizophrenia

Ana Maria Andia, M.D., Psychiatry/Outpatient, Univ of California, 3427 Fourth Avenue, San Diego, CA 92103; Sidney Zisook, M.D., David L. Braff, M.D., John T. Moranville, M.D., Robert Heaton, Ph.D.

Summary:

Gender is an important risk factor for schizophrenia, with lower prevalence rates and a later age of onset in females. Women have been reported to have more first-rank symptoms but better coping and social skills, and are generally noted to recover more fully and be more functional. Premenopausal women respond to lower doses of neuroleptics than men or postmenopausal women. There remains great controversy concerning gender differences in brain morphology and cognitive performance. This report assesses differences between 40 male and 21 female schizophrenics who are part of an outpatient longitudinal study. The women are older by five years and have two more years of education. Thirteen percent of the women are married as compared with 2% of the men. Only 35% of the women are unemployed in contrast to 65% of the men. Despite being prescribed five times lower doses of neuroleptics, women are no different from men in positive, negative or total symptom intensity. MRI scans reveal structural brain abnormalities in a majority of subjects (women = 64%, men = 54%). While neurocognitive impairment is widespread, there are no gender differences on WAIS subscales or global impairment ratings. Potential mechanisms and clinical implications of the gender differences will be discussed.

NR2 Monday May 13, 9:00 a.m.-10:30 a.m.

Glutamate Receptor Gene Expression in Kindling

Ma-Li Wong, M.D., Department of Psychiatry, West Haven VAMC, 950 Campbell Avenue, West Haven, CT 06516; Susan R.B. Weiss, M.D., Mark Smith, M.D., Phillip W. Gold, M.D.

Summary:

The encoding processes for learning and memory involve synaptic changes that persist for several days. This process, known as long-term potentiation (LTP), is thought to underlie cognitive processes, such as memory. The activation of N-methyl-D-aspartate (NMDA), a glutamate receptor, is essential for the initiation of LTP. The phencyclidine receptor is a subunit of the NMDA receptor complex. As phencyclidine can induce a chronic psychotic state similar to schizophrenia, it is hypothesized that abnormalities in the NMDA receptor complex may be of importance in the pathophysiology of schizophrenia. We have utilized kindling, an enduring neuronal model of memory, to study the expression of a kainate receptor (a subtype of glutamate receptor) gene in rat brain utilizing *in situ* hybridization histochemistry with 35-S-dATP labelled oligodeoxynucleotide probes. Sections were apposed to films, and the autoradiographic images were quantified. We report a transient inhibition of kainate gene expression following kindling (ANOVA, $p<0.05$). This finding confirms the hypothesis that glutamate receptors may be involved in brain changes related to neuronal memory. Further studies are needed to clarify the role of glutamate receptors in cognitive disorders such as schizophrenia.

NR3 Monday May 13, 9:00 a.m.-10:30 a.m.

Neurocognitive Components of Chronic Schizophrenia

Abraham Fiszbein, M.D., Psychiatry, Albert Einst. Col of Med., 3411 Wayne Avenue, Apt. 12-D, Bronx, NY 10467; Lewis A. Opler, M.D., Stanley R. Kay, Ph.D. (Posthumously), Carl E. Rosenkilde, M.D., Paul M. Ramirez, Ph.D., Julio Moizeszowicz, M.D., Amy S. Gorelick, M.D.

Summary:

We developed a battery of neurocognitive tests in an effort to clarify the diverse neuropsychological abnormalities in schizophrenia. A sample of 42 neuroleptic-treated, chronic schizophrenic inpatients (29 males and 13 females, mean age 35.9 years and mean duration of illness 3 years) were examined on this battery and on a series of independent, clinical, psychometric, and historical variables. From a principal component analysis of the neurocognitive battery, six orthogonal factors emerged that reflected different facets of the schizophrenic disorder: stimulus processing, hyperarousal, negative syndrome, ontogenic variables, general intelligence, and autism. Multiple regression analysis indicated that these factors are associated with separate sets of criterion variables. This suggests that the six neurocognitive components may reflect the heterogeneity of schizophrenia, which is manifested in different types of neuropsychological consequences. Of particular interest was the emergence of neurocognitive factors that (a) relate to positive vs. negative symptom profiles and (b) are consistent with both the developmental and information processing models of cognitive disorder. Our findings thus suggest that the emergent neurocognitive components derive from independent dysfunctions in schizophrenia.

NR4 Monday May 13, 9:00 a.m-10:30 a.m.

Schizophrenia Candidate Gene Association Study

Alan R. Sanders, B.S., Department of Psychiatry, Baylor College of Med., Box 300982, Houston, TX 77230; Joseph D. Hamilton, II, M.D., William E. Fann, M.D., Pragna I. Patel, Ph.D.

Summary:

There is growing evidence that some genetic predisposition is important in the etiology of schizophrenia. Our laboratory has undertaken a search for a major gene by performing a candidate gene association study comparing the allele frequencies of seven restriction fragment length polymorphisms (RFLPs) at six loci in both a psychiatrically normal control group ($N=51$) and an affected (schizophrenia or schizoaffective disorder) group ($N=55$). Each group was comprised of Caucasians of northern European origin. The candidate areas selected — D5S39, D5S78, dopamine receptor D2 (DRD2), D11S29, porphobilinogen deaminase (PBGD), and D11S84 — were based on prior cytogenetic findings in schizophrenia, linkage studies, and/or implicated gene products. The PBGD MspI 2.2-kbp allele (A2) showed a highly significant association with the presence of illness ($P = 0.00048$). The relative risk of possessing the A2 allele was 2.18, and the A2A2 genotype imposed a higher risk for affection than the A1A2 genotype. Increased severity of illness as indicated by earlier age of onset ($\leq$ 30 years old) was associated with the A2A2 genotype ($P=0.019$). No significant associations were found with the six other RFLPs. Our data suggest that the PBGD gene itself or an unknown gene tightly linked to and in linkage disequilibrium with the PBGD locus predisposes some individuals to schizophrenia.

NR5 Monday May 13, 9:00 a.m.-10:30 a.m.

Neuropathology in Schizophrenia: An MRI Study

Laura Marsh, M.D., Clinical Brain Disorders, NIMH Neuroscience Ctr, 2700 MLK Jr. Ave., SE, Washington, DC 20032; Godfrey D. Pearlson, M.B., Stephanie Richards, B.A., Patrick E. Barta, M.D.

Summary:

Experimental methods used to investigate the neuropathology

of schizophrenia might be integrated by replicating the morphometric methods used in both postmortem and neuroimaging studies. Using MRI, we attempted to replicate the postmortem brain measurements reported by Brown et al. (1986) in which schizophrenic (SCZ) subjects had enlarged anterior and temporal horns of the lateral ventricles and reduced coronal brain area and parahippocampal width, especially on the left, compared with patients with affective disorder (AD).

In this study, a 3mm coronal MRI slice, located identically to that in the Brown et al. study, was used to compare brain areas between SCZ (N = 40) and AD (N = 16), plus normal controls (N = 43). Compared to normals (N), SCZ had smaller areas of coronal brain and both temporal lobes and enlarged left lateral sulci. SCZ had reduced coronal brain and right temporal lobes compared with all AD and smaller right parahippocampal area compared to nonpsychotic AD (N = 13). AD had increased right temporal horn and decreased right insula/brain area compared with N and SCZ.

This MRI study supports postmortem evidence of structural brain changes, especially of the temporal lobe, in schizophrenia. Although we did not replicate the same changes or lateralized results of the postmortem study, in both studies parahippocampal pathology is implicated as possibly pathogenically important. Additional subjects are currently being analyzed for this study. The limitations of interpreting measurements obtained from a single coronal slice must also be considered.

NR6 Monday May 13, 9:00 a.m.-10:30 a.m.

Eye Tracking, CPT and Schizotypal Traits in Relatives of Schizophrenics

Richard Keefe, Ph.D., Psychiatry, Mount Sinai School of Med, One Gustav L. Levy Place, New York, NY 10029; Jeremy M. Silverman, Ph.D., Jackie Moskowitz, Ph.D., Philip D. Harvey, Ph.D., Lee Friedman, Ph.D., Larry J. Siever, M.D.

Summary:

The biological relatives of schizophrenics demonstrate increased prevalence of schizotypal traits, eye tracking deficits and continuous performance test (CPT) deficits, suggesting that these factors may be associated with a schizophrenia-related gene or genes. Previous research from our center suggests that eye tracking and backward masking tasks discriminate schizophrenics from normal controls, yet they do not contribute significant discriminating variance independent of CPT deficits. The current study assesses the independence of these deficits and the association of deficits with schizotypal traits as measured by the Chapman perceptual aberration and social anhedonia scales in a sample of 43 nonpsychotic first-degree relatives of schizophrenic probands and 22 normal controls. Relatives produced significantly worse eye tracking qualitative ratings (p.001) and made more CPT errors of commission in degraded and undegraded conditions ($p < .05$). Backward masking performance did not differ significantly between groups. In multiple regression analysis, independent discriminating variance between normals and relatives beyond general intelligence was accounted for by eye tracking qualitative ratings ($r^2 = 8.6$, $p < .05$) and CPT errors of commission ($r^2 = 6.3$, $p < .05$). Perceptual aberration scores were correlated with CPT errors of commission ($r = .37$, $p < .05$) and errors of omission ($r = .53$, $p < .005$). The data from this study suggest that, in contrast to findings in schizophrenics, the neurocognitive deficits reflected by poor eye tracking and CPT performance in relatives may be independent, and that CPT deficits may be related to schizotypal personality traits in relatives.

NR7 Monday May 13, 9:00 a.m.-10:30 a.m.

An Eight-Year Follow-Up of DSM-III-R Major Psychoses

Debby W. Tsuang, M.D., Department of Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; William H. Coryell, M.D.

Summary:

A review of medical records at the University of Iowa Psychiatric Hospitals between 1979 and 1982 identified 91 inpatients with functional psychoses. Seventy-one were located and personal interviews conducted eight years later. A rater, blind to the follow-up data, rediagnosed the index admission using DSM-III-R criteria. Baseline diagnosis was a powerful predictor of outcome. Of the 17 patients with baseline diagnosis of major depression with mood-congruent psychotic features, 10 (58.8%) were free of psychosis with insight, whereas four out of 15 patients (26.7%) with major depression with mood-incongruent psychotic features had recovered. In contrast, none of the 11 patients with schizoaffective disorder and none of the 22 patients with schizophrenia were judged to be recovered (Fisher's exact test over the four diagnostic groups, $p < 0.001$). Patients with major depression were significantly more likely to be free of psychosis than patients with schizophrenia at follow-up. Results showed no outcome differences, either in recovery or social/occupational status, between schizoaffective disorder and schizophrenia patients.

NR8 Monday May 13, 9:00 a.m.-10:30 a.m.

Clinical Study of Kraepelinian Schizophrenia

Ede Frecska, M.D., Department of Psychiatry, Bronx VA Medical Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Richard Keefe, Ph.D., Seth Apter, M.A., Michael Davidson, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

Summary:

Based on Emil Kraepelin's original description, our research center has developed operationalized criteria for defining a group of very poor outcome schizophrenic patients. Severely deteriorated schizophrenic patients, who for five years prior to evaluation were either continuously hospitalized or completely dependent on others for food, clothing and shelter are designated "Kraepelinians." In an extensive study, descriptive clinical and noninvasive biological measures have been used for the validation of this classification. This poster presents data on the clinical validators. Twenty-nine Kraepelinian patients were compared with 84 acutely exacerbated chronic schizophrenics by seven diagnostic systems. Descriptive measures such as severity of positive and negative symptoms, thought disorder, and response to neuroleptic treatment were assessed by items on the BPRS, SANS, TLC, and a standardized haloperidol protocol, respectively. Kraepelinian patients were 100% positive for schizophrenia by the three major diagnostic systems (RDC, DSM-III-R, ICD-9). None were schizoaffective, while eight schizoaffectives were found among the other chronic schizophrenic patients ($p < 0.1$). Kraepelinians exhibited more severe negative symptoms ($p < 0.05$), more formal thought disturbances ($p < 0.001$), and less of a prospective response to a standard dose of haloperidol. Severity of positive symptoms did not distinguish Kraepelinian schizophrenic patients from acutely exacerbated chronic schizophrenic patients. These analyses help support the assumption that certain schizophrenics, who resemble Emil Kraepelin's dementia praecox patients, represent a more homogeneous subgroup of schizophrenia than other chronic schizophrenic patients.

NR9 Monday May 13, 9:00 a.m.-10:30 a.m.

Family History of Kraepelinian Schizophrenia

Jeremy M. Silverman, Ph.D., Department of Psychiatry, Bronx VA Medical Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Ede Frecska, M.D., Richard Keefe, Ph.D., Michael Davidson, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

Summary:

We have previously reported an increased morbid risk (MR) for schizophrenia-related (SR) disorders in a group of a very poor outcome schizophrenic patients, called "Kraepelinian," compared with other chronic schizophrenic patients. Using the same operationalized criteria for Kraepelinian schizophrenia, i.e., RDC or Feighner criteria for chronic schizophrenia and either continuous hospitalization or full dependency on others for food, clothing and shelter for at least the past five consecutive years, we have now investigated the MR for SR disorders in 350 first-degree relatives of an independent series of Kraepelinian and non-Kraepelinian chronic schizophrenic probands using family history methodology identical to the earlier sample. Blind, telephone family history interviews with multiple informants were conducted using full Family History RDC criteria as well as supplementary criteria for schizophrenia related personality (SRP; derived from DSM-III criteria for schizotypal personality disorder) to assess every first-degree relative of 18 Kraepelinian and 46 non-Kraepelinian chronic schizophrenic probands. As observed in the previously investigated sample, the age-corrected MR for SR disorders (including chronic schizophrenia, chronic schizoaffective disorder and SRP) was significantly higher in the 97 relatives of the Kraepelinian probands (MR = .333) compared with the 253 relatives of the non-Kraepelinian schizophrenic probands (MR = .152; $p < .01$). The current sample was then combined with the earlier sample to assess the specificity of the increased familial loading in Kraepelinian schizophrenia. While the MR for SR disorders was increased ($p < .01$) in the 184 relatives of the combined sample of 36 Kraepelinians (MR = .24) compared to the risks for combined sample of 603 relatives of the 115 non-Kraepelinian schizophrenic probands (MR = .13), the MRs for no other diagnostic category, including the major affective, alcohol and substance abuse disorders, similarly differentiated these two groups of schizophrenic patients. These data provide further support for a subgroup of very poor outcome schizophrenia patients with an increased familial loading for the SR disorders. Furthermore, they suggest that the increased risk to these relatives is specific for these disorders.

NR10 Monday May 13, 9:00 a.m.-10:30 a.m.

Identifying the Schizophrenia-Related Phenotype

Jeremy M. Silverman, Ph.D., Department of Psychiatry, Bronx VA Medical Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Larry J. Siever, M.D., Lynn Pinkham, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

Summary:

Linkage studies of schizophrenia require the accurate identification of a schizophrenia-related (SR) phenotype. Although the assessment of schizotypal personality disorder (SPD) may augment the "informativeness" of a schizophrenic proband's family, genetic epidemiological evidence suggests that SPD may lack specificity for schizophrenia. Recent high-risk-offspring and adoption studies have indicated an increased prevalence of SPD in relatives of major affective disorder patients as well as in relatives of schizophrenia patients. In addition, the psychotic-like and social deficit symptoms associated with SPD are common in patients with borderline personality disorder (BPD), a disorder with no familial relationship to schizophrenia and characterized in part by affective personality disorder traits (APD). This suggests that psychotic-like traits associated with APD may satisfy currently defined SPD criteria, but nevertheless represent a variant of BPD with psychotic-like symptoms unrelated to schizophrenia. In contrast, SPD with no comorbid APD, may be more specifically related to schizophrenia. We tested these hypotheses using blind family history interviews to assess FHx criteria for schizophrenia-related personality (SRP) and APD traits (similar to SPD and BPD traits, respectively) in 404 age-corrected relatives of schizophrenic, BPD and "other" (i.e. neither BPD nor SPD) PD probands. The risk for concurrent SRP and APD was 8.7% among relatives of BPD probands, significantly higher than the 2.2% ($p < .01$) in the relatives of schizophrenic probands and 1.4% ($p < .05$) in those of OPD probands. In contrast, the morbid risk for SRP with no co-morbid APD was 14.7% in the relatives of schizophrenic probands, significantly higher than the 4.9% risk ($p < .01$) in the relatives of BPD probands or 2.9% risk ($p < .01$) in the relatives of OPD probands. These results have implications for those genetic linkage studies of schizophrenia assessing SPD in family members. Current criteria for SPD may identify psychotic-like and social deficit symptoms that are not genetically related to schizophrenia. Excluding affective-related SPD features may more accurately identify an SR phenotype.

NR11 Monday May 13, 9:00 a.m.-10:30 a.m.

Effects of Monoaminergic Agents in Schizophrenia

David G. Daniel, M.D., NRH, NIMH, 2700 MLK Jr. Ave., SE, Washington, DC 20032; Nancy Breslin, M.D., James A. Clardy, A. Abi-Dargham, J. Linnoila, M.D., Daniel R. Weinberger, M.D.

Summary:

We have conducted double-blind, placebo-controlled, randomized crossover studies of the effects of apomorphine, amphetamine, L-dopa, and fluvoxamine on clinical ratings, cognitive function, and regional cerebral blood flow (rCBF) measurement (XE-133 dynamic SPECT) performed during a prefrontal activating paradigm (WCS). Fluvoxamine (a selective inhibitor of presynaptic serotonin reuptake) was studied because under certain experimental conditions, the activity of serotoninergic and dopaminergic systems appear to be related. Apomorphine increased relative prefrontal rCBF during performance of the WCS in each patient with chronic schizophrenia (N = 6). Whereas activation of rCBF during performance of the prefrontal activation paradigm appeared disorganized and random on placebo, with amphetamine (N = 10) and L-dopa (N = 7) the activation pattern was relatively focused in the anterior frontal cortex and suppressed elsewhere. The results are consistent with animal studies suggesting that dopaminergic agents improve signal to noise in the cortex, and with human evidence that dysregulation of mesocortical dopamine activity plays a role in metabolic hypofrontality in schizophrenia. None of the agents produced statistically significant changes in clinical or cognitive ratings in the group as a whole, although in the L-dopa study four patients demonstrated clinically meaningful improvement in positive or negative symptoms. Additional patients are enrolled in the L-dopa, amphetamine, and fluvoxamine studies.

NR12 Monday May 13, 9:00 a.m.-10:30 a.m.

Selegiline in the Treatment of Akathisia

William C. Wirshing, M.D., Department of Psychiatry, West Los Angeles VAMC, 11301 Wilshire Blvd., Los Angeles, CA 90073; Donna Ames, M.D., Theodore Van Putten, M.D., Stephen R. Marder, M.D., George Bartzokis, M.D., Jeffrey L. Cummings, M.D.

Summary:

Eight schizophrenic patients with treatment-unresponsive akathisia were treated, open label, with 5mg bid of selegiline — a selective and irreversible inhibitor of MAO-B — for one week. Medications were unchanged during the week prior to and throughout the trial. Subjects had their psychiatric symptoms evaluated three times in the week before and during the trial with the Brief Psychiatric Rating Scale (BPRS) and had their extrapyramidal complaints measured with both the Barnes Akathisia Scale (BAS) and a specially designed sway platform that measures and records movement of the lower extremities. During the week on selegiline, no subject had any adverse reaction, and there were no significant changes on the BPRS (although the depression, tension, and posturing items showed a trend toward improvement). On the BAS, six of the eight subjects showed improvement on both subjective

distress (mean 2.8 before vs. 1.95 after, $p = 0.05$) and objective manifestations (mean 1.9 before vs. 1.5 after, $p = 0.08$). The sway platform data mirrored these results with a decrease in the energy of the lower extremity movements in the 0.5 - 2 Hz range (typical of akathisia movements) during the week on selegiline. We speculate that selegiline's apparent antiakathisic effect is mediated by either augmentation of dopaminergic transmission or by a reduction in the neuroleptic-related generation of neurotoxic free radicals.

NR13 Monday May 13, 9:00 a.m.-10:30 a.m.

Fluoxetine and Suicidality: A Consequence of Akathisia

William C. Wirshing, M.D., Department of Psychiatry, West Los Angeles VAMC, 11301 Wilshire Blvd., Los Angeles, CA 90073; James Rosenberg, M.D., Theodore Van Putten, M.D., Stephen R. Marder, M.D.

Summary:

Fluoxetine is a potent blocker of serotonin reuptake and has, in recent years, been widely used in the treatment of a variety of mood-based psychiatric syndromes. While it has a relatively benign side effects profile, it has been reported to induce severe suicidal ideation in a small subset of patients. In a case series of five patients treated with fluoxetine (20 mg-40 mg), we have observed the development of agitation, restless motor movement, dysphoria, pacing, an internal sense of desperation, and suicidal ideation. All subjects were female; none had a history of clinically significant suicidal ideation; all described their distress as an intense and novel emotional state; all experienced the suicidal thoughts at the peak of their restless agitation; and all had their agitation, restlessness, and suicidality remit after the fluoxetine was discontinued. Two subjects had symptomatic improvement with concomitant benzodiazepines, and a third had a return of the entire symptom complex upon rechallenge with fluoxetine. In these subjects the fluoxetine apparently caused akathisia, and this profoundly uncomfortable condition led them all to contemplate suicide. This case series suggests that fluoxetine-induced akathisia can lead to suicidal ruminations and that this state might be amenable to conventional antiakathisic regimens (e.g. anticholinergic, antiadrenergic, gabaergic, dopaminergic).

NR14 Monday May 13, 9:00 a.m.-10:30 a.m.

Multidimensional Analysis of CSF Amines in Schizophrenia

Fuad Issa, M.D., NPB-NIMH Neuroscience Ctr, St. Elizabeths Hospital, 2700 MLK Jr. Ave., SE, Washington, DC 20032; Darrell G. Kirch, M.D., Greg A. Gerhardt, Ph.D., Richard L. Suddath, M.D., Robert Freedman, M.D., Richard Jed Wyatt, M.D.

Summary:

An extensive study of the cerebrospinal fluid of schizophrenic patients and normal controls was performed. Twenty-one different biogenic amines, metabolites, and related compounds were simultaneously measured using a gradient high pressure liquid chromatography (HPLC) system coupled with a 16-channel coulometric electrochemical array system (CEAS, ESA Inc.). The statistical analysis comparing the group of drug-free schizophrenics ($n = 30$) with the normal controls ($n = 13$) using a t-test showed lower kynurenine (schizophrenics 5.3 ng/ml, controls 11.3 ng/ml, $p = 0.02$), higher tryptophan ($p = 0.02$) and a strong trend toward higher 5-hydroxytryptophan ($p = 0.06$) in the schizophrenic group. Otherwise no significant differences ($p < 0.05$) were seen. Twelve of the schizophrenic patients were studied on and off neuroleptic treatment and compared using matched-pairs t-tests. While drug-free, the patients had higher MHPG ($p = 0.04$), lower 5-hydroxytryptophan ($p = 0.04$) and a trend toward lower tyrosine ($p = 0.10$). Kynurenine was not significantly different in this matched-pairs analysis. No significant correlations were seen between global psychopathology ratings and the amine concentrations and, as expected, there were significant intercorrelations both within and between neurotransmitter systems. The multidimensional analysis allows the simultaneous studying of several biogenic amine pathways in the brain. The above results support the role of the noradrenergic system in schizophrenia. They also indicate that the kynurenine pathway of tryptophan metabolism might play a role in schizophrenia similar to what has been observed in Huntington's and Alzheimer's diseases.

NR15 Monday May 13, 9:00 a.m.-10:30 a.m.

Psychomotor/Psychosensory Symptoms in Psychiatric Patients

Nutan Atre-Vaidya, M.D., Department of Psychiatry, UHS/ Chicago Medical Sch., 3333 Green Bay Road, North Chicago, IL 60064; V. Chowdary Jampala, M.D., Chandra Vedak, M.D., Rukhsana Khan, M.D., Michael Alan Taylor, M.D.

Summary:

Psychiatric symptoms frequently accompany epileptic disorders. Schizophrenic-like psychosis and depression are most commonly diagnosed. Bipolar disorders have, however, also been associated with epilepsy. Unfortunately, similar attention has not been given to epileptoid symptoms in psychiatric patients, and there are very few studies in which the presence of psychosensory/psychomotor symptoms have been systematically studied in psychiatric, particularly bipolar, patients.

We evaluated 22 outpatients and 36 inpatients for the presence of psychomotor/psychosensory symptoms. Psychosensory symptoms were assessed using POPS (Profile Of Psychomotor symptoms), and psychopathology was assessed using the SANS, SAPS, and Emotional Blunting Scale. We further divided the POPS scale into Classic Psychiatric and Epileptoid subscales. Total epileptoid score was highly correlated with total SAPS score in outpatients ($r = .53$, $p = .05$) and inpatients ($r = .53$, $P = .00$). In addition, among the inpatients, the total affective score was also highly correlated ($r = .30$, $p = .03$) with the total epileptoid score, while among outpatients, recent but not past epileptoid score was highly correlated to past mania ($r = .46$, $p = .01$). These findings suggest that the presence of epileptoid symptoms reflects limbic disturbance that may be related to either current depressive and psychotic symptoms or past manic symptoms.

NR16 Monday May 13, 9:00 a.m.-10:30 a.m.

Serotonin Dysfunction in Schizophrenia

Naveed Iqbal, M.D., Psychiatry, Montefiore Medical Center, 111 East 210th Street, Bronx, NY 10467; Gregory Asnis, M.D., Scott Wetzler, Ph.D., R. S. Kahn, M.D., B. J. Schwartz, M.D., Herman M. van Praag, M.D.

Summary:

The present study investigated the serotonin (5 hydroxytryptamine, 5HT) receptor sensitivity of schizophrenic patients. m-Chlorophenylpiperazine (MCPP), a selective 5HT agonist, was administered in a placebo-controlled double-blind design to male schizophrenic patients ($n = 7$) and normal male controls ($n = 8$) in an oral dose of 0.25 mg/kg. Behavioral (Positive and Negative Syndrome Scale; PANSS) and hormonal (cortisol, prolactin) variables were measured over the subsequent 210 minutes. The schizophrenic patients experienced an overall exacerbation of psychopathology on MCPP as compared with placebo ($p < 0.05$), with specific worsening of PANSS positive symptoms ($p < 0.025$) and PANSS activation ($p < 0.001$). In addition, the schizophrenic patients

showed significantly lower cortisol ($p < 0.05$) and prolactin ($p < 0.05$) responses than the normal subjects. The schizophrenic patients had lower peak MCPP blood levels than did the normal subjects, although this difference was not statistically significant. The increased behavioral response might be indicative of a 5HT receptor hypersensitivity, whereas the blunted hormonal response might be indicative of a 5HT receptor hyposensitivity. Although the hormonal and behavioral dissociation needs further evaluation it is supportive of a 5HT receptor dysfunction in schizophrenic patients.

NR17 Monday May 13, 9:00 a.m.-10:30 a.m.

Cardiolipin Antibodies in Schizophrenic Patients

Kadiamada N.R. Chengappa, M.D., Psychiatry, WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213; A. Bettes Carpenter, Ph.D., Z.W. Yang, Ph.D., R.H. Kelly, Ph.D., B.S. Rabin, M.D., R. Ganguli, M.D.

Summary:

We have previously reported that schizophrenic patients demonstrate antibodies to brain, though the target antigens remain elusive. Recently, membrane phospholipid abnormalities were reported in the frontal lobe of drug-naive, first-episode schizophrenic patients. To determine if phospholipid antibodies play a role in the pathogenesis of schizophrenia, we determined the prevalence of IgG and IgM cardiolipin antibodies in drug-naive and medicated patients.

Sera from 79 RDC schizophrenic patients (18 were first-episode, drug-naive) and 85 age- and sex-matched controls were screened for anticardiolipin antibodies (ACA) using an enzyme-linked immunoassay (ELISA). Excluded were those with conditions known to raise ACA.

Thirteen patients (16.5%) had raised IgG-ACA compared with four controls (4.7%) [$X^2 = 6.08$, $P = 0.01$]. Nine (12%) patients had raised IgM-ACA compared with two controls (2.7%) [$X^2 = 4.71$, $P = 0.03$]. Three first-episode, drug-naive patients had raised IgG-ACA and IgM-ACA. The raised IgM-ACA (but not IgG-ACA) was associated with neuroleptic treatment ($p = 0.01$). These observations suggest that IgG-ACA may be a marker of autoimmune reactivity or may play a direct role in altered phospholipid metabolism in schizophrenia.

NR18 Monday May 13, 9:00 a.m.-10:30 a.m.

Congenital Brain Anomalies in Psychosis Versus Controls

George J. Jurjus, M.D., Department of Psychiatry, Ohio State University, 473 W. 12th Avenue, Columbus, OH 43210; Henry A. Nasrallah, M.D., Martha A. Brogan, M.D., Stephen C. Olson, M.D., Steve B. Schwarzkopf, M.D.

Summary:

Many of the structural brain abnormalities found in schizophrenia (SC) and bipolar disorder (BD) over the past decade are believed to reflect impaired neurodevelopmental processes: Therefore, we hypothesized that congenital anomalies may be more frequently present in the brains of subjects with SC and BD compared with healthy controls.

The MRI scans of 167 subjects (SC = 67, BD = 63, controls = 37) were systematically assessed by a neuroradiologist blind to the diagnosis, for the presence of 23 congenital anomalies involving cortical and subcortical structures. Recruitment into the study excluded subjects with medical and neurological illness or substance abuse. No differences were noted among the groups for the total number of congenital anomalies (SC: 34% BD: 31%, controls 27%). No differences were found between SC paranoid (33%) and nonparanoid (26%) subtypes, or between all males (32%) and all females (27%). None of the specific anomalies was overrepresented in any diagnostic group.

Our data suggest that although certain neuroanatomical abnormalities in SC are attributed to disruption of normal brain development this does not imply that there is a general excess of congenital anomalies in schizophrenia and bipolar disorder compared with controls. The implications of these findings for the neurodevelopmental hypothesis of schizophrenia are discussed.

NR19 Monday May 13, 9:00 a.m.-10:30 a.m.

The Scale of Questions and Investigations of Restless Movements: A Scale for the Treatment of Akathisia

John Lauriello, M.D., Department of Psychiatry, Univ. of CA –San Diego, 9500 Gilman Drive, La Jolla, CA 92093; Peter Weiden, M.D., Andrew Leon, Ph.D.

Summary:

Introduction: The Scale of Questions and Investigations of Restless Movements (S.Q.I.R.M.) studies akathisia treatment response. We subjected the scale to tests of reliability, validity and then compared its measurements to clinical assessment.

Methods: 24 of 27 patients treated for suspected neuroleptic-induced akathisia were followed using the scale for three days.

Results: Interrater reliability showed both initial subjective and objective kappas were 1.00 and the final subjective and objective kappas were .46 and .60, respectively. Internal consistency for both the subjective and objective ratings (R squares) ranged from .61 to .96. Criterion validity, as measured by correlation analysis, yielded a poor –.06 result. Predictive validity showed prediction by the objective rating of the feet $p = .01$ and both the subjective and objective ratings of the trunk .03 and .01, respectively. Akathisia treatment outcome, rated by the patient's clinician, showed 39.4% improved after 72 hours compared with 28% improved, measured by the S.Q.I.R.M.

Conclusion: We satisfied both reliability (interrater and internal consistency) and validity (predictive but not criterion validity) for our treatment scale, but did not agree with clinician improvement ratings.

NR20 Monday May 13, 9:00 a.m.-10:30 a.m.

Assessment of Prosodic Deficits in Schizophrenia

Barbara G. Haskins, M.D., Department of Psychiatry, University of Virginia, 1429 Foxbrook Lane, Charlottesville, VA 22901; Michael S. Shutty, Jr., Ph.D.

Summary:

Ross has suggested that affective components of language are governed by the right hemisphere analogously to left hemisphere organization of propositional language. This hypothesis has been based on unstandardized clinical interviews. We describe development and standardization of an assessment for psychiatric patients utilizing audio tapes and visual stimuli to assess receptive and expressive prosody and recognition of facial affect. The Emotional Blunting Scale assessed spontaneous prosody. Twenty-four state hospital inpatients with no CNS disease and 26 age-matched controls were tested. Interrater reliability for prosodic repetition was high (interclass correlation = .96). Control group comparisons revealed patients performed significantly ($p < .01$) less well. Patients had the most difficulty with comprehension of happy versus sad, angry, or neutral statements. Prosodic impairment did not correlate with length of illness or neuroleptic dose. Prosodic comprehension errors and EBS score showed significant ($p < .05$) inverse relationships with MMSE. Patients demonstrated these dysprosodias: motor (4), global (1), transcortical motor (2), conduction (3), mixed transcortical (2), none (3), other (6). Using Ross's model of cortical dysfunction in aprosodia, our findings indicate both anterior and posterior right cortical dysfunction in patients with schizophrenic and schizoaffective disorder.

NR21 Monday May 13, 9:00 a.m.-10:30 a.m.

Third Ventricle and P300 Findings in Schizophrenia

Louis W. Kraft, B.S., Psychiatry, Ohio State University, 473 W. 12th Avenue, Columbus, OH 43210; Steve B. Schwarzkopf, M.D., Michael W. Torello, Ph.D., Stephen C. Olson, M.D., Henry A. Nasrallah, M.D.

Summary:

Previous studies have demonstrated left temporal scalp voltage attenuation of the auditory P300 waveform in medicated chronic male schizophrenic *inpatients.* In an attempt to replicate Faux et al (1988), we used a full set of 28 scalp electrodes and examined the auditory "oddball" P300 waveform in medicated chronic male schizophrenic *outpatients.* As part of a larger study that included magnetic resonance imaging (MRI), 29 male schizophrenic subjects (DSM-III-R diagnosed) (21-44 yr, mean age 30.6) were compared with 22 male control subjects (21-47 yr, mean age 26.8). Using the SPM analysis technique (296-396 ms), we found a broad central and posterior symmetrical attenuation of P300 in the schizophrenic group. This was confirmed using a subset of 10 electrodes (Cz, Pz, C3, C4, P3, P4, T3, T4, T5, T6) (MANOVA, $p < .05$). However, we were unable to demonstrate the between-group left temporal attenuation. Although analysis of left vs. right electrodes within the schizophrenic group showed significantly smaller left temporal P300 amplitudes (paired T-test, $P < .05$), this was not the case within the control group. Additionally, no significant differences in P300 amplitude based on third ventricle size were found; however, significantly increased P300 latency at the Cz electrode (electrode showing highest signal-to-noise) was seen in schizophrenics with enlarged ventricles (T-test, $p < .05$). Consistent with earlier studies, these results suggest that P300 is attenuated over the left temporal lobe in schizophrenic *outpatients.* Further, P300 latency is related to third ventricle enlargement.

NR22 Monday May 13, 9:00 a.m.-10:30 a.m.

Subsequent Treatment in Dysthymia Unresponsive to TCA

Nina L. Miller, B.A., Department of Psychiatry, Cornell Medical Center, 525 East 68th Street, New York, NY 10021; James H. Kocsis, M.D.

Summary:

Introduction: We investigated response to subsequent treatments given to patients having DSM-III Dysthymic Disorder, who either failed to respond to or were intolerant of an initial trial of imipramine (IMI) or desipramine (DMI) during two separate studies.

Method: Clinical and research records of eligible patients from the above trials were reviewed independently by the two authors. Response to each subsequent treatment trial was rated on a three-point scale: 1 = Responder, 2 = Partial Responder, and 3 = Nonresponder.

Results: Of 90 patients entering treatment (39 IMI, 51 DMI), 27 were nonresponders and 25 were intolerant to treatment. Thus, 52 patients were eligible for a subsequent treatment trial. Fifteen refused further treatment, 17 were referred out, in five the disposition was unknown, and 15 received a variety of subsequent treatments. Results of subsequent treatment are shown in the table. Overall, nine patients (60% of the sample) eventually recovered.

First Subsequent Treatment

	Interpersonal Therapy + DMI	MAOI	Other TCA	Other Med	Total
Responder	3	0	1	1	5
Partial Responder	0	2	0	1	3
Nonresponder	2	2	1	2	7

Later Subsequent Treatment

	MAOI	Other TCA	Other Med	Overall Total
Responder	3	0	1	9
Partial Responder	1	2	0	6
Nonresponder	0	0	2	9

Discussion: Although this report is based upon unsystematic sampling and treatment choice, the eventual outcome of the subsequently treated sample was remarkably good. These preliminary data suggest the clinical wisdom of adequate sequential trials of pharmacotherapy and/or a psychotherapy (IPT) for chronically depressed outpatients who either fail or do not tolerate an initial TCA treatment.

NR23 Monday May 13, 9:00 a.m.-10:30 a.m.

Autoantibodies to DNA in Multicase Families with Schizophrenia

Pinkhas Sirota, M.D., GA, Abarbanel Hospital, Keren Kayemet NS, Bat Yam, Israel; Klara Schild, M.D., Michael Firer, Ph.D., Amir Tanay, M.D., Elizur Avner, M.D., Dina Meytes, M.D.

Summary:

An autoimmune disorder was proposed as one possible etiology for schizophrenia. In this study we have investigated both patients and their healthy relatives for the frequency of a series of antinuclear autoantibodies (ANA) in an attempt to define the autoimmune status of members of multicase families with schizophrenia. The sera of 28 such families (117 patients and 65 first-degree healthy relatives) were tested by ELISA for ANA, anti-dsDNA and anti-ssDNA autoantibodies; 210 healthy subjects matched for age, sex and ethnicity served as controls. The incidence of ANA, anti-dsDNA and anti-ssDNA autoantibodies was significantly increased in schizophrenics compared to normal subjects. The incidence of ANA and anti-dsDNA was significantly increased in healthy relatives compared to controls. No significant differences were found in autoantibody systems between the schizophrenics and their healthy relatives. The data support the contention that autoimmunity, while not being the sole determining factor, plays a role in the etiology of schizophrenia.

NR24 Monday May 13, 9:00 a.m.-10:30 a.m.

Negative Symptoms and Dyskinesia in Schizophrenia

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Summary:

Studies of the relationship between negative symptoms and tardive dyskinesia have yielded disparate findings. Only one study involved unmedicated patients. Since neuroleptics can influence both dyskinesia and negative symptom ratings, it needs to be determined whether neuroleptic treatment may be a confounding factor in such studies.

We examined this issue in a within-subject, on-off haloperidol repeated-measures study in 23 DSM-III-R chronic schizophrenic patients (mean age 32.1 ± 5.5 years; mean duration of illness 12.9 ± 6.3 years). BPRS and dyskinesia ratings were completed on two occasions: first after patients received haloperidol for at least four weeks (average $49.5 \text{ mg} \pm 17.6$ mg daily), and then after a drug-free period (average 13.3 ± 3.7 days).

Negative symptoms (BPRS withdrawal-retardation factor) were significantly correlated with orofaciolingual ($r = .44$; $P < .05$), but not

limb-axial (r = .19), dyskinesia scores when drug free, but not when medicated (r < .10 both). Negative symptoms were not related to tardive dyskinesia examined as a categorical measure (present vs. absent). BPRS psychosis ratings were unrelated to dyskinesia. These findings suggest a specific relationship between negative symptoms and orofaciolingual dyskinesia that may be obscured by differential effects of neuroleptics when studies involve medicated patients.

NR25 Monday May 13, 9:00 a.m.-10:30 a.m.

Regional Brain Density: Schizophrenics Versus Controls

Charles L. Bowden, M.D., Department of Psychiatry, UT-Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284; James L. Maas, M.D., Ermias Seleshi, M.D., Linda Funderburg, M.D., Salvador Contreas, M.D.

Summary:

Objective: To correlate brain density determined by computer tomography (CT) with both behavioral measures of positive and negative symptoms and with amine metabolite levels.

Method: Seventeen patients meeting DSM-III-R and RDC criteria for schizophrenia and 10 age- and sex-matched controls underwent CT scans, and measurements were made of third ventricular maximum width, of ventricular-brain ratios, and of the densities of specific brain regions. While drug-free for at least two weeks, the Brief Psychiatric Rating Scale was scored, and blood, CSF, and urine were obtained for levels of HVA and MHPG.

Results: Patients had higher density in each of the brain regions examined and the increase was statistically significant ($P < .05$) for the R thalamus, L and R frontal, and L cerebellar regions. However, within the schizophrenic sample, blunted affect was strongly negatively correlated with brain density. Levels of MHPG and HVA were also negatively associated with density of the cerebellar region.

Conclusion: The increased density of schizophrenia brain compared with that of controls suggests diffuse histopathological change are part of the illness. However, certain measures of severity are negatively associated with density, suggesting a compounding atrophy.

NR26 Monday May 13, 9:00 a.m.-10:30 a.m.

Expressed Emotion in Nonfamilial Relationships

Robert K. Heinssen, Ph.D., Research, Chestnut Lodge Hospital, 500 W. Montgomery Avenue, Rockville, MD 20850; Steven B. Israel, M.D., Maureen E. Laferty, B.A., Wayne S. Fenton, M.D.

Summary:

An atmosphere of hostility, criticism, and/or emotional overinvolvement (i.e., expressed emotion, or EE) is frequently associated with higher relapse rates among psychiatric patients. To date, correlations between EE and illness course have been examined solely in familial situations; other potentially important relationships have been overlooked. This investigation measures EE in a sample of psychiatric caretakers (psychiatrists, social workers, nursing personnel) and explores how EE ratings vary according to specific staff/patient qualities.

Methods. Five-minute speech samples are obtained from treatment personnel ($N = 15$) who describe their feelings toward 23 schizophrenic patients enrolled in an inpatient behavioral rehabilitation program. Transcripts of verbal records are reliably rated to determine EE properties. Caretakers also complete self-report measures of attributional style, problem-solving strategy, self-efficacy, and work experience. Information about patients includes reliable ratings of premorbid functioning, illness history, current symptoms (positive and negative), social skills, instrumental performance, and personality features.

Analysis. Univariate tests will explore correlations among EE ratings, caretaker self-report data, and patient variables. Multiple regression analyses will evaluate the proportion of EE variance explained by (a) caretaker characteristics, (b) patient qualities, and (c) interactions among staff and patient dimensions.

Contributions. By adopting the perspective of caretaker-patient dyads, we evaluate for the first time the significance of EE in nonfamilial relationships. Consequently, our results may (a) advance understanding of the EE construct, and (b) illuminate factors that influence the treatment course of hospitalized psychiatric patients.

NR27 Monday May 13, 9:00 a.m.-10:30 a.m.

MRI Study of Caudate Nucleus in Major Depression

Patricio R. Escalona, M.D., Psychiatry, Duke Univ Med. Center, Box 3215, Durham, NC 27710; William M. MacDonald, M.D., P. Murali Doraiswamy, M.D., Mustafa M. Hussain, M.D., Charles B. Nemeroff, M.D., K. Ranga Krishnan, M.D.

Summary:

Using high-field MR images, we measured the volumes of the caudate nuclei in 25 patients with major depression (DSM-III) (mean age ± SD, 49 ± 19 yrs.) in comparison with 36 normals (53 ± 19 yrs.) free of major neurologic and psychiatric disorders.

Depressed patients had significantly smaller caudate ($p < 0.0004$) than controls. There were no significant gender differences. These results are consistent with our earlier studies as well as with prior clinical, experimental and PET studies suggesting that basal ganglia dysfunction may be associated with major depression.

NR28 Monday May 13, 9:00 a.m.-10:30 a.m.

Dopamine Competes for 123 I-IBZM Binding in Vivo

Robert T. Malison, M.D., Department of Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Mohammed Al-Tikriti, Ph.D., Elzbieta Sybirska, Ph.D., Sami S. Zoghbi, M.D., Ronald M. Baldwin, Ph.D., John Ellsworth, Ph.D., Robert H. Roth, Ph.D., Dennis S. Charney, M.D., George R. Heninger, M.D., Paul B. Hoffer, M.D., Robert B. Innis, M.D.

Summary:

In a series of non-human-primate experiments ($n = 30$), the effects of body temperature, amphetamine, haloperidol, and reserpine on brain uptake of the dopamine D2 receptor radioligand [^{123}I]IBZM (iodobenzamide) were measured. Specific brain uptake of [^{123}I]IBZM (defined as the radioactive density in striatum minus that in non-striatal regions) reached peak values by 100 minutes post injection of radioligand. After reaching maximal levels, washout of specifically-bound radioligand was greater under normothermic conditions (26% of peak value/hr; core body temperature 35-37°C) than under controlled hypothermic conditions (11%/hr; 32-34°C). The slower washout of brain radioactivity at hypothermic body temperatures was used in subsequent experiments. Administration of haloperidol (0.02 mg/kg iv) at the time of peak specific uptake resulted in a dramatic increase in washout (60%/hr; $p < .0001$ compared with controlled hypothermic state), consistent with its potent D2 receptor antagonist properties. D-amphetamine ($N = 10$; 1.0 mg/kg iv), which has negligible affinity for the D2 receptor, but rather induces the release of endogenous stores of dopamine, also enhanced washout (34%/hr; $p < .0005$). Reserpine pretreatment of two animals (1.0 mg/kg iv, a dose shown postmortem in these animals to cause greater than 90% depletion of striatal dopamine) blocked amphetamine-enhanced washout (10%/hr; $p < .05$) but not that of haloperidol.

These results are consistent with the hypothesis that stimulant-induced release of endogenous dopamine may effectively compete for *in vivo* radioligand binding of [^{123}I]IBZM to dopamine D2 receptors and suggest that similar results would be obtained for the structurally related PET radioligand [^{11}C]raclopride.

NR29 Monday May 13, 9:00 a.m.-10:30 a.m.

Quantitative Morphology of the Basal Ganglia

Jay N. Giedd, M.D., Department of Psychiatry, Duke University, 4600 University Drive #1004, Durham, NC 27707; C. Edward Coffey, M.D., Ioanis Parashos, M.D.

Summary:

Basal ganglia dysfunction has been implicated in many of the most severe psychiatric disorders. Although advanced imaging techniques may help unveil the neurobiological basis of these dysfunctions, relatively little is known about the normal morphology. An understanding of the normal morphology will be instrumental in appreciating psychopathological changes in these structures.

Methods: To examine the effects of age on basal ganglia morphology, 77 normal volunteers aged 30 to 90 years were recruited from the community. All were right-handed with no history or clinical evidence of neurologic or psychiatric impairment. A quantitative MR imaging protocol permitted area and volume measurements of basal ganglia nuclei from contiguous T1-weighted coronal sections.

Results: There was a highly significant (p 0.001) effect of age on the volume of the caudate nucleus that involved interactions of age with both sex and height. The area of the lentiform nucleus did not appear to change with increasing age. These data suggest that the effects of age on basal ganglia size are complex and may vary with the particular nucleus under study.

NR30 Monday May 13, 9:00 a.m.-10:30 a.m.

Brain Imaging in Geropsychiatric Inpatients

Aseem Rawal, M.D., Psychiatry, Duke University, Box 3215 Duke University, Durham, NC 27710; P. Murali Doraiswamy, M.D., William M. McDonald, M.D., Charles B. Nemeroff, M.D., K. Ranga Krishnan, M.D.

Summary:

A retrospective chart review of 105 elderly (over 60 yrs.) patients admitted consecutively over a 12-month period was conducted to determine the prevalence of neuroradiologic abnormalities in patients at a tertiary care geropsychiatric setting. Psychiatric diagnoses (DSM-III-R) included Major Depression (64%), Bipolar Disorder (7%), Dementia (16%), and other diagnoses (13%). Brain MRI (N = 59) or CT (N = 11) scans were obtained on 67% of these patients during their admissions. Only nine patients (13%) had scans interpreted by neuroradiologists as being free of significant findings. In the remaining group, the most common finding was small vessel disease and/or areas of increased signal on T2 MR images (N = 53, 74%). Other findings were cortical atrophy (N = 42, 60%), hyperintensities in the basal ganglia (N = 14, 20%), thalamus (N = 3), midbrain (N = 6), pons and brain stem (N = 10), cerebellum (N = 3), meningiomas (N = 2), metastasis (N = 1), parasellar aneurysm (N = 1) and subdural hematoma (N = 1). These findings suggest that there is a high prevalence of neuroradiologic abnormalities in elderly psychiatric inpatients at tertiary care centers. This study also supports the utility of brain imaging as a diagnostic adjunct in geriatric psychiatry. Potential clinical and prognostic implications of these findings will be highlighted.

NR31 Monday May 13, 9:00 a.m.-10:30 a.m.

Pet Studies of Brain Activation in Alzheimer's Disease

Susan R. Wisebrod, M.D., Dept. of Psych/Neurology, McGill University, 4333 Cote St. Catherine Road, Montreal PQ, CANDA H3T 1E4; Howard Chertkow, M.D., Edith Hamel, Ph.D., Ernst Meyer, Ph.D., Albert Gjedde, M.D., Serge Gauthier, M.D.

Summary:

The lack of physiologic and metabolic measures to confirm the diagnosis of early Dementia of the Alzheimer's Type (DAT) is a major problem in geriatric psychiatry. Baseline fluorodeoxyglucose positron emission tomographic (PET) studies measuring local cerebral glucose metabolism, while encouraging, are not sufficiently sensitive to produce an abnormal pattern in all early DAT patients. Recently, the development of the intravenous O_{15} labelled water bolus technique has allowed investigators to map the response of the human brain to a variety of stimuli including higher mental functions. Our hypothesis is that PET activation studies, which "stress" the cognitive system to a greater degree, will prove more sensitive than baseline studies in indicating pathological cerebral function even in mild DAT. In previous investigations with young normals, our lab demonstrated specific patterns of brain activation during vibrotactile sensation, passive viewing of words, and picture naming. In the present study, the same activation states will be assessed in 10 elderly normals and 10 early probable DAT patients. Each PET scan will be anatomically mapped onto the patient's MRI and correlated with results of extensive neuropsychological testing. Results from the first three DAT subjects suggest that sensory (vibrotactile) activation is maintained but cognitive activation is disrupted in early DAT. Elderly controls appear similar to younger normals.

NR32 Monday May 13, 9:00 a.m.-10:30 a.m.

Increased Sylvian Fissure Size in Schizophrenia

Joseph M. Schwartz, M.D., Department of Psychiatry, Johns Hopkins, 600 N. Wolfe St., Meyer 3-166, Baltimore, MD 21205; Elizabeth Aylward, Ph.D., Patrick E. Barta, M.D., Godfrey D. Pearlson, M.B.

Summary:

While numerous studies show ventricular enlargement in schizophrenia, few specifically address sylvian fissure widening. Such sylvian fissure differences are thought to reflect reduced temporal lobe tissue. The current study compared 48 schizophrenics and 51 age- and sex-matched normal controls with regard to visual assessment of CSF spaces using the MRI rating protocol of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD), which provides photographs of representative MRI scans illustrating varying degrees of atrophic changes of CSF spaces. Intrarater reliability using the Kappa coefficient was determined to be 0.60 or greater for all measurements. Schizophrenics had bilaterally increased sylvian fissure width even after Bonferoni correction. Mean right sylvian fissure values for schizophrenics and controls were $0.34(\pm 0.31)$ and $0.13(\pm 0.22)$ respectively ($X^2 = 14.04$, $p = .0009$). Mean left sylvian fissure values were $0.19(\pm 0.24)$ and $0.05(\pm 0.15)$, respectively ($X^2 = 10.64$, $p = .0011$). A two-way repeated measures analysis of variance using sylvian fissure ratings as the dependent variable indicated significant main effects for both diagnosis ($F = 10.33$, $p < .001$) and side ($F = 21.09$, $p < .001$), but no diagnosis-by-side interaction ($F = 2.23$, $p = .13$).

NR33 Monday May 13, 9:00 a.m.-10:30 a.m.

D2 Receptor Activity in Tourette's Syndrome

Mark S. George, M.D., Neuropsychiatry, Institute of Neurology, Queen Square, London WC1N 3BG, England; Mary M. Robertson, M.B., Durval C. Costa, M.D., Peter J. Ell, M.D.

Summary:

Dopamine overactivity or supersensitivity may produce the tics and other abnormal behaviors seen in GTS. Dopaminergic marker abnormalities have recently been found in GTS postmortem striatal specimens. To investigate whether dopamine dysregulation might be seen with SPET scanning, we studied and imaged 15

GTS patients, seven of whom were drug-naive, and compared them with four normal controls. Following injection of 185MBq ^{123}I-IBZM, serial images were obtained at the level of the basal ganglia from 0 to 60 minutes p.i. using a multi-detector SPET system. ^{123}I-IBZM activity in the frontal and visual cortex and right and left basal ganglia was determined in a blinded fashion using region of interest analysis and ratios. Significant differences were found between controls and GTS patients in left basal ganglia/frontal cortex IBZM uptake from 30 to 50 minutes (multiple t-tests, p values ranged from 0.005 to $<.001$). Further data analysis will examine whether ^{123}I-IBZM activity correlates with clinical symptoms or response to treatment with D2 specific drugs.

NR34 Monday May 13, 9:00 a.m.-10:30 a.m.

HMPAO SPET Scans of Comorbid OCD and Tourette's Syndrome Patients

Mark S. George, M.D., Neuropsychiatry, Institute of Neurology, Queen Square, London WC1N 3BG, England; Mary M. Robertson, M.B., Durval C. Costa, M.D., Michael R. Trimble, M.B., Peter J. Ell, M.D.

Summary:

Studies using PET and SPET have demonstrated frontal lobe and basal ganglia changes in OCD patients. There has been recent interest in the links between GTS and OCD. OCD and GTS may be two different manifestations of the same disease, but with OCD predominantly affecting the frontal lobes and GTS having more basal ganglia activity. To examine this theory, we performed high-resolution 99Tcm-HMPAO SPET scans in 19 patients with GTS, 14 of whom also had OCD. Using ROI analysis and blinded to the patients' OCD status, we measured frontal, basal ganglia, visual and cerebellar activity. We compared frontal lobe/basal ganglia ratios between those patients with pure GTS ($n=5$) and those with comorbid OCD/GTS ($n=14$). The ratios differed between the two groups, with the GTS-only group showing higher right frontal and lower basal ganglia activity than the group with comorbid OCD (right frontal/total basal ganglia ratio, GTS mean 0.49, OCD/GTS mean 0.46, $p=0.058$). These findings are discussed in light of previous neuroimaging work in GTS and OCD, and neuroanatomical models of these disorders.

NR35 Monday May 13, 9:00 a.m.-10:30 a.m.

A Demonstration of Parietal Lobe Activation with SPET

Howard A. Ring, M.B., Department of Psychiatry, Institute of Neurology, Queen Square, London WC1N 3BG, England; Mark S. George, M.D., Durval C. Costa, M.D., Kypros Kouris, Ph.D., Peter J. Ell, M.D.

Summary:

This study sought to develop a technique to reliably detect regional changes in cerebral blood flow during performance of a task requiring changes in brain activity. Four normal volunteers received two SPET scans, each following the intravenous injection of an average of HMPAO. For six minutes around the first injection each subject sat still with eyes and ears open and was then scanned using high-resolution collimators in a triple-headed camera. Immediately after the first scan the subject received the second injection in identical circumstances to the first, except that on this occasion a finger opposition task was performed with one hand. Subjects were then rescanned. Following reconstruction, images were subjected to region of interest analysis, and the percentage change in regional counts between scans was calculated. The greatest change was a mean 9.4% activation in the contralateral parietal region. Maximum inter-scan regional variation in two additional subjects not activated was 3.2%. These results correspond to known details of the cortical control of movement. This ability to demonstrate neuronal activation with SPET allows a role for this technique in clinical and research neuropsychiatric investigation.

NR36 Monday May 13, 9:00 a.m.-10:30 a.m.

Does Tardive Dyskinesia Cause Dysphagia?

Chandragupta S. Vedak, M.D., Department of Psychiatry, UHS/Chicago Medical Sch., 3333 Green Bay Road, North Chicago, IL 60064; Kathy Yedor, M.A., Rukhsana Khan, M.D., Caryn Conlon, M.A., V. Chowdary Jampala, M.D.

Summary:

Choking and dysphagia are common problems in long-term psychiatric wards. As neuroleptic medications are known to be associated with difficulties in swallowing. We evaluated 23 long-term psychiatric patients receiving neuroleptics for more than 12 months for abnormal involuntary movements and dysphagia using modified AIMS and modified barium swallow. The raters for movement disorder and dysphagia were blind to each other's ratings. Seventeen out of the 23 patients exhibited significant dysphagia. Thirteen out of these 17 patients also had significant tardive dyskinesia ($Chi^2=10.55$, $df=1$, $p=.019$). All of the patients with significant dyskinesia also had severe dysphagia. The patients with dysphagia were rated to have more bucco-oral dyskinesia than those without dysphagia ($F=8.9764$, $df=1, 21$, $p=.007$). The severity of dysphagia was not related to the age of the patients, but was related to the summed modified AIMS score ($F=6.11$, $df=1,21$, $p=.022$). Evaluation for tardive dyskinesia, particularly bucco-oral dyskinesia, can help identify patients at risk for choking.

NR37 Monday May 13, 9:00 a.m.-10:30 a.m.

Treatment of Tardive Dyskinesia with Vitamin E

Michael F. Egan, M.D., Neuroscience Center, NIMH, 2700 MLK Jr. Avenue, SE, Washington, DC 20032; Thomas Hyde, M.D., Greg Albers, M.D., Ahmed Elkashef, M.D., Robert C. Alexander, M.D., Richard Jed Wyatt, M.D.

Summary:

Vitamin E (alpha-tocopherol), a potent free-radical scavenger, has been reported to improve symptoms of tardive dyskinesia (TD) in two previous studies. These results supported the hypothesis that free-radical formation may be involved in the pathophysiology of TD. In an attempt to replicate this finding, we gave vitamin E (1600 I.U./d) for six weeks to 18 patients with TD in a double-blind, placebo-controlled crossover study. Videotaped AIMS exams were rated at the end of the study by two independent, trained raters. A modified AIMS rating scale was used which included separate scales for dystonia and choreoathetosis. Vitamin E levels were markedly higher ($p=.0001$) during the vitamin E phase (35.0 mg/L) compared to the placebo phase (13.2 mg/L). There was no significant difference ($df=17$, $p=.71$, 2-tailed, paired t-test) in mean AIMS scores after vitamin E (16.8) compared to ratings after placebo (17.3), or in separate ratings of choreoathetosis and dystonia. We conclude that vitamin E did not have a significant beneficial effect on TD ratings in this selected group of patients with moderate and severe TD.

NR38 Monday May 13, 9:00 a.m.-10:30 a.m.

Early Antipsychotic Effect of Neuroleptics in Patients with Chronic Schizophrenia

Robert G. Stern, M.D., Psychiatry, Bronx VAMC, 130 W. Kingsbridge Road, Bronx, NY 10468; Rene S. Kahn, M.D., Michael Davidson, M.D., P.D. Harvey, Ph.D., R.T. McQueeney, M.D., Farooq Amin, M.D., K. Dumont, B.A., S. Apter, M.A., K.L. Davis, M.D.

Summary:

The clinical impact observed early in the course of neuroleptic treatment has been often attributed to sedation or to other medication unrelated factors. This study hypothesized that neuroleptics produce an early specific antipsychotic effect. After a two-week drug-free period, 79 RDC chronic schizophrenic inpatients were treated with haloperidol 20 mg po/d or an equivalent neuroleptic dose. BPRS and CGI ratings were performed on the last drug-free day and on days 8, 15, 22 and 29 of treatment. Patients showing a decrease of at least one CGI point form baseline at day 29 were defined as "responders," and those without such change as "non-responders." The two groups were compared using repeated measures MANOVA with one between subjects variable, Group and one repeated measure, Time. When significant Group interactions were found, follow-up within Group MANOVA's and paired t-tests were used. There were 29 responders and 50 non-responders. Within Group analyses showed that responders had a significant reduction in total BPRS ($p < 0.0001$) and psychotic symptoms ($p < 0.01$) as well as in negative, anxiety and hostility symptoms *after only one week of treatment.* Contrary to the common belief, these results suggest that a specific antipsychotic effect occurs after a few days of neuroleptic treatment.

NR39 Monday May 13, 9:00 a.m.-10:30 a.m.

Measuring Centrally Produced HVA in Plasma in Humans

Farooq Amin, M.D., Psychiatry, VA Medical Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Michael Davidson, M.D., Robert Stern, M.D., Rene S. Kahn, M.D., James Schmeidler, Ph.D., Peter Knott, Ph.D., Seth Apter, M.A., Kenneth L. Davis, M.D.

Summary:

Dopamine (DA) metabolite homovanillic acid (HVA) in plasma originates mainly from two sources: peripheral noradrenergic (NA) neurons and central DA neurons. Debrisoquine (DBQ), which is an MAOI and does not cross the blood-brain barrier, has been used to suppress the peripheral contributions of HVA to plasma and thereby enhance the degree to which plasma HVA can reflect central DA neuronal activity. Significant residual amounts of HVA are still formed in the periphery after DBQ treatment. To circumvent this problem and better estimate the component of plasma HVA derived from the central DA neurons, the following paradigm was utilized (Kopin, 1988, Life Sci.).

HVA and NA metabolite MHPG were measured daily in plasma for 10 days in a group of schizophrenic patients ($n = 9$) during DBQ treatment (10 mgs bid). After 10 days, DBQ had suppressed the plasma HVA to 48% and MHPG to 30% of their baseline concentrations. Daily plasma HVA and MHPG concentrations correlated strongly with each other ($r = 0.67$, $df = 82$ $p < .0001$). This is consistent with the origin of a part of plasma HVA from the peripheral NA neurons. Plotting HVA concentrations on y-axis and MHPG concentrations on x-axis, the regression line of HVA on MHPG produced a y-intercept (value of y at $x = 0$) which was significantly greater than zero ($t = 5.75$, $df = 82$, $p < .0001$). The magnitude of y-intercept represented the amount of HVA formed in the hypothetical absence of NA metabolism and consisted mainly of HVA produced by the central DA neurons. The results suggested that about 24% (3.14 ng/ml) of the mean baseline plasma HVA concentrations (13.02 ng/ml) were contributed by the central DA neurons.

NR40 Monday May 13, 9:00 a.m.-10:30 a.m.

Perceived Criticism in Late Luteal Phase Dysphoric Disorder

Kimberly A. Yonkers, M.D., Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Jill Hooley, Ph.D., Paul Cneo, B.A., Annie Penn, B.S., Amy Vitale, B.A.

Summary:

Premenstrual mood complaints are common. Late luteal phase dysphoric disorder (LLPDD) is the proposed DSM category that indicates a severe form of premenstrual mood complaints. In order to better understand the cognitive phenomenon involved in premenstrual mood complaints, we administered a perceived criticism form to subjects during two phases of the menstrual cycle (the follicular phase and the luteal phase of the cycle). Subjects were previously administered a SCID and SADS-L and were asked to keep daily ratings of mood and behavior along the menstrual cycle. Sixty-four percent of the sample met criteria for LLPDD and 28% had mild symptoms or symptoms that were merely an exacerbation of another disorder. As hypothesized, both the perceived criticism and degree of upset increased significantly during the luteal phase of the cycle in both groups. We also hypothesized a greater degree of upset relative to criticism in the luteal phase secondary to the cyclic mood disturbance. The contribution of perceived criticism and cycle phase in causing upset among women with cyclic mood disturbance will be discussed.

NR41 Monday May 13, 9:00 a.m.-10:30 a.m.

History and Biology Predict Late Luteal Phase Dysphoric Disorder Subtypes

Candace S. Brown, Pharm.D., University of Tennessee, 26 S. Dunlap-Feurt Bldg. 210B, Memphis, TN 38163; Frank W. Ling, M.D., Carolyn M. Chesney, M.D., Richard G. Farmer, M.D.

Summary:

Platelet serotonin (5-HT) uptake was measured in 19 subjects meeting DSM-III-R criteria for Late Luteal Phase Dysphoric Disorder (LLPDD) and 19 age-matched controls. When subgrouped by personal and family history of depression, LLPDD subjects with positive histories ($N = 6$) had a lower V_{max} (Mann Whitney $U = 19$, $df = 17$, $p = 0.09$) while LLPDD subjects with negative histories ($N = 13$) had a higher K_m ($U = 18$, $df = 17$, $p = 0.07$) during the follicular phase. Subjects with affective histories showed significantly enhanced prolactin responses to thyrotropin-releasing hormone during treatment with placebo (AUC: $U = 11$, $df = 17$, $p < 0.01$) and the serotonergic agonist buspirone (AUC: $U = 6$, $df = 17$, $p < 0.01$) compared with subjects with negative histories during the luteal phase. Because prolactin response may be mediated by serotonergic receptors, augmentation in conjunction with reduced V_{max} in LLPDD subjects with depressive histories may indicate supersensitive receptors secondary to a hyposerotonergic state. In contrast, the increased K_m in the LLPDD subgroup with no psychiatric history may partially re-establish serotonergic function through a compensatory mechanism. Our findings suggest that at least two subtypes of LLPDD exist based on affective history and biological response.

NR42 Monday May 13, 9:00 a.m.-10:30 a.m.

The Cross-Cultural Examination of Women Utilizing the Premenstrual Assessment Form

Judith Marks, M.A., Psychiatry, The Univ of Conn., 10 Talcott Notch Road, Farmington, CT 06032; Ana Lucrecia Ramirez Restrepo, M.D., Javier Escobar, M.D., Catherine Hair, M.D., Susan Caruso-Klock, Ph.D.

Summary:

A high percentage of women from various cultures are reported to experience mood and physical changes during the premenstrual phase (Snowden & Christian, 1983).

Ana Lucrecia Ramirez Restrepo, M.D., has used the Spanish-translated version of the Premenstrual Assessment Form (PAF)

(Halbreich et al. 1982) to investigate premenstrual symptom reporting in a normative sample of 50 Colombian women. We have compared the frequency by which these women met criteria for PAF typological categories with frequencies reported in the literature for several other normative samples from the U.S., Canada, and Korea (Halbreich et al. 1982; Christensen et al. 1989; Youdale & Freeman 1987; Yuk et al. 1990; Kim et al. 1990).

The typological category frequencies for the American and Canadian populations did not differ significantly for the majority of categories. The Colombian women, however, met criteria for PAF categories at a much lower rate. Fifty-eight percent of the Colombian women met criteria for "No Significant Change," whereas the range for this category in the other populations was 0% to 3%. Subtype differences are discussed along with possible explanations for the difference found in the Colombian group. In addition, we will discuss the utilization of the PAF in various populations, including an ongoing study at the University of Connecticut Health Center.

NR43 Monday May 13, 9:00 a.m.-10:30 a.m.

Depressive Symptoms in Bereaved Children and Parents

Julie A. Guthrie, M.D., Psychiatry, The Ohio State University, 473 West 12th Avenue, Columbus, OH 43210; Ronald A. Weller, M.D., Mary A. Fristad, Ph.D., Elizabeth B. Weller, M.D.

Summary:

A depressive syndrome is a frequent sequela of bereavement in adults. Recent research demonstrates many bereaved prepubertal children also experience depressive symptoms following parental death. However, the effect of the surviving parents' bereavement reactions on their parent-bereaved children is unknown. To determine if presence/absence and severity of depressive symptoms in grieving parents and children are correlated, 38 recently bereaved prepubertal children and their 26 surviving parents were studied two months post parental death. Standard structured interviews and clinical rating scales were used to assess depressive symptoms in children (CDRS-R, CDI and parents (Ham-D, PDI). Mood disturbance in the child (i.e. dysphoria, irritability, depressed affect, weeping, guilt, and suicidal and morbid ideation) was significantly correlated ($r = .59$, $p < .0006$) with mood disturbance in the parent (i.e. dysphoria, guilt, worthlessness, and suicidal ideation). Presence of a neurovegetative symptom complex (psychomotor, sleep, and appetite disturbances) in children and their parents was significantly correlated ($r = .41$, $p < .02$). Severity of depression in children and their parents also correlated significantly (r-.55, $p < .004$). Thus, presence/absence and severity of affective symptoms in bereaved child and parent dyads were correlated. Further studies should examine links between affective symptoms of parents and their children, as these would have important theoretical and clinical implications.

NR44 Monday May 13, 9:00 a.m.-10:30 a.m.

Platelet Phospholipids: A New Tool to Study Mania

Alan S. Brown, M.D., Department of Psychiatry, University of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213; Alan G. Mallinger, M.D.

Summary:

We have adapted a newly developed method of quantitating membrane phospholipids, in order to study the platelet inositol phospholipid (PL) second messenger system in bipolar affective disorder. Our hypothesis is that monoaminergic neurons of bipolar manics have an increased relative content of membrane phosphatidylinositol-1,4-bisphosphate (PIP-2). When hydrolysis of PIP-2 is initiated by incoming 5-HT-2 receptor stimulation, this leads to an exaggerated increase of intraneuronal calcium, and subsequent enhanced exocytosis of monoaminergic neurotransmitters. Evidence suggests that the platelet is an excellent model of this system. Our method, originally used to study erythrocytes, enables us to analyze nanomolar amounts of nine membrane PL classes in platelets. The procedure involves platelet isolation from whole blood, extraction of PL using methanol:chloroform:HCl, PL separation by two-dimensional high performance thin layer chromatography, and quantitation by scanning laser densitometry. The nanoscale nature of this method renders it more sensitive and direct than those used in previous studies, which employed phosphate analysis and radioactive labeling. We have studied several control subjects and have obtained values of relative PL composition which are comparable to those reported in the literature using other methods. We have thus developed and successfully implemented a highly sensitive and reliable method of quantitating relative amounts of platelet membrane PL's. As this method is well suited to the clinical investigation of manic patients, we have begun studies of this type in order to improve our understanding of the biological mechanisms underlying bipolar affective disorder.

NR45 Monday May 13, 9:00 a.m.-10:30 a.m.

The Diagnosis of Mania by Self-Report

Douglas B. Marlowe, M.A., Department of Psychiatry, Montefiore Medical Center, 111 E. 210th Street, Bronx, NY 10467; Scott Wetzler, Ph.D.

Summary:

This study examined the diagnostic efficiency of self-report tests for mania. The MMPI ($N = 185$), MCMI ($N = 148$) or MCMI-II ($N = 110$), and SCL-90R ($N = 256$) were administered to psychiatric inpatients upon admission, including approximately 15% diagnosed by experienced psychiatrists as bipolar disorder, manic phase, and 85% with a variety of other psychiatric conditions. The diagnostic efficiency of individual mania scales was evaluated by comparing test-based diagnoses with clinical diagnoses. To make the test diagnosis of mania, a T score ≥ 70 was used for the MMPI Hypomania scale, and Base Rate scores ≥ 85 for the MCMI and MCMI-II Hypomania scales. Overall classification rates were impressive for the MCMI and MCMI-II Hypomania scales (85%). The MMPI Hypomania scale was much less successful (24%). In general, all the scales were highly specific, but had inadequate sensitivity (45%). When the two tests were used in combination, sensitivity improved to a moderate level (60%). Using the entire multidimensional profiles for each test, the manic patients had significantly different profiles on the MMPI, MCMI and SCL-90R in comparison to psychiatric controls ($p < 0.001$). The manic patients' test profiles were characterized by elevations on: SCL-90R (paranoid ideation and psychoticism), MMPI (mania and psychosis), MCMI (hypomania, substance abuse, paranoia and narcissism). The profiles were characterized by the presence of manic symptomology, paranoia and grandiosity, and relatively lower levels of depression and anxiety. Finally, discriminant function analyses using these multidimensional test profiles generated impressive classification rates of up to 84%. In summary, these self-report psychological tests may be used to rule in mania with a fair degree of certainty, but may not be used in lieu of a psychiatrist's interview for identifying manic patients.

NR46 Monday May 13, 9:00 a.m.-10:30 a.m.

Type of Psychotic Features and Outcome in Mania

Mauricio Tohen, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Ming Tsuang, M.D.

Summary:

Fifty-four patients with psychotic mania were followed prospectively for four years to evaluate risk of relapse and overall psychoso-

cial outcome. Type of psychotic features were evaluated as possible predictors of outcome. Baseline and outcome assessments were obtained with structural instruments. Statistical analyses included survival analysis and logistic regression models. Remarkably, there was no loss to follow-up cases.

Thirty (56%) patients experienced mood incongruent psychotic features, including 11 (20%) with Schneiderian first rank symptoms. Mood incongruent psychotic features during the index manic episode predicted a shorter time in remission (Hazard ratio = 2.6, 95% C.I. = 1.2-5.5, P = .01). Presence of first rank symptoms predicted poor residential (odds ratio = 20.5, 95% C.I. = 1.8-228.3, P = .01) and occupational (odds ratio = 5.1, 95% C.I. = 1.1-24.2, P = .04) status at four years.

It appears that the assessment of mood congruence is useful in the diagnosis of psychotic mania and should be retained in the American Psychiatric Association's DSM diagnostic system.

NR47 Monday May 13, 9:00 a.m.-10:30 a.m.

Depression in Dementia Clinic Outpatients

William E. Reichman, M.D., COPSA Institute, UMDNJ-CMHC, 667 Hoes Lane, PO Box 1392, Piscataway, NJ 08855; Andrew C. Coyne, Ph.D., Hilary T. Hanchuk, M.D.

Summary:

A sample of 205 clinic outpatients was screened for depression using DSM-III-R criteria. Patient and family histories of depression were recorded. Mean patient age was 75.0 ($\pm$ 8.1) years; average duration of intellectual impairment was 4.2 years ($\pm$ 3.3); and average Mini-Mental State Exam (MMSE) scores were 15.3 ($\pm$ 6.5). Seventy-nine (42.7%) patients had Alzheimer's disease (AD); 48 (25.9%) had multi-infarct dementia (MID); and 58 (31.4%) received other diagnoses. Controlling for duration of impairment and MMSE, DSM-III-R scores were found to vary according to diagnosis, $F(4,165) = 3.1$, $p < .05$. Scores for AD, other dementias, and MID groups were 2.3, 2.6, and 3.1, respectively. Additional analyses indicated that DSM-III-R scores did not correlate with dementia severity as indexed by MMSE ($r = -.001$, $p > .05$) or Blessed Dementia Scale ratings ($r = -.09$, $p > .05$).

Family history of depression was found to be related to patient depression. Patients with a family history of depression were more likely to be depressed at the time of evaluation than were those without a family history ($X^2 = 7.3$, $p < .01$). Among patients with a family history, 35.7% were currently depressed; without a family history, 10.6% were depressed. A personal history of depression, however, did not influence current patient depression ($X^2 = 1.5$, $p > .05$). The findings of this study underscore the importance of patient and family variables in understanding the relationship between depression and dementia.

NR48 Monday May 13, 9:00 a.m.-10:30 a.m.

Depression in a Geriatric Medical Clinic

Linda C. Barr, M.D., Department of Psychiatry, Payne Whitney Clinic, 525 E. 68th Street, New York, NY 10021; James H. Kocsis, M.D.

Summary:

More than half of all identified episodes of treatment of depression occur in the primary medical care sector (Regier et al. 1978), where underrecognition and undertreatment have been reported (Niesen and Williams, 1980; Wells et al., 1989). As the population ages, diagnosing depression in the geriatric population becomes increasingly important.

Patients attending a geriatric primary care clinic were approached for participation in a study examining the prevalence and characteristics of depression in this setting. Those with profound dementia and those not speaking English were excluded. Those consenting to participation received a screening instrument for depression, described by Burnam et al. (1988). All screeners were administered by the investigator. SCID interviews were attempted for all those with screener scores above .06. Those found to have DSM-III-R major depression or dysthymia were offered treatment with antidepressants.

A total of 164 individuals presented for care; 97 (59%) were approached for participation in the study; 17 patients were excluded, three refused participation and 76 (78%) completed the screening. Average age was 78.7 years. 82% of the sample was female. Twenty-five (33%) had screener scores greater than .06, indicating the presence of depressive symptoms. Thirteen (52%) of these patients completed a SCID interview. Five depressive syndromes were identified: two chronic major depression, one recurrent major depression, one dysthymia, one secondary depression. Estimated prevalence rates were 14% for DSM-III-R diagnosis of depression and 13% for depressive symptoms without a DSM-III-R diagnosis. Three of the patients with major depression were treated with antidepressants. Two have shown a favorable response with a drop in Hamilton score (19 to 9 and 23 to 9). These preliminary results suggest that chronic depression is common in the geriatric medical clinic and that some of the depressive syndromes are responsive to treatment.

NR49 Monday May 13, 9:00 a.m.-10:30 a.m.

Pregnancy Resolution and Depression in Adolescent and Young Women

John D. Mesaros, M.D., Psychiatry, Michigan State Univ., 4704 Burton SE., Grand Rapids, MI 49546; David B. Larson, M.D., John S. Lyons, Ph.D.

Summary:

This case/control study investigated the effects of pregnancy resolution on depressive symptoms in 17- to 25-year-old women. The 17-19-year-old group represented 48% of the total sample while the remaining 52% were 20-25 years old. The 250 subjects, primarily college students, were divided into the following groups: induced pregnancy termination, delivery, spontaneous pregnancy termination, and never pregnant. There was a 72.5% rate of response from subjects surveyed at two clinical centers. They completed a 64-item questionnaire that included the Center for Epidemiologic Studies Depression scale (CES-D). Subjects were statistically matched on relevant demographic and depression risk factors. Unexpectedly, it was found that the induced termination group had the highest frequency of depressive symptoms for CES-D scores greater that 15 ($p < .02$). At the level of severe symptoms (CES-D scores > 30) the induced termination group had a rate of 16.7%; never pregnant controls had a rate of 4.7%; and the delivery group had a rate of 0%. Factors related to this severe level of depression in the induced pregnancy termination group included: perceived loss of control regarding the decision to terminate; negative feelings about the termination; and few meaningful spiritual values.

NR50 Monday May 13, 9:00 a.m.-10:30 a.m.

Onset Age Within Families with Bipolar I Disorder

Francis J. McMahon, M.D., Psychiatry, Johns Hopkins University, Meyer 4-181 600 N. Wolfe St., Baltimore, MD 21205; Sylvia G. Simpson, M.D., O. Colin Stine, Ph.D., Deborah A. Meyers, Ph.D., J. Raymond DePaulo, M.D.

Summary:

Age of onset is an important variable in genetic studies: empirical determination of age-dependent penetrance requires knowledge of the age of onset distribution. This distribution could help identify subgroups in which epigenetic factors play an etiologic role or in which genetic heterogeneity exists. We have been collecting a

group of nuclear families ascertained through a bipolar I (BPI) proband with two or more affected sibling. Probands and all available family members (N = 418) have been interviewed by a psychiatrist using the SADS-L, and all diagnoses conform to the RDC. The following onset ages were determined: first outpatient treatment, first hospitalization, first mania, and first major depression. Analysis of these onset ages reveals that: 1) the overall distribution is unimodal, but with a skew toward younger ages; 2) variance of onset age among first-degree relatives is significantly smaller within than between pedigrees; and 3) onset age is most closely correlated for age at first outpatient treatment of BPI probands and their BPI first-degree relatives ($r = 0.724$, $p < 0.001$). Although further analysis is required, these data should prove useful for linkage studies and other investigations into genetic factors in bipolar disorder. Within nuclear families with multiple affected members, onset age appears to be a strongly heritable characteristic of bipolar I disorder.

NR51 Monday May 13, 9:00 a.m.-10:30 a.m.

Hypersomnia in Bipolar Depression

Eric A. Nofzinger, M.D., University of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213; M.E. Thase, M.D., C. F. Reynolds, III, M.D., J.M. Himmelhoch, M.D., A. Mallinger, M.D., D.J. Kupfer, M.D.

Summary:

Objective. This study attempted to characterize objectively the hypersomnia frequently seen in the depressed phase of bipolar affective disorder. From previous work in sleep and affective disorders, the hypothesis that the hypersomnia may be related to rapid eye movement (REM) sleep pressures was tested by a multiple sleep latency test (MSLT) comparison with narcolepsy, a well defined primary sleep disorder associated with known REM-sleep dysfunction. *Method.* A prospective sample (N = 25) of bipolar depressed patients was selected on the basis of complaints of clinical hypersomnia. They underwent two nights of polysomnography followed by an MSLT study. Their nocturnal sleep and daytime naps were compared with similar studies previously performed for 23 narcoleptic patients who were referred to our sleep evaluation center. *Results.* Despite their complaints of hypersomnia, no abnormalities were noted on MSLT studies for the bipolar group. Contrary to our working hypothesis, REM sleep was notably absent during daytime naps in marked contrast to the narcoleptic group. *Conclusions.* The complaint of sleepiness in the hypersomnic bipolar depressed patient appears to be related to disinterest, withdrawal, decreased energy or psychomotor retardation inherent in the anergic depressed condition, rather than reflective of a true sleep propensity or increased REM sleep pressure.

NR52 Monday May 13, 9:00 a.m.-10:30 a.m.

Risk of Discontinuation of Lithium in Bipolar Disorder

Trisha Suppes, M.D., McLean Hospital, 115 Mill St., Belmont, MA 02178; Mauricio Tohen, M.D., Gianni Faedda, M.D., Ross J. Baldessarini, M.D.

Summary:

We reviewed the literature asking the question: "After a symptom-free period, what is the likelihood of recurrence of bipolar illness if lithium is discontinued?" An extensive search found 12 papers that met our inclusion criteria: DSM-III-R diagnosis of bipolar disorder; patients clinically stable prior to lithium discontinuation; minimum study period of five days; and a minimum of four subjects. Eight double-blind studies including lithium and placebo conditions averages a 75% recurrence of bipolar illness in the placebo group (n = 86) vs. 15% of those given lithium (n = 77). In four other open crossover studies (n = 113) the average recurrence rate of bipolar illness was 70%. Seven of the 12 studies provided data allowing survival analysis, which showed a 38% chance of recurrence in the first eight weeks off lithium, and 50% of the subjects had relapsed by three months (n = 72). At three months 29% of subjects had relapsed into mania and 10% into depression. The average onset of recurrence of mania was much sooner than the pre-lithium course or than predicted from reports on the natural history of bipolar disorder. In sum, this review supports the clinical impression of a high risk of recurrence of bipolar illness if lithium is stopped. The basis and best management of the evident rebound following discontinuation of lithium requires further study.

NR53 Monday May 13, 9:00 a.m.-10:30 a.m.

Comorbidity in Bipolar Disorder at First Episode

Stephen M. Strakowski, M.D., McLean Hospital, 115 Mill Street, Belmont, MA 02178; Mauricio Tohen, M.D., Shelly F. Greenfield, M.D., Gianni L. Faedda, M.D.

Summary:

Psychiatric comorbidity in bipolar disorder has been little studied. To examine this, 30 subjects meeting DSM-III-R criteria for bipolar disorder were assessed at first hospitalization using the Structured Clinical Interview for DSM-III-R diagnosis. Forty percent (12/30) of subjects had comorbid psychiatric diagnoses: substance abuse or dependence (n = 7), obsessive-compulsive disorder (n = 4), simple phobia (n = 2), bulimia nervosa (n = 2), panic disorder (n = 1), and agoraphobia without panic (n = 1). There were no significant demographic differences between the subgroups with and without comorbid diagnoses. Substance abuse prevalence was significantly higher in subjects with another comorbid diagnosis (Fisher Exact Test, $p = 0.026$); this included three of four with comorbid obsessive-compulsive disorder (OCD), and two of four with comorbid anxiety disorder. In 75% (9/12), the onset of the comorbid disorder preceded the hospitalization by more than one year; it is unclear whether this comorbidity represents truly separate disorders or the early symptoms of bipolar illness. These results suggest that the presence of comorbid OCD or anxiety disorder may be associated with an increased risk of substance abuse; substance abuse has been correlated with a worsened course and treatment response in bipolar disorder. These subjects are involved in a longitudinal study of predictors of recovery and outcome.

NR54 Monday May 13, 9:00 a.m.-10:30 a.m.

Erythrocyte Choline in Bipolar Disorder

Andrew Stoll, M.D., Psychotic Disorders Prgrm, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Bruce Cohen, M.D., Marjorie Snyder, M.D., Israel Hanin, Ph.D.

Summary:

Erythrocyte choline concentrations were measured in hospitalized patients with bipolar disorder, manic phase (n = 36), and controls (n = 19). There was a significant elevation in mean erythrocyte choline in the patients with mania ($p < 0.05$, Wilcoxon). This elevation in erythrocyte choline was due to a subgroup of patients with especially high choline values (n = 8). Significant clinical differences were apparent between the patients with "high" and those with "low" erythrocyte choline concentrations. The subgroup of manic patients with elevated erythrocyte choline (≥ 34 nmol/ml) had a more severe illness at admission, a worse outcome at discharge, and required significantly more neuroleptic during and after hospitalization than their low choline counterparts ($p = 0.003$, Fisher); that is, they were less likely to respond well to lithium alone. Furthermore, the bipolar patients with low erythrocyte choline concentrations, as a whole, had more than four times more previous manic episodes than depressive episodes, while the patients with high choline values had approximately the same number of past manias and depressions ($p = 0.013$, Fisher). These results are dis-

cussed in light of the evidence implicating cholinergic neurotransmission in the pathophysiology of affective disorders.

NR55 Monday May 13, 9:00 a.m.-10:30 a.m.

Sequence of Episodes Predicts Response to Lithium in Bipolar Disorders

Gianni L. Faedda, M.D., OPC, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Ross J. Baldessarini, M.D., Mauricio Tohen, M.D., Stephen M. Strakowski, M.D., Christine Waternaux, Ph.D.

Summary:

Meta-analysis of five available studies of response to lithium treatment in bipolar patients, classified according to the sequence of their episodes, supports an association between sequence and response to lithium. The sequence of mania/hypomania-depression-interval has a response rate averaging 72%, while the sequence of depression-mania/hypomania-interval has a response rate averaging 41%. A test of inhomogeneity between studies is nonsignificant ($p = 0.06$), while the different outcome among groups is highly significant (chi-square = 35.6, p 0.000001). The authors discuss possible explanations for the difference in outcome and applications of this classification in clinical practice and research.

NR56 Monday May 13, 9:00 a.m.-10:30 a.m.

Outcome After Lithium Discontinuation in Mood Disorders: A Prospective Study

Gianni L. Faedda, M.D., OPC, McLean Hospital, 115 Mill Street, Belmont, MA 02178; L. Tondo, M.D., M. Tohen, M.D., G.F. Floris, M.D., R.J. Baldessarini, M.D.

Summary:

Patients (N = 66) with DSM-III-R diagnosis of Mood Disorder, treated with lithium, were followed prospectively after discontinuation of lithium. Current age was 43.9 ± 16.1, age at onset was 26.4 ± 12.1 with an excess of women (66.7%). Ninety-seven percent of the patients were bipolar (BP), with mania (BPI = 57%) or without mania (BPII = 40%); only 3% were nonbipolar (NBP). The average duration of lithium treatment was 44 months, with good response in 71%. Rapid discontinuation (two weeks or less, 53% of patients) and gradual discontinuation (more than two weeks, 47% of patients) were compared for rate and latency of relapse. Following rapid discontinuation, 94% of patients relapsed, with a latency of 10.8 months ($F = 12.9$, $M = 6.1$, $p < 0.01$); following gradual discontinuation the relapse rate was 55%, with a latency of 21.4 months ($F = 20.8$, $M = 22.6$, $p < 0.01$). The authors provide a survival analysis of the population and discuss possible explanations of the difference in rate and latency of relapse, as well as the clinical implications of these results.

NR57 Monday May 13, 9:00 a.m.-10:30 a.m.

ECT in Depressed Patients with Neurological Disease

Alexander S. Zwil, M.D., Department of Psychiatry, Univ. of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104; Thomas W. McAllister, M.D., Trevor RP Price, M.D.

Summary:

A pilot study was performed to evaluate the safety and efficacy of ECT in patients with brain lesions. The charts of all patients with the diagnosis of organic mood disorder, major depression, or bipolar disorder-depressed phase, having a concurrent neurological disorder, and receiving ECT at the Hospital of the University of Pennsylvania (HUP) between January 1, 1985, and December 31, 1989, were reviewed. Twenty-five patients met these criteria; two of these patients received ECT on two separate hospital admissions (n = 27). Neurological diagnoses included Parkinson's disease, acquired encephalopathies, primary degenerative dementias, cerebrovascular disease, seizure disorders, neurosurgical lesions, a pituitary microadenoma, mild mental retardation and an intracranial meningioma.

On 26 occasions, patients were judged to be affectively improved following ECT, by clinical criteria. Standardized rating scales (either Ham-D or Carroll) were performed on a subsample of patients and confirmed the clinical impression of improvement. Eight patients, of whom five had degenerative brain diseases and the other three diffuse or multi-focal encephalopathies, experienced disorientation during the course of ECT, but this was not serious enough to discontinue ECT.

ECT appears to be an effective treatment for depression in patients with concurrent neurological diseases. Patients with degenerative brain diseases and diffuse encephalopathies may be prone to ECT-induced delirium.

NR58 Monday May 13, 9:00 a.m.-10:30 a.m.

Natural Killer Cells, Gender and Depression

John M. Petitto, M.D., Psychiatry, Univ of North Carolina, Campus Box #7160, Chapel Hill, NC 27599; James D. Folds, Ph.D., Howard Ozer, M.D., Susan G. Silva, M.S., Carol Murphy, R.N., Dwight L. Evans, M.D.

Summary:

Several research groups have demonstrated that natural killer activity (NKA) is reduced in patients with depression. Despite this observation there is little empirical data relating these changes in NKA to levels of key circulating NK effector cell phenotypes. Postulating that reduced circulating levels of the Leu-11 NK cell phenotype would underlie depression-related reductions in NKA, we examined both peripheral blood NK cell phenotypes and NKA in major depressed and normal control subjects. Depressed subjects evidenced: 1) reductions in Leu-11 (CD16) NK effector cells and NKA; 2) a dissociation of the normal positive correlation between the percent of Leu-11 lymphocytes and NKA, thus suggesting that alterations in both the killing capacity and availability of circulating Leu-11 NK cells appear to be responsible for depression-related reductions in NKA. Moreover, when the data were analyzed by gender, male major depressed subjects showed marked reductions in Leu-11 cells, NKA, and Leu-7 (HNK-1) lymphocytes compared with normal control males. Conversely, depressed females did not differ significantly from normal control females on any of these three immune parameters studied. Severity of depression as assessed by Hamilton depression (HAM-D) rating was not associated with NKA or Leu-7 lymphocyte levels in either major depressed male or female subjects. HAM-D severity ratings were, however, strongly correlated with lower Leu-11 cell phenotype levels among major depressed males, but not females. These data begin to elucidate the immunological mechanisms by which NKA is altered in depression, and suggest that some parameters of immunity may be differentially affected in males and females with the syndrome of major depression.

NR59 Monday May 13, 9:00 a.m.-10:30 a.m.

Altered Natural Killer Cells Diurnal Variation in Depression

John M. Petitto, M.D., Psychiatry, Univ of North Carolina, Campus Box #7160, Chapel Hill, NC 27599; James D. Folds, Ph.D., Howard Ozer, M.D., Dwight L. Evans, M.D.

Summary:

Disturbances in the diurnal variation of several biological parameters including cortisol, TSH, temperature regulation, and the

sleep-wake cycle have been associated with the syndrome of major depression. Recent clinical studies have shown that natural killer cell activity (NKA) is altered in individuals with major depression. There is increasing evidence that the CNS may modulate components of immune system function. Preclinical studies indicate that NKA may be regulated by some neural (e.g., noradrenergic) and endocrine (e.g., cortisol, ACTH) modulators which have been implicated in the neurobiology of depression. Thus, several lines of evidence suggest that alterations in the diurnal variation in some mediators of CNS function associated with depression may lead to changes in the normal diurnal variation of this important parameter of cellular immunity. To test this hypothesis we examined circulating NK cell phenotypes and NKA in 45 subjects (19 control and 26 major depressed) at 8 a.m. and 4 p.m., times that have been shown in normal healthy individuals to approximate the peak and nadir respectively of these immune measures. Control subjects exhibited the expected diurnal variation in NKA ($p < .001$) and circulating Leu-11 (CD16) NK cells ($p < .01$) between these time points. By contrast, this diurnal variation in NKA and Leu-11 cells was absent among the major depressed subject group. Neither the control nor major depressed group evidenced statistically significant differences in Leu-7 (HNK-1) lymphocyte levels between the time points examined. These data suggest that alterations in the diurnal variation of this parameter of cellular immunity may track stress-related diurnal disturbances in CNS function and may be an important avenue of research for clinical as well as basic studies in psychoneuroimmunology.

NR60 Monday May 13, 9:00 a.m.-10:30 a.m.

Expression of G Protein-Coupled Receptors in Depressed Patients

Donatella Marazziti, M.D., Psychiatry, University, Via Roma 67, Pisa 56100, Italy; Daniela Marazziti, Dr. Biol. Sci., Giovanni B. Cassano, M.D.

Summary:

Molecular cloning techniques have permitted the identification and sequencing of the primary structure of several receptors that might have a role in the pathophysiology of psychiatric disorders. Analysis of deduced amino acid sequence from complementary DNA (cDNA) and expression studies of cloned receptors has clarified that pharmacologically defined receptor subtypes do correspond to genetic variants of multigene families.

Our study aim was to measure the expression levels of various G protein-coupled receptor genes, such as serotonin 1 and 2, dopamine 2, alpha 2 and beta 2 adrenergic, in lymphocytes of depressed patients, as compared with healthy controls. Ten patients of both sexes with a major depressive episode, according to DSM-III-R criteria, who had never taken psychotropic drugs, were included. Ten healthy, drug-free subjects who volunteered for the study, served as the control group. The results showed the presence of statistically significant differences between the two groups.

NR61 Monday May 13, 9:00 a.m.-10:30 a.m.

Distribution of Alexithymia in Depressive Subtypes

Larry V. Amsel, M.D., Department of Psychiatry, New York Hospital-WD, 21 Bloomingdale Road, White Plains, NY 10605; Mark J. Russ, M.D., Richard Hahn, M.D.

Summary:

This is the first inpatient study to assess the prevalence of alexithymia among the DSM-III-R subtypes of major depression. Alexithymia involves a dysfunction in the processing and expression of affective states. Traditional dynamic formulation would predict that in such patients with depression the unexpressed negative affect might be manifested in somatic and psychotic symptoms leading to higher rates of melancholic and psychotic depression. In a retrospective design, charts of patients discharged with a diagnosis of major depression were reviewed. Using DSM-III-R criteria and a standardized checklist we divided patients into simple depression, psychotic depression, and melancholic depression. Admission MMPI's were scored for the 22-item alexithymia subscale as described by Kleigr and Kinsman. Twenty percent of our sample scored within alexithymia range. This finding is consistent with previous publications and intermediate between reported rates for normal controls and psychosomatic patients. Statistical analysis on a preliminary sample of 24 indicates a trend in which alexithymia score distinguishes among depressive subtypes ($P = .085$). Alexithymia scores decreased from simple depression to melancholic to psychotic depression. This finding may offer evidence against earlier formulations of the psychic processing of strangulated affects.

NR62 Monday May 13, 9:00 a.m.-10:30 a.m.

Stigma and the Use of Alternative Codes for Major Depression in the Primary Care Setting

Kathryn M. Rost, Ph.D., Psychiatry, Univ of Ark. Med. Sci., 4301 W. Markham Slot 554, Little Rock, AR 72205; G. Richard Smith, M.D.

Summary:

Although a number of primary care providers have informally recognized their preference for alternative diagnostic codes when patients present with depressive disorders, little is known about the prevalence of this practice or the reasons for its occurrence. Widespread use of alternative coding is problematic because many of the new outcomes management systems are triggered by diagnostic codes. To investigate the prevalence of this occurrence, we surveyed 634 randomly selected members and fellows of the American Academy of Family Physicians and American College of Physicians who were currently seeing patients in nonspecialty outpatient settings. Preliminary analyses of 176 respondents indicated that 58% have used alternative coding for one or more depressed patients in the last two weeks. The most commonly cited reasons for the occurrence of alternative coding will be analyzed to investigate the extent to which practicing physicians' perceptions of stigma against depression may inadvertently interfere with innovative efforts to improve mental health services.

NR63 Monday May 13, 9:00 a.m.-10:30 a.m.

The Validation of an Outcomes Management System for the Treatment of Depressive Disorders

Kathryn M. Rost, Ph.D., Psychiatry, Univ of Ark. Med. Sci., 4301 W. Markham Slot 554, Little Rock, AR 72205; G. Richard Smith, M.D.

Summary:

In order to understand how health policy decisions affect outcomes as well as costs of care, tools are needed to evaluate the effectiveness of usual care. These tools need to measure variation in the types and extent of care patients receive across a large number of sites, the outcomes of that care, and patient characteristics that influence the outcome of care. Few outcomes management systems have been tested to determine whether reliable and valid information can be readily collected in settings where clinical care is routinely provided. This session will introduce an outcomes management system for adolescent or adult patients who are diagnosed with major depression and dysthymia, including (1) a three-item screener to identify patients at high risk; (2) patient and clinician baseline assessment; (3) patient follow-up protocol; and (4) a medical records review. Data from our longitudinal pilot testing in 40 patients indicate that outcomes differ for those sub-

jects who do or do not receive adequate pharmacologic treatment (p=.07), and who do or do not receive psychotherapy (p=.02). Thus, brief outcomes tools can measure key constructs precisely enough to demonstrate expected between-group differences.

NR64 Monday May 13, 9:00 a.m.-10:30 a.m.

DST Findings in Major Depression with Early Trauma

Kristin L. Lengowski, M.D., Clin. Res. Unit, Dorothea Dix Hospital, Ruggles Drive, Raleigh, NC 27611; Mark H.N. Corrigan, M.D., Gregory M. Gillette, M.D., George A. Mason, Ph.D., J.C. Garbutt, M.D.

Summary:

Failure to suppress cortisol following dexamethasone(dex) occurs in about 40% of patients with major depression. We have studied 27 hospitalized, drug-free women who met DSM-III-R criteria for major depression or bipolar depression who also gave a history of sexual (unwanted contact) and/or physical abuse prior to age 18. Each of these women was in an acute depressive episode with a Hamilton Depression score (items 1-17) of at least 17. One patient was diagnosed as melancholic and four as psychotic. Each patient received a dexamethasone suppression test (DST) with one mg. of dex given at 11:00 p.m. and cortisol drawn at 4:00 p.m. and 11:00 p.m. the next day. In our lab a cortisol value >6.7 ug/dl at either time point is considered nonsuppression.

Only 3/27 (11%) of these women exhibited nonsuppression. Serum levels of dex are currently being analyzed. No factors that might produce artificially high dex levels have been identified in our patient population.

These findings suggest that patients with major depression and a history of early sexual or physical abuse may have a different neurobiologic profile from what is seen in major depressed patients without such a history. This may explain some of the variance observed in DST studies of depressed patients and highlights the need to understand the neurobiologic and psychopathologic sequelae of early trauma.

NR65 Monday May 13, 9:00 a.m.-10:30 a.m.

Fluoxetine Reduces CSF 5-HIAA and MHPG in Depression

Michael D. De Bellis, M.D., CNE Branch, NIMH Bldg 10 RM 3S231, 9000 Rockville Pike, Bethesda, MD 20892; Thomas Geracioti, Jr., M.D., Margaret Altemus, M.D., Mark A. Demitrack, M.D., Philip W. Gold, M.D., Mitchel A. Kling, M.D.

Summary:

Fluoxetine (FLX) is a highly selective serotonin uptake blocker that has become widely used in the treatment of major psychiatric illnesses. However, relatively little is known regarding its effects on central serotonergic and other monoaminergic function in such patients. We report here a study in which we measured cerebrospinal fluid (CSF) levels of the monoamine metabolites 5-HIAA (serotonin), MHPG (norepinephrine), and HVA (dopamine) in nine patients with DSM-III-R and RDC major depressive disorder (mean age 40.7 ± 4.0; 5 male) both while medication free and following at least four weeks (mean, 80 ± 15 days) of FLX treatment at 20 mg/d, and in 37 healthy volunteers (mean age 30.8 ± 1.6; 20 male). Lumbar punctures (LPs) were done at 9:00 a.m. following an overnight fast and at least three hours of bed rest. Blood was drawn (in all subjects) before LP. The mean HAM-D and Beck scores were 22.3 ± 2.2 and 21.0 ± 4.3 off, and 16.9 ± 2.0 and 14.5 ± 1.2 on FLX, respectively. Mean FLX and norfluoxetine levels were 77.0 ± 11.8 and 111.9 ± 15.3 ng/ml, respectively. Monoamine metabolites were measured by HPLC-EC according to standard methods. CSF 5-HIAA levels in medication-free patients were slightly, but not significantly, lower than controls (85.1 ± 5.3; 92.4 ± 7.0 pmol/ml, respectively). However, CSF 5-HIAA decreased significantly (to 50.9 ± 4.8 pmol/ml) following FLX treatment ($t = 5.34$, $p < 0.001$). CSF MHPG levels were similar to controls, but decreased significantly following FLX treatment ($t = 2.6$, $p < 0.03$). CSF HVA levels were also similar to controls and were slightly but not significantly decreased on FLX ($p < 0.1$). One patient, whose 5-HIAA level dropped sharply to 32 pmol/ml on FLX, was found on follow-up to have suicided after 18 months of treatment with FLX. These results suggest that FLX strongly reduces central serotonin turnover and significantly reduces norepinephrine turnover in depressed patients, but appears to have little effect on dopamine metabolism. The magnitude of reduction of CSF 5-HIAA levels is of interest in the light of recent reports of violent, self-destructive, and/or impulsive behavior in some patients treated with this agent, and studies associating reduced serotonin function with such behaviors. Moreover, these data suggest the hypothesis that measures of central serotonin function in patients treated with FLX and related drugs may represent a predictor of such behavior.

NR66 Monday May 13, 9:00 a.m.-10:30 a.m.

Risk and Benefit Analysis of REM Latency in Depression

Douglas Mossman, M.D., Department of Psychiatry, VA Medical Center, 3200 Vine Street, Cincinnati, OH 45220; Eugene C. Somoza, M.D.

Summary:

Though the clinical interview has retained its central role in psychiatric diagnosis, recent research has suggested that "biological markers" may ultimately increase the precision of clinicians' nosologic and therapeutic decisions. Evaluating and operationalizing diagnostic tests require mathematical techniques that reflect the tests' essential features and limitations, and that guide clinicians in particular clinical situations. In this article, we develop a technique that combines signal detection methods and utility-based decision theory, and apply the technique to published data in which sleep architecture was used as a biological marker for depression. We show how the optimum REM latency cut-off varies with the utility ratio and how this relationship is influenced by the prevalence of depression in the population being tested. We also make specific calculations of the practical limits that must be imposed on uncertainties in utilities to properly operationalize a diagnostic test for a specific clinical situation.

NR67 Monday May 13, 9:00 a.m.-10:30 a.m.

Protein Phosphorylation in the Rat Anterior Pituitary

James C. Pryor, M.D., Psychiatry, Vanderbilt Univ. SOM, MCN A2215, Nashville, TN 37232; Fridolin Sulser, M.D.

Summary:

Regulation of the hypothalamic-pituitary-adrenal axis is important in the pathophysiology of major depression. To better understand the regulation of the HPA axis, we have been investigating the importance of protein phosphorylation in the metabolism of the anterior pituitary of the normal rat.

Anterior pituitaries were removed from normal male rats and homogenized; these were centrifuged to separate particulate and soluble fractions. Protein phosphorylation was performed on each of the fractions in the presence and absence of calmodulin, the calcium calmodulin kinase II inhibitor mastoparan, phosphatidyl serine, and calcium. The samples were electrophoresed on SDS-PAGE gels. Autoradiographs of the gels were prepared and analyzed by scanning densitometry.

Proteins with molecular weights of 80.0 and 54kD were identified in the cytosolic fraction to be phosphorylated in the presence of calmodulin (putative calcium/calmodulin kinase II activity), and

those with molecular weights of 138 and 20 kD were identified in the cytosolic fraction to the phosphorylated by protein kinase C. Those with molecular weights of 54, 24 kD, 19 kD, and 16.6 kD were identified in the particulate fraction to be phosphorylated by calcium/calmodulin kinase II, and those of 57, 43 & 29 kD were phosphorylated by protein kinase C. (Supported by USPHS grants MH-18921 & MH-29228)

NR68 Monday May 13, 9:00 a.m.-10:30 a.m.

Neuroimmunomodulation of Natural Killer Cells by Steroids

Irene E. Ortiz, M.D., Department of Psychiatry, University of New Mexico, 2400 Tucker NE/4th FL FP BLDG, Albuquerque, NM 87131; Arthur D. Bankhurst, M.D., Raul N. Mandler, M.D.

Summary:

It is well established that the general course of autoimmune disease (and affective and anxiety disorders) in women is characterized by suppression of the illness during pregnancy followed by postpartum exacerbation of the illness. Our research was postulated on the speculation that since progesterone increases as much as 2500-fold and b-estradiol increases 30-fold during pregnancy, they may be implicated in this process. Natural killer (NK) cells are lymphoid cells that play a role in the regulation of B cell response and are sensitive to some neurotransmitters. The hypothesis then arose as to whether the alteration in progesterone and b-estradiol that occurs in pregnancy would alter the activity of NK cells. Purified NK cells were obtained from 10 normal non-pregnant women (20-30 years old) by Ficol-Hypaque, glass adherence, the sheep rosette method and incubated with 51Cr-labeled K562 tumor target cells for 4 hours. In vitro treatment with progesterone (10^{-4} to 10^{-6}M) for one hour produced 50%-60% inhibition of cytotoxicity, while in vitro treatment with b-estradiol (10^{-4} to 10^{-6}M) for one hour produced 35%-60% enhancement of cytotoxicity. These data provide new information on the modulation of NK cell activity by progesterone and estrogen, which may be relevant to the pathophysiologic mechanisms of somatic and psychiatric illness unique to women during and immediately after pregnancy.

NR69 Monday May 13, 9:00 a.m.-10:30 a.m.

Valproate and Lithium in Mania: A Chart Review

Abigail M. Stanton, M.D., Psychiatry, WLA-VAMC Brentwood, 1472 S. Crest Drive, Los Angeles, CA 90035; Robert H. Gerner, M.D.

Summary:

To assess the use and effectiveness of valproic acid on acutely manic inpatients, 20 charts from the West Los Angeles VA Hospital were initially reviewed. Variables abstracted included discharge diagnosis, length of stay, use of adjunct medications (neuroleptics, benzodiazepines, other anti-manics), admission and discharge GAS, and two symptom scales, the Mood and the Hypomanic scales. For seven cases, previous admissions when patients had been treated with lithium were also reviewed.

The group contained many chronic patients, 50% had BAD I and 40% had schizoaffective disorder; 55% were substance abusers; 30% were on two anti-manics; 55% were discharged on neuroleptics; and 94% had a GAS at discharge of less than 70. Descriptive statistics (means) showed few differences between patients treated with lithium and VPA. Both groups improved with hospitalization. More neuroleptic (777 chlorpromaz. equiv./d vs 512/d) and less benzodiazepine (0.8 mg clonazepam vs 1.1 mg/d) were used during lithium admissions. This may reflect a clinical tendency to use lower doses of neuroleptics that began in 1987. A nonparametric matched pairs comparison of the seven cases with two admissions (a lithium and a VPA admission) showed no significant differences between admissions on any of the variables. In this population VPA appears to be as effective as lithium in the treatment of acute mania.

NR70 Monday May 13, 9:00 a.m.-10:30 a.m.

Growth Hormone Dynamics Following GHRH Challenge

Cheng-Jen Chen, M.D., Psychiatry, Cornell Univ Med. College, Payne Whitney Clin 525 E 68th, New York, NY 10021; Peter E. Stokes, M.D., Carolyn R. Sikes, Ph.D., Sobhan Mathew, M.D.

Summary:

Diurnal hypersecretion and blunted GH responses to provocative pharmacologic probes have been reported in patients with major depression; however, these findings provide little insight into the complex regulatory mechanisms that control GH release. In order to explore further the underlying pathophysiology of aberrant hypothalamic-pituitary-somatotropic function, we administered GHRH (1 ug/kg) to depressed inpatients and age/sex/weight-matched controls. Blood samples for GH and somatomedin were obtained at –60, –30, –10, 0, 5, 10, 15, 20, 30, 45, 60, 75, 90, 105, and 120 minutes. The stimulation study was repeated at hospital discharge for the patients, and at a comparable time for controls. A 1 mg dexamethasone suppression test (DST) was also performed. Baseline GH levels were comparable for patients and controls, and within normal limits. There was marked heterogeneity in the stimulated GH response. No correlation between baseline GH values and peak responses was observed in individual groups or in the sample as a whole. Peak GH concentrations, as well as somatomedin response over time, are compared between patient and control groups, as a function of clinical state. The relationship between functional status of the axis at testing and stimulated response, as well as possible mechanisms for aberrant GH secretory dynamics will be discussed.

NR71 Monday May 13, 9:00 a.m.-10:30 a.m.

Disturbed Neuroendocrine Regulation in Depression

Robert L. Trestman, M.D., Department of Psychiatry, Bronx VA Medical Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Martin Teicher, M.D., Emil F. Coccaro, M.D., David Harper, B.S., Theresa Mahon, B.A., Vivian Mitropoulou, M.A., Larry J. Siever, M.D.

Summary:

The hypothesis of dysregulated monoamine/neuroendocrine systems in major depression implies that, compared with normal controls 1) the relative amplitude of circadian alterations in plasma metabolites of these systems will be reduced or flattened, 2) the phase relationships among the monoamine/neuroendocrine systems will be disturbed, and 3) normally dominant circadian rhythms will be replaced with higher frequency ultradian harmonics. Nonlinear multioscillator cosinor analysis of serial plasma metabolite concentrations is a tool that allows these questions to be addressed.

Concentrations of plasma MHPG were sampled hourly, and plasma norepinephrine, cortisol, growth hormone, and prolactin were sampled at half-hour intervals over 24 hours in 16 patients with acute major depression and 12 normal controls. Preliminary findings in a subsample of 13 acutely depressed patients and six normal controls revealed a decrease in circadian ($p<0.05$) and a trend toward a decrease in ultradian ($p<0.1$) relative amplitudes of plasma cortisol, a phase advance of plasma MHPG ($p<0.05$), and increased variability in MHPG rhythms in acutely depressed patients compared with normal controls. These results support the utility of the multioscillator model and offer partial support for the dysregulation hypothesis of depression.

NR72 Monday May 13, 9:00 a.m.-10:30 a.m.

Ultradian Cycles in Depression

Donald Hall, M.D., Psychiatry, Walter Reed AMC, Washington, DC 20307; Helen Sing, M.S., Alan Romanoski, M.D.

Summary:

We monitored the variation of mood in a group of patients (n = 9) diagnosed as having DSM-III-R-defined depressive disorders and a group of nondepressed subjects (n = 9) over a period of 12 consecutive hours. We detected cyclical patterns of mood variation (ultradian cycles) and circadian trends in both groups. We also found that the depressed group demonstrated greater hour-to-hour variability of mood than the nondepressed group. This increased variance was found to be primarily due to changes in the character of the respective group's ultradian cycles. The amplitude of the ultradian cycles of mood was significantly greater in the group of depressed patients. These differences in hour-to-hour variations (ultradian cycles) may have implications for both clinical and research studies of depression.

NR73 Monday May 13, 9:00 a.m.-10:30 a.m.

Effect of Anticholinergics on Mood

William M. Kenny, M.D., Psychiatry, Univ of CA San Diego, 3350 La Jolla Village Drive, San Diego, CA 92161; John Lauriello, M.D., J. Christian Gillin, M.D.

Summary:

Introduction: Janowsky and associates have proposed that depression results from an increased ratio of cholinergic to aminergic central neurotransmission. Subsequent work has established that centrally active cholinomimetic drugs can induce depressive symptomatology; however the effect of centrally active anticholinergic agents on depressed patients has not been investigated. We hypothesize that the centrally active anticholinergic, biperiden, will have antidepressant effects on depressed patients.

Methods: Ten unmedicated SCID-diagnosed patients from both the inpatient and outpatient SDVAMC Clinical Research Center were studied in a randomized, double-blind, parallel design over six weeks. Inclusion criteria were a HDRS score of 14 and no contraindication to receiving tricyclics and anticholinergic agents. The patients remained drug-free for the first week of the study, then beginning week 2, patients received biperiden 12 mg/day or glycopyrrolate 1 mg/day for four weeks, and then placebo for one week.

Results: Mean scores for HDRS in active group at weeks 1 and 5 were 21.5 and 16.8 vs. placebo group scores of 21.2 and 17.8, the difference not being statistically significant.

Conclusion: In this small group of depressed patients biperiden was not found to be more efficacious than placebo in alleviating depressive symptomatology.

NR74 Monday May 13, 9:00 a.m.-10:30 a.m.

Hypothalamic-Pituitary-Adrenal Dysfunction and Family Subtypes of Depression

Adrienne C. Lahti, M.D., Psychiatry, University of MI, 1500 E. Medical Ctr Dr. 0018, Ann Arbor, MI 48019; Roger F. Haskett, M.D., Virginia Murphy-Weinberg, R.N., Elizabeth A. Young, M.D., Stanley J. Watson, M.D., Huda Akil, Ph.D.

Summary:

Many patients with major depressive disorder are found to have disturbed functioning of the hypothalamic-pituitary-adrenal (HPA) axis. Indicators of this dyregulation include the escape of B-endorphin (B-end) and cortisol secretion from dexamethasone suppression. Although the bipolar(BP)/unipolar(UP) distinction appears to be the most widely validated characteristic for subgrouping mood disorders, this classification has not been shown to predict cortisol nonsuppression with the dexamethasone suppression test (DST). In a preliminary study of the B-end response to dexamethasone in 19 patients with major depression, however, we found that 50% of the BP patients and 35% of the UP patients were B-end nonsuppressors. We hypothesized that inclusion of the family history data in the UP/BP categorization of patients, in addition to the proband's diagnosis, would enhance this association. Family history data on all first-degree relatives have been obtained from 11 families by an interviewer who was blind to the proband's diagnosis, using the Family Informant Schedule and Criteria (FISC) with at least two informants. In patients with either a personal or a family history of BP disorder, 66% were B-end nonsuppressors compared with 20% of the UP patients. These data suggest that the relationship between HPA dysregulation and depression may be more frequent in patients from families with evidence of BP disorder.

NR75 Monday May 13, 9:00 a.m.-10:30 a.m.

Hypothesis to Explain the Nature of Responsiveness to Tricyclic Antidepressant Drugs

Atul Luthra, M.D., Psychiatry, Camp Hill Hospital, 1763 Robie Street, Halifax N.S., Canada B3H 3G2

Summary:

Approximately one-third of patients with major depression fail to respond to the first choice of tricyclic antidepressant (AD), and often there is a need to change the drug or add adjuncts in the form of lithium, methlyphenidate, another AD drug or T3 to produce a response. The nature of responsiveness to AD drugs is not well understood.

A study was undertaken to investigate the role of norepinephrine (NE) disposition on the wide interindividual variability in the dose of infused NE required to produce a 50% reduction in dorsal hand vein diameter (EC50). The results obtained on NE disposition are noted and used to generate a hypothesis to explain the nature of responsiveness to AD drugs.

Individuals ranged from "low" to "high" disposers of NE. ADs also have a wide interindividual bioavailability, ranging from low to high. It is hypothesized that a pattern of disposition, similar to that observed with exogenous NE, exists for endogenous increases in NE secondary to AD drugs. Patients who represent different permutations of the variables, NE disposition and AD bioavailability at each end of the spectrum are divided into four cohorts and used to provide a model to explain the nature of responsiveness to AD drugs.

NR76 Monday May 13, 9:00 a.m.-10:30 a.m.

Buprenorphine in Refractory Depression

Gwen L. Zornberg, M.D., Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178; J. Alexander Bodkin, M.D., Jonathan O. Cole, M.D.

Summary:

Buprenorphine, a mixed opioid agonist-antagonist, has mood elevating and anxiolytic properties similar to morphine, but is much less likely to cause physical dependence, even with chronic use.

In the treatment of severe depression, monoaminergic agents have proven to be neither universally effective nor free from adverse effects of their own. For patients unresponsive to or intolerant of these agents, pharmacotherapy directed at the endogenous opioid system needs to be evaluated.

We report on the first five subjects in an open study of buprenorphine in treatment refractory depression. Subjects were nonpsychotic unipolar depressives, average baseline Ham-D = 30.8 (range 26-37). Adequate trials of antidepressants from at least two

chemical classes had been unsuccessful (average number of different antidepressants previously tried = 9.2, range = 5-20).

Four of five patients responded, with an average end-point Ham-D = 8 (74% reduction, range = 52–87%). All responders wished to continue on the medication after the trial concluded. This group showed a 44.7% increase in GAS scores (range = 30-60%).

These findings indicate a marked benefit for some treatment refractory depressives. Placebo effect is unlikely to account fully for this observation in subjects unresponsive to multiple previous drug trials.

NR77 Monday May 13, 9:00 a.m.-10:30 a.m.

Depression Versus PTSD: Diagnosing Via Neural Networks

Ibrahim Gunay, M.D., Department of Psychiatry, University of Cincinnati, 231 Bethesda Avenue, Cincinnati, OH 45267; Eugene Somoza, M.D.

Summary:

The similarities between different psychiatric illnesses often present the clinician with a diagnostic challenge. This is especially true for patients with PTSD, since this disorder has symptoms that overlap with those of depression. It would be interesting to study this symptom overlap, as measured by an 18-item BPRS. Additionally, it would be useful to train an artificial neural network to distinguish between these two symptom patterns to learn that combination of symptoms that is most important in separating them. The study population consisted of all walk-in patients in a VA psychiatric evaluation center over a one-year period with a diagnosis of either PTSD (N = 189) or depression (N = 335). PTSD patients had higher BPRS scores than depressed patients on 12 of the 18 BPRS items, including depressed mood, suicidality and guilt feelings. A 126-input node neural net utilizing backpropagation was trained on half of the patients and tested on the other half. The sensitivity for detecting depression (over PTSD) was 82%. The specificity was 53%. Methods of optimizing this to improve indices of diagnostic performance by varying the number of training cycles, the number of hidden nodes, and other network parameters will be discussed. The relative importance of the BPRS items in discriminating between these two disorders will be addressed.

NR78 Monday May 13, 9:00 a.m.-10:30 a.m.

Levoprotiline Versus Amitriptyline in Depression

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Summary:

Noradrenergic, serotonergic and even dopaminergic mechanisms have been implicated in the mediation of the antidepressant effects of established agents. The present study is a double-blind, placebo-controlled comparison between levoprotiline (LVP) and amitriptyline (AMI) in the treatment of depression. Levoprotiline is a pure R (–) enantioner of oxaprotiline, but unlike oxaprotiline and the predecessor maprotiline, it lacks monoaminergic effects. In addition to testing the potential antidepressant effects of the new compound, the results of the study will have important implications on the monoamine hypothesis of depression. Twenty-three outpatients who met DSM-III-R criteria for major depression and maintained the degree of symptom severity after one week placebo washout, were randomized and completed six week's trial with LVP (N = 10, dose = 197.5 mg/day) AMI (N = 6, dose = 142.5 mg/day) or placebo (PBO, N = 7). ANOVA, using Beck Depression Inventory (BDI) as dependant measure revealed no group differences at pretreatment, and the average sample score was 24.6. However, at posttreatment, group differences emerged that were accounted for by the AMI-PBO contrast [T(20) = 2.47; p = 0.02], and a trend between AMI and LVP was observed [T(20) = 1.47; p = 0.08]. In clinically meaningful terms, with AMI there was 79% improvement and 83.3% response (posttreatment BDI score $\leq$9) with LVP 48.8% and 50% and with PBO 30.6 and 28.6%, respectively. These findings revealed that LVP was more similar to PBO than to AMI and thus fail to challenge the monoamine hypothesis of depression.

NR79 Monday May 13, 9:00 a.m.-10:30 a.m.

Cyproheptadine in Major Depression

Enrico G. Camara, M.D., Department of Psychiatry, Cleveland Clinic, 9500 Euclid Avenue – P68, Cleveland, OH 44195

Summary:

The objective of this pilot study was to assess the antidepressant efficacy of cyproheptadine in drug-free, unipolar, treatment-resistant, depressed patients exhibiting hypothalamic-pituitary-adrenal (HPA) axis dysfunction. Patients were referred by other psychiatrists in our department or recruited from a newspaper ad. Eleven patients showing either elevated urinary free cortisol (UFC) (n = 4), nonsuppressed dexamethasone suppression test (DST) (n = 2) or both (n = 5) completed a four-week trial of cyproheptadine 24-32mg PO per day in three divided doses. Seven patients (64%) showed at least 50% reduction in depression scores (Beck Depression Index; Hamilton Depression Rating Scale). Four patients (36%) had complete resolution of their depressive symptoms. Responders showed reduction of their UFCs to the normal range and/or converted to suppressors in the DST. All patients tolerated the medication well. Six of the seven patients had depressive symptoms return within two weeks after the discontinuation of the cyproheptadine. The clinical implications of these preliminary findings are discussed.

NR80 Monday May 13, 9:00 a.m.-10:30 a.m.

Vitamin E in the Treatment of Tardive Dyskinesia

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Summary:

Alpha-tocopherol (vitamin E), a potent antioxidant, was compared to placebo in a double-blind, randomized crossover study of 33 subjects with Tardive Dyskinesia (TD). Six subjects terminated prematurely, while the remaining 27 subjects (17 female; 10 male) had a mean age $\pm$ SD of 42.9 $\pm$ 12.6 and an age range of 19–69. Twenty-two subjects satisfied DSM-III-R criteria for schizophrenia and five for bipolar disorder. All subjects met Schooler and Kane Criteria for at least mild TD. Patients' psychopathology and psychotropic drug regimen remained stable throughout the study. Subjects were randomly assigned to two six-week treatment periods, each with vitamin E and placebo. A two- to three-week placebo washout was conducted between each treatment period. Study drugs were administered double-blind on a fixed dosage schedule of one 400 I.U. capsule of vitamin E, or one identical placebo capsule, TID. The Abnormal Involuntary Movement Scale (AIMS) and the Extrapyramidal Symptom Rating Scale (ESRS) served as primary outcome measures. Scores on the ESRS subscales I-VI and AIMS total score, at termination of vitamin E and placebo treatment from analysis of variance for the two-period crossover design, revealed no significant differences (with alpha levels set at .05). Our results suggest that vitamin E, at the dosage level used, confers no consistent *short-term* symptomatic benefit to patients with TD.

NR81 Monday May 13, 9:00 a.m.-10:30 a.m.

A Test of Hopelessness in Depression and Suicide

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Summary:

Data from the Epidemiological Catchment Area (ECA) survey are used longitudinally to examine the role of hopelessness as a predisposing risk factor for major depression and suicidal ideation. Residents living in the community in the three ECA sites that collected incidence information at waves one and two are included in the analysis. A dichotomous global measure of hopelessness is used. Logistic regression modeling was employed for the analysis. Age, sex, race, marital status, SES, health care utilization, disability, and diagnosis of depression at wave one are covariates in the regression models.

In the two longitudinal analyses, hopelessness predicts major depression and suicidal ideation in the year following the wave one interview, even controlling for initial levels of the variables. In the former, depression at or before wave one is controlled for in the model. In the latter, depression ever in lifetime at wave two is included as a covariate. Hopelessness is significant at the $p < .0001$ level for both predictive models. The results are generally supportive of a cognitive model of depression and suicide with hopelessness as a predisposing risk factor.

NR82 Monday May 13, 9:00 a.m.-10:30 a.m.

Oculomotor Function in OCD

Allen Y. Tien, M.D., Mental Hyg., Johns Hopkins Univ., 624 North Broadway Street, Baltimore, MD 21205; Steve Machlin, M.D., Godfrey Pearlson, M.B., Fred Bylsma, Ph.D.

Summary:

Current oculomotor knowledge suggests that for goal-guided saccadic eye movements, neuroanatomical circuits encompassing frontal cortex and basal ganglia are important. Because MRI and PET studies suggest basal ganglia abnormalities in subjects with obsessive compulsive disorder (OCD), it was logical to investigate oculomotor function in such individuals. Eleven OCD subjects (mean age = 39, five males) and 14 normal subjects (mean age = 38, seven males) were assessed. Goal-guided performance was measured with an antisaccade task, in which subjects must look to an imaginary point opposite a stimulus, and inhibit glancing at the stimulus. To assess basic oculomotor parameters of reaction time, velocity, and accuracy a reflexive saccade task to temporally random targets was given.

In the control reflexive saccade task no significant performance differences were seen. In the goal-guided antisaccade task, a highly significant difference in mean error rate (glancing at the stimulus) was observed (separate variance $t = -3.42$, 2-tailed $p = .004$). The mean in the OCD group was 0.38 (SD = 0.23), while the mean rate of errors in the control group was 0.13 (SD = 0.11). The distribution of error rate in the OCD group appeared bimodal.

The results suggest a deficit in goal-guided saccade performance in a subset of individuals with obsessive compulsive disorder.

NR83 Monday May 13, 9:00 a.m.-10:30 a.m.

Community Age/Gender Incidence of Hallucinations

Allen Y. Tien, M.D., Mental Hyg., Johns Hopkins Univ., 624 North Broadway Street, Baltimore, MD 21205

Summary:

A primary manifestation of psychosis is occurrence of hallucinations. However, there is little knowledge on age and gender distributions for incidence of hallucinations. To provide information, data from the NIMH Epidemiologic Catchment Area (ECA) program were examined. The ECA assessed occurrence of psychopathology using the NIMH Diagnostic Interview Schedule (DIS). Subjects were given the DIS at baseline and a year later at follow-up, with 15,258 participants. Subjects reporting hallucinations at baseline were excluded, so that follow-up reports of hallucinations were new occurrences.

To observe age distributions, a Generalized Additive Interactive Model (GAIM) computer program was employed. The GAIM algorithm uses a cubic spline smoothing function to estimate a nonlinear age curve.

The incidence of visual hallucinations was slightly higher in males (about 20 per 1000 per year) than females (about 13 per 1000 per year) across the age span from 18 to 80 years old, with a subsequent increase in the rate for females (up to about 40 per 1000 per year) after age 80. For auditory hallucinations there was an age 25-30 peak in males with a trough for females, and a later age 40-50 peak for females.

Although the DIS data are "noisy," these curves demonstrate age- and gender-varying forces in the population for the occurrence of psychotic conditions.

NR84 Monday May 13, 9:00 a.m.-10:30 a.m.

Mood Symptoms of Professional Cheerleaders

Joseph Henry, M.D., Department of Psychiatry, University of Miami, 1400 NW 10th Ave., Suite 304A, Miami, FL 33136; Paul Goodnick, M.D.

Summary:

The spectrum of bipolar disorder (BPD) may include subclinical forms, e.g., a significant number of writers experience hypomanic-like episodes (Jamison, 1989). These hypomanic symptoms (sx) might lead to choice of extroverted types of vocation. The biological basis for the hypomanic sx may simultaneously increase vulnerability to depressive sx. Cheerleaders (Ch) for professional football teams undergo a demanding schedule of practices in addition to FT employment or education. As a logical intermediate in the spectrum of mood sx, NFL Ch completed the General Behavior Inventory (Depue, 1981) for lifetime (L) and past month (PM) subclinical sx. Results to date from 76 Ch are contrasted to 17 similar-aged controls (C) and 33 bipolar patients (BP) in remission, who have been shown to have sx between episodes (Goodnick, 1987). ANOVA showed significant differences among the groups: L Means were C(2.7 ± 5.9), Ch (9.4 ± 8.2), BP (11.1 ± 13.0), $F = 4.93$, $p = .009$; PM, were C (2.0 ± 3.8), Ch (10.3 ± 10.8), BP (11.5 ± 13.0), $F = 4.89$, $p = .009$. When the employment of non-student Ch's was classified by extroversion (E) (n = 34,63%)/introversion(I) (n = 20,37%), more hypomanic sx were seen in E over I for both L (6.0 vs 3.2, $p = .009$) an PM (6.3 vs 2.8, $p = .004$). No significant differences were found in rate of depressive sx. Thus, an individual's vocation and avocation may reflect the presence of subclinical forms of mood symptoms. Discussion will focus on spectrum forms and symptoms of BPD that may be beneficial, rather than detrimental, for the individual.

NR85 Monday May 13, 9:00 a.m.-10:30 a.m.

Tricyclic-Antidepressant-Induced Seizures

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Summary:

Eight cases of tricyclic antidepressant (TCA) induced seizures during routine therapy were reviewed. The only risk factor that emerged was elevated TCA plasma levels (mean + S.D. = 734 + 249 ng/ml, range = 438 to 1200 ng/ml). TCA-induced seizures can present with or without a prodrome or associated CNS toxicity. Although

there have been no previous studies in which the incidence of seizures has been correlated with TCA plasma levels, we do know that elevated TCA plasma levels exceeding 450ng/ml increase the risk of delirium. Utilization of therapeutic drug monitoring can identify patients who develop toxic TCA concentrations during routine therapy.

NR86 Monday May 13, 9:00 a.m.-10:30 a.m.

Antidepressant Effects on Melatonin Elimination

Helen L. Miller, M.D., Psychiatry, Yale University, W. Haven VAMC 950 Campbell Ave, West Haven, CT 06516; Robert N. Golden, M.D., R. Bruce Lydiard, M.D., George Mason, Ph.D., David Ekstrom, M.P.H.

Summary:

Melatonin production by the pineal gland has been used as a marker for noradrenergic function, since pineal activity is regulated primarily by the sympathetic nervous system. Previously, we reported an increase in 24-hour urinary excretion of 6-hydroxymelatonin, the principal metabolite of melatonin, after treatment of depressed patients with desipramine, buproprion, clorgyline, and tranylcypromine. We now report our preliminary findings on the effects of two other antidepressants, the serotonin reuptake inhibitor fluvoxamine, and the mixed reuptake inhibitor imipramine, on the excretion of the sulfated hydroxy metabolite of melatonin (S-MEL) in depressed patients.

Patients meeting DSM-III-R criteria for major depression were randomly assigned to double-blind treatment with fluvoxamine ($n = 13$), imipramine ($n = 10$), or placebo ($n = 13$). We collected 24-hour urine samples at baseline and after six weeks of treatment. Excretion of S-MEL, as measured by radioimmunoassay, did not change following placebo or fluvoxamine treatment. In contrast, there was a strong trend, which did not reach statistical significance, towards increased S-MEL excretion after imipramine treatment. These results, together with our earlier findings, suggest that increased melatonin formation may be limited to those antidepressant treatments in which the parent compound and/or active metabolite have direct effects on norepinephrine.

NR87 Monday May 13, 9:00 a.m.-10:30 a.m.

Benzodiazepines and Human Vision

Thomas E. Schlaepfer, M.D., Psychiatry, University of Bern, Mutenstrasse 21, Bern CH 3010, Switzerland; Hans-U. Fisch, M.D.

Summary:

Psychophysical experiments allow us to establish correlations between Single Retinal Ganglion Cells (SRGC) in cats and human visual receptive fields. In the cat, bicuculline decreases the activity of the inhibitory surround of SRGC. Human center and inhibitory surrounds of visual receptive fields were determined with subthreshold summation. Stimuli were three vertical parallel lines displayed for 120ms on a CRT. The contrast of the flanking lines was 3/8 of the contrast of the central line. Dependent variable was the threshold of the central line, independent variable the distance between the central and the flanking lines. In four experiments ($n = 6$ subjects each) midazolam (M) p. o. increased the threshold in the inhibitory part of the receptive fields (0.24° of the visual angle) in a dose-dependent manner (ANOVA: M 4mg: $p < 0.1$; M 8mg: $p < 0.05$, M 15mg: $p < 0.01$). After six hours, predrug values were obtained. After dark-adaptation (eight subjects) no effect of M on visual receptive fields was found. Control experiments without drugs, atropine (1mg i.v.), sulpiride (100mg i.m.), and levodopa (100mg p.o.) had no effect.

Specific actions of GABA on cat SRGC are replicated with M in humans. After dark-adaptation, no free GABA may be available and M, therefore, have no effect. The visual system may be a useful model to bridge the gap between animal and human psychopharmacology.

NR88 Monday May 13, 9:00 a.m.-10:30 a.m.

Alprazolam Versus Behavioral Treatment Post-Rape

Kathleen A. Hughes, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; Dean G. Kilpatrick, Ph.D, James C. Ballenger, M.D., Heidi S. Resnick, Ph.D., Connie L. Best, M.D., Michelle Laraia, R.N.

Summary:

Rape and its long-term sequelae are a public health problem of significant proportions (Kilpatrick, Best, Veronen, 1984). Many of the chronic symptoms displayed by victims are similar to those of other anxiety disorders including panic disorder with and without agoraphobia. Because of the documented efficacy of the drug alprazolam in the treatment of panic disorder, an open-trial flexible dosing of alprazolam vs. a known efficacious treatment (i.e., cognitive-behavioral treatment) was conducted. Seventeen females aged 18-50 (mean 38 years) more than three months post-rape were randomly assigned to the drug or behavioral treatment. Baseline measures included a history and physical, a battery of psychological assessments (e.g., SCL-90, Hamilton Anxiety, etc.), and DSM-III diagnosis. Repeated measures of the psychometric testing, in addition to clinical assessments, were collected at two and eight weeks. Doses of alprazolam ranged from 1 mg to 6 mg (mean 2.8 mg).

Differential attrition was noted in that only 2/10 subjects remained in the drug group compared with 6/7 in the behavioral treatment. Limiting side effects included sedation, depression and irritability. Significant differences between groups were not found, although trends for a greater reduction of symptoms in the behavioral group were noted. Conclusions were limited by several technical and practical problems including recruitment, maintenance, and coordination of two separate research groups. Possible solutions to these problems will be addressed.

NR89 Monday May 13, 9:00 a.m.-10:30 a.m.

Somatization and Conversion Disorders: A Comparison

Kristinn Tomasson, M.D., Psychiatry, Univ of Iowa Col of Med, 500 Newton Road, Iowa City, IA 52242; David A. Kent, M.D., William H. Coryell, M.D.

Summary:

Somatization disorder (SD) and conversion disorder (CD) are both characterized by unexplained medical symptoms and have a common ancestor, hysteria. To further compare these disorders we identified through a chart review 51 CD and 65 SD patients, and conducted a four- to six-year follow up. There was a female predominance, particularly among the SD patients. The peak age at onset was late teens for SD patients, but CD patients had onsets throughout the life span. The SD patients were more likely to have a history of depression (48% vs. 18%), panic disorder (20% vs. 0%), alcohol abuse (32% vs. 18%) and substance abuse (18% vs. 2%), suicide attempts (50% vs. 15%) and divorce (57% vs. 31%). Thirty-two of the CD patients and 38 of the SD patients were reevaluated four to six years later; one CD and four SD patients had died, including one (a SD) by suicide. Few had a medical explanation of the index chief complaint at follow up. Overall morbidity was higher among the SD patients according to the Short form health survey, and SCL-90, with 41% of the SD patients compared with 75% of the CD patients rating their physical health as good.

NR90 Monday May 13, 9:00 a.m.-10:30 a.m.

Body Dysmorphic Disorder: A Report of 20 Cases

Katharine A. Phillips, M.D., McLean Hospital, 115 Mill Street, Belmont, MA 02178; Susan L. McElroy, M.D., Paul E. Keck, Jr., M.D., Harrison G. Pope, Jr., M.D., James I. Hudson, M.D.

Summary:

Problem: Body dysmorphic disorder (BDD), a preoccupation with an imagined defect in physical appearance, has long been recognized in the European literature but largely neglected in American psychiatry. *Method:* We assessed in 20 patients with BDD, its phenomenology, age of onset, course, associated features, treatment history and response, and comorbid DSM-III-R disorders, using the Structured Clinical Interview for DSM-III-R and a supplemental semi-structured interview. Family history was obtained by a blinded investigator. *Results:* BDD's average age of onset was 15 (range of 6-28) and tended to be chronic, with an average duration of illness of 15 years. The 13 men and seven women studied reported a lifetime average of five bodily preoccupations. Associated features included ideas and delusions of reference, excessive mirror checking, and attempts to camouflage the "deformity." Most patients were significantly impaired by their symptoms, avoiding such activities as school, work, and dating. Ninety percent of the sample had an associated lifetime diagnosis of major mood disorder; 35%, a psychotic disorder; and 80%, an anxiety disorder. Patients had received an average of five psychotropic medications, as well as cosmetic surgery and dermatologic treatments, with generally poor response to all except fluoxetine and clomipramine (50% complete or partial response vs. 5% with all other medication trials). *Conclusion:* BDD is an often-secret, chronic disorder that can cause significant distress and impairment, has high comorbidity with other psychiatric disorders, and may respond to psychiatric treatment.

NR91 Monday May 13, 9:00 a.m.-10:30 a.m.

A Comparison of Doxepin, Trazodone and Biofeedback Therapy in the Adjunctive Treatment of Chronic Back Pain

Edward A. Workman, M.D., Psychiatry, Univ of Virginia, VAMC Dept of Psychiatry, Salem, VA 24153; Delmar D. Short, M.D., Frank F. Tellian, M.D.

Summary:

Thirty consecutive patients entering an outpatient, community-based pain management program were included as subjects in this investigation. All patients were treated with weekly physical therapy sessions (consisting of hot and cold packs, structured exercise and stretching therapies). In addition, all subjects were treated with weekly electromyographic biofeedback sessions with training and homework practice in progressive deep muscle relaxation. Additionally, 20 patients were randomly assigned to treatment with either Doxepin titrated within 10 days to 150 mg qhs, or Trazodone titrated within 10 says to 300 mg qhs. All patients suffered from chronic back pain.

Dependent measures included visual analogue scale patient ratings of typical weekly pain levels, activity levels, and mood. The Beck Depression Inventory was also used as an outcome measure. Patients were measured at entry into the study, after one month of treatment, and after four months of treatment.

The data from this investigation were analyzed via One Way Analyses of Variance with Bonferonni follow-up tests. Patient ratings on the above measures, and Beck scores were converted to change scores for data analysis. The ANOVAs for change in pain and activity levels were nonsignificant at one month of treatment. However, the ANOVAs for mood improvement and Beck Depression Inventory change scores were significant at $p < .01$. Bonferonni follow-up tests revealed that Doxepin and Trazodone were equally effective on these outcome dimensions, and both were significantly superior to the biofeedback control condition ($p < .001$).

Evaluation of the data at four months of treatment yielded results not inconsistent with those found at one month. However, side effects were clearly more prominent with Doxepin (particularly antihistaminic and antimuscarinic effects, as predicted by the drugs' respective receptor affinities) than with Trazodone. These results are discussed in terms of characteristics of our sample (as compared to prior studies), the general use of antidepressants in pain medicine, and the apparent specificity of these agents for the affective components of chronic pain syndromes.

NR92 Monday May 13, 9:00 a.m.-10:30 a.m.

Amitriptyline Myocardial Toxicity

Claudi Udina, M.D., Psychiatry, Hosp Gral Catalunya, Gomera SN Sant Cugat, Barcelona 08190, Spain; Manuel Ballester, M.D., Ignasi Carrio, M.D., Vicens Marti, M.D.

Summary:

In order to assess the presence of TAD-induced myocardial damage, a series of 22 young patients with major depression treated with imipramine, clomipramine or amitriptyline were studied with antimyosin (AM).

A heart-to-lung ratio (HLR) was used to quantitate relative AM uptake. HLR in a normal group was 1.39 ± 0.07. Patients on imipramine (HLR: 1.40 ± 0.08) or clomipramine (HLR: 1.43 ± 0.06) showed normal uptake. Those on amitriptyline had a higher ratio (HLR: 1.60 ± 0.12) compared with nonamitriptyline or normal groups ($p < 0.05$). None of the 15 patients on imipramine or clomipramine showed abnormal HLR; while four of seven on amitriptyline did ($p < 0.05$). In these four patients, a second AM study after amitriptyline withdrawal decreased HLR from 1.68 ± 0.09 to 1.48 ± 0.1 ($p < 0.05$), and normalized HLR in three of four patients. Ejection fraction was normal in all TAD patients except in one, on amitriptyline treatment and abnormal HLR, who disclosed the features of dilated cardiomyopathy.

The present study provides a description of TAD-induced reversible myocardial cardiotoxicity identified by AM. This study was carried out at Hospital de Sant Pau in Barcelona (Spain) and was supported by the FISS, grant no. 0723/89.

NR93 Monday May 13, 9:00 a.m.-10:30 a.m.

Primate Behavioral Response to Lactate and Yohimbine

Jeremy D. Coplan, M.D., Dept of Psychiatry, SUNY-HSCB, 450 Clarkson Avenue, Brooklyn, NY 11203; Leonard A. Rosenblum, Ph.D., Steven Friedman, Ph.D., Trina B. Bassoff, M.A., Jack M. Gorman, M.D.

Summary:

Randomized, placebo-controlled, blind observations of behavioral responses to two human panicogens (sodium lactate and yohimbine) were conducted in eight unrestrained bonnet macaques. Four of the subjects were normally reared and four were isolate reared. Intravenous administration of yohimbine (0.2 mg/kg — over 10 minutes) produced significant increases in enervative behaviors with all subjects showing the effect. Sodium-lactate (0.5 molar at 10 cc./kg — over 10 minutes) produced definite anxiety responses in some subjects of each rearing condition, but these effects were not statistically significant overall. In contrast to our previous study using oral yohimbine, no rearing effect for either compound was evident in the current study. Although the enervative effects of yohimbine contrast with the usually reported primate response to external threat, behavioral inhibition and withdrawal appears to represent an important and relevant aspect of anxiety in these animals. The absence of a consistent effect of lactate contrasts with the con-

sistent yohimbine response. This finding suggests that whereas the substrate on which yohimbine operates is present in all our subjects, the as-yet-unknown mechanism triggering anxiety responses to lactate only appears in a portion of these nonhuman primates.

NR94 Monday May 13, 9:00 a.m.-10:30 a.m.

Renal Side Effects of Long-Term Lithium Treatment

Hakan Coskunol, M.D., Psychiatry, EGE University, Tip Fakultesi Bornova, Izmir 35100, Turkey; Simavi Vahip, M.D., Evert J.D. Mees, M.D., Ali Basci, M.D., Oya Bayindir, M.D., Isik Tuglular, M.D., Refet Saygili, M.D.

Summary:

In this study our aim was to investigate the excretion of beta 2-microglobulin and glycosaminoglycans (GAG) in urine as indicators of lithium-induced renal damage.

We compared beta 2-microglobulin and GAG excretion in 108 patients with bipolar disorder who were on lithium treatment for 1-15 years, with 29 matched psychiatric control patients. We used 24-hour urine collections to determine daily urine volume, GAG, beta 2-microglobulin levels and creatinine clearances. Maximal urinary osmolality was measured after 16 hours of fluid restriction period. Three measures were taken consecutively with one-hour intervals.

Twenty-four-hour urine volume and urine beta 2-microglobulin values were significantly higher and maximal urinary osmolality was significantly lower in patients on lithium than controls. No relationship was found between creatinine clearances and duration of disorder time on lithium and daily lithium dosages. Time on lithium did not affect concentrating capacity. Both 24-hour urine volume and maximal urinary osmolality showed significant correlations with lithium dosages.

NR95 Monday May 13, 9:00 a.m.-10:30 a.m.

Dermatological Side Effects of Lithium

Isil Vahip, Psychiatry, EGE University, Tip Fakultesi Bornova, Izmir 35100, Turkey; Tevhide Dincer, M.D., Simavi Vahip, M.D., Gunseli Ozturk, M.D., Isik Tuglular, M.D,, Refet Saygili, M.D., Atilla Varol, M.D.

Summary:

The aim of this study was to determine the frequency and the types of dermatological side effects of lithium. Three groups were studied: 1) Patients with bipolar disorder in remission, who were receiving only lithium ("Lithium group"; 42 women, 57 men = 99 cases) 2) Same diagnosis (most were newly remitted from a manic or hypomanic episode) but on lithium and neuroleptic combination treatment ("Combination group"; 23 women, 23 men = 46 cases) 3) Cases with no mental disorders and not taking any drugs ("Control group"; 33 women, 45 men = 78 cases).

All cases were examined by two dermatologists. They were blind on cases diagnosis, past histories and medications. Some important results are: 1) There were significant differences in the frequency of glossitis, xeroderma, acneiform eruptions, palmoplanter hyperkerotosis, kerotosis pilaris, alopecia, perleche and ungual deformities between the lithium group and the control group. 2) Only glossitis was found more frequently in the lithium group than in the combination group. 3) There was no significant differences between the lithium group and the combination group in having one or more than one dermatological lesion. But the lithium group was having significantly more lesions than the control group.

NR96 Monday May 13, 9:00 a.m.-10:30 a.m.

Subjective Versus Objective Memory Measures in ECT

Iannis Zervas, M.D., Department of Psychiatry, SUNY-at Stony Brook, HSC T10 Rm 020, Stony Brook, NY 11794; Max Fink, M.D., Lina Jandorf, M.A.

Summary:

Fifteen depressed subjects (11 female, 4 male), mean age of 51.3 years (SD: 19.6) received an average of 7.8 ECT (SD: 1.8) in a prospective study to assess memory factors before and after treatment. Testing conditions were kept similar pre and post ECT. The patients were assessed objectively with standardized instruments for depression, global functioning, and immediate and delayed (24 hours) memory, both verbal and visual. At the same testing intervals a subjective memory scale was used to assess the patients' own impressions of their memory functioning. All clinical measures improved significantly ($p < 0.0001$). Memory measures indicated a nonsignificant change in immediate memory and a highly significant decrease ($p < 0.0006$) in delayed memory. The subjective scale however indicated that the patients were not aware of the deficit showing a trend to consider their memory improved after ECT, probably reflecting the improvement in their emotional state.

NR97 Monday May 13, 9:00 a.m.-10:30 a.m.

The Effect of ECT on EEG Coherence

Andrew D. Krystal, M.D., Department of Psychiatry, Duke University, Box 2995, Durham, NC 27710; Richard D. Weiner, M.D., C. Edward Coffey, M.D., Pamela Smith, Rebekka Arias

Summary:

ECT has been reported to increase low-frequency activity, decease high-frequency amplitude and alter interhemispheric symmetry in the electroencephalogram. In order to further study EEG changes induced by ECT we studied interhemispheric and intrahemispheric coherence in the resting EEG of 22 subjects with unipolar major depression from eyes-closed, bipolar EEG recordings made prior to and three days after a course of either pulse unilateral (PUL) or pulse bilateral (PBL) treatments. With this method we hoped to study how ECT affects the degree of physiologic coupling between different parts of the brain. In terms of overall ECT effects, there was a consistent posttreatment decrease in alpha coherence in every electrode pair studied, with the greatest differences being in temporal (p less than 0.0001) and frontotemporal (p less than 0.0006) interhemispheric coherence. There were also increases in low-frequency coherence, the largest being in fronto-central interhemispheric coherence (p less than 0.0002). Differences between PUL and PBL ECT were greatest in the coherence between anterior and centroparietal leads. Here theta coherence was greater on the left than right after PUL but not PBL ECT (p less than 0.0095). The relationship of these findings to ECT-induced changes in EEG spectral amplitude and symmetry, memory change, and treatment efficacy will be discussed.

NR98 Monday May 13, 9:00 a.m.-10:30 a.m.

Coding Interpersonal Processes in Family Therapy

Carol Tingle, M.D., Department of Psychiatry, Univ. of Mississippi-SOM, 2500 N. State Street, Jackson MS 39216; Mark McLain, M.D., Dinesh Mittal, M.D., Nancy Krejmas, M.D., Jeanetta Rains, Ph.D., James L. Griffith, M.D., Melissa E. Griffith, M.S.N.

Summary:

In-session consultations by therapist teams are widely used in

family therapy, but have seldom been studied empirically. In this study a detailed analysis of family and therapist interactions during "reflecting team" consultations was undertaken to: (a) describe the interpersonal process underlying reflection techniques in therapy, and (b) delineate the nature and course of symptom change within the distressed family.

Participants were physician-referred families in which the identified patients were diagnosed with a somatoform disorder. Initial treatment sessions of six families (10-minute preconsultation, during-consultation, 10-minute post-consultation segments; videotaped with verbatim transcripts) were coded by external raters using the Structural Analysis of Social Behavior (SASB). SASB is a well-validated observer-rated coding system for characterizing social communications according to focus of attention (i.e., other, self, intrapsychic) and two orthogonal dimensions of affiliation and interdependence.

Interactions among reflecting team members during the consultation (observed by family members) showed 87% high affiliation and low interdependency codes (e.g., 1-4: "Nurturing and Protecting"; 2-4 "Trusting and Relying"; p.01). Immediate post-consultation shifts in structural interactions among family members were observed for five of six families (e.g., increased 2-4: "Trusting and Relying"; decreased 1-6: "Belittling and Blaming"; p.05).

NR99 Monday May 13, 9:00 a.m.-10:30 a.m.

Personal Therapy for Psychiatry Residents

Anne I. Koplin, M.D., Psychiatry, Sinai Samaritan, 2000 W. Kilbourn Avenue, Milwaukee, WI 53233; Mary Gutmann, Ph.D.

Summary:

Despite the shift of psychiatry to more biologic models of care, the question of psychotherapy for psychiatric residents remains relevant, perhaps even more so.

A survey was sent to all psychiatric residents and full-time faculty in the three residency programs in the state of Wisconsin to assess attitudes about therapy, barriers to therapy and experience in treatment. The one-page questionnaire consisted of seven questions, both open ended and multiple choice.

A total of 72 questionnaires were returned from 120 sent (60%). The majority (72.2%) believed that therapy should not be obligatory for residents. However, 59% of faculty and 50% of residents indicated they were in therapy during residency. Both residents and faculty considered personal issues to be the primary reason for entering therapy. Common barriers included cost, time availability and perceived severity of problem. Beliefs about therapy were independent of years in training or experience in therapy. The choice for therapy is based more on personal than educational goals.

These results suggest that it is important for training programs to recognize and reinforce the personal value of therapy for residents.

NR100 Monday May 13, 9:00 a.m.-10:30 a.m.

A Basic Computer Curriculum for Psychiatry

T. Bradley Tanner, M.D., Psych WPIC, Univ of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213; Stuart Gitlow, M.D., Michael D. Rancurello, M.D.

Summary:

The explosive growth of computer software and hardware is daunting to many health care professionals. Computerese with its ROMs, RAMs, CPUs and Megabytes is often unintelligible. The novice can easily abandon the process of learning how to use a computer and return to the more comfortable, yet much less complicated, world of clinical practice.

Little attention has been directed toward teaching physicians the basics of computers. Each specialty can utilize certain basic computer skills; however, no one has attempted to define a core curriculum for a certain specialist, such as the psychiatrist. A basic computer curriculum was developed at Western Psychiatric Institute and Clinic of the University of Pittsburgh. The goal was to allow psychiatric residents to interact productively with a computer and realize their full potential through the use of computer technology.

Recommended basic skills and applications will be provided during the talk and in the distributed syllabus. Examples include the use of word processors, on-line and CD-ROM literature searches, multimedia computer-assisted instruction, the university electronic mail system and graphic slide preparation. The basic computer curriculum for psychiatry provides a means by which the educator can open the opportunities of computing to psychiatric colleagues and residents in training.

NR101 Monday May 13, 9:00 a.m.-10:30 a.m.

Personality Ratings Predict Criminal Recidivism

Julie A. Tinklenberg, M.S., Child Psychiatry, Stanford University, 520 Sandhill Road, Palo Alto, CA 94309; Jared R. Tinklenberg, M.D., Norman I. Dishotsky, M.D., Kristen Levitan, M.D., Hans Steiner, M.D.

Summary:

Predicting recidivism of juvenile delinquents poses a difficult but important problem. Using the constructs of distress and restraint, two independent raters, blind to outcome, categorized the personalities of 78 male juvenile delinquents incarcerated in the California prison system during 1973-76. Data for the personality classification were obtained by semistructured research interviews of juveniles while they were still incarcerated and a review of their clinical records at that time. Recidivism rates were computed from criminal records compiled by the California Department of Justice in 1987. These records were a comprehensive composition of crime data from the entire state of California and federal government. The severity of crimes was weighted according to the parole boards, usual length of sentences in years, e.g. murder = 7, robbery = 5, burglary = 1. A total recidivism score was computed by adding the weighted numbers for each individual.

We found that juveniles classified into either of the two categories lowest in restraint significantly predicted a higher recidivism score, as defined by severity and frequency of subsequent criminal activity, when compared with the four categories of higher restraint ($p = .01$, $p = .03$). Our results suggest that this categorization may be a useful aid in predicting which juveniles are at high risk for further criminal activity and also those at greatest risk of committing the most serious crimes.

NR102 Monday May 13, 9:00 a.m.-10:30 a.m.

Sex and Racial Bias on the Covers of The Journal of Hospital & Community Psychiatry

Gene A. Nakajima, M.D., Department of Psychiatry, NYU Medical Center, 550 First Avenue, RM 20N11, New York, NY 10016; Howard C. Rubin, M.D., Kewchang Lee, A.B.

Summary:

Since 1983, a distinguishing feature of *Hospital and Community Psychiatry (H&CP)* has been the artwork on its covers. We examined 97 covers for their racial and gender role content and obtained biographical information about the artists.

Of the 68 covers in which race could be determined, 50 depict only white people; seven, only people of color (four African-American, two Native American and one Pacific Islander); and 11, whites with non-whites. Thirty-nine percent of those covers that have people of color contain stereotyped images.

Twenty-one covers show men and 19 show women in traditional gender roles. None depict people outside traditional gender or racial stereotypes.

Eighty-nine artists are represented. Of the artists for which demographic data could be obtained, all are American. Only two are African-American, and two Native American. Eleven are women.

The median date of composition is 1909. Only 17 covers date from 1960 to the present, a period with greater numbers of female artists and artists of color.

For a publication that aspires to represent recent advances in psychiatry, its choice of art belies its mission. *H&CP* should consider choosing contemporary art that reflects the demographics of our diverse communities.

NR103 Monday May 13, 9:00 a.m.-10:30 a.m.

Diagnosis in the Psychiatric Literature: 1948-1988

R. Andrew Schultz-Ross, M.D., Psychiatry, Harvard Medical, MCI BSH 20 Administration Road, Bridgewater, MA 02324

Summary:

This paper reviews the changing focus of attention of psychiatric diagnosis in the academic literature. The contents of *The American Journal of Psychiatry* and *The British Journal of Psychiatry* were reviewed for the years 1948, 1968, and 1988. The titles of all full articles and editorials were assessed for reference to a diagnosis.

Articles related to mood and anxiety disorders increased sizably from 1948 to 1988. Articles on schizophrenia and organic diagnoses both declined. These trends occurred in both journals, but were more striking in *The American Journal of Psychiatry.*

While there are factors that limit the interpretation of these findings, diagnostic focus has changed, transatlantic differences in nosology, changes in the definition of nosology, decline in the incidence of neurosyphilis and psychopharmacological developments likely contribute to the results. However, the data also seem to reflect cultural, historical and philosophical influences that have been less addressed. Better understanding of the forces that shape psychiatric thought may improve future research and therapy.

NR104 Monday May 13, 3:00 p.m.-5:00 p.m.

HMPAO SPECT Abnormalities in Infantile Autism

Mark S. George, M.D., Neuropsychiatry, Institute of Neurology, Queen Square, London WC1N 3BG England; Durval C. Costa, M.D., Kypros Kouris, Ph.D., Howard A. Ring, M.B., Michael R. Trimble, M.B., Peter J. Ell, M.D.

Summary:

Recently, MRI scans have shown abnormalities of neuronal migration in patients with infantile autism. PET studies have failed to demonstrate consistent changes in these patients, despite their obvious disabilities. We sought to determine if SPET functional neuroimaging with 99Tcm-HMPAO might reveal changes consistent with the known structural pathology. Using a triple-detector SPET system (IGE neurocam) we studied four patients with infantile autism (ages 24-32) and four normal age- and sex-matched controls. Using ROI analysis of the frontal, temporal and visual cortex and the cerebellum, we found significant decreases in temporal and frontal activity in the autism patients (a) when compared to controls (c) (frontal/visual ratio 0.81 +/- 0.031 (c), 0.66 +/- 0.007 (a), $p = < .035$; temporal/visual ratio 1.7 +/- 0.007 (c), 1.4 +/- 0.005 (a), $p < .001$). High resolution SPET can demonstrate metabolic abnormalities in this condition. The implications of these findings will be discussed.

NR105 Monday May 13, 3:00 p.m.-5:00 p.m.

Sexual Behavior Problems in Sexually Abused Girls

Clare E. Cosentino, Ph.D., Dept. of Pediatric Psych, Columbia-Presbyterian, 6222 W. 168th St, 619N, New York, NY 10032; Dr. Heino F.L. Meyer-Bahlburg, Richard Gaines, Ph.D.

Summary:

Sexual behavior disturbances and psychopathology symptoms in sexually abused girls were investigated. Twenty sexually abused girls age 6–12 years from a child abuse clinic were contrasted with two demographically comparable control groups, 20 girls from a child psychiatry outpatient clinic, 20 girls from a general pediatric clinic. All girls and their mothers underwent an evaluation protocol comprised of a series of self-report inventories, systematic interviews and psychometric tests, including the Child Sexual Behavior Inventory (Friedrich et al. 1986) and the Child Behavior Checklist (CBCL; Achenbach & Edelbrok, 1983). Sexually abused girls manifested more sexual behavior disturbances than the other two groups: masturbating openly and excessively, exposing their genitals, indiscriminately hugging and kissing strange adults and children, and attempting to insert objects into their genitals. Abuse by fathers or stepfathers involving intercourse was associated with particularly marked sex behavior disturbances. There was a subgroup of sexually abused girls who tended to force sexual activities on siblings and peers. All of these girls had experienced prolonged sexual abuse (over two years), involving physical force, which was perpetrated by a parent. Their behavior more closely resembled that of adolescent or adult sex offenders.

NR106 Monday May 13, 3:00 p.m.-5:00 p.m.

The Increase of Multiple Television Sets and Rise in Youth Suicide

Michelle Sredy, Department of Psychiatry, Penn State University, Hershey MC-P.O. Box 850, Hershey, PA 17033; Paul Kettl, M.D., Edward O. Bixler, Ph.D.

Summary:

The explosion of youth suicide over the last 40 years correlates with the growth of television as a social force in American popular culture. To examine the link between television and youth suicide rates between 1950 and 1988, we compared yearly suicide rates for those aged 15-24 to yearly estimates of the number of TV's in use per 100,000 population, the number of TV households per 100,000, and the number of multiple-set TV households per 100,000.

The growth of television dramatically correlated with the increase in youth suicide rates. The number of TV's in use ($r = 0.94$), number of TV households per 100,000 ($r = 0.86$) and the number of multiple-set TV families per 100,000 ($r = 0.96$) all very strongly correlated with the rise in youth suicide since 1950 ($p < 0.001$). When separated by sex, all correlations were stronger for male suicide rates than female suicide rates.

These dramatic correlations for television to youth suicide are higher than correlations of total drug use, alcohol use, marijuana use or cocaine use as determined by six NIDA surveys or 14 Senior High Student Surveys between 1974 and 1988 with youth suicide, using the same methodology.

Thus, the social effects of television, broadcasting seven hours per day to the average American home, may have contributed to the rise in youth suicide since 1950. Viewing repetitive depictions of televised violence may influence susceptible individuals to commit suicide, and thousands of hours of TV viewing may lead to anomie in our children.

NR107 Monday May 13, 3:00 p.m.-5:00 p.m.

The Invisible Children: Are They Still Invisible?

James A. Van Haren, M.D., Child Psychiatry, Pine Rest Hospital, 300 68th Street SE, Grand Rapids, MI 49509;

Summary:

Over the last 37 years, much information has been collected on high-risk children, i.e. children whose parents suffer from psychiatric illness. Research has shown that many of these children experience significant psychopathology that is evident from birth through adulthood. There have been few investigations examining whether high-risk children are receiving mental health assistance. The purpose of this study was to investigate the degree of parent reported utilization of mental health services by the children of psychiatrically ill adults; 50 adult inpatients and 50 adult outpatients were interviewed. Structured interviews and chart reviews were used to assess the use of mental health service by high-risk children as reported by their parents. Results indicated that a significant number of the adult patients had school-aged children, and in many instances, no inquiry had been made concerning their children's psychological health. Furthermore, few of the children were reported to have received treatment. Based on these results, it is recommended that clinicians working on inpatient wards be aware of this at-risk population and make it part of their routine practice to inquire about possible problems for children of hospitalized adults. In cases in which problems are discovered, referral should be made to a mental health professional.

NR108 Monday May 13, 3:00 p.m.-5:00 p.m.

Pictorial Instrument for Child Psychopathology

Monique Ernst, M.D., Department of Psychiatry, NYU Medical Center, 198 E. 7th Street, #4, New York, NY 10009; Raul R. Silva, M.D., Katherine A. Godfrey, M.D., Maria Solomou, Murray Alpert, Ph.D.

Summary:

This instrument was developed to measure psychopathology in children 6 to 12 years old. It consists of pictures of DSM-III-R criteria arranged by diagnostic subscales, which are rated by the child on a 5-point visual analogue scale. In a preliminary study (presented at The Child and Adolescent Meeting, 1990), we selected 130 pictures out of 330 drawings, tested in 30 normal children for clarity. The present study involves 36 child inpatient admissions who completed the instrument. DSM-III-R diagnoses, independently made by clinicians, were 10 schizophrenia, nine atypical psychosis, and 17 conduct disorder. Descriptive data show that the psychosis, anxiety and obsessive-compulsive subscales were rated highest by the schizophrenia group, and lowest by the conduct disorder group. The reverse was found for the conduct disorder subscale. Mood disorder subscales were rated highest by the atypical psychosis group, and lowest by the conduct disorder group. In contrast to the psychotic children, conduct disorder children rated the mania higher than the depression subscales. Internal consistency (Cronbach Alpha analysis) and diagnostic discriminative function will be assessed. In addition, 12 children have been retested at discharge to assess sensitivity to change.

NR109 Monday May 13, 3:00 p.m.-5:00 p.m.

Validity of Fluorescent Polarization Immunoassay of Plasma Cortisol For Use in the DST in Prepubertal Children

Shahnour Yaylayan, M.D., Psychiatry, The Ohio State University, 473 West 12th Ave Upham Hall, Columbus, OH 43210; Elizabeth B. Weller, M.D., Ronald A. Weller, M.D., Mary A. Fristad, Ph.D.

Summary:

The two most commonly used assay methods for determining plasma or serum cortisol levels have been competitive protein binding (CPB) assay and radioimmunoassay (RIA). Recently, a fluorescent polarization immunoassay (FPIA) technology has been introduced. It is highly sensitive and specific for cortisol and it does not use radioactive isotopes. However, its use has not been validated in children. To accomplish this, 21 prepubertal psychiatric inpatients who satisfied DSM-III-R criteria for major depressive disorder were studied. A 0.5 mg oral dose of dexamethasone was given at 11 p.m. and cortisol levels were measured by RIA and FPIA at 8 a.m. and 4 p.m. the next day from split samples. Children with medical illnesses and those who were on medication known to affect the DST were excluded. Correlation between FPIA and RIA determined cortisol levels was highly significant. Regression analyses demonstrated a significant linear relationship between the two measures. Y(FPIA) = .9878 (RIA) − 0.1383. $F = 486.69$; df = 1,31; $R^2 = .94$; $P < .001$). To determine if this degree of association would be found at varying absolute values or cortisol levels, we divided the sample in three <3, >3 <8, >8. Results remained consistent (<3 $R^2 = .81$, $F = 33.18$, df = 1,8, $P < .0004$; >3<8 $R^2 = .77$, $F = 54.83$, df = 1, 16, $P < .0001$; >8 $R^2 = .89$, $F = 23.80$, df = 1,3, $P < .02$). RIA values were consistently higher such that a value of 5.0 ug/dl (RIA) corresponded with a value of 4.75 ug/dl (FPIA).

NR110 Monday May 13, 3:00 p.m.-5:00 p.m.

Correlates of Violence Risk in Hospitalized Adolescents

Sophia Eldar, M.D., Child Psychiatry, Albert Einstein, 1000 Waters Place, Bronx, NY 10461; Graciela Finkelstein, M.D., Deborah Lipschitz, M.D., Daniel Grosz, M.D., Robert Plutchik, Ph.D.

Summary:

Violence among adolescents is a significant social and public health concern. To further investigate risk factors for violence among this age group, we interviewed and administered self-rating scales to 76 psychiatrically hospitalized adolescents: 52 with a history of violent behavior and 24 with no past history of violence. Self-ratings included: Zung Depression Scale, Impulse Control Scale, Suicide Risk Scale, Social Support Scale and Violence Risk Scale (Plutchik et al., 1989), and Life Events Checklist (Johnson, 1986). The two groups did not differ in terms of demographics, social support, life events, and depression scores. Violent adolescents were more impulsive ($t = 3.60$, $p = 0.001$) and scored significantly higher in the Suicide Risk Scale ($t = 2.32$, $p = 0.023$) than the nonviolent adolescents. The scales were then correlated with indices of violent risk for the whole cohort. Significant positive correlations were found between violent risk and depression ($r = 0.43$, $p < 0.001$), impulsivity ($r = 0.68$, $p < 0.001$), negative life events ($r = 0.28$, $p < 0.05$); a significant negative correlation was found between violence risk and social network ($r = -0.33$, $p < 0.005$). Implications of these results within a model of risk and protective factors for adolescent violence will be discussed.

NR111 Monday May 13, 3:00 p.m.-5:00 p.m.

Child Psychiatry Consultation in the Emergency Room: Presenting Problems and Disposition

Keith Cheng, M.D., Department of Psychiatry, OHSU School of Medicine, 10000 SE Main Street, Portland, OR 97216; William Gabriel, M.D., Terri Lee, M.D., Michel Mennesson, M.D., Melvin Lewis, M.D.

Summary:

The purpose of this study was to delineate the types of present-

ing problems seen and dispositions made by an emergency room child psychiatry consultation team at a major urban community hospital. All patients admitted to the Yale New Haven Hospital pediatric emergency room unit, who received a child psychiatry consult during the calendar years 1989 and 1990 were included in the study (n = 215). The age of subjects ranged from 4 to 15. Sixty percent of those studied were evaluated for suicide risk, and 20% for disruptive, assaultive, runaway, or other out-of-control behavior. The other 20% of patients were seen for psychotic, somatic, anxiety, or affective symptoms. About 50% of the patients seen in the emergency room were hospitalized for further observation and treatment; 45% were not hospitalized and referred for outpatient follow up. A small percentage of patients, less than 5%, were not referred for follow up. Disposition for these children included return to foster care, placement in a community shelter, or juvenile detention. The findings show that the management of suicidal behavior in children and adolescents often starts in the emergency room. Further research is needed to measure the effectiveness of emergency room interventions.

NR112 Monday May 13, 3:00 p.m.-5:00 p.m.

Rural Children's Reactions to Hurricane Hugo

Mitsuko Shannon, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; A J Finch, Ph.D., Charlotte Taylor, M.Ed., Pam Imm, M.A., F.R. Sallee, M.D.

Summary:

Very few surveys of children's reactions to natural disasters have been gathered. Few studies have included standardized measures for anxiety and stress. We present here an extensive survey of over 6000 school-age children from Berkeley County, SC, three months after Hurricane Hugo. Questionnaires were distributed to public school children in grades 5-12 which included: 1) demographic data; 2) responses assessing the extent of trauma; 3) responses assessing grades before and after the trauma; 4) Revised Children's Manifest Anxiety Scale (RCMAS) and 5) Frederick Reaction Index (RI) for children. The data were analyzed using stepwise multiple regression with the RI being the independent variable. Several variables were found to contribute significantly to the multiple regression with the final multiple R being .68. The most significant variables predicting stress symptoms on the RI were as follows: General level of anxiety (as scored by the RCMAS), extent of damage to the house, age (younger children being most affected), race, loss of job by a parent, severity of the hurricane, where the child was located, and being female.

NR113 Monday May 13, 3:00 p.m.-5:00 p.m.

Siblings in Foster Care: Factors Affecting Outcome

Marilyn B. Thorpe, M.D., Psychiatry, Univ of Western Ontario, 86 Devonshire Avenue, London ON., Canada N6C 2H7; GT Swart, M.D.

Summary:

Is being with ones siblings a protective factor in foster care? A retrospective chart review of 115 children who were taken into the care of a Children's Aid Society together was conducted. Many had been neglected. We examined risk and protective factors. The number of risk factors correlated significantly with the number of symptoms in the receiving home and the time spent in care. Poorer functioning children made up their losses. Protective factors correlated with fewer symptoms at home. In care, 53% were separated from their siblings. One was more likely to be separated if one was older, had a physically ill father, and had parents who separated. Separated children had more placements, fewer symptoms in the receiving homes, and fewer symptoms and better school functioning at discharge. Admission to care resulted in better functioning at school, fewer symptoms, and more involvement with extracurricular activities. Children with developmental delays were treated. Only 6% received psychiatric treatment. The number of placements correlated with poorer school functioning. Seven percent of the children had more than five placements, putting them at risk for jail, residential treatment and more symptoms at discharge. Twenty-three percent experienced significant rejection by foster parents.

NR114 Monday May 13, 3:00 p.m.-5:00 p.m.

Predictive Value of 24-Hour $LiCo_3$ Levels in Children

Rameshwari V. Tumuluru, M.D., Psychiatry, The Ohio State University, 473 West 12th Avenue, Columbus, OH 43210; Ronald A. Weller, M.D., Mary A. Fristad, Ph.D., Elizabeth B. Weller, M.D.

Summary:

In adults, measuring lithium levels 24 hours after a test dose has been shown to be a rapid means of predicting subsequent dosage requirements (Cooper et al, 1973). Although a dosage guide based on weight is available for children (Weller et al, 1986), it has not been compared with the 24-hour test dose level method for predicting dosage requirements in prepubertal children. In this study, 42 prepubertal children aged 6-12 received a test dose of $LiCo_3$ 600 mg. Pearson correlation coefficients were calculated between test dose levels (i.e., levels obtained 24 hours after the test dose), and the following variables: admission weight, Dose I (dosage begun after test dose), Level I (the first lithium level obtained on Dose I), Dose II (the second dose given to children in whom dosage adjustment was necessary) and Level II (the first lithium level obtained on Dose II). Twenty-four-hour test dose levels were significantly correlated with weight ($r = -.38$, $p < .01$), Dose I ($r = .38$, $p < .01$), Level I ($r = .33$, $p < .04$) and Dose II ($r = -.35$, $p < .03$) but not Level II ($r = -.13$, $p < .46$). Thus heavier children had lower 24-hour test dose levels and received higher doses of $LiCo_3$ using the weight-based dosage guide (Weller et al, 1986). To determine whether weight or a 24-hour test dose was a better predictor of subsequent dosage, regression analyses were done. These indicated weight was a better predictor of dosage than were 24-hour test dose levels. Thus, compared with adults, a weight-based dosage guide may be a more effective way of predicting subsequent therapeutic lithium dosages in children.

NR115 Monday May 13, 3:00 p.m.-5:00 p.m.

Psychiatric Comorbidity in Communication Disorders

Charlotte A. Hobbs, M.Sc., School of Medicine, McMaster University, 1200 Main Street West, Hamilton, Canada L8N 3Z5; I.B. Pless, M.D.

Summary:

Psychological maladjustment is known to occur with many chronic physical disorders of childhood. Little is known, however, of the long-term psychiatric consequences of chronic disorders. In this paper I determine whether children with communication disorders are more likely than healthy children to develop mental health problems by young adulthood or to persist in having such problems. Cross-sectional and cohort analyses were conducted on 2,638 children from the Ontario Child Health Survey and 11,744 children from the British National Child Development Study (NCDS). Children with communication disorders from both populations were found to have more emotional and behavioral problems than those who were healthy (adjusted prevalence rate ratio = 2.9, C.I. = 1.6, 5.1) or those with other chronic physical disorders. Among children from the NCDS sample who were maladjusted at age 7, those with communication disorders were more likely than children with no chronic physical disorder to have psychological problems at age

23. Among children who were not maladjusted at age 7, those with communication disorders had no greater risk of developing psychological problems by age 23 than did healthy controls. Results are consistent with theories suggesting a persistence of early psychiatric comorbidity among children with communication disorders but not with theories suggesting greater risk of development of psychiatric comorbidity among nonmaladjusted children with communication disorders.

NR116 Monday May 13, 3:00 p.m.-5:00 p.m.

Classroom Academic Performance of ADHD Boys Improved by Stimulants

Josephine Elia, M.D., Child Psychiatry, NIMH-BLDG 10 RM 6N-240, 9000 Rockville Pike, Bethesda, MD 20892; Patricia Welsh, M.Ed., Charles Gulotta, B.A., Judith H.L. Rapoport, M.D.

Summary:

This study evaluated and compared the effects of dextroamphetamine and methylphenidate on actual daily academic tasks.

Thirty-three children, 6 to 12 years of age with attention-deficit hyperactivity disorder (ADHD) were treated with various doses of dextroamphetamine (up to 1.5 mg/kg/day), methylphenidate (3.0 mg/kg/day) and placebo in an 11-week double-blind crossover trial. Both number of attempts and percent correct on a reading and math series, commonly used in schools, rated performance.

Results indicate that all children attempted more reading and math problems with methylphenidate and dextroamphetamine than placebo.

Methylphenidate improved percent correct in one of the reading series, while dextroamphetamine improved percent correct in one of the math functions. Higher doses of each stimulant did not compromise achievement.

NR117 Monday May 13, 3:00 p.m.-5:00 p.m.

A Two-Year Prospective Follow-up of Predictive Value of CSF 5-HIAA and Autonomic Measures in Children and Adolescents with Disruptive Behavior Disorders

Markus Kruesi, M.D., Child Psychiatry, NIMH-BLDG 10 RM 6N-240, 9000 Rockville Pike, Bethesda, MD 20892; Euthymia D. Hibbs, Ph.D., Theodore Zahn, Ph.D., Judith H.L. Rapaport, M.D.

Summary:

Follow-up studies of hyperactive children find a wide range of outcomes with about half undiscernible from normal controls and a substantial minority (about 25%) having antisocial outcomes (Gittelman et al. 1985). Follow-up studies of delinquents have concentrated on psychosocial measures. However, Rutter et al. have argued that biologic factors may be more important than environmental factors in the subgroup of conduct disorders persisting into adult life. The two biologic variables that have differentiated aggressive and antisocial subjects from controls in multiple studies, CSF 5-HIAA concentration and autonomic nervous system activity, were selected as possible predictors of outcome. A two-year, prospective follow-up of 28 of 29 (96.7%) children and adolescents with disruptive behavior disorders found baseline lumbar CSF 5-HIAA concentration correlated significantly and in the expected direction with severity of aggression during the follow-up interval as assessed with the Modified Overt Aggression Scale (pearson $r = -.57$. $p < .002$). Mean heart rate as assessed during psychophysiologic testing was also significantly correlated in an inverse direction with severity of aggression during the two-year follow-up (pearson $r = -.41$, $p = .03$).

NR118 Monday May 13, 3:00 p.m.-5:00 p.m.

Difference in Caloric Utilization in Eating Disorder Adolescents

Afsaneh Nasserbakht, M.A., Child Psychiatry, Stanford University, Children's Hosp. 520 Sand Hill, Palo Alto, CA 94304; Sigrid Inthealer, M.D., Grace H. Shih, R.D., Hans Steiner, M.D.

Summary:

Caloric utilization is an important issue for the clinical management of eating disorders. Bulimic patients often complain of a tendency to gain weight easily despite following a restrictive diet. Anorectics, on the other hand, complain of not gaining weight in spite of large dietary intakes. This claim has been checked in adults, but not in adolescents. Caloric intake and body weight of 32 inpatient adolescents bulimics and anorectics (ranging from 12 to 20 years old) were measured on a daily basis over a three-month period. Subjects were closely observed to rule out any binging and purging behavior. Thirty normal adolescents ranging from 12 to 19 years old, were used as the control group.

ANOVA showed that bulimics (normal weight) ate fewer calories per kilogram body weight than the normal group adolescents. (bulimics: 24.48 ± 5.33 and normal: 27.14 ± 2.34 cal/kg). Both the restrictor anorectics and anorectics with bulimic features ate more calories/kg body weight than the control group. (restrictor anorectics: 61.42 ± 2.52 $p < 0.0001$, anorectics w/ bulimic features: 40.49 ± 5.47 cal/kg $p < 0.0212$). As we can see from these data, nonbulimic anorectics consumed more caloric intake in cal/kg than the bulimic anorectic subgroup. This difference in caloric utilization has been replicated in adult group. These data suggest that being anorectic and bulimic for a long time alters caloric utilization compared to normal group in eating disorder. The origins of altered caloric utilization need to be explored further in experimental design.

NR119 Monday May 13, 3:00 p.m.-5:00 p.m.

Regional Cerebral Glucose Metabolism in Bulimia

Paul J. Andreason, M.D., Brain Imaging, NIMH, 9000 Rockville Pike, 10-4N317, Bethesda, MD 20892; Margaret Altemus, M.D., Alan Zametkin, M.D., Anna C. King, Julio Licinio, M.D., Robert M. Cohen, M.D.

Summary:

Regional cerebral glucose metabolism was measured in patients with bulimia ($n = 11$) and controls ($n = 18$). Significantly lower regional cerebral glucose metabolic rates (rCMRglu) were found in the right mid-frontal cortex, and significantly higher rCMRglu were found bilaterally in the temporal lobes. Previously reported hemispheric asymmetry in the mid-frontal region in bulimia ($L > R$) was observed (Wu, J., et al., Am J Psychiatry 147:3 309-312). In contrast with obsessive compulsive disorder (OCD) (Nordahl, T. et al., Neuropsychopharm 1989, 2:1, 23-38), orbito-frontal metabolism was neither greater than in controls nor did the orbito-frontal metabolism increase with increasing OCD symptoms (Maudsley scale). Though patients with bulimia complain of obsessive thought and compulsions to binge eat, the metabolic patterns are different from that of OCD. The metabolic changes seen in this sample of patients closely resemble metabolic patterns of mood-disordered patients previously studied by this group (Cohen, R.M. et al., Neuropsychopharm 1989, 2:241-254). These findings suggest that bulimia is more closely related to mood disorders than to OCD.

NR120 Monday May 13, 3:00 p.m.-5:00 p.m.

Season Subgroups in Bulimia Nervosa

Robert D. Levitan, M.D., Eating Disorder Section, Toronto General Hospital, 101 College Street CW 311, Toronto,

Canada M5G 2C4; Allan S. Kaplan, M.D., Russell T. Joffe, M.D., Anthony J. Levitt, M.D.

Summary:

A modified version of the Season Pattern Assessment Questionnaire (SPAQ) was administered to 41 consecutive patients with bulimia nervosa (BN), to identify individuals with potentially important seasonal changes in mood and/or core symptoms of BN. Patients who reported significant seasonal changes in mood or core symptoms of BN on the modified SPAQ were designated "seasonal positive" and administered structured clinical interviews using the SADS and a modified version of the Eating Disorders Examination (EDE), to more thoroughly assess seasonal symptom change.

Twenty-nine BN patients (70% of total) were designated "seasonal positive" based on the modified SPAQ, consistent with earlier studies showing a high rate of self-reported seasonal symptoms in BN patients. Structured clinical interviewing of these 29 patients identified 10 with clinically significant seasonal symptom change, including three patients with both BN and seasonal affective disorder (SAD), and seven patients with at least a 50% increase in bingeing frequency across seasons (all with maximum binge frequency in the fall/winter period) independent of SAD.

We conclude that: 1) The SPAQ as a screening instrument in this BN population has high sensitivity but low specificity, identifying a large group of BN patients with clinically insignificant season symptoms; 2) the results support the existence of important seasonal subgroups in BN, in particular a subgroup with SAD (BN-SAD), and a subgroup experiencing at least a 50% increase in binge frequency in the fall/winter period independent of SAD (Seasonal BN-non-SAD). These findings may have implications for treating subgroups of BN patients with light therapy.

NR121 Monday May 13, 3:00 p.m.-5:00 p.m.

Impulsivity in Bulimia: A Serotonin Connection?

Barbara E. Walton, M.S.N., Psychiatry, Beth Israel Hospital, 330 Brookline Avenue, Boston, MA 02215; David C. Jimerson, M.D., Michael D. Lesem, M.D., Debra Franko, Ph.D., Jeffrey M. Levine, M.D., Nicholas A. Covino, Psy.D.

Summary:

Frequent binge eating in bulimic patients and frequent impulsive behaviors in other psychiatric groups have been linked to decreased serotonin function. This study explored relationships between impulsivity and binge eating in bulimia.

Subjects included 20 medication-free, normal-weight female outpatients (age 24.7 $\pm$ 4.4 years, binges per week 6.1 $\pm$ 3.3) meeting DSM-III-R criteria for bulimia nervosa; 18 healthy age-matched controls; and 15 bulimic patients (age 26.2 $\pm$ 3.7, binges per week 16.6 $\pm$ 9.6) hospitalized at NIMH. Subjects completed modified Barratt Impulsivity scales and the Eating Attitude Test (EAT).

For outpatients, impulsivity ratings (54.3 $\pm$ 16.7) were higher than for controls (39.1 $\pm$ 14.2, $p<0.005$); were correlated with EAT Factor II (preoccupation with food) ($p<0.005$); but failed to show a relationship to binge frequency. For inpatients, binge frequency also failed to show a relationship to impulsivity ratings, but was positively correlated with a brief obsessive-compulsive (O-C) subscale. For inpatients, CSF levels of the serotonin metabolite 5-HIAA were positively correlated with impulsivity ($r=0.58$, $p<0.05$) and negatively correlated with O-C scores ($r=-0.81$, $p<0.001$).

This study shows that increased impulsivity in bulimic patients is not directly predictive of binge frequency. Pilot data suggest that intentional or compulsive components of bulimic behaviors might be associated with altered serotonin function.

NR122 Monday May 13, 3:00 p.m.-5:00 p.m.

Two-Year Follow-up of Family Function in Bulimia

D. Blake Woodside, M.D., Psychiatry, Toronto Hospital, 200 Elizabeth Street, Toronto ON, Canada M5G 2C4; Lorie Shekter Wolfson, M.S.W., Allan Kaplan, M.D., Marion Olmsted, Ph.D., Margus Heinmaa, B.S.

Summary:

This study reports on perception of family functioning on the part of a cohort of 24 patients with bulimia nervosa (BN) at three points — admission to an intensive Day Hospital Program (DHP) for BN, discharge from the DHP, and at two-year follow-up. Family functioning was measured by the General (G) and Self-Rating (SR) scales of the Family Assessment Measure (FAM), a valid, reliable measure of family functioning. BN outcome status was defined by information gathered by direct interview using the Eating Disorders Examination (EDE). Good outcome was defined as total abstinence from binging/purging in the month prior to assessment; all other outcomes were defined as poor. Analyses were performed by MANOVA with a repeated measures design. When BN outcome as determined at two-year follow-up was held as a constant, the analysis demonstrated only a main effect for time (GS $p=0.013$, SR $p=0.003$). However, the main effect for outcome approached significance on the SR ($p=0.154$). Examination of the mean FAM scores for good and poor outcome suggests that the failure to demonstrate a significant main effect of outcome is related to our small sample size. The demonstration of a main effect for time across the three measurement supports and extends to two years our previous work showing that diminished BN symptoms are associated with improved patient self-reporting of family functioning. However, the lack of main effects for outcome makes it difficult to conclude whether these observations are casual or a result of BN outcome status.

NR123 Monday May 13, 3:00 p.m.-5:00 p.m.

Promoting Condom Use Among College Students

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Summary:

Despite awareness of the importance of condom use in AIDS prevention, previous research has indicated that the majority of sexually active college students do not use condoms. Communication about condom use has proven problematic for some young adults, who have reported they are unaware of their sexual partners' intent or disposition regarding condom use. This study assessed factors associated with the effectiveness of seven videotaped interactions between a man and woman as models of condom use discussion among college students. Stepwise regression analyses of ratings obtained from 14 male and 14 female undergraduates revealed that the effectiveness of each interaction as a model of condom use discussion was positively associated with students' identification with the interaction ($p<.001$), perceptions that the relationship would last or develop further ($p<.01$), and with the judgment that condom use appeared crucial to the depicted relationship ($p<.001$). However, among men — but not women — perceived spontaneity of the relationship was positively associated with its effectiveness as a model of condom use discussion (p .05). Condom use interventions emphasizing relationship spontaneity may be particularly effective among college men.

NR124 Monday May 13, 3:00 p.m.-5:00 p.m.

Subtle, Early Cognitive Impairment in HIV Disease

Susan E. McManis, M.D., Department of Psychiatry, Lackland AFB, Wilford Hall, San Antonio, TX 78236; George R. Brown, M.D., James R. Rundell, M.D., Robert Zachary, Ph.D., Sarah Kendall, B.A.

Summary:

We report on the results of Rey-Osterreith Complex Figure Copy

(ROC) and Memory (ROM) tests as a measure of neuropsychiatric impairment (NPI) in HIV seropositive persons compared with matched seronegative controls. Ninety-seven HIV+ subjects (63 men, 34 women/85% asymptomatic, 8% ARC, 5% AIDS) underwent standard psychiatric and medical evaluations, including Hamilton anxiety (HAMA) and depression (HAMD) scales, ROC and ROM tests, Walter Reed staging (WR), CD4a, and cerebrospinal fluid (CSF) measures. Parametric and nonparametric comparisons were made with 49 HIV- age/race/sex/rank-matched controls. HIV+ patients scored significantly worse than controls (p=.001, effect size .60) on the ROC, but not on the ROM, test. WR 2-6 patients performed significantly worse than WR 1 asymptomatic patients (ROC p=.016, ROM p=.007). ROC scores negative correlated with WR*, CSF IgG synthesis, CSF nucleated cells, HAMA, HAMD; ROM scores negatively correlated with WR, CSF protein*, CSF IgG synthesis, HAMD* ($p<.01$, $*p<.05$). We conclude NPI is present early in the course of asymptomatic HIV infection. This may represent a biologic process, as supported by correlations with CSF abnormalities. Performance correlations with HAMA/HAMD scores suggest a contribution from affective state, which may result from progression of the disease itself. No gender differences were noted, a finding not previously reported.

NR125 Monday May 13, 3:00 p.m.-5:00 p.m.

Cognitive Impairment and CSF Values in HIV Disease

Susan E. McManis, M.D., Department of Psychiatry, Lackland AFB, Wilford Hall, San Antonio, TX 78236; George R. Brown, M.D., James R. Rundell, M.D., Robert Zachary, Ph.D.

Summary:

We report on the relationship between cerebrospinal fluid (CSF) abnormalities and neuropsychiatric impairment (NPI) in HIV+ persons. Ninety-seven HIV+ subjects (63 men/34 women, 85% asymptomatic/8% ARC/5% AIDS) underwent standard psychiatric and medical evaluations including Rey-Osterreith Complex Figure Copy (ROC) and Memory (ROM) tests as a measure of NPI, Hamilton anxiety (HAMA) and depression (HAMD) scales, CD4a, Walter Reed staging (WR), and CSF measures. ROC negatively correlated with WR*, CSF IgG synthesis, CSF nucleated cells, HAMA, HAMD; ROM negatively correlated with WR, CSF protein*, CSF IgG synthesis, HAMD*; HAMA correlated with CSF protein*, CSF IgG synthesis*; HAMD correlated with CSF protein ($p<.01$, $*p<.05$). Negative correlations of ROC/ROM scores with CSF abnormalities suggest a biologic process is involved in NPI, while those with HAMA/HAMD scores suggest a contribution from affective state. While HAMA/HAMD scores may result from biologic processes, another possibility is that separate biologic and emotional influences result in significant NPI largely when occurring together.

NR126 Monday May 13, 3:00 p.m.-5:00 p.m.

Cognitive Impairment and Gender in HIV Positive Persons

Susan E. McManis, M.D., Department of Psychiatry, Lackland AFB, Wilford Hall, San Antonio, TX 78236; George R. Brown, M.D., Robert Zachary, Ph.D., Sarah Kendall, B.A., James R. Rundell, M.D.

Summary:

As part of a larger multicenter collaborative study, we assessed gender effects on HIV-related neuropsychiatric infection. Sixty-three male and 34 female HIV+ subjects underwent standard psychiatric and medical evaluations including Rey-Osterreith Complex Figure Copy (ROC) and Memory (ROM) tests as a measure of NPI, Hamilton anxiety (HAMA) and depression (HAMD) scales, Walter Reed staging (WR), CD4a, and cerebrospinal fluid (CSF) tests. Male and female groups were comparable in WR, race, rank, age. Subjects were also compared with 33 male and 16 female comparable HIV- controls. No significant group differences were found between male and female subjects on ROM, ROC, HAMA, HAMD scores or CSF abnormalities. Female ROC scores were significantly lower than those of controls ($p=.004$) as were male ROC scores ($p=.0001$). Male ROC correlated negatively with HAMA*, HAMD*, CSF protein, CSF IgG synthesis; female ROC with IgG synthesis, CSF nucleated cells; male ROM with HAMA*, HAMD*, and female ROM with none of the aforementioned. We conclude gender does not play a major role in the level of NPI. Differences in male/female correlations suggest affective state plays a larger role in male than female NPI; but male HAMA/HAMD also correlated with CSF abnormalities, suggesting a biologic component to affective state not seen in women. This study suggests women need not be excluded from NPI studies.

NR127 Monday May 13, 3:00 p.m.-5:00 p.m.

Prospective Study of HIV-Associated Psychosis

Daniel D. Sewell, M.D., Department of Psychiatry, UCSD, La Jolla, CA 92093; Dilip V. Jeste, M.D., J. Hampton Atkinson, M.D., James Chandler, M.D., Igor Grant, M.D., The HNRC Group

Summary:

Information regarding new-onset psychosis in patients infected with human immunodeficiency virus (HIV) is quite limited. *Methods:* We prospectively evaluated HIV-positive and AIDS patients with new-onset psychosis ($N=15$) using neurologic, neuropsychological, and magnetic resonance (MRI) examinations. Exclusion criteria included: functional psychosis prior to HIV infection and the presence of delirium or substance-induced psychiatric disorder. We analyzed our results using a control group of 15 HIV-positive nonpsychotic patients matched according to CDC stage. Psychotic subjects were randomly assigned to haloperidol or thioridazine. *Results:* Psychotic patients were spread among CDC stages II-IV. All 15 psychotic patients had delusions, usually paranoid (66%). Fourteen of 15 (93%) had hallucinations that were usually auditory. Spinal fluid was normal in all cases except one with mild pleocytosis. Clinical reports for 13 of 15 (87%) of the MRI scans were normal. Abnormal scans had either mild ventricular enlargement or white matter hyperintensities. We compared rate of abnormality detected by clinical reports with systematic ratings. Interestingly, neuropsychological performance on an expanded Halstead-Reitan battery showed impairment (mild to moderate) in 80% of the psychotic subjects. Both neuroleptics reduced symptoms, but a greater incidence of side effects was observed with haloperidol than with thioridazine. *Conclusion:* Neuropsychological impairment suggests that new-onset psychosis in patients infected with HIV may be secondary to mild-to-moderate brain dysfunction. The absence of notable abnormalities on clinical MRI indicates that profound psychotic disturbance may precede detectable structural brain abnormalities. Our CSF findings are consistent with HIV-related brain disease not associated with an inflammatory response.

NR128 Monday May 13, 3:00 p.m.-5:00 p.m.

Mood and Neuropsychological Interactions in HIV

Robert A. Stern, Ph.D., Psychiatry, Univ of North Carolina, Campus Box #7160, Chapel Hill, NC 27599; Diana O. Perkins, M.D., Naomi G. Singer, B.A., Susan G. Silva, M.A., Dwight L. Evans, M.D.

Summary:

The neuropsychological impairments associated with HIV are described as representing a subcortical dementia, frequently including motor slowing and mood alterations. It is unknown whether

changes in mood state are psychological in nature (i.e., reactive) or are part of a syndrome of CNS-related symptoms directly associated with HIV infection. We studied 25 asymptomatic HIV seropositive gay men and 34 seronegative controls, using strict exclusion criteria to preclude confounding effects of substance abuse, head injury, learning disability, or zidovudine use. There were no significant group differences in Hamilton Depression Rating Scale (HDRS) or Profile of Mood States (POMS) scores, and neither groups' mean scores feel in the depressed range on the HDRS. Comprehensive neuropsychological and psychiatric evaluations were conducted as part of a larger, longitudinal HIV study, the Coping in Health and Illness Project (CHIP). Significant group differences were found only in measures of motor functioning ($p < .05$), with seropositive subjects performing more slowly than controls. These findings persisted when controlling HDRS, POMS, and education. However, among seropositives, mood state was significantly correlated with individual motor test scores (e.g., HDRS with Finger Tapping Dominant Hand, $r = -.43$, $p < .05$). These results suggest that motor slowing occurs early in the course of HIV infection, appears to be related to CNS effects of HIV, and cannot be accounted for solely by mood state or depressive symptoms.

NR129 Monday May 13, 3:00 p.m.-5:00 p.m.

SPECT Regional Cerebral Blood Flow in HIV Disease

Christopher H. van Dyck, M.D., Psychiatry, Yale University, 333 Cedar Street, New Haven, CT 06510; Scot W. Woods, M.D., Stephanie O'Malley, Ph.D., Lawrence H. Price, M.D., Christopher J. McDougle, M.D., Thomas R. Kosten, M.D.

Summary:

Other investigators using PET have reported an abnormal pattern of relative subcortical hypermetabolism early in the course of HIV dementia (Ann Neurol 1987; 22:700). The present study aimed to extend this finding to HIV + patients not yet manifesting clinical dementia using a more widely available SPECT technique. Ten HIV + methadone patients (5M, 5F, 32 $\pm$ 8 yrs), 10 HIV– methadone patients (5M, 5F, 36 $\pm$ 5 yrs), and 10 healthy controls (6M, 4F, 30 $\pm$ 7 yrs) participated. Subjects underwent SPECT scanning using the Strichman 810X Brain Imager after injection of 20 mCi Tc-99m HMPAO. Regions of interest (ROIs) corresponding to left and right striatum (ST), thalamus (TH), and the whole slices (WS) containing these structures were delineated by an operator blind to diagnosis. The ST/WS ratio was increased in HIV + patients compared with healthy subjects on the left ($1.26 \pm .08$ vs. $1.19 \pm .05$, $p < .05$) but not on the right. HIV– patients showed intermediate ST/WS ratios not significantly different from either of the other groups. The TH/WS ratio did not differ significantly among the three groups. SPECT rCBF data will also be shown for cortical ROIs in all three groups. HIV + and HIV– groups are being rescanned after one year to study longitudinal effects of HIV infection on rCBF. Follow-up rCBF data will be presented. The increased relative striatal blood flow in HIV + patients suggests that SPECT may be able to detect changes in subcortical function before dementia is clinically evident.

NR130 Monday May 13, 3:00 p.m.-5:00 p.m.

Early HIV Infection and Health Locus of Control

Irvin P. Brock, III, M.D., Psychiatry, Wilford Hall Med. Center, 8430 Dorsetshire, San Antonio, TX 78250; George R. Brown, M.D., Richard Jenkins, Ph.D., James R. Rundell, M.D.

Summary:

As part of a large multicenter collaborative study we assessed the multidimensional health locus of control (MHLC) and subscale values of 85 HIV + individuals without AIDS, (50 males/35 females) to see how normative data for chronically ill patients and healthy adults compared. In healthy adults the mean Chance Health Locus of Control (CHLC) was 16.21 and Powerful Others Health Locus of Control (PHLC) was 19.16. In chronically ill patients mean CHLC was 17.46 and mean PHLC was 22.54. Male HIV + patients' mean CHLC score was 19.86 (SD 6.47) and mean PHLC score was 21.56 (SD 5.69). Female HIV + patients' mean CHLC score was 15.48 (SD 9.74) and mean PHLC was 16.55 (SD 9.58). The mean values for PHLC for both genders fall in between the normative data for healthy adults and chronically ill patients. However, the mean CHLC scores for both sexes were 0.5 to 1 standard deviation higher than those of healthy adults and chronically ill patients. These data suggest that both men and women with early HIV infection express less personal control over health outcomes than chronically ill or healthy populations. Further, HIV + patients of both genders viewed valued health outcomes in their lives as being influenced by chance events to a greater extent than controls. This finding has implications for compliance and treatment outcomes with HIV treatment regimens.

NR131 Monday May 13, 3:00 p.m.-5:00 p.m.

Affect and Health Locus of Control In HIV Disease

Irvin P. Brock, III, M.D., Psychiatry, Wilford Hall Med. Center, 8430 Dorsetshire, San Antonio, TX 78250; George R. Brown, M.D., Richard Jenkins, Ph.D., James R. Rundell, M.D.

Summary:

We report on the relationship between affective state as measured by Hamilton anxiety scale (HAM A) and Hamilton depression scale (HAM D) and multidimensional Health Locus of Control (MHLC) scores in 85 HIV + patients without AIDS (50 males/35 females) assessed as part of a large multicenter collaborative study. In male HIV patients HAM A scores positively correlated with Powerful Other Health Locus of Control (PHLC) ($r = .28, p < .03$) and with Chance Health Locus of Control (CHLC) ($r = .48, p < .001$). HAM D scores also correlated positively with PHLC ($r = .39, p < .005$) and with CHLC ($r = .50, p < .001$). In female HIV patients HAM A scores correlated positively with CHLC ($r = .45, p < .007$); a trend was noted for PHLC ($r = .28, p < .07$). Similarly, HAM D scores correlated positively with PHLC ($r = .33, P < .04$) and CHLC ($r = .47, p < .004$). In early stage HIV patients of both genders, Hamilton scores were highly correlated with external locus of control beliefs. They also scored 0.5 to 1.0 SD greater on CHLC subscales than that of healthy adult controls or chronically ill patients. Our data lend credence to previous work that suggested a relationship between depression and external HLC (especially CHLC) and have important implications for early diagnosis, treatment, and secondary prevention of psychiatric morbidity in HIV patients.

NR132 Monday May 13, 3:00 p.m.-5:00 p.m.

Primary Versus Secondary Depression in HIV

Snezana Cvejin, M.D., Psychiatry, Univ of North Carolina, Campus Box #7160, Chapel Hill, NC 27599; Diana O. Perkins, M.D., Carol Murphy, R.N., Bettina Knight, R.N., Dwight L. Evans, M.D.

Summary:

Evaluation and treatment of depression in HIV-infected individuals require special consideration regarding etiology. Depression frequently occurs in HIV-infected individuals. For example, we have studied 29 asymptomatic HIV-positive gay men in our current HIV project, the Coping in Health and Illness Project (CHIP). We found that 10% had a current and 38% had a lifetime major depression, as determined by a structured diagnostic interview (modified SCID). The frequent occurrence of depression in HIV-infected gay men raises questions of whether depression may be a symptom of CNS HIV infection (secondary depression), or a

primary (functional) depression.

We have now studied six patients who appear to have depression secondary to the CNS effects of HIV. In these patients depressive symptoms were alleviated following initiation of zidovudine (ZDV). This suggests two possibilities: (1) HIV infection may be associated with an organic mood disorder, since significant improvement in depressed mood occurred coincident with retroviral treatment, and/or (2) ZDV may itself have mood elevating effects. We also studied two HIV-infected patients with symptoms of major depression who were successfully treated with fluoxetine, suggesting that these patients may have had a primary depression.

Thus, the etiology of depression in HIV is heterogeneous. Depression may be a symptom of CNS HIV infection (secondary). It may be prudent to delay antidepressant treatment in patients for whom ZDV is initiated for HIV infection. Depression may also be functional. Furthermore, as HIV-infected patients are sensitive to the side effects of traditional antidepressants, new generation antidepressants may be efficacious and well tolerated for the treatment of primary depression.

NR133 Monday May 13, 3:00 p.m.-5:00 p.m.

Therapeutic Alliance and Distress After HIV Testing

Cheryl Card, M.A., Department of Psychiatry, Cornell University, 445 E. 68th Street, New York, NY 10021; Samuel Perry, M.D., Baruch Fishman, Ph.D., Robert Russell, Ph.D., Donald Rock, Ph.D.

Summary:

Objective: To assess the effect of the therapeutic alliance on the outcome of a six-session, stress prevention training program after HIV testing and counseling. *Method:* 23 seropositive and 32 seronegative men participated. Nonparticipant clinician observers applied the CALPAS-R to audiotapes. The Brief Symptom Inventory, Speilberger State Trait Anxiety Scale, Beck Depression Inventory, and the Hamilton Depression Rating Scale were administered at intake and at a follow-up visit for assessment of outcome. *Results:* Most partial r's, controlling for initial distress scores, between alliance and initial distress scores in the middle (sessions 3 or 4) and the end (sessions 5 or 6) were moderate to strong (.2-.5) for the seropositive subjects. For the seronegative subjects most of the alliance scores correlated best with outcome in the end sessions. *Conclusion:* This study suggests that therapeutic alliance, which has been shown to be important for understanding the process of psychotherapy, is also an important variable for the efficacy of psychoeducational interventions and specifically for interventions offered to individuals tested for HIV.

NR134 Monday May 13, 3:00 p.m.-5:00 p.m.

Bereavement and Unresolved Grief in Seropositive Men and Men at High Risk for HIV

Jacquelyn Summers, M.S.W., Psychiatry, Univ of Calif. San Diego, 2760 Fifth Avenue #200, San Diego, CA 92103; Sidney Zisook, M.D., J.H. Atkinson, M.D., Tom Patterson, Ph.D., J. Chandler, M.D., J. Malone, M.D.

Summary:

Objective: To examine the 12-month prevalence of bereavement and unresolved grief in men seropositive for human immunodeficiency virus (HIV+) and in seronegative (HIV–) men.

Methods: HIV+ men (n=127) and HIV– homosexual men (n=27) in a longitudinal cohort study were examined for bereavement within the last 12 months using the Texas Revised Inventory of Grief. Resolution of grief was determined on a 0-4 point Likert scale evaluating: (1) experience of grief for the deceased, (2) adjustment to the loss, and (3) capacity to discuss the loss without discomfort. Men categorized with "unresolved grief" exceeded standard cutoff scores. Differences in proportions between groups were compared using Chi Square.

Results: Prevalence rates of loss and unresolved grief were:

# Deaths	HIV+ (N=127)	HIV– (N=27)	p
One Loss (%)	24.4	40.7	ns
2 or more (%)	33.1	29.6	ns
Total % with loss	57.5	70.3	ns
Resolution	**HIV+ (n=71)**	**HIV– (n=19)**	
Resolved (%)	84.5	100.0	ns
Unresolved (%)	15.5	0.0	$p<.05$

A majority of both HIV+ men and HIV– homosexual men have experienced losses. A significant difference was evident in resolution of grief between the two groups. All cases of unresolved grief were found in the seropositive cohort. Of these HIV+ men reporting unresolved grief, 91% failed to attend funeral or memorial services for the deceased compared with 43% of the men with resolved grief who reported not participating in services.

Conclusion: Given the association of grief with depression and physical distress, it is critical to monitor the impact of this high rate of loss within HIV+ men and HIV– homosexual men. Since a minority of HIV+ men report unresolved grief, this group may warrant intervention to encourage grief resolution.

NR135 Monday May 13, 3:00 p.m.-5:00 p.m.

Suicide Attempts and AIDS Among Drug Addicts in Vienna, Austria

Peter Hofmann, M.D., Department of Psychiatry, University Graz, Waehringer Guertal 18-20, Vienna A-1090, Austria; Norbert Loimer, M.D., Elisabeth Werner, M.D.

Summary:

The number of drug-related deaths increases in Austria from year to year; the victims are mostly young people in their twenties. Until now no special analyses were carried out to identify suicide and accidently fatal overdose among these deaths. Suicide is one of the major health problems in Austria; among young Viennese the number of suicides as well as suicide attempts increased dramatically from 1970 to 1989. The drug-related deaths are not included in the Austrian suicide register. The aim of this study is to distinguish between accidental overdosing and suicide attempts among drug addicts in Vienna. Furthermore, we define a high-risk group for suicidal behavior among drug addicts. At the drug outpatient clinic of the Psychiatric University Hospital of Vienna 223/176 patients were investigated in February 1989 and in February 1990 in order to examine the connection between suicide, parasuicide and drug addiction.

About 60% had overdosed accidently; 32% reported suicide attempts. This suggests that the availability of illegal drugs seems not to have a higher suicidal potential than drugs prescribed by physicians. In contrast to the common opinion, HIV-1 positive IVDUs seem to be the group with the highest incidence of overdosing but not of suicide attempts. Furthermore these data suggest that the major reason for overdosing seems to be the variable purity of drugs available on the streets. A possibility for preventing fatal intoxications among drug addicts is decriminalizing the possession of drug.

NR136 Monday May 13, 3:00 p.m.-5:00 p.m.

Sexual Functioning in HIV Positive Women Without AIDS

Edwig K. Plotnick, M.D., Psychiatry, Wilford Hall Med. Center, 3766 Tupelo Lane #1507, San Antonio, TX 78229; George R. Brown, M.D.

Summary:

We prospectively assessed the sexual functioning and use of safer sex practices during the natural history of HIV infection (non-AIDS) detected as part of a mandatory HIV screening program in the United States Air Force (USAF). Patients were active duty women or spouses of USAF servicemen who have tested positive since 1986. Patients were psychiatrically evaluated every 12-18 months by the same evaluators. Initial evaluation (T1) was completed by 35 HIV+ non-AIDS women (average knowledge of conversion = 11 months). Twenty-one women were evaluated at T2 (average knowledge = 28 months). At T1, 34% had no change in sexual functioning, 23% had at least a 33% decrease in libido (excluding a four-week adjustment period following diagnosis), 34% reported no libido and/or were abstinent. Safer sex was practiced 100% of the time by 62%, at least 25% of the time by 14%, and less than 25% by 9%; 9% admitted to never using safer sex techniques. At T2, 43% had no change in their sexual functioning, 23% had at least a 33% decrease in libido, 29% had no libido and/or were abstinent. Safer sex was practiced 100% of the time by 48%, at lease 25% of the time by 10%, less than 25% by 0%, and never by 19%; 23% chose not to answer. We conclude there is continued persistent impairment in sexual functioning over time in HIV+ women. In spite of intensive, HIV-related education, an increasing percentage (38%, T1 to 52%, T2) engage in unsafe sexual practices.

NR137 Monday May 13, 3:00 p.m.-5:00 p.m.

Comparison of DSM-III-R and RDC Diagnostic Systems

Elizabeth Davidson, M.D., Psychiatry, Univ of North Carolina, Campus Box #7160, Chapel Hill, NC 27599; Diana O. Perkins, M.D., Carol Murphy, R.N., Bettina Knight, R.N., Duanping Liao, M.D., Dwight L. Evans, M.D.

Summary:

For the past year our research program, the Coping in Health and Illness Project (CHIP), has used an integrated interview (SCID-RDC) developed from the Schedule for Affective Disorders and Schizophrenia (SADS) and the Structured Clinical Interview for DSM-III-R Disorders (SCID). This integrated interview simultaneously assigns RDC and DSM-III-R diagnoses. We present data on the diagnostic agreement between the two systems for 109 HIV-positive or HIV-negative men who were at risk for HIV disease due to hemophilia or homosexuality. The following are the chance-corrected agreement (kappa) for the DSM-III-R diagnoses vs. the RDC diagnoses: 1) lifetime major depression vs. lifetime definite major depression (kappa = 1.0); 2) lifetime major depression vs. lifetime definite or probable major depression (kappa = .83); 3) lifetime alcohol dependence vs. lifetime definite alcoholism (kappa = .67); 4) lifetime alcohol abuse vs. lifetime probable alcoholism (kappa = .25); 5) lifetime drug dependence vs. lifetime drug dependence (kappa = .66); 6) lifetime drug abuse vs. lifetime drug abuse (kappa = .12). These findings demonstrate an excellent agreement between the two diagnostic systems for affective disorders, indicating the potential for good comparability for mood disorders across studies using DSM-III-R and RDC criteria. The substantial differences in DSM-III-R and RDC led to moderate-to-poor agreement for alcohol or drug use disorders. This suggests caution when comparing substance use disorders across studies using DSM-III-R and RDC criteria.

NR138 Monday May 13, 3:00 p.m.-5:00 p.m.

A New DSM-III-R Based Questionnaire: The Behavior Emotions Questionnaire

Diana O. Perkins, M.D., Psychiatry, Univ of North Carolina, Campus Box #7160, Chapel Hill, NC 27599; Snezana Cvejn, M.D., Elizabeth Davidson, M.D., Carol Murphy, R.N., Lenn Murrelle, B.A., Dwight L. Evans, M.D.

Summary:

A self-report questionnaire providing DSM-III-R diagnoses would be a valuable tool both in clinical psychiatric practice and in epidemiological research. We have developed a self-report instrument based on the SCID, the Behavior and Emotions Questionnaire (BEQ), and report preliminary validity statistics. The validity of the BEQ to assign current and lifetime psychiatric diagnoses was determined in a larger research project with 109 HIV-positive or HIV-negative men at risk for HIV disease due to hemophilia or homosexuality. Each subject received the SCID-RDC (modified SCID), a structured clinical psychiatric interview, with consensus DSM-III-R diagnoses assigned at a diagnostic conference. Subjects completed the BEQ on the day prior to the psychiatric interview by indicating "YES" or "NO" to questions concerning psychiatric symptoms. The questions are organized like the SCID and are similar in content. The following data show the agreement for lifetime psychiatric diagnoses between the BEQ and the SCID-based consensus diagnosis, based on chance corrected percent agreement (kappa), sensitivity, and specificity, respectively: 1) major depression (.59, .73, .85); 2) bipolar disorder (1.0, 1.0, 1.0); 3) alcohol dependence (.73, .90, .88); 4) alcohol abuse (.86, .44, .91); 5) alcohol use disorder (.82, .93, .89); 6) drug dependence (.56, .53, .96); 7) drug abuse (.60, .58, .96); 8) drug use disorder (.70, .69, .97); 9) eating disorder (1.0, 1.0, 1.0); 10) anxiety disorder (.94, 1.0, .94) 11) presence of any psychiatric disorder (.89, .97, .90). These data suggest that this time-efficient self-report assessment tool has substantial validity, high sensitivity and specificity. Thus, the BEQ has potential as a valuable DSM-III-R self-report questionnaire. Further studies in other patient populations are needed and are underway.

NR139 Monday May 13, 3:00 p.m.-5:00 p.m.

Undetected Alcohol-Related Burn Trauma

Lawson F. Bernstein, M.D., Department of Psychiatry, New York Hospital, 525 E. 68th Street, PWC, New York, NY 10021; Lawrence Jacobsberg, M.D., Theresa Ashman, M.A., Gloria Musagui, R.N., Cleon Goodwin, M.D., Samuel Perry, M.D.

Summary:

Studies have shown that alcohol abuse is a significant risk factor for severe burn trauma and for subsequent morbidity and mortality, but it is not known how frequently alcoholism is diagnosed by the treatment team. At a large inpatient burn center, we examined the correspondence between a history of alcohol-related trauma and/or alcoholism in the medical record (MedRec) and the results from a standardized and blinded interview for alcoholism, the CAGE questionnaire. To determine if admission blood alcohol concentration (BAC) could improve detection we examined the correspondence between BAC and CAGE.

Of 124 burn patients interviewed, 24 (19%) were CAGE+; however, only nine patients (7%) were MedRec+. Although a significant correspondence was found between CAGE and BAC ($p < .003$), 70% of CAGE+ were BAC–.

The results not only confirm a high rate of alcoholism among burn patients, but also indicate that this disorder is frequently not diagnosed by the treatment team and, further, that admission BAC is not adequately sensitive for early detection. We conclude that clinicians should administer a brief questionnaire for alcoholism to burn patients to assess needs for acute treatment and referral.

NR140 Monday May 13, 3:00 p.m.-5:00 p.m.

Adolescent Alcohol Use and Psychological Symptoms

John F. Aruffo, M.D., Psychiatry, Univ of Arkansas, 800

Marshall Street, Little Rock, AR 72202; John B. Jolly, Psy.D.

Summary:

Based on previous studies assessing the relationship between alcohol abuse and depression, we hypothesized that the level of alcohol abuse was related to severity of depression in psychiatric inpatient adolescents. Eighty-eight inpatient adolescents were assessed by a structured clinical interview (the Diagnostic Interview for Children and Adolescents-Revised [DICA-R] to determine level of alcohol abuse. Subjects were divided into three groups based on self-report: those who had never been drunk (ND), those who reported they have been occasionally drunk (OD), and those who reported being frequently drunk (FD). Severity of depression was assessed specifically (the Children's Depression Inventory) and globally (the Youth Self-Report), that is, general internalizing symptoms, by self-report. Depression was also assessed by clinician rating (Hamilton Rating Scale for Depression). Contrary to our prediction, depression severity was not significantly related to level of alcohol abuse in our inpatient sample, on either self-report or clinician rating. Interestingly, our alcohol-abusing groups (OD and FD) reported a significantly higher level of externalizing behaviors ($F = 3.96$, $df = 79$, $p < .05$) on the YSR than our nonabusing group (ND). Our results would suggest that, at least within our inpatient sample, level of alcohol abuse is not related to severity of depression, but is related to self-reported acting-out behaviors. Further assessment of the relationship between level of abuse and acting out with more sensitive measures appears warranted.

NR141 Monday May 13, 3:00 p.m.-5:00 p.m.

A Family Study: Bulimia Nervosa and Alcoholism

Barbara A. Johnson, M.D., Psychiatry, Univ of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213; Walter H. Kaye, M.D., Cynthia Bulik, Ph.D., Theodore Weltzin, M.D., L.K. George Hsu, M.D.

Summary:

Considerable controversy has been raised over the issue of whether or not bulimia nervosa is related to major affective disorder. However, recent studies have suggested that bulimia nervosa may have a substantial relationship to alcohol abuse. Such studies have found a high lifetime rate of alcohol abuse and dependency in bulimic subjects and their relatives. Our preliminary data replicate and extend this possibility. Inpatient bulimic probands ($N = 4$) and their first-degree relatives ($N = 15$) were directly interviewed with semistructured interviews to assess current and lifetime Axis I and II psychopathology, while history on second-degree relatives ($N = 41$) was obtained from the subjects noted above as well as from second-degree relatives on each side using the Family History Research Diagnostic Criteria method. We found psychoactive substance abuse to be present in 25% of probands, 33% of first-degree relatives, and 24% of second-degree relatives. However, these subjects also had high rates of affective and anxiety disorders. Our study is intent upon answering the question of whether or not bulimia nervosa, alcohol abuse, and affective disorders are expressions of common transmissible factors or are separate, but coexisting disorders.

NR142 Monday May 13, 3:00 p.m.-5:00 p.m.

Alcohol and Sedative Use in Panic and OCD Patients

Joan R. Birnberg, B.A., c/o Roger Cambor, M.D., 441 E. 69th St. Rm 226, New York, NY 10021; Roger Cambor, M.D., Laura Portera, B.A., Andrew C. Leon, Ph.D., Robert B. Millman, M.D., M. Katherine Shear, M.D.

Summary:

While benzodiazepine therapy is one effective treatment for anxiety disorders, concern exists about sedative addiction. To assess substance use in an anxiety disorder sample, consecutive patients presenting to an anxiety disorders clinic are undergoing evaluation using the Structured Clinical Interview—DSM-III-R and Addiction Severity Index. Of 26 patients assessed, 21 met criteria for Panic Disorder (PD) and five for Obsessive Compulsive Disorder (OCD). Among PD patients, one had comorbid OCD and four endorsed several OCD symptoms. Nine of 21 (43%) PD patients and four of five OCD patients had evidence for current and/or past dependence, abuse, or excessive use of alcohol or sedatives. Comparing subjects without OCD symptoms with those who endorsed at least some SCID criteria for OCD revealed significantly greater substance use in the latter group ($p < 0.015$). Trends suggested that female PD patients had more affective disorder comorbidity and less substance abuse, while males had more substance abuse and less affective comorbidity. Thus, 1) anxiety disorder patients may have a high degree of excessive alcohol and sedative use, 2) patients with OCD symptoms may have increased risk for substance use, and 3) there may be a gender difference in comorbidity patterns with potential etiologic and treatment implications.

NR143 Monday May 13, 3:00 p.m.-5:00 p.m.

Phenomenology of Comorbid Anxiety and Alcoholism

Ihsan M. Salloum, M.D., Psychiatry, Univ of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213; Juan E. Mezzich, M.D., Joe Plial, M.A.

Summary:

Numerous studies have demonstrated high prevalence of comorbid anxiety and alcohol use disorders. The phenomenological features of this important clinical population are still largely undetermined. This study attempted to elucidate the clinical profile of patients with anxiety disorder (AD) plus alcohol use disorder (AUD), as compared to those patients with either diagnosis only. A large sample of adult general psychiatric patients presenting for care at a metropolitan university hospital and diagnosed with a semistructured procedure according to DSM-III criteria during a nine-year period (1981-1989) constituted the initial data base.

Three subgroups were selected for analysis; 1) AD group (1449 patients), 2) AUD group (355), and 3) coexisting AD and AUD group (60 patients). These subgroups were compared along demographic, symptom, social and personal history, past treatment history, and multiaxial variables (axes II through V).

The comorbid group more closely resembled the AD group than the AUD group regarding symptom variables, multiaxial variables, past treatment history, and demographic variables. It differed from the AD group mainly on those social and personal history variables indicating difficulties in interpersonal and occupational functioning, and from the AUD group on symptom profile with the AUD group having more severe symptoms of impulsive, violent, and antisocial behavior, as well as depressive and suicidal behavior.

NR144 Monday May 13, 3:00 p.m.-5:00 p.m.

Aggression and Immunity in Inner-City Alcoholics

Angela Lignelli, B.S., Department of Psychiatry, UMDNJ-Med School, 185 S. Orange Avenue, Newark, NJ 07103; Steven J. Schleifer, M.D., Steven E. Keller, Ph.D.

Summary:

Aggressive behavior has been shown to influence several major biological systems and may influence susceptibility to infectious and neoplastic diseases. Little is know, however, about the association of anger and aggression with the immune system. We have explored the possibility of such a relationship in an urban indigent population consisting primarily of minorities.

Thirty clients from a university-based alcoholism recovery center

in Newark, NJ participated. Aggression was measured in relation to two parameters: Psychiatric Symptom Index (anger) to determine general aggressive attitudes; and a modified version of the Yudofsky scale to examine focused aggression. Correlation analyses revealed no association between the two domains of aggression, indicating that they tap distinct behavioral areas. General anger/aggressiveness was correlated with the functional activity of Natural Killer cells ($P < 0.05$); targeted aggression was related to activated T cells ($p < 0.05$). Regression analyses, controlling for age and sex, supported the association between increased NK activity and general aggressiveness ($p < 0.06$). Similarly, targeted aggression, controlling for age and sex, was associated with increased activated T cells ($p < 0.06$). These data are consistent with our earlier findings of an association between aggression and increased NK activity in adolescents. They suggest a complex interaction between aggressive states and immunity that may have significant health consequences.

NR145 Monday May 13, 3:00 p.m.-5:00 p.m.

The North Carolina Family Study on the Genetics of Alcoholism

Lenn Murrelle, B.A., Department of Psychiatry, Univ. of North Carolina, UNC Campus Box 7175, Chapel Hill, NC 27599; Diana O. Perkins, M.D., Jane Doody, M.S., David S. Janowsky, M.D.

Summary:

Family studies provide a useful tool for investigating hereditary, biological, and environmental factors that contribute to the onset of alcoholism. Recruitment of alcoholic probands through three major North Carolina alcoholism treatment facilities has resulted in the identification of 106 multigenerational families with 716 members. This sample of volunteer families is unique due to its geographic stability, relatively large sibships, and its tendency to be cooperative and densely affected. Our research strategy emphasizes comprehensive phenotype assessment. To date, extensive self-report screening information has been collected through mailed questionnaire on 93 probands and over 350 of their first- and second-degree relatives. The screening questionnaire includes multiple measures to evaluate alcohol use history (Michigan Alcoholism Screening Test, Alcoholism Dependence Scale, Alcohol Use Inventory, CAGE Questionnaire, MacAndrew Scale, DSM-III-R criteria). Also included are screening items for major psychiatric illnesses, including other substance use, mood, anxiety, eating, psychotic, and gambling disorders (Behavior and Emotions Questionnaire—a DSM-III-R-based diagnostic questionnaire, Drug Abuse Screening Test). Clinical records are obtained for all general medical, alcoholism, substance abuse, and psychiatric treatment. Pedigrees on selected families will be presented. Studies are planned that will examine issues of comorbidity, proposed typologies, putative neuroendocrine markers, and linkage analysis.

NR146 Monday May 13, 3:00 p.m.-5:00 p.m.

Cocaine Withdrawal, Locomotion and Mood State

Huan-Kwang Ferng, M.D., Department of Psychiatry, UCLA/NPI, 760 Westwood Plaza, Los Angeles, CA 90024; Martin P. Szuba, M.D., Lewis R. Baxter, M.D.

Summary:

While disturbances in locomotor activity, mood and sleep are essential features of cocaine withdrawal, there have been no systematic studies examining the relationship between circadian locomotor activity and mood state in cocaine withdrawal. We hypothesize that subjective mood state would significantly correlate with locomotor activity and would show a prominent diurnal variation in subjects withdrawing from cocaine.

Seven males, ages 22-35 (mean = 28.7 ± S.D. 3.5), suffering from cocaine withdrawal underwent continuous locomotor activity monitoring using a mercury tilt switch device worn on the non-dominant wrist for up to 72 hours. Subjects completed the profile of mood states and internal state scale, both validated self-reporting instruments of mood at 10:00 and 18:00 hours each day of the monitoring. All subjects met DSM-III criteria for cocaine withdrawal and cocaine dependence but suffered from no other psychiatric or medical illnesses.

Average daily locomotor activity gave a significant negative correlation with POMS subscales of anger/hostility (tau = −1, P = 0; $R_s = -1$, P = .05) and confusion/bewilderment (tau = −1., P = 0; $R_s = -1$, P = .05). Average daily locomotor activity correlated significantly with internal states scale of well-being (tau = .8, P = .05; $R_s = .9$, P = .07).

Subjects appear to experience a diurnal variation in mood. The POMS fatigue subscale and internal state scale depression subscale tended to be worse in the morning in subjects (Wilcoxon P = .05 and .07, respectively).

Additional subjects currently being studied will be reported.

NR147 Monday May 13, 3:00 p.m.-5:00 p.m.

Time-Limited Cocaine Treatment: Program Evaluation

Lisa Newell, Psychiatry, Yale University, 904 Howard Avenue, New Haven, CT 06519; Douglas Ziedonis, M.D.

Summary:

Few treatment outcome studies or program evaluations have been reported for outpatient cocaine treatment. In this survey 45 patients were assigned to a Time-Limited Cocaine Treatment (TLCT) group over a six-month period. This group combined elements of relapse prevention and psychoeducational approaches in a 10-week format. In this treatment population, the average age was 29, 60% were male, 60% black, 38% white and 2% Hispanic. Of those patients who continued to be engaged in treatment after three weeks (n = 20), 60% successfully completed treatment. A comparison of clinical and demographic differences between those who completed treatment and those who didn't was made, focusing on factors in the program that could be revised to improve retention rates, particularly in the first three weeks of treatment (such as additional treatment contacts and use of anticraving medication). Findings will also be useful in revising the TLCT format and matching patients and treatment modalities for more cost-effective treatment.

NR148 Monday May 13, 3:00 p.m.-5:00 p.m.

Neuropsychiatric Effects of Anabolic Steroids

Tung-Ping T. Su, M.D., BPB, NIMH, 9000 Rockville Pike, Bethesda, MD 20892; David R. Rubinow, M.D., Michael Pagliaro, R.N., Christine Ollo, Ph.D., David Pickar, M.D., Owen Wolkowitz, M.D.

Summary:

Much concern has been generated by reports of widespread use of anabolic steroids (AS) by young athletes and bodybuilders. While neuropsychiatric symptoms are frequently described to accompany AS use, no data exist regarding the effects of AS on CNS function. We report the first longitudinal study of the acute neuropsychiatric effects of low- and high-dose AS administration in human volunteers. Normal volunteers receive in a blind fashion six days of placebo and three days each of methyltestosterone (MT) 40 mg/day and MT 240 mg/day. Mood and behavioral ratings are accompanied by measurement of cognitive function, motor activity, cerebral blood flow, and plasma and CSF biochemistry. Of the six volunteers who have thus far completed the protocol, marked irritability and aggressiveness have been observed during high-dose

MT in all. The severity of these symptoms resulted, in one case, in the subject's request to be placed in seclusion. Motor activity and mood lability increased during high-dose MT, albeit inconsistently. Libido increased during low-dose but decreased during high-dose MT. Striking but inconsistent evidence of neuropsychiatric changes appears to accompany even brief exposure to AS. The behavioral and cognitive changes induced by AS in the full sample (n = 20) will be presented and discussed.

NR149 Monday May 13, 3:00 p.m.-5:00 p.m.

Characterization of Buprenorphine Withdrawal

Haydn M. Thomas, M.D., Department of Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Marc I. Rosen, M.D., Martin E. Waugh, D.O., Herbert R. Pearsall, M.D., Scott W. Woods, M.D., Thomas R. Kosten, M.D.

Summary:

The acute behavioral withdrawal syndrome from the mixed agonist/antagonist buprenorphine may be different from the withdrawal from methadone. This study proposed to determine the behavioral and rCBF changes associated with acute withdrawal from buprenorphine. We have previously described decreases in cortical and increases in brainstem regional cerebral blood flow (rCBF) during acute withdrawal from methadone. *Methods:* Thus far, five opiate addicts have participated following maintenance on buprenorphine (2mg sublingually) for seven days. Naltrexone was then administered: placebo on day 8, 50mg on day 10, and 50mg with 0.2 mg clonidine preload on day 12. On each of the three days, withdrawal symptoms were assessed at baseline, 30, 45, 60 and 90 minutes after naltrexone was given and Tc-99m HMPAO was injected 90-120 minutes after naltrexone. A clinician completed an abstinence rating scale documenting the severity (range 1 = none to 5 = severe) of 16 signs or symptoms associated with opiate withdrawal. Single photon emission computed tomography (SPECT) rCBF scans were acquired using an ASPECT cylindrical crystal device. *Results:* Oral naltrexone treatment produced definite and measurable signs and symptoms of opiate withdrawal in all treated subjects. The mean peak in abstinence severity score was lower in buprenorphine withdrawal compared with our previous study of methadone withdrawal (methadone withdrawal peak = 43 and buprenorphine withdrawal peak = 36), even though a 50-fold increase in naltrexone was utilized. Clonidine preload significantly decreased the abstinence severity score (buprenorphine withdrawal peak with clonidine = 18). Data on rCBF changes during buprenorphine withdrawal, and the effects of clonidine, will be presented and compared with the methadone results.

NR150 Monday May 13, 3:00 p.m.-5:00 p.m.

Substance Abuse in Chronic Schizophrenia

John R. DeQuardo, M.D., Department of Psychiatry, Univ. of Mich. Med. Ctr., 1500 E. MED CTR DR, 9C-9150, Ann Arbor, MI 48109; Christopher Carpenter, B.S.E., Rajiv Tandon, M.D.

Summary:

Substance abuse is a prevalent problem; its influence has extended to involve individuals with schizophrenia. Illicit substance use has an increased prevalence in schizophrenia and is associated with earlier onset, treatment noncompliance, and poor outcome. To examine these relationships further, we reviewed charts of 68 schizophrenic patients (DSM-III-R, RDC) admitted between 1987 and 1990, for age, sex, age of onset, age at first hospitalization, family history, and substance abuse. Each patient was rated at medication-free baseline and four weeks post-treatment on the BPRS, SANS and HRSD to assess positive, negative and depressive symptoms. Neuropsychological evaluation and CT scans (VBR) were also performed. One-year follow-up data were obtained via phone contacts with patients and family. Our results indicate that females abused substances less often (20%) than males (53%) ($p < .05$). Substance abusing patients were younger on admission ($p = .06$) and at first hospitalization ($p = .06$), had lower pre- and post-treatment HRSD rating ($p < .01$), and poorer post-discharge treatment compliance ($p < .001$) than nonabusers. Substance abuse was unrelated to positive or negative symptoms, family history, IQ or VBR. Alcohol (54%) and cannabis (46%) were used most often; cocaine, stimulants, inhalants, barbiturates and hallucinogens were all consumed much less frequently. Substance abuse in schizophrenia appears to influence onset, clinical features, course and outcome, and is worthy of further inquiry.

NR151 Monday May 13, 3:00 p.m.-5:00 p.m.

A Controlled Study of Adolescent Gasoline Huffers

Dorothy Grice, M.D., Med. Univ of South Carolina, 171 Ashley Avenue, Charleston, SC 29425; Ann L. Taylor, M.D., Robert Malcolm, M.D.

Summary:

Restrictions were placed on the content of tetraethyl lead in gasoline with the Clean Air Act in 1979. Since that time the practice of inhaling gasoline as an intoxicant (huffing) has been seen as a transient recreational fad. There have been few recent controlled studies of gasoline huffers. The present study surveyed 1,143 adolescent charts from 1986-1990 for a history of recurrent gasoline inhalation. The prevalence of gasoline huffing in inpatient adolescent substance abusers was found to be 1.3%. Fifteen adolescents hospitalized for chronic gasoline inhalation were identified and compared with a control group of non-gasoline-inhaling adolescent substance abusers matched for age, race, and sex. The mean age of all subjects was 13.4 years, with 13 males and two females in each group. In the huffing group, there was a mean use of 2.8 years and an average last use three days prior to admission. Huffers and controls were compared on multiple social and psychiatric variables using Fisher's exact test, chi-square or a Student's t-test. Six of the huffers were admitted with psychotic diagnoses vs. none of the controls ($p = 0.008$). Four of the huffers were admitted as direct consequences of violent acts vs. none of the controls ($p = 0.04$). Huffers were twice as likely to have T-scores >70 on MMPIs ($x^2 = 6.78$; $p = 0.009$). Huffers had abused twice as many drugs as controls ($x^2 = 4.85$, $p = 0.03$). Four huffers had CTs or MRIs of the head with one abnormal scan. T-test comparisons were made of WISC-R Full Scale, Verbal, and Performance IQs with no significant differences between groups. In the present sample, gasoline huffing appeared to be uncommon among a general inpatient population of adolescent male and female substance abusers. When hospitalization did occur, huffers were more likely to be psychotic, have higher levels of psychopathology, have abused more substances, and to be more violent than controls. Cognitive functions did not appear impaired in the huffer group.

NR152 Monday May 13, 3:00 p.m.-5:00 p.m.

Evaluation of Salivary Concentrations of Methadone for Monitoring Drug Therapy

Norbert Loimer, M.D., Department of Psychiatry, University of Vienna, Waehringer Guertel 18-20, Vienna A-1090, AUSTRIA; Rainer Schmid, Ph.D., Christian Wolf

Summary:

Objective: The correlation between plasma and saliva concentration of d,1 methadone has been examined. Collection of saliva for routine drug monitoring is easy to perform; furthermore it minimizes the discomforts to patients as well as the infectious risk for medical staff. *Methods:* In 20 former opiate addicts under d,1 methadone maintenance therapy, d,1 methadone levels were com-

pared in venous blood samples and in unstimulated and citric acid stimulated saliva. Samples were collected 24 hours after the last methadone intake and d,1 methadone concentrations were determined by HPLC. *Results:* A correlation between plasma levels and stimulated saliva was observed. *Conclusions:* For monitoring methadone maintenance therapy stimulated saliva is an appropriate specimen with obvious advantages.

NR153 Monday May 13, 3:00 p.m.-5:00 p.m.

Defining Substance Use in a Mentally Ill Population

Lisa Dixon, M.D., Department of Psychiatry, MPRC, P.O. Box 21247, Baltimore, MD 21228; Erica Dibietz, LCSW, Robert Conley, M.D., Timothy W. Santoni, M.A., Deborah Medoff, Ph.D.

Summary:

The high prevalence of substance abuse comorbidity in mental illness emphasizes the importance of examining the predictive value of differing definitions of substance use and the effects of such use on service utilization. *Methods:* Trained assessors evaluated 476 randomly selected psychiatric inpatients in the Maryland state psychiatric hospital system by direct patient interview and chart review. *Results/Conclusions:* Possible definitions of "drug user" include previous drug/alcohol treatment (N = 117, 25%), Axis I drug/alcohol diagnosis (23%), history of daily use (41%), history of weekly use (59%), or use in 30 days prior to admission *and* a period of daily or weekly use (37%) reflects current use with a history of sustained use. Regression analysis showed that DU's thus defined were more likely to be young ($p < .0001$), male ($p < .001$), non-schizophrenic ($p < .01$), and to have a history of arrest ($p < .001$) and DWI's ($p < .001$). DU's were more likely to have had previous inpatient treatment at the same facility ($p < .05$) and previous outpatient psychiatric treatment ($p < .001$). Drug ($p < .001$) and alcohol ($p < .001$) treatment needs were more likely to be barriers to discharge, but not mental health counseling/therapy or behavioral management programs.

NR154 Monday May 13, 3:00 p.m.-5:00 p.m.

Behavioral Syndrome of Alzheimer's Disease

Daniel S. Javier, M.D., Department of Psychiatry, SUNY-Health Sciences Ctr., Stony Brook, NY 11794; Barry Reisberg, M.D., Steve Sclan, Ph.D., Emile Franssen, M.D., Carol Torossian, Ph.D., Steve Ferris, Ph.D.

Summary:

The characteristic behavioral symptoms accompanying cognitive deterioration in Alzheimer's disease (AD) are a major source of burden for their caregivers. Despite the importance of the behavioral symptoms, limited information is available regarding their nature, course and treatment. Previous research with a 25-item scale--the Behavioral Pathology in AD Rating Scale (BEHAVE-AD)--separating these symptoms into seven major categories (paranoid and delusional ideation; hallucinations; activity disturbances; aggressiveness; sleep disturbances; affective disturbances; anxieties and phobias), has indicated that specific symptoms peak in occurence at certain stages (Reisberg, et al. 1989). In order to gain a better understanding of the pattern of behavioral symptoms in AD, we evaluated 271 aged subjects with or without AD and examined the relationships between the symptom clusters identified with the BEHAVE-AD (Reisberg, 1987). After partialling out the effects of cognition, we observed highly significant correlations (p's $< .01$) between paranoid and delusional ideation and each of the remaining six BEHAVE-AD categories. These findings provide initial support for the hypothesis that the BEHAVE-AD symptomatic categories comprise a clinical syndrome. Relevance for pharmacologic treatment of the symptoms of AD and for the future development of novel psychopharmacologic intervention strategies are discussed.

NR155 Monday May 13, 3:00 p.m.-5:00 p.m.

Environments and Assessed Quality of Life

Jill S. Meyer, M.D., Psychiatry, Creighton-Nebraska, 2205 South 10th Street, Omaha, NE 68108; Robert L. Schalock, Ph.D.

Summary:

Sixty elderly (mean age, 78 years) persons were administered the 1990 *Quality of Life Questionnaire,* a standardized questionnaire that measures a person's perceived level of satisfaction, independence, and social belonging. Ten females and 10 males were selected, based on purposeful sampling in New York, Kansas and Nebraska, from each of three living environments, including independent (living on own), semi-independent (retirement center), or supervised (nursing home or care center). Significant ($p < .05$ or .01) results based on ANOVA (with Tukey's Test for group comparisons) or Pearson Product Moment correlations included:

- Measured satisfaction and social belonging are higher for those living independently than supervised.
- Independence is higher for those living independently or semi-independently than supervised.
- There are no significant differences on the three factors between those living independently and those living semi-independently.
- Age is negatively correlated with independence and social belonging.
- Marital status is positively correlated with satisfaction.

Results are discussed in terms of the role of environments on quality of life, and the improvement of a person's perceived quality of life through environmental modification.

NR156 Monday May 13, 3:00 p.m.-5:00 p.m.

Early Versus Late Dementia: Patient and Caregiver Issues

Hilary T. Hanchuk, M.D., COPSA Institute, UMDNJ-CMHC, 667 Hoes Lane, PO Box 1392, Piscataway, NJ 08855; Andrew C. Coyne, Ph.D., William E. Reichman, M.D.

Summary:

Impact of age of symptom onset on patient and caregiver functioning was considered in 192 patients evaluated for cognitive impairment. Mean patient age was 75.0 ($\pm$8.0) years; average length of cognitive impairment was 3.8 ($\pm$2.5) years. Seventy-six (43.7%) patients had Alzheimer's disease (AD); 45 (25.9%) had multi-infarct dementia (MID); and 53 (30.5%) had other diagnoses (18 diagnoses were missing). Mean patient Mini-Mental State Exam (MMSE) scores were 15.4 ($\pm$6.4); mean Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) scores were 3.0 ($\pm$2.0) and 2.6 ($\pm$2.2).

Thirty-eight patients (19.8%) displayed early onset of dementia (before age 65); 154 (80.2%) showed late onset (65+). It was hypothesized that early onset cases would show more rapid decline in functioning than late cases, thus placing caregivers of the former under more stress than the latter, as measured by Zarit's (1982) Burden Inventory and Kinney and Stephens' (1984) Hassles scale. This expectation was not supported: Although early onset cases were evaluated slightly further into the disease process than late cases (4.6 vs. 3.6 years; $F(1,185) = 4.22$, $p < .05$), there were no group differences in MMSE's, ADL's, or IADL's (all p's $> .05$). Furthermore, caregiver stress was equivalent across groups—Burden Inventory and Hassles scores for caregivers of early onset cases were 28.5 and 23.3; for late cases, scores were 37.2 and 23.5 (all $p >$'s.05). These findings suggest that the impact of various dementing illnesses on both patients and caregivers is not dependent on age of onset.

NR157 Monday May 13, 3:00 p.m.-5:00 p.m.

Effect of Age on Psychiatric Patient Requests

Eve J. Wiseman, M.D., Department of Psychiatry, UCLA/NPI, 760 Westwood Plaza, Los Angeles, CA 90024; Gary W. Small, M.D.

Summary:

Despite recent research on psychiatric outpatient requests, no prior study has focused on the relationship of age to the nature of requests. To this end, we studied the requests made by 120 walk-in patients at a psychiatric admission and evaluation clinic. Patients completed a 14-item questionnaire adapted from a larger 84-item instrument validated for young adult populations. Each questionnaire item tapped into a specific request category. We predicted that older patients would have fewer social supports and thus would be more likely to request succorance, advice, and ventilation than young patients.

The 120 patients were divided into three age groups: 18 to 34 years (n = 64, mean age = 27.1 ± 5.2[SD]), 35 to 49 years (n = 37, mean age = 40.6 ± 4.0), and 50 and older (n = 19, mean age = 61.7 ± 9.3). Although younger patients were less likely to have been married than older ones, 26% of the old group were widowed, compared with none in the other groups (chi-square = 21.5, $p < .001$). In general, older patients were more likely to endorse request items indicating succorance, advice, and ventilation. They also were more likely to request confession and community triage. These results suggest that age does influence the nature of psychiatric patients' requests. Degree of social support may partly explain this effect.

NR158 Monday May 13, 3:00 p.m.-5:00 p.m.

Age-Related Effects of Lithium on the Phosphoinositide System

Krishna Dasgupta, M.D., Geriatrics, Middleton VA Hospital, 2500 Overlook Terrace, Madison, WI 53705; Molly H. Weiler, Ph.D.

Summary:

Although there is considerable evidence for age-related alterations in brain neurotransmitter systems, little information is available regarding age-related changes in central nervous system second messenger system function. In order to determine whether lithium's effects on the phosphoinositide (PI) second messenger system change with age, neostriatal slices prepared from 3, 10, and 24-26 month Fischer 344 rats were labeled with [3H]myoinositol, then incubated with oxotremorine-M (a muscarinic agonist) and varying lithium chloride (LiCl) concentrations (0-10mM). Radioactivity of the [3H]inositol phospholipid fraction in the organic phase and [3H]inositol phosphates in the aqueous phase was determined. Results were expressed as [(aqueous/(organic + aqueous)] x100% = % inositol phosphate (IP) accumulation.

Significant differences among the three age groups were found at the following lithium concentrations: 0.2mM ($F = 4.11$, $df = (2,17)$, $p < 0.05$), 0.3mM ($F = 7.14$, $df = (2,19)$, $p < 0.05$), and 0.5mM ($F = 6.88$, $df = (2,22)$, $p < 0.05$). At these concentrations, post-hoc t tests showed that % IP accumulation was significantly greater in 10 and/or 24-26 month rats than in 3 month rats.

These results suggest that lithium's effects on muscarinic receptor-activated PI hydrolysis in the neostriatum of Fischer 344 rats are enhanced with age.

NR159 Monday May 13, 3:00 p.m.-5:00 p.m.

The Rate of Progression in Alzheimer's Dementia

Robert G. Stern, M.D., Psychiatry, Bronx VAMC, 130 W. Kingsbridge Road, Bronx, NY 10468; Richard C. Mohs, Ph.D., Michael Davidson, M.D., Terena Searcey, B.A., Kelly Ware, James Schmeidler, Ph.D., Kenneth L. Davis, M.D.

Summary:

Patients with NINCDS-ADRDA probable Alzheimer's dementia [AD] were given the 0-33 points Blessed test [BT] version for information, memory and concentration at six-month intervals over a period of up to 60 months. For each patient the change in the total BT score between each two consecutive visits at six- and 12-month intervals was calculated. Pairs of ratings with initial BT scores higher than 30 were not included. This computation obtained 221 six-month delta values from 100 patients and 182 12-month delta values. The correlation between the baseline score and the six- and 12-month BT scores delta was calculated using polynomial regression analysis. Variance was calculated for the effect of sex, age of onset and presence of family history. There was no significant correlation between the degree of dementia on the BT and the size of deterioration after six or 12 months and no significant difference in the mean deterioration after six or 12 months, between males/females, presenile/senile-onset or between family history for AD positive/family history negative groups. Mean +/–SD deterioration at six and 12 months was 2.1579 +/– 3.2922 and 4.1703 +/– 4.3160 respectively. The absence of correlation between severity and progression of AD and the large SD values for the mean change found in this study have multiple implications for the design of clinical pharmacological studies.

NR160 Monday May 13, 3:00 p.m.-5:00 p.m.

Cortisol Response to CRF in Alzheimer's Disease

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Summary:

Although hypercortisolism occurs in up to 50% of patients with Alzheimer's disease (AD), the exact site of dysregulation in HPA axis functioning remains unknown. The cortisol and ACTH responses to CRF challenge have previously been used to explore the mechanism of hypercortisolism in depression, and suggest that there is enhanced secretagogue (CRF) drive from the hypothalamus. A similar paradigm was examined in this study to further elucidate the site of dysregulation of cortisol secretion in AD.

Serial cortisol was measured in 13 patients (mean age 67.9 ± 6.7 years; nine males, four females) meeting NINCDS criteria for AD, and 12 age-matched controls (NC) (mean age 66.27 ± 6.5 years; 10 males, two females) following ovine CRF (100 ug/kg IV) and placebo. One milligram DSTs were available on 13 AD patients and 11 controls. The data were analyzed by repeated measures ANOVA.

There were no differences in basal cortisol levels between AD and NC subjects. Furthermore, there were no differences between the groups in the maximum postCRF cortisol release (AD:12.35 ± 4.5 ug/dl; NC:14.69 ± 5.0 ug/dl; p = NS). Four of 13 AD subjects demonstrated DEX resistance, compared with one of 11 controls, but there was no difference in the maximum change in postCRF cortisol between these two groups (nonsuppressors: 15.15 ± 6.57 ug/dl; suppressors: 11.10 ± 3.12 ug/dl; p = NS).

These data indicate that the adrenal response to CRF challenge is normal in this group of AD patients, and that the cortisol response to CRF is no different between suppressors and nonsuppressors. The ACTH or beta-lipotropin response to CRF, therefore, appears critical to the interpretation of the most likely site of HPA axis dysregulation in AD, and is currently under study at this site.

NR161 Monday May 13, 3:00 p.m.-5:00 p.m.

Risk Factors for Alzheimer's Disease: A Case Control Study From China

Ge Li, M.D., Department of Psychiatry, Bronx Va Medical Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Yu-Cun Shen, M.D., Cuang-Hui Chen, M.D., Yong-Tong Li, M.D.

Summary:

Seventy Alzheimer's disease (AD) patients (mean age = 65.3 years, SD = 14.6; males = 33, female = 37) were clinically identified by NINCDS-ADRDA and ICD-10 (draft) in China. Two normal controls were matched for each patient by age, sex, and neighborhood. Extensive demographic, medical, family history and environmental exposures were collected on both cases and controls from family informants to assess possible risk factors associated with AD. Inter-informant and test-retest reliability were assessed and most items showed good agreement. Factors significantly associated with AD cases were family history of dementia (odds ratio [OR] = 7.5, confidence interval [CI]: 1.6-36.3), family history of other mental illnesses (OR = 9.5, CI:2.0-45.6) and left-handedness (OR = 3.6, CL: 1.2-11.1). Logistic regression analysis revealed statistically significant results for the family history variables (dementia [$p = .01$]; mental illness [$p = .03$]), but not for handedness ($p > .05$). Neither family history of Down's syndrome nor antecedent history of head trauma or other conditions that might support the immune and viral hypothesis in AD were significantly associated. These data support the role of familial/genetic factors in Alzheimer's disease.

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Medial Temporal Lobe Size P300 and Subjects At Risk for Alzheimer's Disease

Bradley S. Jacobs, B.S., Psychiatry, Ohio State University, 473 West 12th Avenue, Columbus, OH 43210; Michael Torello, Ph.D., Robert Bornstein, Ph.D., Elizabeth Burns, Ph.D., Henry A. Nasrallah, M.D.

Summary:

Previous work has shown that brain potentials during the processing of visual and auditory stimuli are altered in Alzheimer's disease.

Auditory brain-event-related potentials were measured using an "oddball" paradigm. In addition, magnetic resonance imaging of the brain was used to detect leukoariosis and medial temporal lobe damage. Testing was performed on subjects who were hereditarily at risk (AR) for AD (N = 17) and a control group (N = 12), all aged 50-60 years, medically healthy, free of any DSM-III-R diagnosis and medication free. The P200 amplitude was significantly smaller in AR subjects who were leukoariosis positive ($p < .02$). The P300 amplitude was found to be negatively correlated with the amount of temporal lobe atrophy ($p < .03$) only in the AR, leukoariosis-positive group. Both the P200 and P300 are thought to have temporal love source generators.

Taken together, these data provide evidence for brain functional and structural changes in the temporal lobes of subjects at-risk for Alzheimer's disease. Studies like these may lead to detection of premorbid markers for Alzheimer's disease and may lead to early detection and treatment of this disorder.

NR163 Monday May 13, 3:00 p.m.-5:00 p.m.

CSF HVA in Schizotypal and Other Personality Disorders

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Summary:

Cerebrospinal fluid (CSF) concentrations of the dopamine metabolite homovanillic acid (HVA) were measured in a group (n = 10) of schizotypal personality disorder (SPD) patients and a control group (n = 14) of other personality disorder (OPD) patients. The personality disorder diagnoses were assessed by DSM-III criteria using the SIDP. DSM-III diagnoses of schizophrenia, schizoaffective and bipolar disorders were ruled out by the SADS interview. All patients were free of significant medical illnesses, free of psychotropic medications for three weeks, used low monoamine diet for three days and were hospitalized at least two days prior to the lumbar puncture (LP). The LP was performed between 9 a.m. and 10 a.m., after at least nine hours of strict bed rest. The LP was done through the vertebral space between L3 and L4. CSF samples representing 12th to 15th ml aliquot were stored at –80°C and assayed for HVA using HPLC. Mean CSF HVA concentrations in SPD patients were found to be significantly higher than OPD controls ($t = 2.74$, $p = 0.01$). The sum of DSM-III SPD characteristics in each patient in the total sample correlated significantly with CSF HVA concentrations ($r = .43$, $p < 0.04$). This correlation appeared to be due to the psychotic-like SPD characteristics (i.e., magical thinking, ideas of reference, recurrent illusions and suspiciousness) and not due to the other SPD characteristics (i.e., social isolation, odd speech, inadequate rapport and undue social anxiety) as CSF HVA concentrations correlated very strongly with the former SPD characteristics ($r = .59$, $p < .002$) but not with the latter ($r = .11$, $p =$ ns). These findings raise the possibility of a central dopaminergic dysfunction in SPD that may modulate the psychotic-like symptoms of this disorder.

NR164 Monday May 13, 3:00 p.m.-5:00 p.m.

A Test of the Tridimensional Personality Theory

Robert G. Ruegg, M.D., John Umstead Hospital, Adult Admission Unit, Butner, NC 27509; John Gilmore, M.D., Mark Corrigan, M.D., David Ekstrom, M.P.H., Bettina Knight, R.N., Robert N. Golden, M.D.

Summary:

Cloninger's Tridimensional Personality Theory links certain dimensions of personality to specific neurotransmitter systems: Harm Avoidance (HA) to serotonergic, Novelty Seeking (NS) to dopaminergic, and Reward Dependence (RD) to noradrenergic systems. To test this theory, we compared Tridimensional Personality Questionnaire (TPQ) profiles with neuroendocrine responses to a serotonergic challenge.

Twenty-two healthy subjects (14 male, eight female) completed the TPQ. Prolactin and cortisol responses to clomipramine (CMI) infusion were then measured.

HA scores showed a moderate correlation with cortisol responses ($r = .39$, $p = .09$), but not with prolactin responses to CMI. NS scores showed a significant inverse correlation with prolactin responses to CMI ($r = -.56$, $p < .02$), especially in men ($r = -73$, $p < .008$). NS was also inversely correlated with cortisol responses ($r = -.49$, $p = .03$), especially in women ($r = -.86$; $p < .02$). RD scores did not correlate significantly with either prolactin or cortisol responses to CMI.

The correlation between cortisol responses to CMI and HA scores supports the hypothesis that the HA component of personality is related to central serotonergic function. Since serotonergic systems may constrain dopamine-mediated aspects of personality, the inverse relationships that we found between NS scores and neuroendocrine responses to CMI are also consistent with the Tridimensional Personality Theory.

NR165 Monday May 13, 3:00 p.m.-5:00 p.m.

Enlarged Ventricle to Brain Ratio in Schizotypal Personality Disorder

Merrill Rotter, M.D., Department of Psychiatry, Bronx VA Medical Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Oren Kalus, M.D., Miklos Losonczy, M.D., Ling Guo, M.D., Robert Trestman, M.D., Emil F. Coccaro, M.D., Michael Davidson, M.D., Ken Davis, M.D., Larry J. Siever, M.D.

Summary:

While enlargement of the lateral ventricles has been demonstrated in schizophrenic patients, CT scan abnormalities have not been studied in clinically selected patients with schizotypal personality disorder (SPD), a diagnosis previously shown to be phenomenologically, genetically and biologically related to schizophrenia. Non-contrast CAT scans of the brain were performed in four diagnostic groups: SPD patients ($n = 24$), schizophrenic patients ($n = 123$), patients with personality disorders other than SPD (OPD; $n = 22$), and normal controls ($n = 23$). Mean lateral ventricle to brain ratio (VBR) was significantly larger in the SPD patients (VBR: 7.07) compared with OPD patients (VBR: 5.33, t-test, $p < 0.05$) and normal controls (VBR: 4.92; t-test, $p < 0.02$). There was no significant difference between the SPD patients and the schizophrenic patients, whose mean lateral VBR was also enlarged (VBR: 6.28). Frontal horn VBR was enlarged in each of the three patient groups (Sz, SPD, OPD) compared with the normal controls ($p < 0.05$). However, only the schizophrenic and SPD patients demonstrated significantly enlarged posterior horn VBR in comparison with the normal controls ($p < 0.05$). These results suggest that SPD patients have structural brain abnormalities comparable to those in schizophrenic patients, including relative enlargement of the lateral ventricles and the posterior horns.

NR166 Monday May 13, 3:00 p.m.-5:00 p.m.

Traumatic Brain Injury in Patients with BPD

Chris A. Conway, Psychiatry, Tufts University, 15 Corporal Burns Road, Cambridge, MA 02138; Robert Van Reekum, M.D., David Bachman, M.D.

Summary:

It has been suggested that neurological dysfunction is especially common among patients with the diagnosis of Borderline Personality Disorder (BPD). We have undertaken a retrospective chart review to determine if traumatic brain injury (TBI) is more common in BPD than in other psychiatric disorders. Forty-three male BPD patients were consecutively identified from a VA acute psychiatric unit and compared with 49 consecutively identified age- and sex-matched controls from the same unit with other psychiatric diagnosis. A chart review was undertaken using a modified version of the Diagnostic Interview for Borderlines (DIB-R). TBI was defined as a head injury sufficiently severe to result in loss of consciousness or in hospital admission. TBI was identified in 15 of 43 patients meeting DIB-R criteria for BPD, but only four of 49 controls (p .005). All patients had sustained a TBI prior to being diagnosed as exhibiting BPD. An analysis of the DIB-R scores and subscores revealed no differences between BPD patients who suffered a TBI and those who did not. The potential contribution of TBI to the clinical presentation of BPD is yet to be defined.

NR167 Monday May 13, 3:00 p.m.-5:00 p.m.

Impulsivity and 5-HT in Personality Disorders

Robert L. Trestman, M.D., Department of Psychiatry, Bronx VA Medical Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Timothy L. Lawrence, M.D., Emil F. Coccaro, M.D., Vivian Mitropoulou, M.A., Susan Weston, M.D., James Weisberg, M.S., Steven Gabriel, Ph.D., Larry J. Siever, M.D.

Summary:

Central serotonergic (5-HT) dysfunction has been linked with impulsive/aggressive behavior in personality disorders (PD) (Coccaro et al. AGP, 1989). We studied 33 patients with DSM-III-R PD to extend our earlier work to include patients from a second medical center, to attempt to confirm the initial finding in a larger sample, and to examine possible gender differences. Central 5-HT function was assessed with plasma prolactin response (delta PRL) to fenfluramine (60 mg orally), a 5-HT releasing/uptake inhibiting agent. The delta PRL correlated inversely with several self-rated measures of impulsivity and aggression ($n = 33$; Barratt Impulsivity Scale (BIS)-Total: $r = -0.43$, $p < 0.01$; BIS-Motor Impulsivity: $r = -0.30$, $p < 0.05$; Buss-Durkee Hostility Inventory (BDHI)-Total: $r = -0.27$, $p < 0.06$; BDHI-Assault: $r = -.063$, $p < 0.001$), consistent with poorly inhibited aggressive impulses, whether directed at the self or others. These results extend our earlier findings in a more restricted sample, and parallel those of other groups who have demonstrated a relationship between decreased 5-HT function and increased impulsivity/aggression. Preliminary data suggesting gender differences will also be presented. These findings will be discussed in the context of hypothesized dimensional characteristics underlying PD diagnoses.

NR168 Monday May 13, 3:00 p.m.-5:00 p.m.

Noradrenergic Activity in Impulsivity/Aggression

Timothy Lawrence, M.D., Department of Psychiatry, Bronx VA Medical Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Emil F. Coccaro, M.D., Robert Trestman, M.D., David Bernstein, Ph.D., Vivian Mitropoulou, M.A., Larry J. Siever, M.D.

Summary:

Prior studies have suggested a relationship between noradrenergic function, impulsive/aggressive behavior and the mediation of environmental response. We therefore hypothesized that noradrenergic function is associated with aspects of impulsive and aggressive behavior, such as irritability, risk-taking, or reactivity to the environment, but not with violence per se, in patients with personality disorder (PD). Basal plasma norepinephrine (NE) and the growth hormone (GH) response to IV clonidine were examined in patients with DSM-III-R PD ($n = 27$). GH response correlated with self-rated measures of impulsivity and aggression in PD patients: (Buss-Durkee Hostility Inventory (BDHI)-Irritability: $r = 0.32$, $p < 0.05$; Barratt Impulsiveness Scale (BIS)-Risk-Taking: $r = 0.44$, $p < 0.01$) but not overt violence (BDHI-Assault: ns). Similar correlations were seen in the male subgroup ($n = 18$), but not in the female subgroup. NE levels correlated with like measures in the whole sample of PD patients (BIS-Risk-Taking: $r = 0.43$, $p < 0.05$; BIS-Total: $r = 0.48$, $p < 0.01$), and again in the male, but not the female, subsample. Similar correlations were found in subsamples divided along diagnostic categories or clusters (e.g., borderline vs. non-borderline, and dramatic vs. non-dramatic). In light of the findings of an inverse relationship between the prolactin response (PRL) to fenfluramine (FEN), and index of serotonergic (5-HT) activity, and impulsivity/aggression in an overlapping population (Coccaro EF, et al. AGP '89), and the absence of a relationship between PRL response to FEN and GH response to clonidine, these preliminary findings suggest that both the NE and 5-HT systems may affect the mediation of impulsivity/aggression.

NR169 Monday May 13, 3:00 p.m.-5:00 p.m.

Assessing Axis II Disorders by Informant Interview

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Summary:

In order to compare two methods of personality disorder (PD) assessment, direct patient interview and informant interview, the Structured Interview for DSM-III Personality Disorders (SIDP) was given to 62 psychiatric patients and a friend or relative of each who served as an informant. Two raters simultaneously interviewed each patient, and a senior clinician reviewed these ratings along with ratings from the informant interview to determine the patient's consensus Axis II diagnosis. Informant-based diagnoses showed poor agreement with diagnoses based on patient interview (mean kappa = .29, range = .11–.45, $p < .001$), and were less highly associated with consensus diagnoses (mean kappa = .45, range = .25–.69, $p < .001$) than were patient interview-based diagnoses (mean kappa = .73, range = .64–.83, $p < .001$). When informant interview and patient interview disagreed, however, the addition of informant-based data contributed to a change in patients' consensus diagnoses in a sizable minority of instances (29.2%). These findings raise the possibility that PD assessment by informant interview may lead to enhanced diagnostic resolution.

NR170 Monday May 13, 3:00 p.m.-5:00 p.m.

Event-Related Potentials in Schizotypal Personality Disorder

Oren Kalus, M.D., Department of Psychiatry, Bronx VA Medical Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Thomas B. Horvath, M.D., Ann Peterson, M.A., Emil F. Coccaro, M.D., Vivian Mitropoulou, M.A., Michael Davidson, M.D., Kenneth L. Davis, M.D., Larry J. Siever, M.D.

Summary:

Auditory event-related cortical potentials (ERP) were compared in patients with schizophrenia (SZ; n = 20), schizotypal personality disorder (SPD; n = 19), and normal controls (NC; n = 20) to determine: 1) if the diminished P300 amplitude (AMP) reported in SZ may extend to SPD, and 2) whether the association between N200 AMP and anhedonia reported in subjects at risk for psychosis might be replicated in SPD patients with negative symptoms. Subjects were healthy, medication free for two weeks, and diagnosed on SADS (SZ) and SIDP (PD). An "Oddball Paradigm" with frequent and rare tones was used and recorded on a Nicolet Pathfinder II with a CZ cortical electrode (linked to mastoids). P300 AMP was significantly different across the three groups ($F = 4.12$, $p < 0.01$, ANOVA) and significantly diminished in the SZ patients compared with normals ($p < 0.05$, Scheffe). The P300 AMP of SPD patients was intermediate between the SZ and NC groups, showing no significant difference with either. N200 AMP was significantly correlated with the sum of negative schizotypal symptoms ($r = +.49$, $p < 0.02$). The results suggest a possible overlap of reduced P300 AMP between SPD and SZ as well as ERP correlates for some schizotypal symptoms.

NR171 Monday May 13, 3:00 p.m.-5:00 p.m.

Generalized Anxiety Disorder: Long-Term Outcome

Mark H. Townsend, M.D., Department of Psychiatry, LSU Medical Center, 1542 Tulane Avenue, New Orleans, LA 70112; Donna M. Mancuso, M.D., James G. Barbee, M.D., Donald E. Mercante, Ph.D.

Summary:

The diagnostic validity and long-term prognosis of generalized anxiety disorder (GAD) remains the subject of considerable controversy. We report the results of an investigation of the long-term outcome of an original sample of 50 patients who participated in a medication trial. Subjects were re-interviewed approximately one year after completion of the study, utilizing standardized interviews.

At the time of this writing 28 of 50 patients have been interviewed (an addition 17 have been scheduled). Interim analysis reveals that 39% continued to fulfill criteria for GAD. Other concurrent Axis I diagnoses were as follows: dysthymia 36%, social phobia 14%, major depression 11%. Thirty-six percent of the original group currently fulfill criteria for one or more personality disorders. Patients who currently have GAD meet criteria for significantly more personality disorders than those without GAD. In addition, follow-up patients with GAD report a statistically equivalent number of recent life events as compared with patients without GAD.

These results suggest that for many patients, GAD is not typically a chronic condition. In addition, the persistence of active symptoms of GAD was associated at follow-up with a higher rate of Axis II pathology, and life events did not appear to significantly influence outcome.

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Classification of Anxiety Disorders: The Controversy

Michael Bach, M.D., Department of Psychiatry, University of Vienna, Waehringer Gurtel 18-20, A-1090 Vienna, Austria; Detlev O. Nutzinger, M.D., Martina de Zwaan, M.D.

Summary:

Assessing only cross-sectional diagnoses in anxiety disorders entails a considerable loss of information and adds weight to hierarchical rules as the probably most weak diagnostic criterion. Using a semi-structured polydiagnostic interview (including St. Louis, RDC, DSM-III, DSM-III-R and ICD-10) we determined lifetime diagnoses in a sample of 82 outpatients with a DSM-III-R anxiety disorder. Seventy-three percent of patients with DSM-III-R panic disorder (PD) without agoraphobia (AP) at onset developed AG subsequently, whereas only 33% of patients with DSM-III-R AG at onset developed PD. In all classification systems more than 80% of patients had additional lifetime diagnoses, ranging from 1.29 mean additional diagnoses in St. Louis to 3.38 DSM-III. Considering hierarchical rules did not substantially affect the overall number of lifetime diagnoses within each classification system, but it caused significant divergencies between the classification systems regarding the individual diagnoses (e.g., hypochondriasis was found in 14.6% of our sample according to DSM-III vs. in 51.2 according to DSM-III-R). Our results underline the importance of a polydiagnostic approach considering lifetime diagnoses in addition to cross-sectional classification, especially for research purposes.

NR173 Monday May 13, 3:00 p.m.-5:00 p.m.

Serotonin Function in Generalized Anxiety Disorder

Mark Germine, M.D., Department of Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Andrew W. Goddard, M.D., George R. Heninger, M.D., Dennis S. Charney, M.D., Scott W. Woods, M.D.

Summary:

In order to assess serotonergic function in generalized anxiety disorder (GAD), the serotonin agonist m-chlorophenylpiperizine (MCPP, 0.1 mg/kg iv) and placebo were administered to 10 GAD patients and 19 healthy subjects. Ratings of 13 mood variables and 27 anxiety symptom variables, and measurements of vital signs, cortisol, human growth hormone, and prolactin were performed. ANOVA revealed significant drug x diagnosis interactions for anger, nervousness, anxiety, fear of going crazy, shortness of breath, fear of dying, choking feeling, tremor, and twitching. On post-hoc analysis, placebo-corrected increases from baseline were significantly higher in GAD patients for each of these measures. The GAD/control difference on anxiety measures was primarily the result of a greater decrease over time on the placebo day for GAD patients. The blockade of this drop by MCPP may reflect a sus-

taining effect on anticipatory anxiety. Anger showed a significantly greater increase on the MCPP day in GAD patients. The peak increase in anger occurred at 30 minutes post infusion, with an MCPP/placebo difference of 22 + 24mm in the GAD group and 2 + 6mm in the healthy subjects ($p < 0.005$). This result suggests a relationship between the regulation of hostile affect and serotonergic activity in GAD.

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CSF Diazepam-Binding Inhibitor Concentrations in Panic Patients

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Summary:

Diazepam-binding inhibitor (DBI) is a neuropeptide found in the brain and CSF of man. Previous studies have suggested the possible role of DBI as a potential endogenous anxiogenic ligand modulating GABAergic transmission at the benzodiazepine-GABA-receptor complex. The measurement of DBI immunoreactivity (DBI-IR) in CSF of panic disorder patients and normal volunteers was undertaken to assess whether these were differences in the CSF concentration of this interesting compound. A lumbar puncture was performed on 18 panic patients (four males, 14 females) and nine controls (five males, four females). Subjects were kept overnight after four days of a low monoamine diet. The samples were immediately stored at -70 degrees centigrade until assay. Results are expressed in pmoles/mL. As a group, no significant differences were found between panic patients' CSF concentration of DBI-IR (1.12 $\pm$ 0.27 pmol/mL) and that of normal volunteers (1.23 $\pm$ 0.27 pmol/mL). No sex differences were demonstrated. These results will be discussed in relation to previous DBI-IR measurements in other neuropsychiatric disorders.

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Long-Term Fate of Specific Agoraphobic Fears in Panic Disorder

Michaela Amering, M.D., Psychiatry, University Vienna, Waehringer Guertel 18-20, Vienna 01090, Austria; Heinz Katschnig, M.D.

Summary:

In two large international multicenter clinical drug trials of panic disorder comparing imipramine, alprazolam and placebo and involving over 1,600 patients 82.2% of all patients suffered from panic disorder with agoraphobia. In a two- to six-year follow-up of roughly a quarter of the original population, a large proportion of patients had improved, especially with regard to phobic avoidance, over and above the amelioration achieved during the original drug trial. The present study examines the long-term fate of specific fears. The main finding is that among those specific fears currently subsumed under the term agoraphobia "fear of large open spaces," i.e., the fear historically and semantically most closely linked to the term agoraphobia, behaves differently from all other "agoraphobic" fears. For instance, it was the least frequent specific fear at baseline (46.1%) and its intensity was significantly lower (5.1 on 0-to-10 scale) than that of other specific agoraphobic fears. Also, it showed by far the largest reduction over time of all agoraphobic fears. The findings suggest that in future studies on panic disorder with agoraphobia specific fears should be analysed separately and in addition to overall phobia.

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Immune Function in Panic Disorder with Agoraphobia

John S. McDaniel, M.D., Department of Psychiatry, Emory Clinic, 1365 Clifton Road, Atlanta, GA 30322; Emile D. Risby, M.D., Rita D. Jewart, Ph.D., Mary B. Eccard, R.N., June Caudle, M.LN., Mark Stipetic, B.S., Donald E. Manning, M.D., Samuel C. Risch, M.D.

Summary:

Immune alterations, including impaired natural killer cell activity (NKA), have been widely reported in depressed patients and bereaved individuals. Few studies have examined immunity in panic disorder, a syndrome clinically and biologically related to depression. Two reports have examined lymphocyte mitogen responses in panic disorder. Surmon et al. (1987) found these patients to have normal mitogen stimulation responses, while Schleifer et al. (1990) found these patients to have impaired lymphocyte proliferative responses compared with controls. No previous reports have determined NKA in this patient population. We have prospectively studied NKA, total white blood cell counts (WBC), and total lymphocyte counts (LC) in 14 medication-free patients with the SCID/DSM-III-R diagnosis of panic disorder with agoraphobia. These patient findings were compared with those of 14 age-, gender-, and race-matched normal controls studied on the same day and time as their matched patients. To date, panic disorder patients have significantly *higher* NKA than controls: (patients 43.9 $\pm$ 8.2 vs. controls 24.1 $\pm$ 4.8, $t = 2.45$, $p < .03$). Patients do not differ significantly from controls in WBC or LC. No significant correlations were found among age, Hamilton Anxiety Rating Scale, Hamilton Depression Rating Scale, NKA, WBC, and LC. These findings may indicate a state of natural killer cell hyperactivity in this patient population, in contrast to the impaired NKA seen in depressed and bereaved states.

NR177 Monday May 13, 3:00 p.m.-5:00 p.m.

Feeling of Unreality as a Panic Disorder Symptom

James Cancienne, M.S., Psychiatry, New York Hospital, 525 East 68th Street, New York, NY 10021; M. Katherine Shear, M.D., Laura Portera, B.A., Andrew C. Leon, Ph.D., Marylene Cloitre, Ph.D.

Summary:

The feeling of unreality is one of the DSM-III symptoms of panic attacks, with a quality that seems distinct from both the typical autonomic symptoms and the other cognitive symptoms. Previous reports suggest that panic patients endorse this symptom with a moderate frequency. We report here the results of preliminary exploratory study evaluating the importance of feelings of unreality as a symptom of panic disorder. *Methods:* We conducted an analysis of two-week self-report diaries of 42 patients who met DSM-III-R criteria for panic disorder. Fifty-seven percent reported feelings of unreality (UR+) in their panic and/or limited symptom episodes. A comparison of this group with those who did not experience feelings of unreality (UR–) revealed significant differences in depression (mean BDI for UR+ = 16.38; UR– = 7.22; $p < .01$) and anxiety (mean Trait anxiety for UR+ = 51.83; UR– = 42.67; $p = .026$). There were significantly more patients with comorbid diagnoses in the UR+ compared to the UR– groups (41% vs. 21%; $p = -.022$). Lastly, a regression analysis indicated that the feeling of unreality contributed significantly to degree of functional impairment. *Conclusion:* These results suggest that the feeling of unreality may be a marker for a clinically distinct subtype of panic disorder.

NR178 Monday May 13, 3:00 p.m.-5:00 p.m.

Personality in Early Dropout From Clinical Trials

Dane K. Wingerson, M.D., Psychiatry, Univ. of Washington, 1959 NE Pacific Street RP-10, Seattle, WA 98195; Peter P. Roy-Byrne, M.D., Mark D. Sullivan, M.D., Deborah Cowley, M.D., Stephen R. Dager, M.D., David L. Dunner, M.D.

Summary:

Patients commonly drop out of clinical trials because of side effects or lack of efficacy. However, in our experience, patients who dropped out early in the trial (first two weeks) gave ambiguous or no reasons. We examined the potential role of personality traits in early dropouts in patients with panic disorder (n = 28) and GAD (n = 49) using Cloninger's TPQ.

Panic study early dropouts (n = 8), compared with completers (n = 20), had significantly higher scores on novelty-seeking subscales for impulsiveness (subscale 2, p = .07) and disorderliness, dislike of regimentation (subscale 4, p = .04), as well as total novelty-seeking (p = .03). Paradoxically, dropouts also had lower scores on the harm avoidance subscale of fear of uncertainty (subscale 2, p = .04).

Early dropout GAD patients (n = 13) compared with completers (n = 36) also had a significantly higher score on the novelty-seeking subscale 4 (p = .03).

For panic and GAD patients combined, dropouts (n = 21) versus completers (n = 55) had significantly higher scores on the novelty-seeking 4 (p = .004), and novelty-seeking total (p = .01) subscales.

These findings suggest that anxious patients who drop out early from clinical trials may not be leaving due to increased anxiety, but perhaps because of personality traits of impulsivity and dislike of regimentation.

NR179 Monday May 13, 3:00 p.m.-5:00 p.m.

Caffeine in Panic Disorder

William J. Apfeldorf, M.D., Department of Psychiatry, NYS Psychiatric Institute, 722 W. 168th Street, New York, NY 10032; Joan R. Birnberg, B.A., Andrew C. Leon, Ph.D., Jack M. Gorman, M.D., M. Katherine Shear, M.D.

Summary:

Objective: Caffeine provokes panic in people with panic disorder, most likely related to its competitive antagonism of adenosine receptors. A recent preliminary study suggested caffeine heightens taste sensitivity to quinine through an adenosinergic mechanism and that this sensitivity is enhanced in panic disorder patients (DeMet et al., 1989). To replicate this finding in untreated medication-free patients, a prospective study of caffeine enhancement of taste is underway in patients presenting to the Anxiety Disorders Unit at Payne Whitney Clinic.

Methods: Fifteen panic disorder patients and 15 normal subjects will be asked to participate in a caffeine taste test. Using a forced selection paradigm (DeMet et al., 1989), subjects are asked to separate four cups containing quinine from four cups containing water. The lowest concentration of quinine at which the cups are correctly identified is the taste threshold. Caffeine sensitivity is determined as the difference between taste thresholds for quinine measured in the presence and absence of 10 micromolar caffeine.

Results: To date, seven patients have completed the taste test. Using DeMet's caffeine sensitivity criterion, six of seven (86%) patients show high caffeine enhancement. In the original study, 80% of panic disorder patients and 17% of normal subjects demonstrated high caffeine taste enhancement.

Significance: These pilot results are consistent with the observed heightened responsiveness of panic disorder patients to dietary caffeine and with a proposed adenosine dysregulation in panic disorder. The caffeine taste test may offer a simple assay to identify potential panic disorder patients.

NR180 Monday May 13, 3:00 p.m.-5:00 p.m.

A Comparison of Limited Symptom Episodes and Full-Blown Panic Attacks

Laura Portera, M.A., Department of Psychiatry, New York Hospital, 525 E. 68th Street, New York, NY 10021; M. Katherine Shear, M.D., James Cancienne, M.S., Andrew C. Leon, Ph.D., Marylene Cloitre, Ph.D.

Summary:

Panic disorder patients regularly report limited symptom episodes (lse's) as well as full-blown panic attacks. The assumption generally made is that lse's represent minor panic attacks. However, this idea has not been empirically tested. The purpose of this study was to compare characteristics of full-blown panic attacks and lse's as reported in two-week panic diaries by a sample of 42 panic patients. We assessed: 1) the correlation between frequency of full-blown attacks and lse's; 2) the correlation between frequency of full-blown attacks and number of panic symptoms reported in those attacks; 3) the correlation between frequency of lse's and number of symptoms reported in those episodes; and 4) differential effects of treatment on panic and lse's. Results of this analyses show: 1) there is no association between full-blown panic frequency and lse frequency, (r = .08, p = .343); 2) there is a strong positive relationship between frequency of panic attacks and number of symptoms (r = .45, p = <.01); 3) conversely there is a strong negative relationship between frequency of lse's and number of symptoms, (r = –.62, p = <.01); and 4) treatment that is highly effective in reducing full-blown panic frequency was not as effective on lse's. These results suggest that lse's may be a distinct phenomenon, different from full-blown panic attacks.

NR181 Monday May 13, 3:00 p.m.-5:00 p.m.

Personality Disorders in Patients with Panic

Naresh P. Emmanuel, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; R. Bruce Lydiard, M.D., J. Allen Melvin, M.D., Virginia Villeponteaux, M.D., James C. Ballenger, M.D.

Summary:

The SCID and SCID II were administered to 73 patients with a primary diagnosis of panic disorder. The sample consisted of 58 females and 15 males with ages ranging from 21-63 years for males and 20-61 years for females. The mean duration of symptoms ranged from one to 30 years. Of the 73 subjects evaluated, 20% (18 subjects) met the criteria for a diagnosable personality disorder. The most frequently encountered Axis II diagnoses were avoidant personality disorder (12.5%), dependent personality disorder (11.1%) and paranoid personality disorder (12.5%). One subject met the criteria for five personality disorders, three for four personality disorders, one for three personality disorders, eight for two personality disorders and seven for only one personality disorder. In general those with more personality disorders tended to have more than one major psychiatric diagnosis. This rate of 20% patients with personality disorder tends to be low compared with earlier findings by Reich, Mavissakalian and Hamann. However, these were arrived at using the patient-rated Personality Diagnostic Questionnaire (PDQ). It has been found that the PDQ tends to overdiagnose personality disorders, while the SCID II permits clarification of an item with the examiner. Effects of personality disorder on treatment outcome will be discussed.

NR182 Monday May 13, 3:00 p.m.-5:00 p.m.

Familial Relationship Between Panic and PTSD

Linda M. Nagy, M.D., Psychiatry, VA Medical Center, 950 Campbell Ave, West Haven, CT 06516; Kathleen R.

Merikangas, Ph.D., Steven M. Southwick, M.D., Nancy Docherty, M.A., Elisheva Dan, M.A., Laurie Harkness, Ph.D., Dennis S. Charney, M.D.

Summary:

Little is known about possible vulnerability factors for PTSD or comorbid disorders. We have observed that spontaneous panic attacks and yohimbine-induced panic attacks are common in PTSD patients. To determine whether comorbid panic in PTSD patients is due to a familially transmitted vulnerability for panic attacks, we examined the family history of PTSD patients with and without comorbid panic disorder or yohimbine-induced panic attacks. *Methods:* Vietnam combat veterans who met DSM-III-R criteria for PTSD (N = 34) were interviewed about DSM-III-R diagnoses in each of their first-degree adult relatives. The interview was blind to comorbid diagnoses in the proband. Families were stratified by comorbid panic disorder in the proband (PTSD + PD; N = 16/34) and yohimbine-induced panic attack in the proband (YOH-PA; N = 17/27). *Results:* Panic disorder was reported in 4/75 (5.3%) relatives of PTSD + PD probands and in 3/115 (2.6%) relatives of the PTSD probands without panic disorder. The rate of panic disorder in relatives of YOH-PA probands was 1/70 (1.4%) and 6/120 (5.0%) in relatives of probands without yohimbine-induced panic attacks. The rate of PTSD was 8/75 (10.7%) in relatives of PTSD probands with comorbid panic disorder and 9/115 (7.8%) in relatives of PTSD probands without panic disorder. PTSD was reported in 8/70 (11.4%) of YOH-PA relatives vs. 9/120 (7.5%) of non-YOH-PA relatives. There were no significant differences in rates of panic disorder or PTSD between relatives of either group. *Conclusions:* Our preliminary findings do not support a familial etiology of panic attacks in PTSD patients, and rates of panic in family members do not appear to be elevated compared with other published reports. This finding suggests that although panic disorder and PTSD may share common pathophysiologic elements, one may be more genetic in origin (panic disorder in patients without PTSD) and the other more environmental (PTSD).

NR183 Monday May 13, 3:00 p.m.-5:00 p.m.

PTSD and Re-Injury Behavior

Cheryl Cottrol, M.D., Department of Psychiatry, UMDNJ, 185 S. Orange Avenue, E-501, Newark, NJ 07103; Jacob Lindenthal, Ph.D.

Summary:

This study was undertaken in an effort to understand factors contributing to the high rates of re-injury seen among physically traumatized individuals. Fifty-eight patients on the trauma service were randomly selected. Inclusion criteria were 1) recent admission following a physical trauma, 2) age range between 18 and 65, 3) English speaking, 4) consent, and 5) achieving a criterion score on cognitive screening measures. Instruments used were 1) Structured Clinical Interview for DSM-III (SCID), 2) Yudofsky Aggression scale, 3) Suicide Probability scale, and 4) a general questionnaire assessing cognitive status, demographics and type of injury.

Findings of the study included: 1) 39% met full criteria for the diagnosis of PTSD; 2) 50% had symptoms of PTSD without meeting full diagnostic criteria; and 3) 10% did not display or report any PTSD symptomatology. An association was found between PTSD symptoms and criteria and 1) other psychiatric diagnoses, and 2) suicide probability and aggression. When the symptom categories of PTSD were delineated to A) Re-experiencing phenomena B) Avoidance phenomena and C) Increased arousal, it was found persons showing positive PTSD symptoms in category A were found to show a higher score on the suicide probability scale and aggression scale. Persons who were found to have PTSD symptoms in category B scored significantly higher only on the suicide probability scale, and persons who stated PTSD symptomatology in category C scored significantly higher on aggression scales than those without symptoms in this group.

Implications of these findings are discussed.

NR184 Monday May 13, 3:00 p.m.-5:00 p.m.

Efficacy of Clomipramine in PTSD

Ramanujam Mohan, M.D., Psychiatry, VA Medical Center, 15th Street 116-A, Augusta, GA 30910; Daniel M. Samonsky, M.D., Bruce I. Diamond, Ph.D.

Summary:

Since some symptoms of post-traumatic stress disorder (PTSD) resemble those observed in obsessive compulsive disorder (OCD) it was thought that clomipramine (CMI) may be useful for combat veterans with PTSD. We reviewed the charts and interviewed 10 patients who met DSM-III-R criteria for PTSD and were on CMI. A clinical global impressions scale for 14 symptoms of PTSD was used. Patients ranged in age from 40-67 years, and were taking daily doses of CMI from 25-200mg/day. Patients who reported homicidal intrusions (2), racing thoughts (8), and suicidal intrusions (5) at baseline, reported no such symptoms after treatment. Eighty percent of the patients who reported depression, insomnia, and intrusive thoughts noted improvement of 2 points or more on these symptoms. The two symptoms that were resistant to improvement were flashbacks and hypervigilance. In some patients improvement was noted as early as three days, with the majority improving in two weeks. Higher doses of CMI were required for the symptoms of depression, guilt, insomnia and suicidal intrusions. These results with CMI suggest that the intrusive thoughts in PTSD and OCD have a similar quality and suggest further studies with CMI and other 5HT reuptake inhibitors.

NR185 Monday May 13, 3:00 p.m.-5:00 p.m.

PTSD and Dissociation in Vietnam Combat Veterans

J. Douglas Bremner, M.D., Department of Psychiatry, West Haven VAMC-116A1, 950 Campbell Avenue, 9th Floor, West Haven, CT 06516; Steven Southwick, M.D., Elizabeth Brett, Ph.D., Alan Fontana, Ph.D., Robert Rosenheck, M.D., Dennis S. Charney, M.D.

Summary:

Objective: This study compared general dissociative symptomatology and dissociation at the time of combat trauma in Vietnam combat veterans with PTSD to Vietnam combat veterans without PTSD. *Method:* The Dissociative Experiences Scale (DES) was used to compare general dissociative symptomatology in PTSD patients (N = 37) to non-PTSD patients (N = 28) seeking treatment for medical problems. Dissociation at the time of combat trauma was measured using the modified Dissociative Experiences Questionnaire (DEQ-M). Combat exposure was measured using the combat Exposure Scale (CES) and PTSD symptom severity using the Mississippi Scale. *Results:* There was a significantly higher level of dissociative symptomatology as measured by the DES in PTSD patients (26.1 $\pm$ 16.9) than in non-PTSD patients (14.6 $\pm$ 17.2)($p < 0.05$). There was also a higher level of combat exposure in the PTSD patients ($p < 0.05$), but when this was controlled for using a multiple linear regression combining the DES and the CES, the DES predicted a significant amount of the variance in PTSD symptomatology as measured by the Mississippi Scale ($p < 0.05$). PTSD patients reported more dissociative symptomatology at the time of combat trauma as measured by the DEQ-M (11.4 $\pm$ 1.7 vs. 1.7 $\pm$ 2.1)($p < 0.001$). *Conclusion:* Our finding of increased dissociative symptomatology in patients with PTSD suggests that dissociation may be a core aspect of the response to trauma. Dissociation at the time of combat trauma may be a measure of individual variations in response to traumatic events.

NR186 Monday May 13, 3:00 p.m.-5:00 p.m.

Dissociation and Trauma in Psychiatric Inpatients

Glenn N. Saxe, M.D., Psychiatry, Mass Mental Health Center, 74 Fenwood Road, Boston, MA 02115; Bessel A. van der Kolk, M.D., Robert Berkowitz, M.D., Gary Chinman, M.D., Kathryn Hall, M.D., Gabriel Leiberg, M.D., Jane Schwartz, M.D.

Summary:

This presentation reports on an investigation of the prevalence of childhood trauma and the subsequent development of dissociative and post-traumatic psychopathology in a population of psychiatric inpatients. The Dissociative Experiences Scale (DES) was administered to all patients and consecutive admissions at a state psychiatric institution. All patients who scored above 25 were matched for age and gender with a group of patients who scored below 5 on the DES. Patients in these two groups were then blindly interviewed and the following interview schedules were administered: 1) The Traumatic Antecedent Questionnaire, 2) The Dissociative Disorders Interview Schedule, and 3) The SCID-PTSD. Results on the first 90 patients screened with the DES (out of an anticipated N of 125) include the following: Seventeen patients (19%) had a high DES score. Each of these patients then met DSM-III-R criteria for a dissociative disorder and for PTSD. These patients reported significantly more experiences of childhood trauma and problems with attachment. Chart reviews revealed no differences in reporting of dissociative and post-traumatic symptoms between groups. These results are discussed in terms of the under-recognition of dissociative and post-traumatic experiences in psychiatric inpatients.

NR187 Monday May 13, 3:00 p.m.-5:00 p.m.

Predictors of Psychological Distress After Burn Injury

JoAnn Difede, M.A., Department of Psychiatry, Payne Whitney, 525 E. 68th Street, New York, NY 10021; Samuel W. Perry, M.D., Lawrence B. Jacobsberg, M.D., Ellen Halpern, M.A.

Summary:

The DSM-IV Task Force is currently debating whether the distress experienced after traumatic events is primarily related to subjective psychological factors or to the objective severity of the stressor. To examine this issue, we evaluated 180 hospitalized patients shortly after burn injury (1.0 +/–0.8 weeks). Emotional distress was measured by the Profile of Mood States (POMS) and by the degree of intrusive and avoidant thoughts (Impact of Event Scale: IES-intrusive; IES-avoidant). The subjective psychological predictor of distress was perceived emotional support (Interpersonal Support Evaluation List (ISEL). The objective severity of the stressor was the percent total body surface area of the burn (TBSA). POMS and IES scores correlated with ISEL (POMS, $r = -.30$, $p = .001$; IES-intrusive, $r = -.38$, $p = .001$; IES-avoidant, $r = -.28$, $p = .001$), indicating that distress after severe trauma was associated with less perceived interpersonal support; however, TBSA did not correlate with the POMS or IES. In fact, subjects with *smaller* burns were more likely to have distress ($F = 4.6$, $df = 1, 170$, $p = .03$). The results suggest that emotional distress after severe trauma is associated more with the psychological state of the individual than the severity of the stressor.

NR188 Monday May 13, 3:00 p.m.-5:00 p.m.

An Open Trial of Fluoxetine for Hypochondriasis

Brian A. Fallon, M.D., Therapeutics, NYS Psychiatric Inst., 722 West 168th Street, New York, NY 10032; Michael R. Liebowitz, M.D., Franklin Schneier, M.D., Raphael Campeas, M.D., Ester Salman, B.S., Sharon O. Davies, R.N.

Summary:

Hypochondriasis is widely regarded as a disorder with a poor prognosis. Case reports of successful treatment of hypochondriasis using serotonin reuptake blockers and the similarity of the obsessions and compulsions of patients with hypochondriasis to those with OCD led us to design the following open trial. *Methods:* Eight patients (mean age 42 + 13, sex 3 M/5 F) with DSM-III-R hypochondriasis were entered in an open trial using fluoxetine. Patients with major depression were excluded. After a one-week, single-blind placebo washout, patients were treated for 12 weeks starting at 10 or 20 mg and increasing as tolerated to 80 mg. Measures included global clinical response (CGI), as well as ratings of hypochondriasis, depression and anxiety. *Results:* Eight patients entered the study, two of whom dropped out. Five of six study completers were much improved at 12 weeks (mean Flu does 53 + 24 mg), while only two of six were much improved at six weeks (mean Flue dose 35 + 17 mg). Statistically significant decreases between baseline and week 12 were noted in the measures of hypochondriasis (Whiteley Index, Illness Behavior Questionnaire) and anxiety (HAM-A) but not depression (HAM-D). *Conclusion:* This study suggests that fluoxetine at high doses may be an effective treatment for hypochondriasis. A placebo-controlled trial is needed.

NR189 Monday May 13, 3:00 p.m.-5:00 p.m.

Are You Benzo or Buspirone Prone?

Christine Reynaert, M.D., Psychiatry, University of Louvain, Cliniques Universitaires, Yvoir B5530, Belgium Europe; Pierre Janne Pascal, Ph.D., Leon Cassiers, M.D., Jean Kinable, Ph.D

Summary:

It still remains difficult to predict, before the prescription, to what extent an anxiolytic drug will succeed. In anxiety disorders, the determinants of a drug's choice are often made on the basis of the drug's efficacy as well as an anticipated short time of response. However, to many patients it is important to avoid any possible addiction so as to keep control over the situation.

In order to be able to predict the patient-molecule appropriateness and to define the profile of the best suitable patient for a buspirone treatment, we have conducted a prospective study of 217 outpatients (general practice). The aims of the study were first, to predict the level of satisfaction obtained with the drug and, second, to assess the clinical efficacy of buspirone (State Trait Anxiety and Hamilton Anxiety Rating Scale). Both variables were evaluated by the patient, the general practitioner and a significant other (e.g. the spouse). The predictors included an evaluation of the family functioning (Olson's Model), the Locus of Control (Rotter's and Waalston's questionnaires) and additional new experimental items especially conceived for the purpose of the study.

Data were analysed by means of successive discriminant and multiple regression analyses. The results of the study indicate that a semi-structured interview including 10 questions enables us to predict to what extent the patient will benefit from buspirone or, on the contrary, would prefer to obtain an immediate "benzodiazepine-like" effect.

NR190 Monday May 13, 3:00 p.m.-5:00 p.m.

A Family Study of Obsessive-Compulsive Disorder

Margaret A. Richter, M.D., Department of Psychiatry, Clarke Institute, 250 College Street, Toronto, Canada M5T 1R8; Richard P. Swinson, M.D., Russell T. Joffe, M.D.

Summary:

Obsessive-compulsive disorder (OCD) is widely accepted as a familial condition, but studies examining prevalence rates of the illness in families of probands are limited and suffer from major

methodological flaws. We therefore carried out a study examining psychiatric morbidity in the first-degree relatives of 12 subjects with primary OCD by RDC criteria. Probands were interviewed using the Family Informant Schedule and Criteria (FISC), a semi-structured interview generating diagnoses according to the Family History-Research Diagnostic Criteria modified for anxiety disorders. Information was thus obtained on 43 first-degree relatives. Nine of 43 (20.9%) first-degree relatives fulfilled criteria for primary OCD. A further five of 43 (11.6%) had significant obsessional features. Eight of 43 (18.6%) met criteria for major depression. This is in excess of that expected based on prevalence rates for the general population obtained in the Epidemiologic Catchment Area study. A very high prevalence of the spectrum of anxiety disorders in the relatives was also noted. Comorbidity of psychiatric diagnoses will be reported in detail.

This study, using systematic data collection and standardized diagnostic criteria, finds that there is a high prevalence of affective and anxiety disorders, particularly OCD, in the first-degree relatives of probands with OCD.

NR191 Monday May 13, 3:00 p.m.-5:00 p.m.

Personality Disorders in Trichotillomania

Gary A. Christenson, M.D., Psychiatry, Univ of Minnesota UMHC, 420 Delaware St SE box 393, Minneapolis, MN 55455; Elizabeth Chernoff, B.A.

Summary:

Trichotillomania, a disorder of chronic self-directed hair pulling, appears to be more common than previously suspected. Some authors have suggested an association with obsessive compulsive disorder (OCD). Few systematic studies of psychiatric descriptors have been conducted on large populations of trichotillomanics, and there are no published reports of systematic assessment of comorbidity with Axis II disorders. As part of a larger study of personality disorders in psychiatric patients, the authors evaluated 51 adult chronic hair pullers (50 outpatient and one inpatient) with the Structured Interview for DSM-III-R personality (SIDP-R). Twenty-one (41.2%) trichotillomanic subjects met criteria for at least one DSM-III-R personality disorder and five (9.8%) met criteria for two or more personality disorders. Histrionic (13.7%), avoidant (9.8%), dependent (9.8%), and obsessive compulsive (9.8%) personality disorders were most common. A comparison of our results with the published comorbidity of personality disorders in OCD suggests both similarities and differences between trichotillomania and OCD.

NR192 Monday May 13, 3:00 p.m.-5:00 p.m.

Treatment of Trichotillomania with Fluoxetine

Gary A. Christenson, M.D., Psychiatry, Univ of Minnesota UMHC, 420 Delaware St SE box 393, Minneapolis, MN 55455; Thomas B. Mackenzie, M.D., James E. Mitchell, M.D., Alan Callies, B.A.

Summary:

Trichotillomania, a disorder of chronic hair pulling, has been proposed by some investigators to be a variant of obsessive-compulsive disorder based on observed similarities in phenemenology, family history and response to treatment. A controlled study of clomipramine and open studies of fluoxetine have suggested the usefulness of these antiobsessional agents in this disorder. Twenty-one adult chronic hair pullers were recruited into an 18-week, placebo-controlled, double-blind crossover study of fluoxetine up to 80 mg/d. Fifteen subjects (14 females, one male) completed the study with an additional female subject dropping out at 16 weeks after developing a drug reaction. The mean $\pm$ SD age of these 16 subjects was 31.6 $\pm$ 6.2 with a mean $\pm$ SD duration of hair pulling of 17.0 $\pm$ 6.7 years. No significant drug-period interactions were found in regard to number of hair-pulling episodes per week, estimated amount of hair pulled per week, weekly subject rating of hair pulling or weekly subject rating of urge to pull.

NR193 Monday May 13, 3:00 p.m.-5:00 p.m.

Effects of Fenfluramine on HVA in OCD and Controls

Dan J. Stein, M.B., Psychiatry, NY State Psych Inst., 722 W. 168th Street, New York, NY 10032; Eric Hollander, M.D., Jihad B. Saoud, M.S., Concetta M. Decaria, M.S., Michael Stanley, Ph.D., Michael R. Liebowitz, M.D.

Summary:

Fenfluramine has been used as a pharmacological probe of net serotonin function. However, there is some concern about its specificity and potential dopaminergic effects. To investigate this, we studied effects of fenfluramine and placebo on the dopamine metabolite plasma homovanillic acid (pHVA) in 12 OCD patients and 10 controls. Fenfluramine, as compared with placebo, significantly lowered pHVA in patients ($t = 3.54$, $p = .005$), but not in controls. Patients significantly differed from controls in pHVA decrease after fenfluramine as compared with placebo (drug x time x group F-3.65, $p = 0.014$). Perhaps upregulated serotonin receptors result in increased sensitivity to fenfluramine and decreased dopaminergic neurotransmission in OCD.

NR194 Monday May 13, 3:00 p.m.-5:00 p.m.

Obsessional Severity in Tourette's Syndrome

Dan J. Stein, M.B., Psychiatry, NY State Psych Inst., 722 W. 168th Street, New York, NY 10032; Ruth Bruun, M.D., Stephen Josephson, Ph.D., Concetta M. Decaria, M.S., Sari Trungold, B.A., Eric Hollander, M.D.

Summary:

Patients with Tourette's syndrome (TS) have long been known to have obsessive-compulsive symptoms, and family studies suggest a genetic relationship between TS and obsessive-compulsive disorder (OCD). Nevertheless, there are few studies that use standard rating scales to assess obsessive-compulsive symptoms in TS. Twenty-four adult TS patients, all of whom had evidence of obsessive-compulsive symptoms on clinical interview, completed a Leyton Obsessional Inventory, a standard self-administered obsessive-compulsive scale. For each subject the score (a measure of the extent of obsessive-compulsive symptoms and traits), interference (a measure of the severity of symptoms), and resistance (a measure of the disability caused by symptoms) was calculated. Results were compared with previous work on OCD patients and normal controls. TS patients with clinical evidence of obsessive-compulsive symptoms had significantly lower measures than OCD patients, but significantly higher measures than normal subjects. Implications of these findings will be discussed.

NR195 Monday May 13, 3:00 p.m.-5:00 p.m.

Nocturnal Penile Tumescence Is Diminished In Diabetic Men

Eric A. Nofzinger, M.D., Department of Psychiatry, University of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213; C.F. Reynolds, III, M.D., J.R. Jennings, Ph.D., M.E. Thase, M.D., Ellen Frank, Ph.D., D.J. Kupfer, M.D.

Summary:

The nocturnal penile tumescence (NPT) study is commonly used to help differentiate psychogenic from organic impotence. The leading cause of organic impotence is diabetes. While the observation of abnormal NPT studies is well documented in impotent diabetics,

little research has been done in a sexually functional diabetic sample to document the normality of NPT in nonimpotent diabetics. In a prospective study, 143 diabetics were referred without controlling for the adequacy of daytime sexual function. Of these, 20 met our exclusion criteria controlling for confounding medical or psychiatric conditions that might affect sexual function. Of the 20, 10 reported no daytime sexual dysfunction, three reported minimal dysfunction, three reported moderate dysfunction, and four reported the complete absence of sexual function. All (n = 20) subjects underwent similar NPT studies that were compared with 20 age-matched controls. Results showed that the condition of diabetes, irrespective of daytime sexual function, is associated with diminished NPT profiles to the point that nine of our sexually functional diabetics (90%) would have had false positive NPT studies based on traditional NPT criteria. The study highlights the need for an age-matched sexually functional diabetic comparison group in the interpretation of the diabetic NPT study due to the variations in NPT associated with the conditions of diabetes, healthy aging, and daytime sexual function.

NR196 Monday May 13, 3:00 p.m.-5:00 p.m.

Length of Stay Determinants on an Inpatient Unit

Joseph V. Pace, M.D., Psychiatry, Wilford Hall Med., 9535 Abe Lincoln, San Antonio, TX 78240; George Brown, M.D.

Summary:

We reported the results of a two-year prospective study of factors associated with length of stay (LOS) in the Air Force's largest teaching hospital. Data were collected on 1019 consecutive admissions; 45 patients with administratively shortened LOS were excluded. Of 974 admissions, 69.3% were active duty military, 30.7% were civilians. Overall average LOS was 13.02d (s.d. 13.06). Multiple regression analysis indicated that a nonclinical factor (military status) was the most important determinant of LOS: civilian LOS was significantly shorter (10.32d;p = .0001) than military (14.21d). Discharge diagnosis was also an important determinant: Adjustment D/O, substance use D/O, and V-codes as primary Axis I diagnoses yielded significantly shorter LOS (8-11d) than bipolar D/O, major depressive D/O, and all psychotic D/O (22-24 d; p = .0001). Black patients' LOS was longer than any other racial group (16.29 d; p = .05). Other factors contributing to longer LOS in both groups included (p < .05): comorbid Axis II diagnosis, use of restraints, and paranoid symptoms on admission. Gender, marital status, homicidality on admission, organic etiology, duration of symptoms prior to admission, alcohol use D/O, and past history of physical or sexual abuse were not associated with LOS in either subgroup.

NR197 Monday May 13, 3:00 p.m.-5:00 p.m.

Repeat Users of Psychiatric Emergency Services

Patrick F. Sullivan, M.D., Psych/WPIC, Univ of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213; Steven D. Forman, M.D., Cynthia M. Bulik, Ph.D., Juan E. Mezzich, M.D.

Summary:

Objective: This study examined characteristics of repeat users of a psychiatric emergency service (PES) to determine differential patterns of use. The largest previous study sampled 2,600 visits in one year. Prior investigations failed to use structured diagnostic approaches.

Method: 16,257 people made 29,214 visits to an urban PES from 1985-1989. A semistructured interview provided DSM-III multiaxial diagnoses. The characteristics of the 202 people who frequented the PES at least 11 times (13.7% of all visits) were compared with groups who frequented 1, 2-4, and 5-10 times.

Results: The most frequent users of PES were significantly more likely than less frequent users to be male, black, unmarried, receive SSI disability, and lack an occupation. In the most frequent use group, schizophrenia was significantly more prevalent than in the other groups. In contrast, major depression, adjustment disorders, and childhood disorders were more prevalent in the nonrepeater group. Heaviest PES usage was in March and October.

Conclusions: Repeat users are distinct from one-time users of PES in diagnosis, demographic characteristics, and seasonal usage. Repeat users consume PES resources disproportionately. Targeted intervention strategies based on these characteristics may enhance efficient resource utilization.

NR198 Monday May 13, 3:00 p.m.-5:00 p.m.

Psychiatric Morbidity in Liver Transplant Patients

Andrea F. DiMartini, M.D., Department of Psychiatry, Western Psych. Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213; Kathleen A. Pajer, M.D., John Fung, M.D., Thomas Starzl, M.D., Paula T. Trzepacz, M.D., Ronald Tringali, M.S.M.

Summary:

Cognitive and psychiatric symptoms may impair organ transplant patients' ability to be compliant. The psychiatric morbidity associated with cyclosporine A (CyA), and FK506, a new immunosuppressant, has not been evaluated.

In a randomized, nonblinded, controlled trial of FK506 vs. CyA in liver transplant patients, cognitive function (Mini-mental State Exam (MMS); Trails A + B) and psychiatric symptoms (Symptom Checklist) were assessed one week post-op (n = 24). Forty-two percent had alcoholic cirrhosis; mean age was 40 ± 9 years; 46% were female; 29% were college-educated. FK506 (n = 14) and CyA (n = 10) patients were demographically similar.

Thirty-five percent of the group had cognitive impairment; 51% had more than four psychiatric symptoms. MMS scores for FK506 and CyA were similar (26 ± 5 vs. 28 ± 2). Trails A (58 ± 45s vs. 37 ± 14s) and Trails B (127 ± 64s vs. 96 ± 37s) scores were not statistically significantly different. The number of psychiatric symptoms was similar (4 ± 3 vs. 5 ± 2). Diagnosis, pre-op cognitive status, and demographic factors did not change the results. The serum levels of FK506 were positively correlated with Trails B scores (r = 61, p = .03). These preliminary data suggest similar overall psychiatric morbidity in FK506 and CyA patients during the first post-op week, although larger sample sizes are needed for confirmation of results.

NR199 Monday May 13, 3:00 p.m.-5:00 p.m.

Popular Remedies for a Society's Debilities: Medicines for Neurasthenia in Victorian America

John B. Stea, M.D., Department of Psychiatry, Maimonides Medical Center, 914 48th Street, Brooklyn, NY 11209; William K. Fried, Ph.D.

Summary:

This paper will provide a historical exploration of the use of medicines for neurasthenia in Victorian America. Also termed nervous exhaustion, neurasthenia puzzled many physicians. Its symptoms included weakness, depression, anxiety and numerous psychosomatic complaints. Physicians, including George Beard, a prominent neurologist, employed a number of regimes for this symptom complex, including medicines that ranged from atropine to zinc oxide. In this paper, theories on the origin of neurasthenia will be explored, as they were reflected in the types of substances used to treat this condition. Advertisements of commercial preparations for neurasthenia will be examined as they reveal methods used to gain the interest of the medical professionals and the general public. Finally, the response of the medical profession to the proliferation and availability of substances such as cocaine, alcohol and opiates will be discussed. The results of this paper reveal that in an

era of little regulation, a wide range of substances were available for neurasthenia. These medicines were used to fill the therapeutic vacuum left by the increased awareness of mood and other disorders collectively known as neurasthenia, and the dearth of effective treatments for them.

NR200 Monday May 13, 3:00 p.m.-5:00 p.m.

A Rehabilitation Program for Chronic Fatigue Syndrome

Andrew John Wilson, M.M., Department of Psychiatry, Prince Henry Hospital, Anzac Parade - Little Bay, Sydney NSW 2036, Australia; Ian Hickle, M.D., Catherine Hickle, M.B., Andrew Lloyd, M.D., Denis Wakefield, M.D.

Summary:

An outpatient cognitive-behavioral and physical rehabilitation (CBPR) program for patients with CFS was conducted in conjunction with a double-blind, placebo-controlled trial of transfer factor (TF). The patients were randomly allocated to the CBPR program, so that an equivalent number in each group received TF injections. The treatment consisted of at least six outpatient sessions with an emphasis on education, cognitive strategies and graded increase in physical activity. A close relative was also interviewed to explain the program and seek their ongoing support. Psychological morbidity was assessed principally by the Profile of Mood States (POMS) questionnaire at trial entry (n = 90), four months later at the end of the TF injections (n = 90) and after a further three months (n = 77). All patients showed a reduction in fatigue, but the CBPR program was not associated with any additional benefit. The intervention, however, was associated with a trend ($p = 0.08$) towards a marked reduction in depression (>1 SD) at the end of TF injections in patients who participated in the CBPR program. At three-month follow-up the patients' levels of depression had returned to pre-intervention levels. This style of psychological intervention may lead to a reduction in depression in patients with CFS but has no specific effect on the key symptom of fatigue. Importantly, non-specific clinic attendance was associated with an equal degree of improvement.

NR201 Monday May 13, 3:00 p.m.-5:00 p.m.

Clinical Correlates of Nonsuicidal Self-Injury

Douglas R. Langbehn, M.D., Department of Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; Bruce Pfohl, M.D.

Summary:

We examined the charts from 660 admissions to the Adult Psychiatric Unit during 1987 and found 32 cases of intentional, nonsuicidal, physical self-injury not associated with mental retardation. The controls consisted of 88 randomly selected admissions for suicide attempts. Women were significantly over-represented among the cases (84% vs 58%, $p = 0.014$) but age did not differ between groups (29.0 + 9.0 vs. 30.6 + 13.3). Among the cases, three of the five men and none of the women had DSM-III schizophrenia.

In comparing the 27 female cases with nonsuicidal intentional self-injury with the 51 female suicide attempters, the cases were more likely to receive an Axis II diagnosis (67% vs 25%, p0.001) and to have a history of substance abuse (63% vs 24%, p0.001). Cases were less likely to receive a diagnosis of depression or adjustment disorder. Childhood sexual abuse was three times more frequent among cases (37% vs 12%, p0.02).

In summary, the current study agrees with several previous studies in finding that the typical patient presenting with nonsuicidal intentional self-injury is a female below the age of 35 with a history of childhood sexual and/or physical abuse, and past or present substance abuse. The most frequent self-injury was cutting the skin with a sharp object. The patient often described the act as a compulsion following several hours of increasing tension. Treatment was frequently complicated by repeated admissions, substance abuse, borderline personality traits and unresolved feelings about childhood sexual abuse.

NR202 Monday May 13, 3:00 p.m.-5:00 p.m.

Crisis Intervention and Suicide: A Follow-Up Study

Anelise Muhlebach, Ph.D., Psychiatry, University of Geneva, Rue Des Vollandes 69, Geneva GE 01207, Switzerland; Antonia Andreoli, M.D., Maryvonne Gognalons, Ph.D., Jeanne Abensur, M.D.

Summary:

Significance: Since the observed (Black 1985) increase of mortality and suicide rates in inpatients may be associated with treatment assignment, we developed a prospective investigation of treatment choice/mortality relationships in hospitalized patients.

Methods: The subjects (N = 78), aged 15-65, were referred to inpatient care in a Geneva (Switzerland) 105,000 inhabitants catchment area within two months and had reliable diagnostic/psychosocial assessment. Clinicians were allowed a choice between standard hospitalization, 24-hour emergency intervention and time-limited combined (drug + psychotherapy) crisis intervention. Treatments were extensively taped by questionnaires. Seventy-five patients (96.1%) had one- and two-year follow-up.

Results: The number of deaths was one (1.9%) at one-year, and seven (8.8%) at two-year follow-up. During the second follow-up year, four subjects committed suicide and the total sample standardized mortality ratio was 9.16 for overall deaths and 170 for suicide. Suicide rate was higher in EI (3; 60%) than in CCI (1; 1.9%) and SH (–; 0%) patients.

Comment: Our preliminary data indicate that 1) completed suicide may occur more frequently than previously reported (Glick 1979) and 2) emergency treatment, but not well-structured crisis intervention programs, may be associated with increased number of suicides at two-year follow-up in patients referred to inpatient hospitalization.

NR203 Monday May 13, 3:00 p.m.-5:00 p.m.

Aftercare Compliance Among Drug Overdose Patients

Jessica Hellings, M.D., Psychiatry, Kansas Univ Med. Center, 39th & Rainbow Blvds, Kansas City, KS 66103; George A.D. Hart, Ph.D., Elizabeth Penick, Ph.D.

Summary:

Should every case of deliberate self-poisoning be admitted? At Johannesburg Hospital in South Africa, this was the policy. We systematically examined and followed 138 consecutive, self-poisoning admissions (96 females; 42 males). This mostly young group of patients were provided intensive crisis counseling within one day after they were considered medically stable. One hundred twenty-five were discharged within a few days and scheduled for a return outpatient aftercare appointment with the same clinician approximately one week later (nine were transferred to the psychiatric inpatient unit and four were referred to their private psychiatrist). Only eight or 6.4% of the 125 scheduled for aftercare kept their appointments (two men and six women). Of the original 138 patients, 78 (56.5%) were contacted one year later. Two suicides occurred during that time. Both suicides were patients who had been transferred to the inpatient psychiatric unit. None of the 125 who participated in the short-term aftercare program attempted or completed suicide within 12 months of their admission to the hospital. These findings suggest that the policy of automatically admitting all self-poisoning patients to inpatient treatment is not cost effective.

NR204 Monday May 13, 3:00 p.m.-5:00 p.m.

Mental Health Risk Factors in Vietnamese Amerasians

Robert S. McKelvey, M.D., Department of Psychiatry, Baylor Coll. of Medicine, 4815 Dickson, Houston, TX 77007; Alice R. Mao, John A. Webb, Ph.D.

Summary:

Mental health professionals have long been interested in the relationship between immigration and emotional disturbance. To develop a risk profile predicting mental health symptoms in a group of prospective U.S. immigrants, 161 Vietnamese Amerasians awaiting U.S. placement were evaluated at the Amerasian Transit Center (ATC) in Vietnam. The Hopkins Symptom Checklist-25 (HSCL-25) and a modified version of Felsman's Personal Information Form were utilized. HSCL-25 symptoms of anxiety and depression were factor analyzed against a variety of demographic, education, familial, health and vocation variables. Those found to be correlated with increased symptoms of anxiety and depression were: 1) history of missing school, 2) delinquency, 3) multiple hospitalizations, 4) separation from mother, 5) low family income, 6) education outside of a public school setting, 7) negative or indifferent feelings toward their American father, 8) hostile relationship with stepfather/foster father, and 9) residence in a camp prior to the ATC. Increasing numbers of risk factors were associated with higher levels of psychological distress.

The risk profile should assist mental health professionals involved in treating newly arrived immigrants and refugees to identify those most in need of mental health support. This is the first *prospective* study of immigrant mental health based on assessment prior to departure from the immigrant's homeland.

NR205 Monday May 13, 3:00 p.m.-5:00 p.m.

Race and Haloperidol-Induced Side Effects

James C-Y Chou, M.D., Clinical Research, Nathan Kline Institute, Orangeburg, NY 10962; Richard Douyon, M.D., Pal Czobor, Ph.D., Jan Volavka, M.D.

Summary:

Seventy-four Black and 22 Caucasian acutely decompensated schizophrenic or schizoaffective patients were treated with haloperidol under double-blind conditions for up to six weeks. The groups were similar in age, weight, sex, diagnosis and duration of illness. Race had no significant effects on severity of baseline symptomatology or amount of improvement, and there were no Black/Caucasian differences in haloperidol dose, haloperidol plasma level, or ratio of haloperidol dose/plasma level. Plasma homovanillic acid levels were also similar (in a subset of 40 subjects). However, Blacks had significantly more new onset extrapyramidal side effects during the initial week of haloperidol treatment than did Caucasians (chi-square = 5.68, df = 1, $p < .02$). This difference was not present in subsequent weeks. This suggests that Blacks are more vulnerable than Caucasians to extrapyramidal side effects early in the course of haloperidol treatment.

NR206 Monday May 13, 3:00 p.m.-5:00 p.m.

Motor Vehicle Fatalities and Mental Illness

Carole Menard-Buteau, M.D., Louis H. Lafontaine, Research Center, 7401 Hochelaga, Montreal PQ, Canada H1N 3M5; Richard Boyer, Ph.D., Alain D. Lesage, M.D., Frederic Grundberg, M.D.

Summary:

Purpose: To investigate the contribution of psychopathology in vehicle accidents as Axis I and II dx. The originality of this research lies in the use of two control groups (general population and suicide group). Traffic accidents among young men are a major public health issue to which psychiatry could provide some answers.

Method: Comparison on rates of DSM-III-R dx found in males (18-35 years old) in the Province of Quebec, adjusted for sociodemographics. Psychological autopsies conducted four months after the tragedy. Same technique was used in all groups. Dx are reached blindly by two psychiatrists.

Preliminary results: Trend show higher prevalence of comorbidity of depression or adjustment disorder or personality disorder with alcohol/drug abuse/dependence among accident victims compared to each control group. Final data will be presented with accident victims: N = 40; Ss in control group: N = 120.

Findings: Congruent with the literature: furthermore, synergic effect of the comorbidity of alcohol abuse/dependence and Axis I/II characterized the accident group. In young males, comorbidity of alcohol/drug problem and Axis I/II dx is a fatal traffic accident factor discriminating this group from suicide victims and the general population.

NR207 WITHDRAWN

NR208 Monday May 13, 3:00 p.m.-5:00 p.m.

Psychiatric Disorders in Patients with Epilepsy

M. Caroline Burton, M.D., Psychiatry, Mayo Clinic, 200 First Street Southwest, Rochesrer, MN 55905; Teresa A. Rummans, M.D., Max R. Trenerry, Ph.D., Gregory D. Cascino, M.D., Frank W. Sharbrough, M.D., Robert J. Ivnik, Ph.D.

Summary:

Goal: To determine the frequency and nature of psychiatric illness preoperatively in patients undergoing surgical treatment for medically intractable seizure disorders and to assess possible factors predictive of these disorders.

Methodology: Retrospective analysis of 193 consecutive adult patients who underwent surgical treatment for medically intractable seizure disorders 1987-1989.

Results: Twenty-five of 193 patients (13%) had a psychiatric history preoperatively. Diagnoses were chemical dependency (48%), affective disorder (32%), suicide attempt (24%), psychotic disorder (12%), and personality disorder (8%). Compared with patients without a psychiatric history, these patients were older at surgery ($T = 2.05$, $p < 0.005$) and had a longer duration of seizure disorder ($T = 5.72$, $p < 0.005$). Sex, age of onset of seizure disorder, and laterality were not associated with psychiatric disorder. Postoperatively, nine of 25 patients (36%) were diagnosed with a psychiatric illness.

Conclusion: Psychiatric illness in this patient population is not uncommon. It is associated with older age at surgery and longer duration of seizure disorder. Postoperatively, the majority of these patients (64%) had no recurrence/exacerbation of their psychiatric problem.

NR209 Tuesday May 14, 9:00 a.m -10:30 a.m.

Meiotic Origin of Nondisjunction in Down Syndrome

Melvin G. McInnis, M.D., Dept. of Psychiatry, Johns Hopkins Univ., 600 North Wolfe St Meyer 2181, Baltimore, MD 21205; Michael B. Petersen, M.D., Patricia Adalsberger, B.Sc., Stylianos Antonarakis, M.D.

Educational Objectives:

Meiosis 1 and 2 errors will be explained and contrasted in males and females. The importance in determining the source of nondisjunction with centromeric markers and relationship to research in nondisjunctive events will be discussed. A description of the population (e.g., age versus meiosis 1 and 2 errors) will be presented.

Summary:

Down syndrome arises from the meiotic nondisjunction of chromosome 21 (trisomy 21) and is the most commonly identified genetic cause of mental retardation. Recent studies of 200 families using multiple DNA polymorphisms have indicated the origin of the extra chromosome 21 is maternal in 95 percent of cases and 5 percent in paternal. This is different than the estimate of 80 percent and 20 percent paternal origin by chromosomal heteromorphisms.

The polymerase chain reaction (PCR) was used to analyze polymorphic loci approximately six centiMorgans from the centromere of chromosome 21 to determine the stage of meiotic error in the nondisjunctive event leading to trisomy 21. Three polymorphisms were due to variable $(GT)_n$ dinucleotide repeat sequences (D21S120, D21S13, and D21S172) and one was a EcoR1 restriction site within an amplified sequence at the D21S173 locus.

Members of 200 families with liveborn trisomy 21 were studies with these markers. The meiotic stage of nondisjunction was determined in 171 families (85.5 percent). In 162 families with maternal origin, 120 (75 percent) were found to be errors in the first meiotic division and 42 (25 percent) were second division errors. Of the nine paternal cases, two (22 percent) were first meiotic errors and seven (78 percent) were meiosis 2 division errors. PCR markers are highly polymorphic and the method of choice for determining the meiotic source of nondisjunction. The mean maternal age for meiotic 1 errors was 32.2 years (SD 6.4) and for meiotic 2 errors was 32.7 years (SD 5.7); the difference was not significant.

References:

1) Petersen MB, et al. Use of short sequence repeat DNA polymorphisms after PCR amplification to detect the parental origin of the additional chromosome 21 in Down syndrome. *AmJ of Human Genetics* 48: 65-71, 1991

2) Warren AC, et al. Evidence for reduced recombination on the non-disjoined chromosomes 21 in Down syndrome. *Science* 237: 652-654, 1987

NR210 Tuesday May 14, 9:00 a.m -10:30 a.m.

Nocturnal Endocrine Profiles of Depressed Teens

Stanley P. Kutcher, Psychiatry, Sunnybrook Hospital, 2075 Bayview Avenue, Toronto, Ont., Canada M4N 3M5; Dina Malkin, M.D., Jay Silverberg, M.D., Peter Marton, Ph.D., Peter Williamson, M.D., Aaron Malkin, M.D.

Educational Objectives:

1) To demonstrate nocturnal secretory profiles of TSH; GH; CRT in depressed adolescents. 2) To identify possible biologic markers of adolescent depression. 3) To develop the understanding of the neurobiology of adolescent depression.

Summary:

Twelve depressed adolescents and 12 controls matched for age, sex, Tanner stage, time of menstrual cycle (females), weight, and time of year assessed were studied over three nights. Measurements for cortisol (CRT), thyroid stimulating hormone (TSH), and growth hormone (GH) were made on serum collected at 2200, 2400, 100, 200, 300, 400, and 600 hours in eight pairs and every 20 minutes from 2000 to 700 hrs. in four pairs. CRT secretion did not significantly differentiate the groups. TSH secretion was significantly elevated in the depressed group at two time points. GH secretion significantly differentiated the two groups at most time points and the depressed teens significantly hypersecreted GH (area under the curve). These findings were not related to basal levels of free T4, cortisol, or to differences in total amount of state 4 sleep between the groups. A 2400 hr GH value of 8 mg/L correctly classified 100 percent of the depressed and 94 percent of the nondepressed groups. The implications for diagnosis, etiology, and treatment of adolescent depression are discussed.

References:

1) Kutcher S, Williamson P, Silverberg J, et al. Nocturnal growth hormone secretion in depressed older adolescents. *J.Am.Acad. Child Adolesc.Psychiat.* 27:751-754 1988.

2) Dahl R, Puig-Antich J, Ryan N, et al. Cortisol secretion in adolescents with major depressive disorder. *Acta.Psychiatr.Scad.* 80:18-20 1989.

NR211 Tuesday May 14, 9:00 a.m -10:30 a.m.

Locomotor Activity and the Diagnosis of ADHD

Martin H. Teicher, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Carol A. Glod, M.S., Kambiz Pahlavan, M.D., David Harper, B.S., Eleanor Magnus, B.S., Frances Wren, M.D.

Educational Objectives:

To understand how locomotor activity and circadian rhythms are affected in children with ADHD or mood disorders. To understand how pharmacotherapy affects locomotor activity levels and biological rhythms in children with ADHD.

Summary:

The diagnosis of Attention Deficit Hyperactivity Disorder has been criticized by some factions for lack of objectivity, and for overreliance on the impression of teachers. Pioneering research from Rapoport's group at the NIMH has shown that locomotor activity levels are increased, on average, in children with ADHD, and that stimulants reduce activity to more normal levels. We have collected detailed activity recordings from normal and hyperactive children to ascertain whether any quantitative parameters specifically identify children with ADHD. Activity recordings (864 epochs over 72 hours) were obtained from 12 normal controls (11.2y), 13 children with ADHD (9.4y), six children with manic or mixed states (10.5y), and 13 children with major depression (13y). The distribution of activity levels was sharply skewed in ADHD, showing a paucity of lower level activity and a marked increase in high level activity. Ten patients with ADHD had distributions that were more skewed than patients in any other group. These ten patients were pervasively hyperactive in all situations, and their activity patterns normalized with effective pharmacotherapy. Phase space trajectories from the field of chaos theory show that children with ADHD oscillate between two strongly attractive states, whereas children with major mood disorders show a weakened diurnal attractor, and prominent circadian dysregulation.

References:

1. Porrino LJ et al. A naturalistic assessment of the motor activity of hyperactive boys: I. Comparison with normal controls. *Arch Gen Psychiatry,* 40: 681-687, 1983.
2. Borcherding BR et al. Differential effects of methylphenidate and dextroamphetamine on the motor activity level of hyperactive children, *Neuropsychopharmacology,* 2: 255-263, 1989.

NR212 Tuesday May 14, 9:00 a.m -10:30 a.m.

Family Genetic Risk Factors in ADHD

Joseph Biederman, M.D., Child Psychiatry, Mass General Hospital, 15 Parkman Street ACC-725, Boston, MA 02114; Stephen V. Faraone, Ph.D., Ming T. Tsuang, M.D., Belinda R. Krifcher, B.A., Kate Keenan, B.A.

Educational Objectives:

Participants will learn about findings indicating important family-genetic influences in ADHD and about the validity of subgrouping of ADHD probands by patterns of comorbidity.

Summary:

In a large sample of children and adolescents with *DSM-III-R* attention deficit hyperactivity disorder (ADHD) (N = 140) and comparison samples of normal controls (N = 120) ascertained from pediatric and psychiatric facilities, we have produced results that are strikingly similar to those we reported previously based on *DSM-III* criteria using a different sample. Using family study methodology, assessments of probands (N = 260) and their first-degree relatives (N = 822) were made by blind raters. ADHD probands were significantly more likely to have comorbid conduct disorder and oppositional defiant disorder, major depression (MDD), and anxiety disorders. Relatives of ADHD probands compared with relatives of normal controls had a markedly higher risk for ADHD (16 percent vs 3 percent, p's, <0.00001), antisocial disorders (25 percent vs 12 percent, $p=0.00002$), MDD (26 percent vs 9 percent, $p=0.0001$), substance (alcohol or drug) dependence (34 percent vs 19 percent, $p=0.001$), and multiple anxiety disorders (22 percent vs 13 percent, $p=0.001$). After stratification of probands based on patterns of comorbidity, familial risk analysis support hypotheses that ADHD and MDD share common familial vulnerabilities, that ADHD plus comorbid conduct disorder may be a distinct subtype, and that ADHD and anxiety disorders segregate independently in families. These results confirm and extend previous findings indicating important family-genetic influences in ADHD and provide further validation of subgrouping of ADHD probands by patterns of comorbidity.

References:

1. Biederman J, Faraone SV, Keenan K, Knee D, Tsuang MT: Family-genetic and psychosocial risk factors in *DSM-III attention deficit disorder. J Am Acad Adoles Psychiatry* 29:526-533; 1990

2. Biederman J, Munir K, Knee D: Conduct and oppositional disorder in clinically referred children with attention deficit disorder: A controlled family study. *J Am Acad Child Adoles Psychiatry, 26:724-727, 1987*

NR213 Tuesday May 14, 9:00 a.m -10:30 a.m.

Adult Outcome of Childhood Hyperactivity

Salvatore Mannuzza, Ph.D., Hillside Res., Long Island Jewish, 270-05 76th Avenue, New Hyde Park, NY 11042; Rachel G. Klein, Ph.D. Abrah W. Bessler, B.A.

Educational Objectives:

At the end of the program, the learner should have a better understanding of the adult fate of clinically-diagnosed hyperactive children, compared to nonhyperactive controls. This study specifically focuses on occupational status, educational achievement, and psychiatric function in adulthood.

Summary:

We previously reported a prospective follow-up investigation of 103 Caucasian male adolescents (ages 16-23 years) who had been diagnosed as hyperactive in childhood (ages 6-12 years), compared to 100 controls. Information was obtained on 98 percent of the original cohort. Blind *DSM-III* diagnoses showed that, compared to controls, probands had significantly higher rates of attention deficit (31 percent vs. 3 percent), antisocial (27 percent vs. 8 percent), and drug abuse disorders (16 percent vs. 3 percent) at average age 18 years. The present study reports on the adult outcome of these subjects. At mean age 26 years (23-30 years), 91 probands (88 percent of childhood cohort) and 95 controls were directly interviewed by trained clinicians. Significant differences were found in occupational rank and in educational achievement in disfavor of probands. Cases continued to show significantly higher rates of antisocial (18 percent vs. 2 percent), drug abuse (16 percent vs. 4 percent), and attention deficit disorders (8 percent vs. 1 percent). In summary, as a group, probands completed less schooling, were less often involved in higher level professions (e.g., lawyers), and were at a significantly increased risk for mental disorder. However, being a hyperactive child did not preclude achieving a higher-level education or profession, and two-thirds of these children showed no evidence of any mental disorder at adult follow-up.

References:

(1). Gittleman R, Mannuzza S, Shenker R, Bonaguar N. Hyperactive boys almost grown up: I. Psychiatric status. *Arch Gen Psych 42, 937-947, 1985*

(2). Mannuzza S, Klein RG, Bonagura N, Malloy P, Giampino TL, Addalli, KA. Hyperactive boys almost grown up: V. Replication of psychiatric status. *Arch Gen Psych* (in press).

NR214 Tuesday May 14, 9:00 a.m -10:30 a.m.

Psychopathology in Male Prostitutes: Implications

Richard R. Pleak, M.D., CADH Box 38, Hillside Hosp, Long Island Jewish Med Ctr, Glen Oaks, NY 11004; Heino F.L. Meyer-Bahlburg, Ph.D.

Educational Objectives:

The learner should be able to identify psychiatric diagnoses prevalent in male prostitutes and discuss its potential significance in the etiology of prostitution and the effectiveness of prevention/intervention programs.

Summary:

The male prostitute has long been assumed to have some degree of psychopathology. Past studies have indicated greater overall psychopathology than in the general population, but no specific data on diagnoses have been available. The first author has formally studied 50 young male prostitutes and has initiated a study of homeless young male prostitutes in New York. Subjects were recruited in their working locales and interviewed using structured diagnostic instruments, including the SCID. Results of the study, substantiated by preliminary results from the work with homeless male prostitutes, show very high rates of psychopathology, primarily childhood-onset and substance abuse/dependence disorders. At least 52 percent had had impulse control disorders (attention-deficit hyperactivity and conduct disorders) and 68 percent had had psychoactive substance abuse or dependence disorders, while fully 82 percent had had any lifetime psychiatric diagnosis. Such psychopathology has importance in the etiology of prostitution and has implications for prevention and intervention programs for this population. For example, AIDS prevention programs for male prostitutes commonly fail to take into account limitations in attention and impulse control of their target subjects. The effectiveness of programs for male prostitutes may be enhanced by tailoring them according to the prevalence and types of psychopathology found here.

References:

1. Pleak RR, Meyer-Bahlburg HFL: Sexual behavior and AIDS knowledge of young male prostitutes in Manhattan. *J Sex Res* 4:557-587, 1990

2. Weisberg DK: Children of the Night: A Study of Adolescent Prostitution. Lexington, MA, Lexington Books, 1985.

NR215 Tuesday May 14, 9:00 a.m - 10:30 a.m.

A Family Study of Social Phobia and Panic Disorder

Abby J. Fyer, M.D., Theraputics, NYS Psychiatric Inst., 722 West 168th Street, New York, NY 10032; Salvatore Mannuzza, Ph.D., Tim Chapman, M.S., Michael R. Liebowitz, M.D., Jack M. Gorman, M.D., Donald Klein, M.D.

Educational Objectives:

To provide information about: 1. heritability of panic disorder and social phobia. 2. use of family study methods to investigate diagnostic validity

Summary:

The relationship of panic disorder and social phobia was examined using the family study method. Rates of panic disorder (± agoraphobia) and social phobia among directly interviewed relatives of four proband groups are compared: Panic Disorder/No Social Phobia (PD), Social Phobia/No Panic Disorder (SocPh), Panic Disorder & Social Phobia (PD/SocPh), Not Ill Controls (NIC).

Relatives (n = 164) of PD probands had an increased rate of PD (6.1 vs. 2.6) but not of SocPh (7.9 vs. 5.2) as compared to relatives of NIC (n = 231). Conversely, relatives (n = 88) of SocPh probands had an elevated rate of SocPh (15.9 vs. 5.2), but not of PD (2.3 vs. 2.6). The pattern among relatives of the comorbid PD/SocPh probands was similar to that seen in relatives of PD subjects i.e., an increased rate of PD (7.9 vs. 2.6) but not of SocPh (1.8 vs. 5.2). Co-occurrence of SocPh/PD was rare among relatives of all groups. In 27/32 comorbid PD/SocPh probands the onset of SocPh preceded the onset of PD by at least a year. In addition, family study results were unchanged by exclusion of those few probands in whom PD preceded SocPh.

These data indicate that SocPh in individuals who subsequently develop PD is distinct with resect to intergenerational transmission from SocPh in individuals who do not have PD. However, further confirmation is needed in larger clinical and epidemologic samples.

References:

1. Liebowitz, MR. Social phobia: Review of a neglected anxiety disorder. *Arch Gen Psych* 42, 729-736, 1985.

2. Understanding the clinical heterogeneity of major depression using family data. Weissman, MM *Arch Gen Psychiatyr,* 43, 430-434, 1985.

NR216 Tuesday May 14, 9:00 a.m -10:30 a.m.

A New Primate Model for Panic Disorder

Frank R. Ervin, M.D., Psychiatry, McGill University, 1033 Pine Avenue West, Montreal, PQ, Canada H3A 1A1; Roberta M. Palmour, Ph.D., Jacques Bradwejn, M.D.

Educational Objectives:

To describe the behavior pharmacology of a new primate model of panic and anxiety produced by the intravenous injection of cholecystokinin tetrapeptide in African green monkeys with anxious temperaments. Behavioral effects in conspecifics with calm temperaments are contrasted.

Summary:

Intravenous injection of cholecystokinin tetrapeptide (CCK-4) in African green monkeys (*Cercopithecus aethiops*) produces behavioral symptoms which have reportedly indicated anxiety in nonhuman primates. This phenomenon is dose responsive (1-20 ug CCK-4), of short duration (5-45 minutes, depending upon dose) and exhibits prompt onset (30 seconds after CCK administration). In the 30 percent of animals hyperresponsive to social threat, doses between 1 and 5 ug stimulate restless behaviors (pacing, rearing, threat, vigilance, and attack if approached), while doses between 10 and 20 ug engender fixed and frozen immobility, with retreat into a corner, self-clasping, shivering, and tremor. In monkeys unresponsive to social threat, low doses of CCK-4 have no overt behavioral effect, but doses of 10-20 ug cause subtle changes in vigilance and threat behavior, as well as occasional rearing and pacing.

Behavioral activation is accompanied by increases in blood pressure and heart rate. The dose response curve is shifted to the right by alprazolam and by adenosine A2 agonists. This model has implications for a wide range of basic and clinical investigations into the neurobiology of anxiety states.

References:

1. Freidman S, Sunderland, GS, Rosenblum LA 1988. A nonhuman primate model of panic disorder. *Psychiat Res 23:* 65-75, 1988.

2. Bradwejn J, Koszycki D, Shriqui C (1991) Cholecystokinin panic: A specificity and dose study in panic disorder and controls. *Arch Gen Psych* (in press).

NR217 Tuesday May 14, 9:00 a.m -10:30 a.m.

Comparison of Cholecystokinin-Tetrapeptide-4E-4 and Oxygen in Normal Controls

Diana Kozycki, M.A., Psychiatry, St. Mary's Hospital, 3830 Lacombe Avenue, Montreal, PQ, Canada H3T 1M5; Jacques Bradwejn, M.D., Michel Bourin, M.D.

Educational Objectives:

To report on the role of cholecystokinin-tetrapeptide in panic disorders and on a comparison of the panicogenic effects of cholecystokinin-tetrapeptide of CO2 in normals.

Summary:

CCK-4 is panicogenic in panic disorder (PD) and normal controls, but with an increased action in PD. We reported that CCK-4 induced panic attacks were qualitatively similar to attacks induced with CO2 in PD patients. This study compared the action of CCK-4 (25ug i.v.) and 35 percent CO2 (single inhalation) in 26 normal controls. *DSM-III-R* criteria, including moderate to severe anxiety were used to judge the occurrence of a panic attack. For the entire sample, the mean (± SEM) number of symptoms was similar for CCK-4 and CO2 (7.4 ± 0.8 vs 6.0 ± 0.8), but the sum intensity of symptoms was greater with CCK-4 (18.9 ± 2.7 vs 10.1 ± 1.8; ($P < .01$). The incidence of panic attacks was 17 percent for CCK-4 and 21 percent for CO2. No differences were found among controls who panicked, suggesting that CCK-4 and CO2 are equipotent panicogenics. A common neurobiological substrate might be shared by these two agents.

References:

1. Bradwejn J, Koszycki D, Meterissian G. Cholecystokinin-tetrapeptide induces panic attacks in patients with panic disorder. *Can J Psychiatry* 35: 83-85, 1990.

2. Bradwejn J, Koszycki D, Shriqui C. Enhanced sensitivity of panic disorder to cholecystokinin-tetrapeptide: Clinical and behavior results. *Arch Gen Psych* (in press).

NR218 Tuesday May 14, 9:00 a.m -10:30 a.m.

Cognitive Mediation of Lactate-Induced Panic

David M. Clark, D. Phil., Psychiatry, University of Oxford, Warneford Hospital, Oxford, England OX37JX; Michael Gelder, M.D., Paul M. Salkovskis, Ph.D., Pavlos Anastasiades, M.A.

Educational Objectives:

To evaluate and distinguish between current biological and cognitive approaches to the understanding of panic disorder.

Summary:

Infusions of sodium lactate reliably induce panic attacks in panic disorder patients but rarely do so in normal controls. Biological theories explain this finding by supposing that the lactate has a direct panic-inducing effect, and that individuals who are susceptible to lactate have a biochemical disorder. In contrast, cognitive theories propose that panic results from the misinterpretations of sensations induced by lactate. In an attempt to distinguish these explanations, 20 panic disorder patients were allocated to one of two pre-infusion instructional sets (experimental or control). Both em-

phasized lactate is harmless and the infusion could be stopped at any time. Experimental instructions also emphasized lactate is a natural substance, it is normal to experience intense sensations and the sensations are not indicative of an adverse bodily reaction. The experiment group was also encouraged to ask questions and given answers supporting the view that strong sensations are a normal consequence of the infusion. Heart rate and anxiety were measured throughout. An experimenter blind to patients' allocation assessed whether a panic occurred. During the infusion, subjects in the experimental group experienced significantly less anxiety, smaller heart rate increases, and were less likely to panic than those in the control group. The implications of these results for controversies about the causes of panic attacks are discussed.

References:

1. Clark DM. A cognitive approach to panic. *Behavior Research and Therapy, 24,* 461-470, 1986.

2. Clark DM, Salkovskis PM, Gelder MG, *et al.* Tests of cognitive theory of panic attacks. In I. Hand, H. Wittchen (eds) *Panic and Phobias II,* Springer-Verlag, 1988.

NR219 Tuesday May 14, 9:00 a.m - 10:30 a.m.

The Use of Alpidem in Generalized Anxiety Disorder

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Educational Objectives:

To inform health care professionals about new, effective and safe anxiolytic agents and to educate the audience about the comparative advantages of these drugs to those of the benzodiazepine class. Underlying mechanisms of action of anti-anxiety agents will be address.

Summary:

Benzodiazepines for Generalized Anxiety Disorder (GAD) are safe and effective treatments; however their potential to produce dependence and impair psychomotor and cognitive functions are drawbacks. In this study the efficacy and safety of the omega 1 and 3 benzodiazepine ligand, alpidem, was compared to placebo using lorazepam as an active control. Although not a benzodiazepine, alpidem inhibits diazepam binding. Thirty patients who met *DSM-III-R* criteria for GAD were randomized in a double-blind fashion to either alpidem (225 mg), lorazepam (4.5 mg), or placebo. The primary efficacy measure was the Hamilton Anxiety Rating Scale (HAM- A). A repeated measures ANOVA was used to determine differences in HAM-A scores. The results showed alpidem to be more effective than the other groups. Half of the alpidem group had a decrease of 50 percent or greater in their HAM-A scores with a greater effect on psychic than somatic symptoms. The most common side effects with alpidem and lorazepam were lightheadedness, drowsiness, and daytime tiredness. Moreover, treatment with alpidem did not manifest any withdrawal symptoms. Thus this novel omega one and three benzodiazepine ligand appears to be an effective and safe treatment for GAD.

References:

1. Musch B, Priore P, Morselli PL: Clinical studies with the new anxiolytic alpidem in anxious patients: an overview of the European experiences. *Pharmacol Biochem Behav* 29:803-06, 1988.

2. Rickels K. Nonbehzodiazepine anxiolytics: clinical usefulness. *J Clin Psych* 11 (part 2):44, 1983.

NR220 Tuesday May 14, 9:00 a.m - 10:30 a.m.

Social Phobia: Morbidity in a Community Sample

Franklin R. Schneier, M.D., Therapeutics, NYS Psychiatric Inst., 722 West 168th Street, New York, NY 10032; Jim Johnson, Ph.D., Christopher Hornig, B.A., Michael R. Liebowitz, M.D., Myrna M. Weissman, Ph.D.

Educational Objectives:

To learn bout features of social phobia in an epidemiologic sample, including sociodemographics, comorbidity, suicidal behavior, financial dependency, and treatment seeking.

Summary:

Selected sociodemographic and clinical features of social phobia were assessed in four US communities among more than 13,000 adults from the Epidemiological Catchment Area (ECA) study. Rates of social phobia were highest among women and persons who were younger (age 18-29), less educated, single, and of lower socioeconomic class. Mean age of onset was 15.5 years, and first onsets after age 25 were uncommon. Lifetime major comorbid disorders were present in 69 percent of social phobics and usually had onset after social phobia. When compared to persons with no psychiatric disorder, uncomplicated social phobia was associated with increased rates of suicidal ideation, financial dependency, and having sought medical treatment, but was not associated with higher rates of having made a suicide attempt or having sought treatment from a mental health professional. An increase in suicide attempts was found among social phobics overall, but this increase was mainly attributable to comorbid cases. Social phobia, in the absence of comorbidity, was associated with distress and impairment, yet was rarely treated by mental health professionals. The findings are compared and contrasted to prior reports from clinical samples.

References:

1. Schneier FR, Liebowitz MR: Social phobia in adulthood, in Hersen M, Last CG (Eds.): Handbook of Child and Adult Psychopathology. N.Y., Pergamon, 1990.

2. Regier DA, Myers JK, Kramer M, et al: The NIMH epidemiologic catchment area program: historical context, major obstacles, and study population characteristics. *Arch Gen Psych,* 41:934-941, 1984.

NR221 Tuesday May 14, 12 noon - 2:00 p.m.

Impact of Support Network on Bereaved Children

Mary A. Fristad, Ph.D., Psychiatry, OSU Hospital, 473 W. 12th Avenue, Columbus, OH 43210; Natalie K. Wolfe, B.A., Elizabeth B. Weller, M.D., Ronald A. Weller, M.D.

Summary:

In adults, good social support networks are associated with better coping following a loved one's death. As this relationship has not been studied in children, we determined bereaved children's social support networks, then assessed their association with psychiatric outcome. Also, effects of mediating variables on these parameters were examined. Subjects were 89 parent-bereaved children aged six to 18 years. They and their surviving parents were administered structured interviews six weeks post-parental death to assess their social support networks (Home Environment Interview, Grief Interview, and Intervention Survey) and psychiatric status (DICA). Additionally, questionnaires were administered to the children, their parents, and teachers (Conners-Parent and Teacher forms, CDRS-R, CDI, and CBCL). Children had talked about the death with others including: surviving parent, 47 percent; a friend, 42 percent; relative outside the nuclear family, 27 percent; a sibling, 26 percent; another parent-bereaved child, 25 percent; a nonrelative adult, 19 percent; and a counselor or therapist, 18 percent. Use of nonfamilial support was associated with greater behavioral problems ($r = .30$; $p < .05$). Adolescent males with living fathers had the most extensive and helpful (by self-report) support networks. Boys with living mothers utilized the most familial support and exhibited the most behavioral difficulties. Implications of these findings are discussed.

NR222 Tuesday May 14, 12 noon - 2:00 p.m.

A Positive and Negative Scale for Children and Adolescents: A Study of Criterion Validity and Interrater Reliability

Joel H. Fields, M.D., Albert Einstein Med Ctr, Bronx Child Psych Hosp., 1000 Waters Place, Bronx, NY 10461; Stanley R. Kay, Ph.D. (Posthumously), Gail Alexander, M.D., Sandra Grochowski, B.A., Daniel Grosz, M.D., Jean Pierre Lindenmayer, M.D., Gary Pawl, M.D., Amoro Reyes, M.D., Len Leven, M.D.

Summary:

An increased interest in assessing positive and negative symptom syndromes in adult schizophrenics has led to widespread syndromal assessment utilizing Andreasen's SAPS/SANS (1982), and Kay's et al. PANSS (1986). These syndromal concepts haven't yet been adequately explored in psychotic children and adolescents and may potentially reveal therapeutically useful differential patterns of pathogenesis, premorbid status, and long-term outcome. The KIDDIE-PANSS (K- PANSS) was developed by the authors in order to assess positive and negative symptoms in a pre-adult population. Thirty-four psychiatric inpatients, age range six to 16 years, were evaluated with the K-PANSS, Achenbach Child Behavior Checklist and the SAPS/SANS as part of a criterion validity and interrater reliability study. Results support the internal reliability of the scales (alpha range from .62 to .89) and interrater reliability (mean Pearson $r = .76$, .78, and .84) for the positive, negative syndromes, and general psychopathology. Criterion-related validity was evidenced from the correspondence between the K-PANSS and the SAPS/SANS with high correlations between the two positive scales ($r = .69$, $p < 0.0001$) and the two negative scales ($r = .89$, $p < 0.0001$). There was a significant correspondence between the Achenbach and the K-PANSS General Psychopathology subscale ($r = .52$, p.005). Implications for applications of the K-PANSS will be discussed.

NR223 Tuesday May 14, 12 noon - 2:00 p.m.

Depressive Disorders in Maltreated Children

Joan Kaufman, Ph.D., Psychiatry, Univ of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213

Summary:

The prevalence of depressive disorders was examined in a sample of 56 seven to 12-year-old maltreated children. All previous investigations of children at risk for depressive disorders have studied the offspring of affectively-ill parents, and the major premise of this study was that abused children comprise another sample at risk for developing depressive disorders. Project data were obtained from parents, children, teachers, social workers, and medical records, with naturalistic and formal child assessments made in a day camp setting devised specifically for this study. Overall, 18 percent of the sample met the criteria for major depression, a rate comparable to that reported in offspring studies. Most of the children in this study, however, were "doubly depressed." Children who met the criteria for depressive disorders were more likely than the other children to have suffered more extreme forms of physical and emotional abuse, been subjected to repeated and prolonged separations from their biological parents, have few social supports, describe their relationship with their parents in antagonistic terms, make maladaptive causal attributions, and have abnormal patterns of cortisol secretion. *A discriminant analysis conducted using a subset of these measures correctly classified 91 percent of the sample in terms of their diagnostic status.*

NR224 Tuesday May 14, 12 noon - 2:00 p.m.

Suicidal Ideation in Children with ADHD

Catherine A. Martin, M.D., Psychiatry, Univ of Kentucky, 820 South Limestone Annex #4, Lexington, KY 40536; Kaye L. McGinty, M.D., Jeanetta F. Smith

Summary:

The association of depression and impulsivity has been described in children with Conduct Disorder (CD) and Attention Deficit Hyperactivity Disorder (ADHD) and in adolescents with suicidal behavior. This study investigated the frequency and character of suicidal ideation in latency aged children with possible ADHD. Forty-three consecutive cases of children being evaluated for ADHD underwent a standard psychiatric interview, completed a Children's Depression Inventory (CDI) and had Parent and Teacher's Conners Scales completed. Twenty-one percent of the population reported suicidal ideation. Children reporting suicidal ideation were remarkably similar to those denying suicidal ideation on a number of variables including age, the total score, and the behavioral problems subscale of the CDI, Teacher's, and Parent's Conners. Of the nine children reporting suicidal ideation all denied actual intent but two had a plan. Precipitants included physical pain, misbehavior and subsequent punishment, sibling favoritism, school difficulties, and paternal hospitalization for minor surgery. This study highlights the importance of asking about suicidal ideation in the children with symptoms of hyperactivity. The CDI used as part of the interview may facilitate reporting of suicidal thoughts. Suicidal ideation in this population appears to follow relatively minor, everyday stress and may be correlated with an immediate depressive, impulsive feeling state which deserves further investigation.

NR225 Tuesday May 14, 12 noon - 2:00 p.m.

Fluoxetine Treatment of Patients With Autism and Mental Retardation

Edwin H. Cook, M.D., Psychiatry, Univ of Chicago, 5841 S. Maryland Avenue, Chicago, IL 60637; Randall Rowlett, M.D., Catherine Jaselskis, D.O., Bennett L. Leventhal, M.D.

Summary:

Behavior of some children and adults with autistic disorder was noted to be similar to more articulate patients of normal intelligence with obsessive-compulsive disorder. An open trial of fluoxetine treatment of children and adults with autistic disorder and/or mental retardation was conducted. Twenty-three patients with autistic disorder (*DSM-III-R;* 7.0 to 28 years; five female, 18 male; Full-scale I.Q. range 15 to 73) were administered doses of fluoxetine ranging from 20 mg every third day to 80 mg per day based on open titration. Dosage was most commonly reduced because of insomnia and/or irritability. Fluoxetine led to a significant improvement in NIMH Clinical Global Impressions (CGI) ratings of clinical severity in 15 of 23 subjects (baseline 5.7 $\pm$ 0.8, fluoxetine 4.9 + 1.1; paired t 4.03, df 22, $p < .002$). Six of 23 subjects had side effects which significantly interfered with function or outweighed therapeutic effects; only one of these were "responders." Mentally retarded, nonautistic subjects with varied Axis I psychiatric disorders (age range 4.8 to 52 years; 12 female, four male; Full-scale I.Q. range 15 to 67) were administered doses ranging from 20 to 80 mg. per day. Ten of 16 subjects had an improvement of one or more on CGI Severity ratings (baseline 5.1 $\pm$ 1.0, mean fluoxetine 4.2 $\pm$ 1.3; paired t 3.57, df 15, $p < .004$). In an open trial fluoxetine improved function in a majority of subjects with autistic disorder and/or mental retardation. All side effects remitted within several days of discontinuation or reduction of fluoxetine. Systematic, double-blind controlled studies of the efficacy of fluoxetine are warranted.

NR226 Tuesday May 14, 12 noon - 2:00 p.m.

Fenfluramine Effects on Cerebral Metabolism

Edwin H. Cook, M.D., Psychiatry, Univ of Chicago, 5841 S. Maryland Avenue, Chicago, IL 60637; John Metz, Ph.D., Malcolm Cooper, M.D., Jin Shin Chou, Bennett L. Leventhal, M.D.

Summary:

A pilot time course study was conducted to determine the effects of fenfluramine (FEN), an agent that releases serotonin and inhibits its reuptake, on cerebral metabolic rate of glucose (CMRglu). Four normal male subjects (ages 31- 35) were each studied on four separate days at least two weeks apart. Six to 7.5 mCi of [^{18}F]-2-deoxyglucose (FDG) was injected after placebo or two, three or four hours after oral administration of 60 mg d,l-FEN. The order of the drug administration was varied and double-blind. Subjects were studied while performing a visual monitoring task during acquisition of PET data with PETT VI. Compared to placebo, FEN did not have any significant group mean effects on regional or global CMRglu at any time point. However, individual subjects were consistent in their responses to FEN; those who had low placebo global CMRglu increased in response to FEN with maximum increase at three hours; those who had high placebo CMRglu decreased in response to FEN with a maximum decrease at three hours. The average absolute percent change from placebo in global CMRglu was 12 percent, 18 percent, and 4.3 percent at two, three, and four hours after FEN, respectively. This pilot study did not reveal significant mean effects of FEN on CMRglu, although individual responses were most robust three hours after FEN. Pharmacological challenge studies with more selective and direct 5-HT agonists may reveal less heterogeneous responses of regional or global CMRglu.

NR227 Tuesday May 14, 12 noon - 2:00 p.m.

Psychosocial Impact of Pediatric Rheumatic Disease

Sharon Silber, Ph.D., Schneider Children's Hosp, 271-16 76 Avenue, New Hyde Park, NY 11042; Cathy Pacyna, M.S.W., Lynn Parker, Ph.D., Theresa Constans, M.S.

Summary:

The psychological functioning of 60 children aged five to 16 ($X = 11.8$) having rheumatic disease was considered in the context of Sameroff and Chandler's "continuum of caretaking casualty." Using the Achenbach Child Behavior Checklist, we found significantly elevated levels of both internalizing and externalizing behavior disorder in these children (40 percent of the sample exceeded clinical norms). Further, families with either family conflict (on the FES) or maternal depression (on the Beck) reported higher levels of behavior disorder in their children. Family cohesion and expressiveness were related to reduced levels of behavior disorder in children. Behavior disorder in children, in turn, was associated with a greater perceived burden of the illness on the family. Again, the family environment moderated this effect. Highly conflictual families with depressed mothers perceived the illness as most burdensome. Maintaining an active-recreational orientation, religiousness, and greater family organization acted as protective factors. No effects were noted for the age or gender of the child, but low SES families were at greatest risk (all findings significant at .05 or lower). Implications of the findings to understand the interaction of child pyschopathology, family functioning, and biosocial stress are discussed.

NR228 Tuesday May 14, 12 noon - 2:00 p.m.

Comorbidity and Methylphenidate Response in ADHD

Richard L. Livingston, M.D., Psychiatry, Ark. Children's Hospital, 800 Marshall Street, Little Rock, AR 72202; Roscoe A. Dykman, M.D., Peggy A. Ackerman, M.A.

Summary:

Comorbid psychiatric disorders are extremely common among people with attention deficit disorder and the clinical relevance of comorbid disorders is only beginning to be explored. Our group tested the hypotheses that ADD children with comorbid disorders would respond differently to methylphenidate than those without comorbid disorders. One hundred nine outpatient boys with ADD were divided according to results of the Diagnostic Interview for Children and Adolescents (DICA) into four groups: No comorbid diagnosis ($N = 52$), Oppositional or Conduct Disorder only ($N = 23$), Depressed or Anxious Only ($N = 16$), and those with both emotional and behavioral disorders ($N = 18$). They were assigned randomly (double-blind) to high (0.6 mg/kg) or low (0.3 mg/kg) doses of methylphenidate a.m. and noon; response was determined by Conners' teacher questionnaire results before and after medication. Two-way analysis of covariance using the pretreatment score as covariate yielded significant differences showing that the boys with comorbid emotional disorders improved much more on high than low dose methylphenidate (ADD index, $p < .01$; hyperactivity index, $p < .05$). Boys without comorbid disorders and those with only comorbid oppositional or conduct disorder responded about as well to low as to high doses. Further research is needed but clinicians are advised to attend to comorbidity and consider higher doses when methylphenidate is prescribed to ADD boys who also have anxiety or depression.

NR229 Tuesday May 14, 12 noon - 2:00 p.m.

Cost of Child Day Treatment Program Versus Inpatient Treatment Program

Natalie Grizenko, M.D., Psychiatry, Douglas Hospital, Lyall Pavilion 6875 LaSalle B1, Montreal Que, Canada H4H 1R3; Danielle Papineau, M.Sc.

Summary:

The cost of treating 23 children age six to 12, with severe behavior problems admitted consecutively to an inpatient unit and 23 children admitted consecutively to the same unit after it was converted to a day treatment program was compared. The two groups were equivalent in terms of age, gender, diagnosis, treatment outcome, and severity of pathology as assessed by the Children's Global Assessment Scale. The average length of treatment for the day treatment group was significantly shorter (6.1 months) than that for the inpatient group (19.7 months) ($p < .001$). Reasons for the dramatic decrease in treatment duration include families, community and schools continuing to be involved with the children, and children being highly motivated to "graduate" to a regular school. The total cost of treatment per child in day treatment (mean $9,213 Canadian dollars) was significantly lower than for inpatient group (mean $61,412 Canadian dollars) ($p < .001$) mainly due to the decrease in length of stay and lower operating cost of day treatment. Implications of the findings will be discussed with respect to health care policy and the need to make the public and professionals aware of the day treatment as a cost effective alternative to inpatient treatment.

NR230 Tuesday May 14, 12 noon - 2:00 p.m.

Effectiveness of Family Therapy in Day Treatment

Natalie Grizenko, M.D., Psychiatry, Douglas Hospital, Lyall Pavilion 6875 LaSalle B1, Montreal Que, Canada H4H 1R3; Danielle Papineau, M.Sc.

Summary:

In recent years, the overall effectiveness of day treatment for

behavior disordered children has been demonstrated. One such program (Grizenko and Sayegh, 1990) was found to be effective as a whole. The present study attempted to determine the usefulness of family therapy as part of the multimodal day treatment package by comparing a group of 25 children receiving weekly family therapy with a group of ten children whose families were contacted briefly each week by front line staff. Treatment was identical in all other respects. The two groups were compared on measures of family and behavioral functioning. The Family Assessment Measure was used to measure change in family functioning. The group receiving family therapy improved significantly more over time than the comparison group on FAM-total (parent, $p < .02$), and on three of the seven subscales according to both the parent and the child. The Revised Child Behavior Checklist was used to measure behavioral improvement. Children in the family therapy group improved significantly more over time on the externalizing subscale ($p < .05$). Implications of the finding will be discussed regarding the need for structured family therapy in day treatment.

NR231 Tuesday May 14, 12 noon - 2:00 p.m.

Effects of Nicotine Haloperidol Versus Nicotine in Tourette's Syndrome

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Summary:

We evaluated the effect of adjuctive noctine gum and haloperidol in ten patients with Tourette's Disorder, using the Yale Global Tic Severity Scale (YGTSS) and the Clinical Global Impression scale for Tourette Syndrome (CGI-TS) amended for repeated measurements. Satisfactory inter-rater reliability was obtained. One-way within subjects MANOVAS, followed by planned comparisons showed highly significant ($p < 0.001$) decreases in tic severity between the 30 minutes baseline and 30 minutes gum chewing periods, with less significant effects between baseline and the first 30 minutes post-gum period ($p < 0.01$), and between baseline and the second 30 minutes post-gum period ($p < 0.05$). Using nicotine gum alone in nine untreated subjects with Tourette's Disorder, no significant differences in YGTSS and CGI-TS were found between the four periods. Total tic frequencies showed modest differences between baseline and gum ($p < 0.05$), and baseline and second post-gum ($p < 0.05$) periods. Five of these nine subjects were subsequently rated over the four periods, using a placebo nicotine gum. No significant differences were found between periods, using total tic frequency counts and the amended YGTSS and CGI-TS. These open studies suggest that nicotine powerfully potentiates the action of haloperidol in Tourette's Disorder, but that nicotine gum alone has less effect. Possible mechanisms will be discussed.

NR232 Tuesday May 14, 12 noon - 2:00 p.m.

Specific Symptoms and Cognitive Deficit in Tourette's Syndrome

Chris N. Larson, M.D., Psychiatry, The Ohio State University, 473 West 12th Avenue, Columbus, OH 43210; Robert A. Bornstein, Ph.D

Summary:

Children and adolescents with Tourette Syndrome (TS) ($n = 88$) were evaluated on a variety of neuropsychological measures and the revised Tourette Syndrome Symptom List (Revised-TSSL). A previous study found that complete motor tic summary scores but not simple tic scores were correlated with neuropsychological deficits (Bornstein, 1990). In this study we examined if specific symptoms were more highly correlated with neuropsychological deficits. Tests included the WISC-R, WRAT, Wisconsin Card Sort, Grooved Pegboard Test, and an expanded Halstead-Reitan Battery. Simple finger and hand movements, arm movements, shoulder, and leg movements were associated with more neuropsychological deficits than simple tics of the head and neck. Similarly, complex motor tic symptoms of touching a body part, other people, or objects were associated with more deficits than with other complex motor tics. It appears that certain specific simple and complex tic symptoms may be associated with different patterns of skill deficit as measured by a battery of neuropsychological tests. This supports the hypothesis that in children and adolescents certain TS tic symptoms may be more strongly associated with neuropsychological impairment.

NR233 Tuesday May 14, 12 noon - 2:00 p.m.

Childhood Sexual Abuse and Adult Personality

Bruce Pfohl, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; Nancee Blum, M.S.W.

Summary:

We examined the association between self-report of childhood sexual abuse among adult psychiatric patients and personality disorder (PD) diagnosis. Personality and history of childhood sexual abuse was assessed in 93 nonpsychotic patients using the Structured Interview for *DSM-III-R* Personality (SIDP-R) to interview both the patient and a knowledgeable informant. Two of the 34 men and 24 of the 59 women reported sexual abuse during childhood.

History of childhood sexual abuse was not globally associated with adult PD but rather appeared to be specifically associated with certain PD diagnoses. Sixteen (76 percent) of 21 women with a diagnosis of Borderline PD reported childhood sexual abuse compared to 21 percent without this diagnosis ($p < 0.001$). A similar rate of abuse (72 percent) was found among the 24 women who met criteria for the experimental diagnosis of Self-Defeating PD ($p < 0.001$). Abuse rates were lower but still significant among women with Dependent PD and Passive Aggressive PD.

Analysis at the trait level indicated that self-report of childhood sexual abuse was most strongly correlated with unstable relationships, periods of intense anger, suicide threats, and feelings of emptiness and boredom. The findings agree with other studies suggesting that childhood sexual abuse (or at least patient's willingness to report this event) is related to very specific personality disorders and traits. There is a need for more detailed studies to determine if the association is etiologic, familial, or represents some type of reporting bias.

NR234 Tuesday May 14, 12 noon - 2:00 p.m.

Cross-Gender Ratings of Boy Outpatients: New Data

Richard R. Pleak, M.D., CADH Box 38, Hillside Hospital, Long Island Jewish Med Center, Glen Oaks, NY 11044; Glenn S. Hirsch, M.D., Dennis A. Anderson, M.D., David E. Sandberg, Ph.D.

Summary:

A previous study of boy psychiatric outpatients (by first author) found higher scores on cross-gender rating scales than a comparison control population. The scores did not correlate as expected with internalizing subscales of the Child Behavior Checklist (CBCL), but did correlate with an externalizing subscale. The present study aims to replicate these findings in a different geographic area and compare these data with a recent locally-obtained school-based control sample (by the fourth author). The study sample consists of five- to 12-year-old boy psychiatric outpatients from Queens and Long Island seen during initial screenings (N presently = 82) or in a day hospital ($N = 40$). Caregivers completed the CBCL and questionnaires for cross-gender behavior (Bates, Bentler, & Thompson). Preliminary results show no significant differences between

this and the previous sample's means on three feminine behavior scales. The new sample scores significantly higher than the 1973 control population; however, when compared to the school-based controls, the sample was significantly higher on only one scale. As previously, the new sample's scale scores correlate significantly with a CBCL externalizing subscale, but not with the internalizing subscales. Results for the complete sample will be presented with discussion of the relevance of these new findings.

NR235 Tuesday May 14, 12 noon - 2:00 p.m.

Neuroleptics and Adolescent Borderline Pathology

Arthur H. Schwartz, M.D., Psychiatry, UMDNJ-RWJMS, 675 Hoes Lane, Piscataway, NJ 08854; Harriet E. Hollander, Ph.D., George T. Pavlidis, Ph.D., Michael A. Gara, Ph.D.

Summary:

This study investigated whether neuroleptics would prove helpful in treating conduct disordered adolescents with associated borderline and/or schizotypal personality disorder. Smooth pursuit eye movements were studied to see if abnormality predicted response to medication. A double-blind, placebo-controlled crossover design was used with 19 court-involved adolescents. Subjects received three weeks of active medication and placebo separated by one week of washout. Neuroleptics impacted significantly on symptomatology as reflected in the Global Assessment Scale, and depression and agression-impulsivity scores. Specific diagnoses did not predict medication response, nor did smooth pursuit eye movements even though they were significantly more impaired for adolescent patients than controls. Conduct disordered adolescents with associated personality disorders respond to neurologic medication, like their adult counterparts, in the short term when they present with symptoms of aggressivity and impulsivity.

NR236 Tuesday May 14, 12 noon - 2:00 p.m.

Unmet Service Demands in Child Disruptive Behaviors

Christopher R. Thomas, M.D., Western Psych. Inst., 3811 O'Hara Street, Pittsburgh, PA 15213; Rolf Loeber, Ph.D., Magda S-Loeber, Ph.D.

Summary:

Youngsters displaying disruptive behaviors (conduct problems and/or attention deficits/hyperactivity) or delinquency have contacts with multiple social agencies: child protection services, schools, mental health clinics, and the juvenile court. This paper presents data on three age-cohorts of 1,517 boys in first, fourth, and seventh grade. By age ten more than 23 percent of the parents had sought professional help for the boy's behaviors. Much of this help seeking concerned learning problems, and to a lesser extent hyperactivity. The higher the severity of boy's lifetime delinquency, the higher the likelihood that parents had sought help for the boy. Typically, school and mental health facilities provided a first tier of system contacts for these boys, followed later by contacts with the police and the juvenile justice system. With the exception of the schools and the court, interventions from the other delivery systems were mostly limited to repeated assessments or record keeping. Implications of the findings are discussed.

NR237 Tuesday May 14, 12 noon - 2:00 p.m.

Fluoxetine in Adolescent Psychiatric Inpatients

Lee S. Cohen, M.D., Psychiatry, Holliswood Hospital, 87-37 Palermo Street, Holliswood, NY 11423; Owen Schneider, M.D., A. Lawrence Rubin, M.D., Dipak Nandi, M.D., Dane Bonn, B.S.

Summary:

Although fluoxetine is not approved for adolescents, its use in clinical populations of depressed adolescents is widespread. Published literature on the use of fluoxetine in adolescents is limited to two reports indicating clinical efficacy in obsessive-compulsive disorder. These studies were limited by the number of patients and their uncontrolled nature. All patients on our adolescent psychiatric unit treated with fluoxetine for a minimum of one week (n = 40, age range 13-18, mean 15.0, 25 female, 15 male) from May 1989 through September 1990 were studied by retrospective chart review. Primary *DSM-III-R* diagnoses were: 20 with major depression (one with psychotic features), 17 with depressive disorder NOS, one dysthymic disorder and two with obsessive-compulsive disorder. Mean starting dose was 21.6 mg/day and final dose was 28.4 mg/day (dose range 5-60 mg/day, Mean: 39 days). Clinical Global Impressions indicated a "marked" severity of illness (CGI mean: 4.68) on admission, 65 percent were much – very much improved on CGI at discharge (mean global improvement of 2.35 and mean efficacy index of 1.84). Seventy-seven percent of patients manifested some side effect (no significant correlation with dose), most commonly nausea, anxiety, insomnia, and headaches; however, only three required discontinuation. Fully 92.5 percent (n = 37) of patients manifested no change in suicidal behavior, two made a suicide attempt and one had an increase in suicidal ideation while on fluoxetine. Ninety-five percent of patients manifested no cardiovascular side effects, 5 percent got dizzy. Our preliminary data suggest that fluoxetine is clinically efficacious in a predominantly depressed adolescent population. Further controlled studies examining fluoxetine's clinical utility may be warranted.

NR238 Tuesday May 14, 12 noon - 2:00 p.m.

Family History in Adolescent Suicide Attempters

Lee S. Cohen, M.D., Psychiatry, Holliswood Hospital, 87-37 Palermo Street, Holliswood, NY 11423; Owen Schneider, M.D., A. Lawrence Rubin, M.D., Jane Salvowitz, R.N., Barbara Sprung, R.N.

Summary:

Studies of adolescent suicide completers and attempters have indicated increased rates of suicidal behavior and psychopathology in the first-degree relatives of this population. A pilot investigation by our group of 30 outpatient adolescent suicide attempters indicated that 40 percent of the patients had a family member and 63 percent had a friend who manifested suicidal behavior (23.3 percent of the attempters had a first-degree relative manifesting suicidal behavior). Inpatient adolescent suicide attempters remain as an understudied group.

The current study is designed to examine 20 consecutive adolescent suicide attempters and 20 nonsuicidal age and sex matched psychiatric controls on an adolescent psychiatric inpatient unit investigating incidence of family and friends' suicidal behavior. Psychopathology in the first-degree relatives is assessed by the Family Informant Schedule and Criteria (FISC). Rating Scales for depression and anxiety will be correlated with family history of suicidality.

Preliminary analysis of the first seven consecutive suicide attempters (Age Range 12-16, mean: 14.6) indicates that 57 percent have a family history of suicidal behavior (29 percent in a first-degree relative and 100 percent of the adolescents have at least one friend who has manifested suicidal behavior. Mean scores on the Ham-D were 18 and on the Ham-A 14. Issues regarding adolescents' exposure to suicide in their environment and family will be discussed.

NR239 Tuesday May 14, 12 noon - 2:00 p.m.

Length of Stay on Latency-Ages Psychiatric Units: A Comparative Study

Richard F. Dalton, M.D., Psych-Neuro., Tulane Med. Center, 1430 Tulane Avenue, New Orleans, LA 70118; Kent M. Ward, M.D.

Summary:

This study was designed to examine different patient, family, treatment variables related to length of stay on both our eight-bed, university unit, and our 24-bed state unit for disturbed children. In this retrospective study, 50 variables specifically related to each patient hospitalized during 1987 were statistically correlated to lengths of stay. The results showed that location was the main predictive variable: 40 days on the university unit and 200 days on the state unit. When examined separately, the 34 university patients' increased lengths of stay were predicted by lack of discharge placement and parental psychopathology. None of the variables proved predictive for the 28 state patients. On closer examination, the major differences between the two locations (numbers of patients, numbers of child psychiatrists and clinical workers, numbers of nursing staff workers, amount of paperwork) contributed to clinical confusion within the state unit, resulting in location being the main predictor when both populations were examined together and leading to no predictors when the state patients were examined separately. The main concern generated by these findings is that state administrators will respond by legislating length of stay instead of correcting obvious problems.

NR240 Tuesday May 14, 12 noon - 2:00 p.m.

Cornell Friendship and Peer Interview

Paulina F. Kernberg, M.D., Psychiatry, NYH-Cornell Med Center, 21 Bloomingdale Road, White Plains, NY 10605; Audrey J. Clarkin, Ph.D., Edward Greenblatt, Ph.D., Jonathan C. Cohen, Ph.D.

Summary:

The Cornell Interview of Peers and Friends (CIPF), a 30 minute, semi-structured interview was designed to evaluate children's perceptions of their relationships with peers and friends. The Cornell Interview was individually administered to a group of nonpatient children (school sample) and to a group of psychiatrically disturbed children. Subjects, both male and female, were between the ages of seven and 11. Significant differences were found between boys and girls and between the psychiatric and nonpatient's based on the CIPF. The CIPF also assesses the level of developmental appropriateness, social skills, and self-esteem for each child and these measures significantly differentiated nonpatient and psychiatric populations. Satisfactory inter-rater reliability was found on the interview's total score as well as on the three subscale scores of developmental appropriateness, social skills, and self-esteem. The CIPF instrument offers the potential for screening children at risk for emotional disturbance and for assessing the outcome of therapeutic interventions.

NR241 Tuesday May 14, 12 noon - 2:00 p.m.

Conduct Disorder and Personality Characteristics in Hospitalized Adolescents

Wade C. Myers, M.D., Psychiatry, Univ of Florida, Box J-234 JHMHC, Gainesville, FL 32610; Roger C. Burket, M.D., Terry Otto, M.D.

Summary:

The relationship between conduct disorder and *DSM-III-R* Axis I and Axis II psychiatric diagnoses in adolescents remains unclear. Robins found that nearly 50 percent of highly antisocial children become highly antisocial adults. McManus et al. found that 45 percent of seriously delinquent adolescents met *DSM-III* criteria for personality disorders, primarily borderline personality disorder. In our study, 25 psychiatrically hospitalized adolescents were evaluated for *DSM-III-R* Axis I and II psychiatric diagnoses. Current and lifetime Axis I *DSM-III-R* psychiatric diagnoses were obtained using the Diagnostic Interview for Children and Adolescents (DICA-R). Panic disorder was assessed using the K-SADS-E. Personality disorders were assessed using the Structured Interview for *DSM-III-R* Personality Disorders (SIDP-R).

Fifty percent of the sample met criteria for conduct disorder. A majority of those with conduct disorders had comorbid major depression and ADHD. The diagnosis of conduct disorder was associated with fulfilling criteria for multiple Axis II personality disorders. More than four personality disorders per case were found in those with conduct disorder, while those without conduct disorder averaged less than one personality disorder. These findings have important clinical, research, and treatment implications, and support the developing view of conduct disorder as a broad-spectrum illness composed of multiple Axis I and II characteristics.

NR242 Tuesday May 14, 12 noon - 2:00 p.m.

Low Dopamine Beta Hydroxylase: A Biological Sequela of Abuse and Neglect?

Matthew Galvin, M.D., Psychiatry, Riley Hospital, 702 Barnhill Drive 3N, Indianapolis, IN 46202; Anantha Shekhar, M.D., Jay Simon, Ph.D., Barbara Stilwell, M.D., Robert Ten Eyck, Ph.D., Gina Laite, M.D., George Karwisch, M.D., Susanne Blix, M.D.

Summary:

Twenty-one psychiatrically hospitalized boys were studied while off psychoactive medication to determine if conduct disorder solitary type and abuse or neglect experiences correlated with low serum dopamine beta hydroxylase activity. Preliminary results supported earlier findings that conduct disorder undersocialized types in boys correlate with low enzyme activity. Possible and definite neglect or abuse prior to 36 months of age was correlated with low enzyme activity. Abuse or neglect was not correlated with low enzyme activity when time of occurrence was not specified. The possibility that low serum dopamine beta hydroxylase is a biological sequela of seriously disrupted attachment is discussed.

NR243 Tuesday May 14, 12 noon - 2:00 p.m.

Activity and Antidepressant Response in Children

Carol A. Glod, M.S., McLean Hospital, 115 Mill Street, Belmont, MA 02178; Martin H. Teicher, M.D., Kambiz Pahlavan, M.D., David Harper, B.S., Eleanor Magnus, B.S., Elyse Duboe, M.D.

Summary:

The treatment of childhood depression is complex, and double-blind studies have yet to demonstrate antidepressant efficacy. Some hospitalized children appear to respond dramatically to the milieu, while others appear to respond to antidepressants or lithium. We monitored locomotor activity levels for 72 hours in hospitalized unmedicated children and adolescents prior to treatment, to ascertain whether any parameters correlate with treatment response. Each child received one of three treatments, based on clinical need. Eleven received antidepressant trials (usually DMI or fluoxetine), 16 received only milieu and individual therapy, and five were treated with lithium. Response was determined by overall clinical global improvement. Discriminant analysis revealed that differences in circadian frequency and diurnal activity most clearly distinguished milieu responders from antidepressant responders ($F(2,13) = 4.69$, $p < 0.05$). Antidepressant responders had a longer circadian period than milieu responders (24.65 vs. 23.97h), and were slightly more active. Patients who failed to respond to both milieu treatment and antidepressants, could be distinguished from milieu responders by

their lack of circadian entrainment, and high intradaily variability ($F(2,12) = 5.23$, $p < 0.05$). Certain activity parameters, obtained shortly after hospitalization, may help identify patients who are less likely to respond to milieu treatment, but more likely to respond to antidepressants or lithium.

NR244 Tuesday May 14, 12 noon - 2:00 p.m.

Altered Immunity in Childhood Major Depressive Disorder

Jacqueline Bartlett, M.D., Psychiatry, UMDNJ-NJMS, 185 South Orange Avenue, Newark, NJ 07103; Steven E. Keller, Ph.D., Steven J. Schleifer, M.D.

Summary:

Major depressive disorder (MDD) in adults is associated with changes in immunity, including age-related differences. While no psycho-immunologic phenomena have been reported in children, they do have hormonal and vegetative disturbances in MDD which may affect immunity. Twenty children with MDD, eight to 12 years old, were compared to healthy, matched controls. Diagnoses were obtained with the DISC-R. Severity of depressive symptoms were assessed with the CDRS and CDI. Immune measures, including cell counts, mitogen response (to PHA, PWM &, ConA) and natural killer cell (NK) activity were obtained.

There were no significant group differences in total numbers of lymphocytes, subtypes, or response to mitogen stimulation. Depressed subjects had significantly lower NK cell activity ($t = 2.3$, $p < 0.03$).

Hierarchical regression analyses controlling for age, sex, and diagnostic group revealed that severity of symptoms was inversely related to lymphocyte ($t = 2.3$, $p < 0.03$), suppressor T ($t = 2.1$, $p < 0.05$) and B cell counts ($t = 2.3$, $p < 0.03$).

The possible mechanisms involved in altered immunity in childhood MDD and the similarities to what is found in adult MDD will be discussed.

NR245 Tuesday May 14, 12 noon - 2:00 p.m.

Alcohol and Depressive Cognitions in Adolescents

John B. Jolly, Psy.D., Psychiatry, Univ of Arkansas Med. Sci, AC 800 Marshall Street, Little Rock, AR 72202; John F. Aruffo, M.D., Richard L. Livingston, M.D.

Summary:

Negative cognitive distortions have been demonstrated to be related to depression in adults, adolescents, and children, but it has been suggested that negative cognitive distortions may be related to general psychopathology, rather than being depression-specific. Alcohol and substance abuse have been found to be related to depression and suicidality in adolescents. The current study is the first to use such a dually-diagnosed sample to test the hypothesis that negative cognitive distortions are depression-specific. We compared the cognitive distortions of nine depressed (DAA) and 33 nondepressed (NDAA), alcohol abusing adolescent psychiatric inpatients (mean age = 15.0, SD = 1.5). The depressed group was defined by a Hamilton Rating Scale for Depression score of 23 or greater. Children's Depression Inventory scores were significantly higher ($t = 2.03$, $df = 40$, $p < .05$) for the DAA group (22.4) than the NDAA group (14.2). Groups were equivalent with respect to age, race, gender, and reading level. Results revealed that the DAA group displayed significantly higher negative cognitive distortions on the Children's Negative Cognitive Errors Questionnaire ($t = 2.41$, $df = 40.$, $p < .05$) than the NDAA group. On the Cognition Checklist, the DAA group demonstrated higher depressed ($t = 2.58$, $df = 39$, $p < .01$) and anxious ($t = 2.25$, $df = 39$, $p < .05$) cognitions on the Depression and Anxious subscales, respectively, than the NDAA group, suggesting that alcohol abuse contributed little to the cognitive distortions in this sample.

NR246 Tuesday May 14, 12 noon - 2:00 p.m.

Cortisol Abnormalities in Sexually Abused Girls

Frank W. Putnam, M.D., Develop. Psych., NIMH 15K NIH, 9000 Rockville Pike, Bethesda, MD 20892; Penelope K. Trickett, Ph.D., Karen Helmers, R.N., Elizabeth J. Susman, Ph.D., Lorah Dorn, Ph.D., Barbara Everett, Ph.D.

Summary:

Childhood sexual abuse is a traumatic experience, increasingly linked to specific psychiatric disorders, including, borderline personality disorder, eating disorders, somatization disorder, multiple personality disorder, and substance abuse disorders. This prospective, longitudinal study of sexually abused girls, aged six to 15, and sex, age, race, and SES-matched controls investigates biological markers of stress and trauma in addition to psychological factors. Morning serum cortisols were obtained on 20 sexually abused girls and 15 matched controls at 0, 20, and 40 minutes. There was a significant group difference for time 0 (Abuse = 8.06 ug/dl, control = 5.28 ug/dl, $F(1,33) = 5.09$, $p = .031$) and a trend at 20 minutes (abuse = 9.10 ug/dl, control = 5.65 ug/dl, $F(1,20) = 3.82$, $p = .065$). On one-year follow-up (still in progress) there is a significant group difference at 20 minutes (abuse = 9.73, control = 4.34, $F(1,9) = 6.38$, $p = .035$) and trends at 0 and 40 minutes. Animal models of stress indicate that sustained elevations of cortisol have deleterious effects on the maturation of the developing CNS.

NR247 Tuesday May 14, 12 noon - 2:00 p.m.

Measuring Therapy Outcome in an Urban Child Clinic

Kathleen P. Longeway, Ph.D., Psychiatry, Sinai Samaritan, 2000 Kilbourn Avenue, Milwaukee, WI 53233; Kathleen P. Longeway, Ph.D., Lucille B. Glicklich, M.D.

Summary:

In order to assess change in parental perceptions of their children's emotional and behavioral functioning as a result of short-term therapy, 120 parents who called to schedule their children (ages four to 16) for therapy were asked to rate their children on the Achenbach Child Behavior Checklist and a personality "Strength" rating and to rate themselves on the Beck Depression Inventory prior to beginning the children's treatment and at the end of eight therapy sessions. Children also rated themselves on the Children's Depression Inventory pre- and post- treatment. Eight sessions were chosen because this represents a standard "dose" of therapy allocated for HMO patients who predominate in clinic settings. Of the 61 mother-child pairs completing pre-treatment measures, 24 completed the eight sessions and post-treatment measures. Conduct and oppositional disorders comprised 50 percent of presenting problems (61 percent if ADHD was included) and were significantly over-represented among indigent patients. Forty-six percent of mothers had not completed high school. It was concluded that even when therapy has a short-term focus, drop-out rates are high enough and literacy rates low enough in urban youth samples (especially among older as opposed to younger children $p < .03$) to render outcome study on standardized measures extremely difficult. This supports Weisz and Weiss's (1989) claim that the outcome of therapy conducted in actual clinic settings with spontaneously referred children may not be measurable in the same manner as university-based research and may call for innovative methods.

NR248 Tuesday May 14, 12 noon - 2:00 p.m.

Marital Change After the Birth of an At-Risk Child

Mary Klinnert, Ph.D., Pediatrics, National Jewish Center, 1400 Jackson ST. K-802, Denver, CO 80206; Leslie A. Gavin, Ph.D., Frederick S. Wamboldt, M.D., David Mrazek, M.D.

Summary:

The transition to parenthood literature suggests that the introduction of a new baby has at least a short term negative effect on the marital satisfaction of the parents. The present study replicates and extends the results of other investigators in a sample of couples with children at medical risk for developing asthma, and probes the mechanisms behind this effect. Longitudinal data on marital satisfaction, birth order, infant illness and temperament, and family life events were collected from 128 couples during prenatal, 6, 12, and 18 month sessions. Results replicated prior work — marital satisfaction scores significantly declined from the prenatal period to 18 months after birth. Results also indicated that family structural burdens and family stress burdens had a significant negative effect on marital satisfaction. Child related burdens were less reliably related. These interesting and provocative results will be discussed within the framework of the literature on both stress and coping and development psychopathology, with the goal of evaluating how this well-documented decline in marital satisfaction relates to more clinically-oriented concerns.

NR249 Tuesday May 14, 12 noon-2:00 p.m.

DSM-III-R Pathological Gambling in Young Adults

Glenn C. Davis, M.D., Psychiatry, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202; Naomi Breslau, Ph.D., Patricia Andreski, M.A.

Summary:

Pathological gambling is a disorder modeled on the generic elements that define the addictions: criteria require disruption of social and occupational functioning and loss of control of behavior. We examined the increased risk for affective disorders and drug and alcohol dependence in subjects with pathological gambling. A random sample of 1,007 young adults in a large HMO in Detroit, Michigan, were interviewed using the NIMH-DIS, revised to cover *DSM-III-R* diagnoses. Seventy-five percent of respondents reported having "ever gambled" while only 5.4 percent reported having "often gambled too much." The lifetime prevalence of pathological gambling was 1.5 percent; 3.4 percent in males and 0.3 percent in females. Mean age at onset was 20 years. Pathological gambling was significantly associated with alcohol and drug abuse/dependence (Odds Ratios: 3.4 and 3.9, $p<0.05$), as well as with mania/hypomania (Odds Ratio: 6.8, $p=.001$). Onset of mania/hypomania always followed pathological gambling, while alcohol abuse/dependence always preceded pathological gambling. Drug abuse/dependence occurred both before and after pathological gambling. We will report data comparing risk factors for pathological gambling with those for affective disorders and psychiatric substance use disorders.

NR250 Tuesday May 14, 12 noon-2:00 p.m.

Childhood Abuse and Types of Adult Anger

Nicholas G. Ward, M.D., Psychiatry, Univ of Washington, 1959 NE Pacific RP-10, Seattle, WA 98195; Albert S. Carlin, Ph.D., Heather Sowell, B.S., Belinda Gustafson, B.S.

Summary:

The relationships of childhood sexual, physical, and emotional abuse with adult anger as measured by Spielberger's anger scales—total (trait), in, out, expressed and controlled—were examined in 265 adult family medicine outpatients. Differences were analyzed by 2x2x2 ANOVA in which physical, sexual, and emotional abuse served as independent variables. The physically abused group had significantly higher mean total anger (31.0 vs. 25.3; $p<.008$), anger in (17.5 vs. 14.6, $p<.001$), anger out (15.9 vs. 13.7, $p<.001$), and expressed anger (26.8 vs. 19.8 $p<.001$), than the nonabused group. The sexually abused group had no significantly higher mean anger subscale scores than the nonabused group. The emotionally abused group only had significantly higher mean scores on the anger total subscale than the nonabused group (31.7 vs. 25.3, $p<.001$). None of the forms of abuse were associated with significantly higher controlled anger scales. Significant interaction effects between different forms of abuse and anger subscale scores were seen. Thus, while physical abuse was most frequently associated with higher subscale scores, its effects cannot be examined in isolation from effects of sexual and emotional abuse, which frequently occur with it.

NR251 Tuesday May 14, 12 noon-2:00 p.m.

Adolescent Suicidality in an Inner-City Population

Beverly Delaney, M.D., Psychiatry, New Jersey Medical Sch., 185 South Orange Avenue, Newark, NJ 07103; Jacqueline Bartlett, M.D., Steven J. Schleifer, M.D., Haftan Eckholdt, M.A., Steven E. Keller, Ph.D.

Summary:

Psychosocial stressors have been associated with suicidal ideation in adolescents. Most studies neglect minority populations and stressors common in inner city life. One such stressor is experiencing death of a peer. We examined the impact of this stressor and depression on suicidality.

Three hundred fifty-four (191 males, 163 females) adolescents, (11-25 years; $x = 16.38 \pm 2.21$) were studied. Participants were accrued from an inner city adolescent medicine clinic and public high school. Eighty percent were black, 15 percent Hispanic, and 5 percent other. Nineteen percent had lifetime major depressive disorder (MDD) using the Diagnostic Interview Scale for Children (DISC-R). Suicidal ideation was identified by responses to relevant DISC-R questions. Seventeen percent reported ever having had suicidal ideation. Of those with ideation, 49 percent had current or past MDD. Forty-one percent had experienced the death of one or more close friends during the past year.

Regression analysis, conducted for participants with current MDD or no history of MDD, determined the contribution of age, gender, and death of a close friend to suicidal ideation. In this model, female gender alone predicted suicidal ideation ($p<0.01$). When current MDD was added to the model, gender, MDD, and death of a close friend significantly predicted suicidal ideation. These findings suggest that the unique experiences of inner city life contribute to suicidal ideation both in association with depressive states and independently.

NR252 Tuesday May 14, 12 noon - 2:00 p.m.

Rurality and Early Adolescent Alcohol Use

Kelly J. Kelleher, M.D., Psychiatry, UAMS, 4301 W. Markham St. Slot 554, Little Rock, AR 72205; Vaughn Rickert, Ph.D., Brian Hardin, M.D., Sandra Pope, M.P.H.

Summary:

Little is known about alcohol use in rural adolescents. A total of 1631 early adolescents (11-14 yrs.) were surveyed at ten junior high schools classified into four areas to represent the urban-rural continuum. Among drinkers, rural youth from the Highlands, an area characterized by poultry industry and a Caucasian population, were more likely to initiate and drink with friends rather than family, drink on the weekends and report easy access to alcohol.

After controlling for other factors, tobacco use and drinking by parents and friends were the important determinants of alcohol use and abuse for the Highlands as well as urban and suburban youth. Rural youth from the Delta, an area characterized by extreme poverty and a largely black population, were different, engaging in less experimentation and less abusive drinking. In regression analyses for the Delta, only parental drinking and approval of drinking along with close friends using alcohol were related to use. For the Highland, urban, and suburban youth, drinking patterns seemed largely related to peer group influence. The Delta youth appeared to be influenced to a greater degree by family patterns of use. Whether this difference and the lower use overall are related to cultural norms or availability of alcohol is not known.

NR253 Tuesday May 14, 12 noon-2:00 p.m.

Carbamazepine Reduces Childhood Rage Symptoms

Sidney Werkman, M.D., Psychiatry, Georgetown University, 2918 33rd Place NW, Washington, DC 20008; Gordon Farley, M.D., Jeanne Van Der Zanden, Ph.D.

Summary:

We report on the treatment with the anticonvulsant carbamazepine [CBZ] of eight boys (age six to ten) consecutively hospitalized for repeated, severe rage symptoms. (Achenbach Aggression Ratings >30 x2 weeks prior to treatment). None had responded positively to previous outpatient treatments. Diagnoses of thought disorder, affective disorder, and mental retardation were excluded.

CBZ was given at 5mg/kg/day for >eight weeks. Systematically recorded aggression and depression ratings, seclusion counts, and clinical change measures, produced the following notable symptom DECREASES:

AGGRESSION: five subjects ($p<.05$)

DEPRESSION: two subjects ($>p.01$)

OPPOSITIONAL-DISRUPTIVE BEHAVIOR AT CREPUSCULAR (evening-night/night-morning) TRANSITIONS: two subjects

["Twilight behaviors reminiscent of laboratory mammal Crepuscular photoperiod patterns as well as those of children with disturbances of attention, activity, and sleep.]

These data support the use of CBZ to treat children with severe repeated rage episodes and present a previously unreported effect on disturbed Crepuscular behaviors.

NR254 Tuesday May 14, 12 noon-2:00 p.m.

Suicidal Youth: The Decision to Hospitalize

Richard Morrissey, Ph.D., Child Psychiatry, Schneider Children's, 269-01 76th Avenue Room 135, New Hyde Park, NY 11042; Robert Dicker, M.D., Howard Abikoff, Ph.D., Harold S. Koplewicz, M.D., Amelia DeMarco, M.S.

Summary:

A questionnaire containing 64 clinical vignettes describing adolescent suicide attempters was distributed to a sample of 36 child and adolescent clinicians. Six variables known to relate to lethality of attempt were systematically varied within the vignettes: sex, presence of depression, presence of conduct disorder/substance abuse, history of previous attempts, first or second degree relative with a previous attempt, and adequacy of family supports. Respondents were asked to make a judgment concerning the appropriateness of hospitalization for the youngster and the degree of confidence in that judgment. Hospitalization preference was found to be reliably measured and inversely related to professional experience. A repeated measures MANOVA analysis suggested that for both male and female patients, raters' hospitalization preferences were significantly affected by family supports, depression, presence of a previous attempt, conduct disorder/substance abuse, and presence of a suicidal relative, in that order, even when partialing out rater effects. Configural cue utilization did not add substantially to the efficacy of a linear model including the six factors, which explained two-thirds of the variance in the preference to hospitalize.

NR255 Tuesday May 14, 12 noon - 2:00 p.m.

Rapid Meclizine-Induced Cerebellar-Vestibular Improvement in Adult Learning Disabled

Harold Levinson, M.D., 600 Northern Blvd., Great Neck, NY 11021

Summary:

The efficacy of meclizine in rapidly reversing the cerebellar-vestibular (CV) dysfunction shown characterizing adults with learning disabilities or dyslexia was tested. Accordingly, 103 learning disabled ranging in age between 19-56 yr. were given either a single oral (12.5mg) dose of meclizine ($N = 48$) or placebo ($N = 55$) under double-blind conditions. CV-based diagnostic neurological and optokinetic tracking parameters were found to significantly improve in response to meclizine vs placebo. These and related data support both the CV dysmetric and dyspraxic hypothesis of learning disabilities or dyslexia as well as the use of CV stabilizing or enhancing antimotion-sickness medications such as meclizine in treating this disorder — even in adults.

NR256 Tuesday May 14, 12 noon-2:00 p.m.

MRI of the Posterior Fossa in Autistic Adults

H. Jordan Garber, M.D., Psychiatry, ANI, 7777 Steubenville Pike, Oakdale, PA 15071; Edward R. Ritvo, M.D.

Summary:

Conflicting results have been reported from morphometric MRI studies of the posterior fossa in autistic subjects, but the use of "medical" controls and differing MRI techniques limit comparisons. Our previous MRI study of young autistics did not detect any significant morphologic differences in the posterior fossa, but could not exclude the possibility of measurable abnormalities being apparent in adulthood. We recently studied 12 adults who met *DSM-III* criteria for autistic disorder, ages 18-38 (mean +/–s.d. = 27.2 +/–5.3 years), and a group of 12 normal volunteer controls matched to the autistic group for age and sex distribution. Contiguous 5 mm sagittal 1.5 T MRI sections were acquired with consistent and precise midsagittal slice positioning by a method for reference to internal landmarks we have previously reported. Magnified MR images were analyzed using computerized morphologic measurements as previously described and consistent with other investigators. There were no significant differences between groups of adult controls and autistics for mean midsagittal areas of the pons, fourth ventricle, or lobules of the cerebellar vermis. No significant structural brain abnormalities were described by radiologic evaluation of all subjects. These results will be discussed in relation to previous MRI studies of autism.

NR257 Tuesday May 14, 12 noon-2:00 p.m.

SPECT in Lithium: Responsive Conduct Disorder

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Summary:

Previous SPECT studies of children with cognitive and developmental disorders have reported various abnormalities. We studied three right-handed adolescent white males (ages 13, 15, 17) who met *DSM-III-R* criteria for conduct disorder using I-123-IMP

SPECT. Patients were consecutive admissions for inpatient evaluation and treatment at a specialized neuropsychiatric facility. Learning disabilities and low grade academic achievement were conspicuous in each patient, with a mean FS IQ of 74 (range 66-82). Comprehensive neuropsychological testing documented generalized impairments in higher cognitive functions, without focal or lateralizing signs. The three patients evidenced similar profiles of neuropsychological impairments and behavioral disturbances, which included impulsivity, inattention, and aggression.

SPECT revealed bilateral posterior parietal hypoperfusion in all three subjects prior to medication. In the one patient who underwent repeat SPECT following lithium treatment, normalization of perfusion deficits was observed. In all three patients, treatment with low-dose lithium carbonate (serum levels 0.31-0.52 mEq/L) was rapidly effective in reducing problematic behaviors. Objective measures of cognitive performance, which assessed generalized attention, on-task vigilance, cognitive flexibility, and impulse control, were markedly improved on lithium. These pilot data will be discussed in relation to prior SPECT studies and current theories of cerebral dysfunction in behavioral disorders and learning disabilities.

NR258 Tuesday May 14, 12 noon-2:00 p.m.

Psychopharmacology of Conduct Disorder

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Summary:

To investigate the short-term efficacy of methylphenidate in a group of conduct disorder children, a placebo-controlled, random assignment, double-blind, five-week treatment study was done. All children and parents received non-specific behavioral counseling during the course of the five weeks. Treatment was fixed flexible dosing—minimum of 30mg a day of methylphenidate titrated to 60mg a day of methylphenidate, if no side effects. The original plan was to include only children with conduct disorder who did not meet criteria for ADHD; however, the great majority presented with concurring ADHD and so subjects (n = 69) were divided between those with ("mixed" subjects) and without pervasive ADHD ("pure" subjects). Classroom and gym observations, cognitive testing, and self and parent report measures were used. All children were significantly helped by the methylphenidate/counseling approach although these results were more dramatic for the mixed group. Significant improvement was seen for specific conduct symptoms as well as for symptoms of ADHD. These results were extremely encouraging and indicate a methylphenidate effect not only on hyperactive-like behaviors but also on conduct disorder behaviors in children with a pervasive pattern of antisocial behavior.

NR259 Tuesday May 14, 12 noon-2:00 p.m.

A Cartoon-Like Questionnaire to Assess Children 6-12 Years of Age

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Summary:

There is no instrument allowing direct, reliable assessment of primary school children, whether for clinical or epidemiological purposes.

Dominic is a cartoon-like questionnaire designed to study mental health status of children six to 12 years of age. Each drawing represents the same child in various situations.

Methods: 300 drawings were developed after *DSM-III-R* criteria for ADHD, Conduct, Oppositional Defiant, Separation Anxiety and Overanxious Disorder, Depression, Simple Phobia. To verify understanding, ten boys and ten girls for every year of age were presented with each drawing. A total of 167 drawings survived the process.

Theses drawings were studied in a sample of 73 children (40 boys and 33 girls), 58 from the general population and 15 from outpatient clinics.

One week after first presentation with *Dominic*, they were reassessed.

Criterion validity was studied against a "clinically enriched" *Dominic*.

Results: Reliability: for the various diagnoses, Kappas ranged from .51 to .66. No reliability differences were observed according to age.

Validity: against the "clinically enriched" *Dominic*, Kappas ranged from .60 to 1, according to diagnoses.

Cronbach alpha ranged from .65 to .82.

Concluding Statement: Picture-based assessment can already be considered a breakthrough to assess mental health of children six to 12 years of age.

NR260 Tuesday May 14, 12 noon-2:00 p.m.

Family and Individuals Adjustment in Cystic Fibrosis Children

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Summary:

Family adjustment to their child's chronic illness has been associated with psychological adjustment and psychiatric symptomatology. However, few studies to date have attempted to systematically evaluate this relationship and its relationship to the illness severity. We studied 45 children ages seven to 15 and their families at a large Cystic Fibrosis center and obtained measures of family impact of illness on the family (the Impact of Illness on the Family scale by Stein), family functioning (the Family Assessment Device by Epstein), behavioral adjustment (the Child Behavior Checklist by Achenbach), ratings of anxiety, depressive, and eating disorder symptoms, and ratings of illness severity and duration. Impact of illness on the family and overall family dysfunction were significantly correlated with illness severity, but not duration. However, impact of illness on the family was significantly correlated with internalizing behavior on the CBCL, ($R = 4516$, $P = .003$), while family dysfunction was correlated with depressive symptomatology ($R = .3395$, p.023). Our findings indicate that illness-related stress is primarily reflected in internalizing symptoms, with family adjustment helping either to ameliorate or exacerbate their development into depressive symptomatology.

NR261 Tuesday May 14, 12 noon-2:00 p.m.

Exclusion of Close Linkage of Tourette's Syndrome to D1 Dopamine Receptor

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Summary:

Many lines of evidence support a dopaminergic mechanism for Tourette's syndrome (TS). We have previously excluded D_2 dopamine receptor (genetic locus DRD2), perhaps the most likely dopaminergic candidate gene, from linkage with TS (Gelernter et al., *Arch Gen Psychiatry* 47:1073-1077 (1990)). D_2 dopamine receptor (locus DRD1) was recently cloned and mapped to chromosome

5q. We developed a genetic map of this region, and have now used this map to do an RFLP linkage study resulting in exclusion of DRD1 from close linkage with TS. We studied DRD1 and linked markers (D5S36, D5S61, and D5S62) in a large Mennonite TS kindred (Kurlan et al., *Neurology* 36:772-776 (1986)). We considered only individuals with the full TS syndrome to be affected (this is the most stringent of diagnostic models). Liability classes were defined to take into account age at onset and sex differences. Dominant inheritance was assumed, with a disease gene frequency of 0.0004; penetrance values were 0.126 to 0.450 for males and 0.048 to 0.170 for females; phenocopies were set at 0 percent for both sexes. Our version of LINKMAP program of the LINKAGE package (Lathrop GM et al. *Am J Human Genet* 37:482-498, 1985) modified to run under distributed parallel processing (LINDA-LINKMAP) was used for the multipoint linkage analysis.

Markers were fixed at 0.0 (D5S36), 0.015 (D5S61), 0.277 (D5S62), and 0.278 (DRD1). Complete (= 0.0) linkage of TS with DRD1 was ruled out (LOD score −10.1). The area of exclusion of linkage (LOD score between −2 and −10.5) extends from map position −0.10 to 0.50.

These results provide strong evidence against linkage of the DRD1 D_2 receptor locus (identified by either probe phD1-Gem or HNR) with Tourette syndrome. Use of multipoint analysis allowed exclusion of a broad genomic area amounting to about 2 percent of the human genome. This exclusion extends our earlier work with the DA system in TS to exclude the two best characterized dopamine receptors from linkage with TS trait.

NR262 Tuesday May 14, 12 noon-2:00 p.m.

Are Parkinson's Disease and ADHD Related?

Amy J. Holland, B.S., Psychiatry, East Carolina Univ, School of Med. c/o Diamond, Greenville, NC 27858; John M. Diamond, M.D., Stephen L. McNeil, M.D.

Summary:

The discovery of striatal dopamine depletion in patients with parkinsonism, animal studies suggesting dopaminergic mechanisms in the development of hyperactive motor behavior, and the therapeutic efficacy of dopamine agonists, have suggested a relationship between Parkinson's disease (PD) and Attention Deficit Hyperactivity Disorder (ADHD). Furthermore, Von Economo's Encephalitis sometimes produced a Parkinsonian syndrome in adults and a behavior disorder similar to ADHD in children. The purpose of this study was to explore the presence of a developmental relationship for these disorders. The subjects (N = 111) were recruited from PD support groups and administered the Parents' Rating Scale (PRS) as a self-report on behaviors during childhood. This was supplemented by additional questions designed to support the diagnosis of ADHD. Six percent of the subjects had significant scores on the PRS consistent with a past history of ADHD. This prevalence is similar to that of three to five percent commonly reported for ADHD in the general population. These results do not support a developmental relationship between ADHD and PD.

NR263 Tuesday May 14, 12 noon-2:00 p.m.

Predictive Value of Brief Alcoholism Screening Tests in a Sample of Hospitalized Adults

Frederic Blow, Ph.D., Psychiatry, Univ of Michigan, 400 E. Eisenhower Parkway Ste A, Ann Arbor, MI 48104; Kirk Brower, M.D., James Young, M.S., Elizabeth Hill, Ph.D., Kathleen Singer, R.N., Thomas Beresford, M.D.

Summary:

In recent years, alcoholism screening measures such as the CAGE and MAST have been shown to be useful in screening hospitalized patients for alcoholism. However, studies to date have not compared these screening tests to the current "gold standard," the *DSM-III-R* diagnosis. This present study compared three screening instruments, the CAGE, MAST, and SMAST, against *DSM-III-R* diagnoses. Semi-structured interviews were conducted with a random sample of 1,139 hospitalized general medical/surgical patients. The prevalence of *DSM-III-R* defined alcoholism (overall sample prevalence = 32 percent) differed between men and women ($p < .001$), and between age groups ($p < .001$), and demonstrated a significant linear decrease as age increased ($p < .001$). Both the MAST and SMAST had low predictive values (ranging from 52 percent to only 77 percent) across gender and age groups. The positive predictive values for both the MAST and SMAST were higher for males and decreased with age, especially for women. In contrast, the CAGE maintained predictive power above 80 percent for both men and women, and remained near 80 percent until the age of 70. In summary, while the MAST and SMAST are gender- and age-biased alcoholism screening instruments, the CAGE appears to have high predictive value for both men and women through age 70. In addition, the CAGE maintained high specificity and moderate sensitivity across the sample. The CAGE instrument, despite limitations in sensitivity for several age and gender subgroups, has the highest positive predictive value of the short alcoholism screening measures tested and consequently is the most appropriate for mass alcoholism screening.

NR264 Tuesday May 14, 12 noon-2:00 p.m.

Alcohol Dependence Among Hospitalized Eating Disorder Patients

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Summary:

This study had two objectives: 1) to assess the prevalence of *DSM-III-R* defined alcohol dependence (AD), and 2) to assess the effectiveness of the CAGE questions and the MAST in recognizing AD. Subjects were 81 female patients admitted consecutively to an inpatient unit for eating disorders. The mean age was 26.5 years (sd = 8.4 years). Eighty (98 percent) were white. All but six were graduated from high school; 70 percent were in or had finished college. Most (62 percent) were single. As assessed by structured interview, 30 subjects (37 percent) met AD criteria. Of those using any alcohol only 15.5 percent reported current heavy drinking (4 days weekly) while 18 percent of the sample reported recent binge drinking. The CAGE questions were significantly more sensitive (80 percent vs 67 percent) and specific (94 percent vs 75 percent) than was the MAST in recognizing AD patients. The CAGE questions correctly identified 89 percent of the patients compared to 72 percent for the MAST. Most (82 percent) of the AD patients and some (18 percent) of the non-AD patients had prior notation of heavy alcohol use. Hypertension (7.6 percent), ulcer disease (6.2 percent) and pancreatitis (1.2 percent) were present while other alcohol related conditions were not. The AD group were more likely to have been drinking alcohol within one week of admission (50 percent vs 26 percent, Chi Square = 4.8, $p < 0.05$). The AD group were more likely to have ever used marijuana (93 percent vs 57 percent, Chi Square = 12.1, $p < 0.001$) and cocaine (53 percent vs 12 percent Chi Square = 7.63, $p < 0.01$). We conclude 1) the prevalence of AD is very high in this group and 2) the CAGE questions are preferable to the MAST in effectively screening this subject group.

NR265 Tuesday May 14, 12 noon-2:00 p.m.

Long-Term Antidepressant Treatment of Alcoholism

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Summary:

Tricyclic antidepressants might reverse or prevent depressive symptoms related to resumed drinking, and may reverse biochemical abnormalities hypothesized to underly both depression and alcoholism, thus prolonging abstinence in newly sober alcoholics. METHOD: Primary alcoholics were randomly assigned to a six-month double-blind trial of desipramine (DMI) or placebo, with stratification by gender and presence or absence of major depression. Monthly DMI plasma levels were obtained to insure compliance and that a standard level of drug was circulating. Depression was assessed with the Hamilton (HAM), and sobriety with the Timeline interview and significant other confirmation. SUBJECTS were 33 males and eight females with an average age of 40.25 years, and a moderate level of alcohol dependence. HAM scores were equivalent between depressed groups (DMI $x = 25.0$, PLA $x = 23.6$) and between nondepressed groups (DMI $x = 7.7$, PLA $x = 9.4$). RESULTS: Depressed PLA subjects were significantly more depressed at the time of their termination from the study (HAM $x = 20.0$) than subjects in the other three groups ($F = 13.06$, $p = .0000$). There was a trend for depressed DMI subjects to have more days sober ($x = 99.9$, nondepressed DMI $x = 44.8$, depressed PLA $x = 67.1$, nondepressed PLA $x = 59.3$). For those with prior treatments, 29 percent depressed PLA, 0 percent nondepressed PLA, 75 percent depressed DMI, and 33 percent nondepressed DMI had their longest period of sobriety on the study. CONCLUSION: Preliminary support was obtained for the efficacy of DMI in the treatment of depression secondary to alcoholism. (Supported by NIAAA grant number R23 AA06866.)

NR266 Tuesday May 14, 12 noon-2:00 p.m.

Psychiatric, Alcoholic and Antisocial Characteristics in Adult Offspring of Alcoholics versus Non-Alcoholics

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Summary:

The clinical clustering of depression, alcoholism, and antisocial personality (ASP) and possible genetic transmission has been proposed in the literature. This study compares nearly equal numbers of age-similar black and white offspring from middle-class families with parental alcoholism (AOPA) versus those without parental alcoholism (AOPNA). A total of 75 AOPA (37 males; 38 females) and 76 AOPNA (38 males; 38 females), similarly balanced for both racial subgroups, were available; Hollingshead-Redlich social class was also determined. Exclusion criteria for parents (except for alcoholism) were: 1) 18 yo; 2) two on SADS-L item for drug use; 3) psychoses or major affective disorder; 4) major medical problems requiring an MD. Psychiatric status for both parents and offspring was determined by blind-rated SADS-L interviews; severity of alcoholism in offspring was determined by MAST scores. Alcoholism, but not drug abuse, is more likely to occur in AOPA (53 percent) vs AOPNA (39 percent) with males accounting for a disproportionate frequency in both groups (67 & 72 percent); AOPNA males (72 percent) drink more frequently than AOPA females (33 percent); AOPNA females drink the least (28 percent). Major depression is more likely to occur in AOPA (36 percent) vs. AOPNA (17.6 percent) with females accounting for a disproportionate frequency in both groups (70 percent & 83 percent). No racial differences are apparent. Coincidence of alcoholism and its severity, drug abuse, major depression, and ASP will be discussed.

NR267 Tuesday May 14, 12 noon-2:00 p.m.

Comparative Validity of Eleven Alcoholism Topologies

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Summary:

The overlap between 11 well-known alcoholism typologies and their comparative clinical validities were examined in a large sample ($N = 36$) of men inpatient alcoholics who underwent a comprehensive examination at entry to the study and again, one year later. The alcoholism typologies studied were: current age; familial vs nonfamilial alcoholism; age-of-onset; Cloninger Types I and II; Sociodemographic; MMPI, Shipley CQ; SCL-90; AUI; psychiatric severity by the number of co-occurring *DSM-III* syndromes; and "dual diagnosis" subtypes based upon the type of syndromes coexisting with alcoholism. We found that *all* of the alcoholism typologies correlated positively with one another at moderate but typically significant levels. We then used factor analysis to search for underlying dimensions that might account for the unexpected overlap. Two dimensions were identified that "explained" over two-thirds of the variance: (1) age-of-onset, and (2) severity of general psychopathology. Moreover, when examining 23 indices of clinical validity (15 derived from intake measures, eight from outcome measures), we found that all of the typologies satisfied at least two or more of the a priori external validity criteria. These findings raise troubling questions about the clinical utility of various alcoholism typologies that have been proposed.

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The Platelet Benzodiazepine Receptor in Alcoholics

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Summary:

The peripheral benzodiazepine (PBZ) receptor has been hypothesized to be anxiogenic and proconvulsant. Since anxiety and convulsions are part of the alcohol withdrawal syndrome, we studied platelet PBZ receptor bindings and psychiatric symptoms in alcoholics at various stages of abstinence. A total of 84 benzodiazepine-free subjects (63 alcoholics and 21 controls) completed the study. Subjects were interviewed using the SCID, an Alcohol Use Inventory, the SCL-90R, and the Spielberger State/Trait Anxiety Scale. Blood was drawn for determination of platelet PBZ receptor binding. Alcoholics who were currently drinking had a significantly elevated ($p < 0.05$) receptor number (Bmax) (2672 ± 1160 fmol/mg protein) over that found in the controls (1328 ± 620), recently detoxified alcoholics (1370 ± 737), and alcoholics with long-term sobriety (983 ± 660). Recently detoxified alcoholics had elevated Kd values (4.52 ± 1.21 nM) whether compared to controls (3.69 ± 1.79 nM), actively drinking alcoholics (3.38 ± 1.58 nM) or alcoholics with long-term sobriety 2.54 ± 1.83 nM). Recently detoxified alcoholics had the greatest elevation in psychiatric scale scores with significant differences from both controls and alcoholics with long-term sobriety. This study suggests that changes in the affinity of the PBZ receptor is associated with psychiatric symptoms in alcoholics. Receptor density changes appear to be related to alcohol consumption alone; and independent of psychiatric symptoms.

NR269 Tuesday May 14, 12 noon-2:00 p.m.

Naltrexone in the Treatment of Alcohol Dependence

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Summary:

Recent reviews of alcoholism treatment show that relapse rates often exceed 50 percent within three months, even after intensive inpatient or residential treatment. This has prompted a search for pharmacological agents that may help decrease the high relapse rates that often occur early in treatment.

New pharmacological approaches to the treatment of alcoholism are suggested by biochemical and behavioral studies demonstrating an interaction between alcohol and opiates. Several animal studies have shown that opiate antagonists such as naltrexone or naloxone will decrease alcohol drinking. This suggests that naltrexone may be a helpful adjunct in the treatment of alcohol dependence.

In our study, naltrexone decreased craving, mean drinking days, and relapse rates. It seemed to be particularly effective in decreasing drinking in subjects who had at least one slip; that is, naltrexone helped stop the "loss of control" over drinking observed among placebo treated subjects. In addition, naltrexone was well tolerated with few side effects and no deleterious effects on mood and psychopathology.

In summary, our study gives preliminary support to the clinical utility of naltrexone as an adjunct to the treatment of alcohol dependence and provides support for the hypothesis that alcohol is reinforcing because of its effects on opioid systems.

NR270 Tuesday May 14, 12 noon-2:00 p.m.

Controlled Trial of Buspirone in Alcoholism Relapse

Robert J. Malcolm, M.D., Psychiatry, Med. Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; Raymond Anton, M.D., Kathleen J. Brady, M.D., Carrie L. Randall, Ph.D., Amanda Johnston, Ph.D., R. Eric Jones, M.D.

Summary:

Two studies with the serotonin $5HT_{1a}$ agonist buspirone have demonstrated either a reduction in alcohol consumed by heavy drinkers or an alteration in severity of drinking as measured by the Alcohol Severity Index (ASI). This double-blind, controlled trial of buspirone versus placebo evaluated 67 male veterans with alcohol dependency and nonpanic anxiety disorders. Subjects were randomized to 60 mg per day of buspirone (N = 33) or placebo (N = 34) in a 24-week outpatient trial. There were no significant differences between groups in routine demographic variables, severity of alcoholism, number of previous treatments, comorbid psychiatric disorders, or other substance abuse. Abstinence and quantity of alcohol consumed were assessed by subjective reports from the patient and significant others, breathalyzer alcohol levels, and clinical laboratory studies. Survival analyses were performed on Time to First Drink, Time To First Intoxication, and Time to Five Consecutive Heavy Drinking Days (>6 oz. alcohol per day). For all of these measures, preliminary analyses did not statistically differ between placebo or buspirone groups. Number of patients abstinent and alcohol severity scores on the ASI did not differ between groups at three or six months. Prestudy alcohol use per day decreased for both groups and did not differ statistically at three or six months. In this study of male veteran anxious alcoholics, treatment with buspirone did not improve or interfere with recovery from alcoholism. Buspirone did not appear to be an effective agent to prevent relapse from drinking in a population of severely dependent, male veteran alcoholics.

NR271 Tuesday May 14, 12 noon-2:00 p.m.

Neuroendocrine Correlates of Alcohol Expectancy

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Summary:

Several studies have suggested that presentation of an alcohol stimulus can increase an alcoholic's subjective desire to drink to a greater extent than that observed in nonalcoholic controls, and can produce increases in skin conductance and heart rate. In one study, the increased desire to drink alcohol following consumption of a perceived alcoholic beverage was also shown to be associated with increases in both plasma insulin and glucose. To date, however, studies have not examined whether neuroendocrinological changes in response to an alcoholic stimulus are mediated by the expectancy of alcohol. In the present study, we employed a within-subject, repeated measures design to explore the effects of expectancy on subjective and neuroendocrine responses to beverage presentation in alcoholics. Eight male inpatient alcoholics were studied under two experimental conditions in the second week of alcohol abstinence. In one condition subjects were told that they would be consuming a glass of beer. In the other condition, the same subjects were told to expect a placebo beer. Subjects actually consumed the same alcoholic-free beer in both conditions. Self-reported mood, neuroendocrine, and psychophysiologic data were collected at 12 intervals during and after presentation and beverage consumption. The results indicated that when subjects believed they had consumed alcohol, the changes in insulin levels from baseline were significantly greater at 10, 20 and 30 minutes following consumption. The findings suggest that the insulin response following ingestion of a carbohydrate-containing beverage is enhanced by the anticipation of ethanol.

NR272 WITHDRAWN

NR273 Tuesday May 14, 12 noon-2:00 p.m.

Hypomania in Post-Acute Alcohol Withdrawal

Ellen M. Cawthra, R.N., Psychiatry, Univ of CO Denver VAMC, 4200 East 9th Avenue C-268, Denver, CO 80262; Kim Nagel, M.D., Lawrence E. Adler, M.D., Merilyne C. Waldo, Ph.D., Robert Freedman, M.D.

Summary:

Although there has been considerable interest in the use of lithium carbonate in recovering alcoholics, there has been little objective evidence of a manic syndrome within this population, perhaps because of the almost universal presence of depressed mood. For this purpose, we have devised a scale which rates psychomotor activitation, independent of mood (Psychomotor Activity Rating Scale, PARS). In this study, 19 subjects were evaluated six to ten days following withdrawal from alcohol and again one week later. Nine had evidence of hypomania, reflected in PARS in the abnormal range at week 1. Plasma MHPG levels were significantly higher in this group compared to 15 normal controls, at both the beginning and ending of a two-week hospitalization, replicating previous studies. There were no significant differences on ratings of mood, although the subjects with normal PARS scores tended to be more depressed. Although both groups had markedly enlarged cerebral ventricles, there were no significant differences between them, nor were they different on the Trails B, another measure of brain function. The severity of alcohol withdrawal was not significantly different between the two groups. What was significant was that subjects with abnormal PARS scores had fewer months of abstinence in the past two years. This finding can be interpreted in two ways: 1) longer exposure to alcohol may predispose individuals to this hypomanic reaction; or 2) the reaction may keep people from abstinence.

NR274 Tuesday May 14, 12 noon-2:00 p.m.

A General Population Survey of Drinking Patterns

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Summary:

A randomized, stratified community survey of 2115 residents of Alachua County, Florida, was carried out to assess alcohol drinking patterns, other substance abuse, and psychopathology. The frequency of abstinence and distinguishing features of this population were determined. A total of 21.4 percent of the population were lifelong (LL) abstainers, 30 percent of the female sample and 8 percent of the male sample. LL abstainers as a group were older, more "fundamentally" religious, from lower SES, much less likely to engage in other addictive behaviors, including smoking, other substance abuse, and food binging. The perceived health of LL abstainers was significantly poorer than that of social drinkers. LL abstainers were also much more likely to have been raised in a childhood home in which one or both parents were themselves abstinent. In female LL abstainers a significantly lower prevalence of major depression was found compared to both social and problem drinkers. Possible biological and cultural determinants of LL abstinence are discussed. In summary, the characteristics that differentiate LL abstainers from social and problem drinkers are many and may aid in our understanding of the etiology of addictive disorders.

NR275 Tuesday May 14, 12 noon-2:00 p.m.

Platelet Mao Activity and Alcohol Dependence: A Study of Patients and their Healthy First-Degree Relatives

Mario Guazzelli, M.D., Dept. of Psychiatry, Clinica Psychiatrica, Via Roma 67, Pisa 56100, Italy; Pietro Pietrini, M.D., Antonio Ciapparelli, M.D., Federica Loprieno, M.D., Ilaria Bianchi, M.D., Pietro Sarteschi, M.D.

Summary:

Several studies show that PMAOA is reduced in AD during alcohol assumptions as well as during long-lasting continence, thus suggesting that PMAOA reduction may be a trait-dependent parameter rather than a direct effect of alcohol. To investigate possible meaning of PMAOA reduction as biological correlate of alcohol use disorder vulnerability, we started a clinical (*DSM-III-R* based diagnostic interview, MALT, MAST, Family History) and biochemical (PMAOA evaluated by a radiometric assay) study in AD patients and their HFDR. Compared to sex- and age-matched AD and HFDR healthy controls, the 11 male AD patients (m.a. 53.4 ± 7.6 yrs) and 11 HFDR (10 M/1 F; m.a. 27.8 ± 12.5 yrs) studied till now showed a significant PMAOA reduction (22.9 ± 5.3 vs 13.2 ± 7.1 and 23.5 ± 3.9 vs 14.3 ± 8.2 nmoles/mg-prot/h, respectively). Further data on a wider sample and the analysis of correlations between PMAOA and clinical AD features, now in progress, will better evaluate the meaning of this parameter as biological correlate of alcohol use disorders.

NR276 Tuesday May 14, 12 noon-2:00 p.m.

Predictive Validity of Two Screen Tests for Alcoholism

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Summary:

To the best of our knowledge, alcoholism screening tests have not been studied longitudinally. The purposes of this study were: 1) to assess the longitudinal response frequencies of both the CAGE questions and the MAST and 2) to characterize the predictive validity of both tests three years after an initial response to each. We interviewed subjects (N^5404), chosen at random from general hospital admission lists, at baseline and again three years later. This was done as part of a structured interview from which *DSM-III-R* diagnoses could be made. Subjects were 51 percent male, 91 percent white, with an age range of 18 to 58 years at baseline.

Positive response rates were (baseline, follow-up): CAGE, 25.5 percent and 21.5 percent, MAST 34.2 percent and 25.2 percent. CAGE positive prevalence was 84 percent of baseline; this was true for 74 percent of MAST responders. There were significant changes within these prevalence figures, however: 24 subjects (6 percent of N) shifted to positive and 40 patients (10 percent of N) shifted to negative at follow-up. For the MAST, similar figures were 25 (6 percent) and 61 (15 percent). Predictive validity characteristics of the baseline screen response vis-a-vis follow-up *DSM-III-R* alcohol dependence diagnosis were (sensitivity, specificity): CAGE, 62 percent and 89 percent, MAST 71 percent and 81 percent. The predictive power of a positive response at baseline for a positive response at follow-up for each test were: CAGE 69 percent and MAST 59 percent. We conclude that baseline screening responses may not be very useful indicators of predictive validity because of confounding variables such as changing clinical state, shifts in the diagnostic standard, setting, and interview method.

NR277 Tuesday May 14, 12 noon-2:00 p.m.

Young Adult Children of Alcoholic Parents: Protective Effects of Positive Family Relationships

Elizabeth Hill, Ph.D., Psychiatry, Univ of Michigan, 400 E. Eisenhower Parkway Ste A, Ann Arbor, MI 48104; Janet Nord, Ph.D., Frederic Blow, Ph.D.

Summary:

The detrimental effect of a positive family history for alcoholism may vary with the degree of family impairment during development. In this study we assessed the effects of family history and family environment on psychological adjustment and alcohol misuse. From ongoing studies, we recruited parents who had a child aged 18-30, 20 with *DSM-III-R* alcohol dependence diagnosis, 20 without. The child then completed a multi-dimensional assessment. The young adult participants included 20 men and 20 women (mean age = 24.8). There were no significant differences in overall social or psychological adjustment between those with and without an alcoholic parent. Differences were restricted to substance abuse behaviors: children with an alcoholic parent were much more likely to be heavy drinkers (47 percent vs 6.3 percent) and to have higher consumption as youths, although they were similar in the incidence of an alcohol dependence diagnosis. Within the group with alcoholic parents, the children who had the most positive relationships with parents showed fewest current symptoms of depression and anxiety. Positive relationships also significantly delayed the age of onset of regular drinking and the frequency of symptoms to dependence on drugs and alcohol. The degree of exposure to parental alcoholism positively increased the frequency of drinking reported in high school and was strongly correlated with the number of dependence symptoms already experienced by the offspring (alcohol $r = .706$). However, this exposure measure was not significantly related to social or psychological adjustment measures. In this sample of subjects from alcoholic families there appear to be strong protective effects of positive family relationships on the potential negative effects of a family history.

NR278 Tuesday May 14, 12 noon-2:00 p.m.

Immunity in Inner-City Alcoholics

Steven J. Schleifer, M.D., Psychiatry, UMD-NJ Med School, 185 South Orange Avenue, Newark, NJ 07103; Steven E. Keller, Ph.D., Stephanie LaFarge, Ph.D., Angela Lignelli, B.S., Hong-Lin Nui, M.B.

Summary:

The extent to which the immune system is altered in alcoholics who are free of overt liver disease is unclear, especially among inner city minority populations. We have studied 29 non-IVDU inner city alcohol-dependent (SCID-*DSM-III-R*) subjects (21 males), ages 22-58 who were free of serious medical disorders. A total of 64 percent also met criteria for abuse of drugs other than alcohol; 55 percent met criteria for a current depressive disorder. About 28 percent resided in shelters. Some 52 percent reported alcohol use during the preceding 24 hours; 77 percent during the preceding two weeks. Hierarchical multiple regression models, controlling for age and gender, revealed that alcohol use during the preceding two weeks and elevated liver enzyme levels were significantly ($p < 0.05$) and independently associated with decreased lymphocyte proliferative responses to phytohemagglutinin. Similar effects were seen for pokeweed mitogen. Elevated liver enzyme levels were also associated with decreased CD4 + cells ($p < 0.02$). Natural killer cell function, in contrast, appeared higher among alcohol users compared with abstainers ($p < 0.1$). Use of other drugs, alcohol use in the preceding 24 hours, and depression were, in general, not associated with altered immune measures. Altered immunity related to active alcohol use among inner city persons with a history of alcoholism may be relevant to the risk of infectious disorders such as AIDS in this population.

NR279 Tuesday May 14, 12 noon-2:00 p.m.

Acute and Chronic Ethanol Effects on Lymphocytes

Martha M. Sarasua, M.D., Surgery, Metrohealth Med. Center, 3395 Scranton Road, #R416, Cleveland, OH 44109; Mariano V. Tolentino, M.D., Ray Hill, B.S., Debra Wentworth, B.S., Robert Smith, Ph.D., Jonathan Dunn, M.D.

Summary:

Ethanol induces immunosuppression *in vivo*, yet the mechanisms underlying this effect remain unknown.[1-2] Here, we have investigated the effects of ethanol on lymphocyte membrane fluidity and the proliferative response to mitogens and interleukin 2 (IL-2). We first utilized a defined culture system of IL-2 dependent cytotoxic T cells (CTLL-N) as a model of ethanol effects *in vitro*. CTLL-N were exposed to ethanol for varying periods of time from one hour to 21 days. Results in this system were compared to measurements on human peripheral blood mononuclear cells (PBMNC) isolated from controls and alcohol dependent patients. The response of the CTLL-N to IL-2 was significantly inhibited by acute (one hour) exposure to ethanol. This effect reached a peak in two days then declined to control levels by seven days of exposure. A corresponding decrease in sensitivity of the CTLL-N to the membrane fluidizing effects of ethanol occurred with chronic ethanol exposure indicating membrane level adaption. PMBNCs from alcohol dependent patients showed a significant elevation in membrane fluidity when compared to controls. The proliferative response to mitogen of PBMNCs from patients was reduced. Thus, ethanol acutely effects lymphocyte membrane fluidity and function both *in vitro* and *in vivo*. Chronic exposure results in membrane level adaption to ethanol.

NR280 Tuesday May 14, 12 noon-2:00 p.m.

Effects of Steroids on Immune Cells

Martha M. Sarasua, M.D., Surgery, Metrohealth Med. Center, 3395 Scranton Road, #R416, Cleveland, OH 44109; Mariano V. Tolentino, M.D., Ray Hill, B.S., Pat Warnaka, B.S.

Summary:

Steroid use and abuse have risen drastically in male adolescents. Reasons ranging from enhancement of physical abilities to improvement of one's appearance have been cited. Behavioral problems typically result in psychiatric consultation. However, it is important to recognize other potential complications of this growing problem. This study was conducted to characterize *in vitro* the effects of steroids on the membrane fluidity and basal proliferation of peripheral blood lymphocytes (PBL). Using the membrane-associated probe diphenylhexatriene (DPH) to monitor fluidity, the fluorescence polarization (FP) of PBL's isolated from healthy volunteers were measured prior to and following titration of 0.5u moles of cortisol for up to 2u moles/L. The FP and basal proliferation of PBL's grown in the presence or absence of 1M cortisol for 72 hours were also measured. Membrane fluidity increased with addition of steroids and was dose-dependent. Following three days of exposure to steroids, membrane fluidity also increased. Steroids did not affect the basal proliferation of PBL's; however, they diminished the proliferative response of PBL's to the standard mitogen, phytohemagglutinin (PHA). These results imply that steroids directly affect the lymphocyte cell membrane fluidity and its response to mitogenic stimulation. This may explain the immunosuppression known to result from adrenocorticosteroid therapy.

NR281 Tuesday May 14, 12 noon-2:00 p.m.

Imipramine Treatment of Depressed Drug Abusers

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Summary:

Methadone maintenance is frequently complicated by continued drug abuse and associated HIV high-risk behaviors. Some of these patients may have affective disorder and use illicit drugs to "self-medicate." Available studies of tricyclic antidepressant treatment in depressed methadone patients have yielded equivocal results with some improvement in mood but little evidence for reduced drug abuse. These studies rely on cross-sectional symptoms to diagnose depression, whereas longitudinal studies suggest most depression in opiate addicts is transient and may not represent "true" affective disorder.

We therefore have used lifetime psychiatric history to select drug abusing methadone patients with depression which is either primary (antedates substance abuse) or chronic. In a 12-week open label trial of imipramine 9/1 (53 percent) improved in both mood and drug abuse, achieving stretches of abstinence of at least four weeks. In an ongoing double-blind trial 8/14 (57 percent) have achieved a favorable response (significant reduction in both depression and illicit drug abuse) compared to 1/19 (5 percent) on placebo. This suggests the potential of a careful psychiatric history in selecting drug abusers for antidepressant treatment.

NR282 Tuesday May 14, 12 noon-2:00 p.m.

Depression Predicts Improved Response to the Use of Medication in Cocaine Treatment

Douglas Ziedonis, M.D., Psychiatry, Yale University, 904 Howard Avenue, New Haven, CT 06519; Thomas Kosten, M.D.

Summary:

The use of amantadine (300mg; n = 24), desipramine (150 mg, n = 24), and placebo (n = 27) in the cocaine treatment of 75 cocaine abusing methadone maintenance patients was compared in a ten-week randomized, double-blind trial. Twenty-five percent of the

patients (n = 19) had major depression or dysthymia. Although with a delay in treatment response, the medicated "depressed" patients had a dramatic 96 percent decrease in cocaine usage compared to the placebo treated "depressed" patients who actually increased their usage to 5 percent above baseline. Using ANCOVA to adjust for baseline differences between the medicated and placebo treated "depressed" patients, significant differences were noted at week 5 ($112 vs $263), F(1,15) = 7.0; $p < 0.02$, and continued to be present at week 10 ($5 vs $92), F(1,11) = 11; p0,01. Also, in the medicated depressed patients showed a significant reduction in cocaine craving relative to placebo (by week 8 $t = 2.4$,df 14, and $p < 0.04$) with mean craving scores dropping 68 percent. Although reduced, the Beck scores of the depressed patients did not improve significantly with treatment. In conclusion, medication usage improved cocaine abuse treatment in all groups. Depressed patients receiving placebo showed no improvement.

NR283 Tuesday May 14, 12 noon-2:00 p.m.

Relapse Prevention Group Therapy is Effective in the Treatment of the Mentally Ill Substance Abuser

Douglas Ziedonis, M.D., Psychiatry, Yale University, 904 Howard Avenue, New Haven, CT 06519; Adam Jaffe, Ph.D., Ellen Davis, Ismene Petrakis, M.D., Izola Hogan, R.N.

Summary:

The treatment of mentally ill substance abusers (MISA) is difficult. This report describes a unique outpatient relapse prevention group approach for the treatment of psychotic disordered psychiatric patients with a substance abuse disorder. The group activities included role playing, social skills training, relapse analysis, psychoeducation, and monitoring of both psychiatric and substance abuse symptoms. Data were collected from these groups to characterize the course for these patients. The nature of their pretreatment substance abuse relapses and intreatment slips was evaluated. A specialized relapse prevention manual has been organized. Thirty-eight patients were treated and evaluated for six months. Of these patients, 25 successfully completed three months or more of treatment. A total of 25 continue to be engaged in treatment. Of the 13 not in treatment, seven completed three months or more of treatment. Urine monitoring revealed that 85 percent of patient's urine were negative after the initial evaluation, and a positive urine was a strong dropout predictor. These patients had lowered rates of unemployment, hospitalizations, legal problems, psychiatric problems, and substance abuse problems. New medication strategies combined with this relapse prevention approach may further improve outcomes for these patients.

NR284 Tuesday May 14, 12 noon-2:00 p.m.

Psychosocial Factors in Adolescent Drug Use

David W. Brook, M.D., Psychiatry, New York Medical College, NYMC Dept. of Psychiatry, Valhalla, NY 10595; Judith S. Brook, Ed.D.

Summary:

This paper describes recent prospective, longitudinal, and cross-sectional research concerning psychosocial etiological factors involved in adolescent drug use and abuse. These findings result from a number of research studies funded by NIDA over the last decade. The studies examine several such psychosocial and familial factors: 1. The interrelationships between family relations, peer influences, and personality attributes, looking at domains of casual influence and their interactions using a developmental approach. Family Interactional Theory stresses the parent-child mutual attachment relationship, and its connection with drug use; 2. Certain risk factors, such as aggression starting in childhood, predispose the child to later drug use, while other protective factors insulate the child against future drug use. Risk-protective interactions are explored; 3. Sibling influences in drug use are examined: a warm sibling mutual attachment relationship protects against drug use; 4. A risk-diathesis model is proposed to synthesize the above findings. This work, combining data-based, large-scale research over several generations of family life, using analyses based on recently-formulated statistical techniques, has already been used as the basis for both further research by others and for the formulation of public policy regarding the prevention of drug use and abuse. The heuristic value of this approach will also be discussed.

NR285 Tuesday May 14, 12 noon-2:00 p.m.

Dual Diagnoses and Recovery From Addictions

Robert C. Ness, Ph.D., Psychiatry, Med. Col. of GA VAMC, 1515 Pope Avenue, Augusta, GA 30912; Lois Cecil, M.A., Lionel Solursh, M.D., William Nolan, Ph.D.

Summary:

We report and interpret significant chi-square relationships among psychiatric illness, substance of addiction, and rates of abstinence within a cohort of 248 male inpatients discharged from a six-week VA addiction treatment program. Twenty-seven percent of the patients also were diagnosed per *DSM-III-R* as follows: PTSD (24), schizophrenia (17), organic personality disorders (13), and depression/anxiety (14). Forty percent of these dual-diagnosed patients were alcohol dependent, 38 percent "mixed users" (cocaine/alcohol), and 22 percent cocaine dependent. Abstinence rates at one and six months were determined by telephone interviews with patients and verified with significant others. Within the full sample, rates of abstinence for those patients with dual-diagnoses did not differ significantly from rates of abstinence for those without dual-diagnoses at either one or six months follow-up. However, within the cocaine dependent sub-group, dual-diagnosis patients were more likely to have used cocaine at both one and six months follow-up than those with solely addictions diagnoses. In addition, patients diagnosed as schizophrenic were significantly more likely to be cocaine dependent, while patients with any other nonaddictions psychiatric diagnosis were more likely to be either alcohol dependent or "mixed users."

NR286 Tuesday May 14, 12 noon-2:00 p.m.

Activation of Locus Coeruleus in Opiate Withdrawal

Gary Aston-Jones, Ph.D., Mental Health, Hahnemann University, Broad & Vine, MS 403, Philadelphia, PA 19102; Hideo Akaoka, Ph.D.

Summary:

Noradrenergic neurons of the locus coeruleus (LC) in morphine-dependent rats are strongly activated by opiate-withdrawal (OW). We examined mechanisms for this activation using extracellular recording of LC neural activity in halothane anesthetized rats.

Direct infusion of the opiate antagonist naloxone (NLX; 10 mM) into the LC of dependent rats did not reliably alter LC discharge (n = 8). There was no evidence that hyperexcitability of LC neurons caused their activation during OW, as chronic morphine did not affect excitability by iontophoretic glutamate, and decreased responses to sciatic nerve stimulation (by 27 percent, $p < .05$; n = 31).

Possible involvement of afferents to the LC from the ventrolateral medulla (VLM) was examined. NLX microinjected in VLM (500 nl) significantly activated LC neurons in dependent rats (24 excited, non inhibited, n = 36). This effect was *specific* to (i) dependent rats, (ii) to VLM, and (iii) to opiate receptors as the inactive enantiomer, +NLX, was ineffective (n = 6, $p < .03$).

The activation of LC cells by NLX was attenuated by kynurenate (antagonist of excitatory amino acids, EAAs) given intraventricu-

larly (0.5 umole; n = 6) or directly infused into LC (n = 4), and was significantly reduced by direct LC infusion of the non-NMDA antagonist, CNQX (10^{-4} M, n = 5, p < .004), or the NMDA antagonist, AP5 (10^{-4} M, n = 3, p < .02). Reversals were complete only for OW-activations induced by NLX injection into VLM.

These results indicate that VLM may be one primary site whereby OW activates LC neurons and that this activation is produced by an EAA input to LC. Supported by PHS grant DA 06214.

NR287 Tuesday May 14, 12 noon-2:00 p.m.

Noradrenergic Function and Ethanol Intoxication

Christopher J. McDougle, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; John H. Krystal, M.D., Lawrence H. Price, M.D., George R. Heninger, M.D., Dennis S. Charney, M.D.

Summary:

Preclinical and clinical studies have demonstrated that ethanol (ETOH) increases norepinephrine (NE) turnover in the brain. The purpose of this investigation was to assess the effects of the alpha-2 adrenergic receptor antagonist, yohimbine (YOH), on the behavioral manifestations of ETOH intoxication in healthy human subjects. METHODS: 12 subjects participated in four double-blind test conditions: placebo ETOH (2.8 ml of 95 percent ETOH floated on an approximate mixer p.o.)/placebo YOH (0.45 percent saline I.V.), ETOH (1.1 mL/kg of 95 percent ethanol p.o.)/placebo YOH, placebo ETOH/YOH (0.4 mg/kg YOH I.V.), and ETOH/YOH. Fifty minutes after subjects consumed the active or placebo ETOH, they received a 10-minute I.V. infusion of active or placebo YOH. Ratings of intoxication (Sensation Scale (SS)), symptoms of anxiety (Panic Attack Symptom Scale (PASS)), and a subjective feeling of euphoria-high were obtained at baseline and throughout the study. RESULTS: The global Analysis Variance (ANOVA) of the four test conditions revealed significant ETOH X YOH X time interactions for total SS score ($p < 0.0001$), total PASS score ($p < 0.0001$), and for self-ratings of high ($p < 0.0001$). The ANOVA of the ETOH/YOH condition vs the ETOH/placebo YOH condition revealed significant YOH X time interactions for total SS score ($p < 0.005$), self-rating of high ($p < 0.001$), and a trend for total PASS score ($p < 0.17$), with the ETOH/YOH condition being highest on all three variables. CONCLUSIONS: The combination of YOH-induced increases in NE and ETOH produces a significantly greater degree of intoxication and high than ETOH alone. This suggests that central noradrenergic function may contribute significantly to the intoxicating and euphorogenic effects of ETOH in man.

NR288 Tuesday May 14, 12 noon-2:00 p.m.

Alcohol Screening in Acute Psychiatric Inpatients

Cynthia A. Pristach, M.D., Psychiatry, SUNY at Buffalo, 462 Grider Street, Buffalo, NY 14215; Cedric M. Smith, M.D., Cathy Perkins, M.D.

Summary:

Identification of alcohol abuse in psychiatric patients is essential, since it can confuse the clinical picture and complicate treatment. The utility and reproduceability of the Self-Administered Alcoholism Screening Test (SAAST) was assessed in 236 acutely ill psychiatric patients. It was administered twice, first at admission and again when patients were ready for discharge. The initial SAAST was completed in 195 (83 percent) patients; 76 (39 percent) had a clinical history of alcohol abuse. The two SAASTs were completed by 173 (73 percent) patients and initial SAAST scores were positive (≥ 8) for 69 (37 percent) with alcohol abuse diagnosed clinically in 70 (40 percent) patients. The majority of patients (63 percent scored within +/- 2 points on both tests. Only 41 (17 percent) patients were unable or refused to complete the initial SAAST; ten more gave stereotyped negative responses. Seven of the initial noncompleters had positive SAAST scores; all had clinical diagnoses of alcohol abuse.

Primary diagnoses included schizophrenia (43 percent), affective disorders (22 percent), personality and adjustment disorders (23 percent). Positive SAAST scores were found in 13/16 patients with alcohol dependence.

The SAAST could be completed by the majority of acutely ill psychiatric patients even at admission, and was clinically useful in the diagnosis of alcohol abuse, especially when used in conjunction with the clinical interview.

NR289 Tuesday May 14, 12 noon-2:00 p.m.

Mentally Ill Chemical Abusers in the VA Psychiatric Programs: 1976-1988

Robert Rosenheck, M.D., NEPEC, VA Medical Center, 950 Campbell Avenue, West Haven, CT 06516; Louis Massari, M.P.H.

Summary:

Introduction: Although mentally ill chemical abusers have been identified as an increasingly important population in US mental health programs, longitudinal trend data on their treatment have not been available. *Methods:* Discharge abstracts were analyzed for all patients discharged from Department of Veteran Affairs (VA) medical centers, nationally, with primary non-substance abuse psychiatric diagnosis over a 12-year period (1976-1988). Patients were classified as Mentally Ill Chemical Abusers (MICAs) if they had a primary mental illness diagnosis and either: 1) a secondary substance abuse diagnosis (alcohol or drug abuse/dependence) or 2) an admission for substance abuse treatment during the same year. The percentage of MICAs discharged from VA psychiatric care doubled, from 22.6 percent to 43.6 percent, during these 12 years. In 1988, MICAs were younger and more likely to be minorities than other VA psychiatric patients. On average MICAs had 1.6 episodes of treatment per year and a total of 36.0 days in the hospital per year as compared to 1.6 episodes of treatment and 76.9 total hospital days per year for psychiatric patients without substance abuse diagnoses or treatment. *Conclusions:* MICAs are a growing population among psychiatric inpatients. Although their numbers are growing they have shorter lengths of stay and consume fewer days of care per year than other psychiatric patients.

NR290 Tuesday May 14, 12 noon-2:00 p.m.

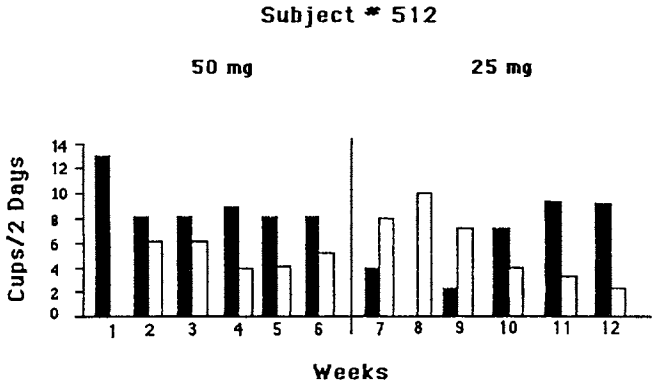
Caffeine Dependence Among Cola Drinkers

John R. Hughes, M.D., Psychiatry, University of VT, HBPL 38 Fletcher Pl. Ira Allen, Burlington, VT 05401; Alison H. Oliveto, Ph.D., William Valliere, B.A., Warren K. Bickel, Ph.D., Stephen T. Higgins, Ph.D.

Summary:

Recent studies by ourselves and others have established that some coffee drinkers reliably self-administer caffeinated coffee in preference to noncaffeinated coffee. The present study attempted to extend these findings to soda drinkers. Caffeinated cola drinkers (24-100 oz/day) were assigned to 50 mg/12 oz of caffeinated cola (the usual dose in colas) and 25 mg/12 oz caffeinated cola conditions in a randomized, double-blind crossover design. Each condition consisted of six independent weekly trials in which each subject had concurrent access to the caffeinated cola (i.e., noncaffeinated cola to which we added caffeine) and a noncaffeinated cola. Thus far, three of seven subjects consistently self-administered the 50 mg sodas in preference to the noncaffeinated sodas (e.g., on five or six of the six trials) and two of eight subjects

consistently self-administered the 25 mg soda ($p < .05$ for individual subjects). Sample results are shown below. These results indicate some cola drinkers use cola for the effects of caffeine.



NR291 Tuesday May 14, 12 noon-2:00 p.m.

Substance Dependence in Psychiatric Patients

Norman S. Miller, M.D., Psychiatry, NYH-WD Cornell, 21 Bloomingdale Road, White Plains, NY 10605; Richard K. Ries, M.D.

Summary:

The subjects for this study were taken randomly from two general acute psychiatric units that are closed voluntary wards. The units do not accept any patients solely for substance abuse treatment or withdrawal. All patients must have a psychiatric condition or complaint which necessitates acute admission or referral for psychiatric diagnostic assessment and treatment. Examination of a sample of 100 consecutive discharges from two general psychiatric units (50 from each) showed that *DSM-III-R* clinical concurrent and longitudinal diagnoses represented in the group include: Axis I: adjustment disorder, depressed 47 percent; major depression 30 percent; dysthymia 5 percent; panic disorder 1 percent; bipolar 20 percent; schizophrenia or other psychoses 40 percent; (more than one diagnosis was possible). Axis II: personality disorder diagnoses were given to 30 percent of the patients and included borderline 50 percent, antisocial 25 percent, narcissistic 15 percent, and other personality disorders 10 percent. The diagnoses are not broken down to primary or secondary; that is, whether the substance dependence came before or after the psychiatric diagnosis. All patients with an Axis II diagnosis also received an Axis I diagnosis. Seventy-five percent of the Axis I and Axis II psychiatric diagnoses had a concomitant Axis I drug and/or alcohol dependence diagnosis. Of these, 80 percent are multiple drug and alcohol dependence diagnoses. According to the following: 80 percent alcohol dependence, 60 percent cannabis dependence, 40 percent cocaine dependence, 30 percent benzodiazepines, 20 percent others.

NR292 Tuesday May 14, 12 noon-2:00 p.m.

Substance Abuse in HIV Infected Males

Patricia Rosenberger, Ph.D., Psychiatry, Ohio State University, 151 Upham Hall 473 W 12th Avenue, Columbus, OH 43210; Robert A. Bornstein, Ph.D, Henry A. Nasrallah, M.D., Michael F. Para, M.D., Robert J. Fass, M.D., Robert R. Rice, Jr., Ph.D.

Summary:

Objective: The present study explored aspects of substance abuse in two groups of HIV infected homosexual males; group 1) males with HIV+ asymptomatic diagnoses (N=84), and group 2) males with ARC/AIDS diagnoses (N=48).

Method: The men participated in structured diagnostic interviews; substance use disorder diagnoses were made using *DSM-III-R* criteria.

Results/Discussion: Alcohol use disorder was the most common diagnosis, with 65 percent of group 1 and 57 percent of group 2 reporting lifetime episodes, including 4 percent of both groups reporting current episodes. No significant difference was found between lifetime highest weekly average of ethanol intake. However, current amount of average weekly ethanol intake was significantly different between the two groups (144 grams, group 1; 67 grams, group 2, $p = .05$) indicating a difference in current use. Drug use disorder diagnoses were also prevalent. Lifetime diagnoses were made in 57 percent of group 1 and 66 percent of group 2 with 11 percent and 7 percent of groups 1 and 2, respectively, meeting criteria for current episodes. The most common diagnosis was cannabis use disorder. No significant differences in rate of drug use disorder were found across all drug categories with the exception of past cocaine use disorder (16 percent group 1; 4 percent group 2, $p = .05$). Group patterns in substance use, examining past versus present use will be discussed.

NR293 Tuesday May 14, 12 noon-2:00 p.m.

Medical Student Substance Use/Parental Alcohol Use

Lon R. Hays, M.D., Psychiatry, Univ of Kentucky, Annex of Kentucky, Lexington, KY 40536; David W. Metzler, M.D.

Summary:

Numerous studies have reported a high incidence of substance abuse by medical students. Other reports have focused on the higher risk of physicians for developing drug or alcohol abuse or dependence than for others with similar educational backgrounds. At the University of Kentucky, students in all four years of medical school were given a questionnaire to elicit information concerning demographic characteristics, past or present substance use, alcohol use by the parents, and use of psychiatric services available for medical students. Although the questionnaires were anonymous, students used code numbers which would allow the investigators to follow them through subsequent years of medical school in this longitudinal study. The survey revealed the following percentages of drug use during their lifetime: Alcohol, 95.5 percent; Caffeine, 88.9 percent; marijuana, 52.5 percent; cigarettes, 31.8 percent and cocaine, 19.2 percent. At least one parent was reported to have a drinking problem by 16.7 percent (compared with 14 percent of the general population). Of the responders, 12.6 percent reported utilizing the psychiatric services available to medical students. As this longitudinal study continues, it is hoped more light will be shed on patterns of substance use by medical students, medical students as children of alcoholics,and perhaps the need for curriculum redesign and program development.

NR294 Tuesday May 14, 12 noon-2:00 p.m.

Subpopulations of Substance Abusers: A New Concept

Nathaniel T. Marvel, M.D., Psychiatry, VA Medical Center, 3200 Vine Street, Cincinnati, OH 45220; Van R. Silka, M.D., Thor Tangvald, IV, M.D., James B. Shackson, M.D., Ibrahim Gunay, M.D.

Summary:

Thirty-seven substance dependent patients not exclusively dependent on alcohol (NDA) were compared with 35 exclusively alcohol dependent patients (EA) in their detoxifications at the same VA Hospital. Chart reviews were performed for a two-year post-admission course. While there was a significant difference in PRN use in recidivist (R) EA patients vs nonrecidivist (NR) EA patients, no differences were found in the NDA population. The NR-EA patients also had a significantly lower rate of using substances on the morning of admission than their NR-NDA counterparts (23 percent vs 42 percent), both being lower than their respective R groups

at 56 percent each. A significantly lower recidivism rate (26 percent vs 46 percent) and AMA rate (0 percent vs 22 percent) were found for the EA vs NDA group. The fact that the predictors for the EA population were not significant for the NDA population, suggests the heterogeneity of the NDA group precludes the application of predictors significant in the EA group. Current literature does not reflect the differences between these groups of psychoactive substance dependent patients, yet the information and operation of effective treatment programs must take this into account. EA patients PRN consumption was found to be a predictor of recidivism, but those criteria were not predictive for NDA patients.

NR295 Tuesday May 14, 12 noon-2:00 p.m.

Geriatric Substance Abusers: Erroneous Assumptions

Nathaniel T. Marvel, M.D., Psychiatry, VA Medical Center, 3200 Vine Street, Cincinnati, OH 45220; James B. Shackson, M.D., Thor Tangvald, IV, M.D., Van R. Silka, M.D., Ibrahim Gunay, M.D.

Summary:

A series of 60 patients ≥55, consecutively admitted to a VA detoxification unit was studied. Previous studies of geriatric substance abuse dependent patients use cut off ages of ≥60, 65, or 70. There is no consistent rationale for these age parameters in the literature other than convention. The ages of all patients admitted to our unit were bi-modal in distribution, with peaks at 35 and 55 years. We found no significant difference in the pattern, years, or age of onset of substance use between patients aged 35-59 and those ≥60. Geriatric substance abuse literature describes two patterns of substance dependency: early-onset and late-onset (>40 years old), with the latter being predominant. While this may be true in general, our patients aged ≥55 have abused substances an average of 34.7 years with the average of onset being 26. Fifty-three (89 percent) had been abusing ≥10 years, and 50 (83 percent) for ≥20 years. Our study suggests that the cutoff age of ≥60 for geriatric substance dependent patients is both arbitrary and incorrect. Furthermore, while studies reflect a predominance of late onset abusers, this is an incorrect assumption in the inpatient setting. In light of the above, those treating geriatric substance dependent patients need to critically evaluate those hypotheses upon which their program is based.

NR296 Tuesday May 14, 12 noon-2:00 p.m.

Acetorphan Blocks Opiate Withdrawal Symptoms

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Summary:

In a double-blind trial versus clonidine, acetorphan, an enkephalinase (EC 3.4.24.11) inhibitor, significantly reduced objective signs and subjective symptoms of opiate withdrawal in ten addicts studied over five days in a hospital setting. On several objective signs, the antiwithdrawal activity of acetorphan was more marked than that of clonidine, studied in nine patients, whereas the two drugs exhibited a similar efficacy on subjective components of withdrawal. No side effect was recorded with acetorphan. The antiwithdrawal activity of acetorphan presumably derives from the protection of endogenous enkephalins from degradation resulting namely in decreased noradrenergic activity and enhanced serotoninergic activity in brain. Enkephalinase inhibition might constitute a novel therapeutic approach to the opiate abstinence syndrome.

NR297 Tuesday May 14, 12 noon-2:00 p.m.

Risk for Alcoholism in Relatives of Drug Addicts

Leonard Handelsman, M.D., Psychiatry, VA Medical Center, 130 West Kingsbridge Road, Bronx, NY 10468; Marc Branchey, M.D., Jeremy Silverman, Ph.D., Laure Buydens-Branchy, M.D., Karen Holloway, M.D., David P. Bernstein, Ph.D.

Summary:

We studied the morbidity risks for alcoholism and addictions in the first degree relatives of male addicts with or without alcoholism. Of the 71 addicts (all of whom were cocaine dependent), 40 (56.3 percent) had a history of alcoholism, and 37 (59.1 percent) had a history of opioid dependence. Twenty-two patients (30.1 percent) also met criteria for a lifetime diagnosis of a major psychiatric disorder. Significant increases in morbidity risks for alcoholism were found among male relatives of cocaine addicts with co-morbid alcohol dependence when compared with relatives of cocaine addicts with no alcohol co-morbidity. Among fathers, risks were .69 vs. .32 ($z = 2.98$, $p < .003$), while among brothers, risks were .38 vs. .15 ($z = 2.35$, $p < .03$). Significantly increased risks were also observed in male relatives when probands with a psychiatric diagnosis were excluded from the analyses. Co-morbid opioid dependence was not related to increased risk for alcohol or drug abuse in relatives. Whether this increased risk for alcoholism in relatives of alcoholic drug addicts is the expression of a specific vulnerability to the development of alcoholism or represents the transmission of a less specific trait could not be ascertained in this study.

NR298 Tuesday May 14, 12 noon-2:00 p.m.

Waiting for Drug Treatment: A Naturalistic Study

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Summary:

Little is known about the behavior and treatment response of drug addicts on waiting lists for inpatient treatment. A total of 88 consecutively presenting male cocaine dependent veterans were enrolled in a two-week waiting list program prior to admission to a detox ward. Two to three days after initial presentation, they were screened medically and psychiatrically. Amantadine 200 mg qd was offered; disulfiram 250 mg qd was also offered when alcohol use was believed to trigger cocaine use. Patients were asked to visit the clinic 5x/wk to complete a drug use and craving form. Of the 88 patients, 40 received amantadine, and additional six patients were treated with both medication, and 42 patients received no medication. The medicated group used less daily cocaine than the group that refused medication ($\$4.90 \pm 9.30$ vs. $\$15.60 \pm 26.5$, $t = 2.35$, $p < .03$). There was no difference in craving levels between the groups. The medicated group demonstrated a modest increase in retention compared to the non-medicated group (13.0 ± 2.9 vs. 10.7 ± 5.4, $t = -2.48$, $p < .02$). Neither self-selection of medication nor the differential response of the medicated patients was predicted by demographic variables or drug history. There were no untoward effects of medication.

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ADHD in Adult Opiate Dependent Outpatients

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Summary:

INTRODUCTION: ADHD has been often related to alcoholism, antisocial P.D. and schizophrenia. Its relationship to opiate dependency has been studied by few authors.

OBJECTIVES: To determine adult ADHD prevalence and its clinical correlations in a severe opiate dependent outpatient population.

METHOD: 104 adult subjects were evaluated by a senior psychiatrist to assess: previous and present history of ADHD. Instruments used: Research Diagnostic Criteria for Axis I and *DSM-III-R* for Axis I and Axis II diagnosis. Utah University Criteria for Adult ADHD and the Addiction Severity Index (ASI)

RESULTS: 1. High prevalence of Adult ADHD: 44.2 percent. 2. Adult ADHD patients showed the following significant data (compared to those not Adult ADHD): a) Lower school achievement ($p<0.01$) b) Higher unemployment rate ($p<0.03$). c) More family history of opiate dependency ($p<0.009$) and delinquency ($p<0.02$). d) More learning disabilities ($p<0.005$). e) Higher rate of previous conduct disorders ($p<0.001$). f) Increased rate of medical pathology ($p<0.01$) and more HIV positives ($p<0.003$). g) More delictive acts ($p<0.001$) longer imprisonment periods. h) Higher rate of schizophrenia ($p<0.03$) and alcohol dependency and antisocial ($p<0.001$).

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Nasal Naloxone: A New Approach to Detect Opiate Dependence

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Summary:

Until now naloxone hydrochloride, was used intravenously, intramuscularly, conjunctively, or subcutaneously as a diagnostic tool for opiate dependence. There was no alternative route of administering naloxone in humans, which provided the same benefits as intravenous application, e.g. rapid onset, high bioavailability, short duration of action, without having the drawback of the risks associated with vessel puncture. In an open clinical trail with a cross-over design, naloxone was administered randomized twice (IV/nasal and IM/nasal) in 18 opiate dependent patients. Naloxone blood levels were taken and measured by means of HPLC. Withdrawal distress was recorded, and pupillary response was measured, pulse rate and blood pressure were obtained. As significant increase in withdrawal distress and in pupillary dilatation was observed after nasal administration of 1mg (1mg/400 ul) naloxone (CuraMed^{R}) in all subjects, and did not differ from the IV route. Both (IV and nasal) differed significantly from IM response. It can be concluded that the nasal route for the administration of naloxone is as effective as the parenteral route. This test is sensitive to identify the physically dependent opiate user and might have further implications for emergency medicine and for withdrawal treatment.

NR301 Tuesday May 14, 12 noon-2:00 p.m.

Short-Term Hospital Course of Personality Disorder

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Summary:

"Regression," (extreme dependency, negativism, withdrawal, and aggression) has been well described in patients with borderline personality disorders (BPD) following admission to inpatient psychiatric units. Despite much consensus, a number of issues remain unanswered: is regression an invariable phase of hospitalization, is it specific to borderline personality disorder, who is most vulnerable, and does it predictably remit? To date, 26 subjects diagnosed using the SCID-II completed baseline self-reports for suicidality, depression, affective intensity, hostility, and other psychiatric symptoms. Three times per week beginning one to two days following admission, subjects were administered a self-report instrument and a brief semi-structured interview to assess the presence and severity of behaviors and feelings associated with BPD and regression. Of the 26, 19 completed the study. Fifteen met criteria for BPD and four met criteria for another personality disorder (NBPD). Our preliminary data suggest that the BPD group were more severely ill (as defined by higher ratings of self-reports) on admission and remained so throughout hospitalization. The pattern of symptomatic improvement was not significantly different between the two groups, nor was a clear pattern of regression noted, although with a greater sample size, we may be able to identify BPD patients at higher risk to regress following admission.

NR302 Tuesday May 14, 12 noon-2:00 p.m.

Lack of Efficacy of Buspirone in Borderline Personality Disorder

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Summary:

The purpose of this study was to assess the efficacy of a serotonergic anxiolytic medication, buspirone, in the treatment of borderline personality disorder (BPD). Forty subjects meeting *DSM-III-R* criteria for BPD were treated with either buspirone or placebo using a randomized double-blind protocol. All subjects also received eight sessions of weekly dynamic supportive psychotherapy. Preliminary data analysis revealed that buspirone was no more effective than placebo over time for the treatment of BPD. Contrary to what was expected, the buspirone group did less well than the placebo group on certain outcome scales and also had more dropouts than placebo group. We conclude that buspirone does not appear to be an effective treatment for this disorder.

NR303 Tuesday May 14, 12 noon-2:00 p.m.

Multiple Regression of Outcome in BPD and Narcissistic Personality Disorder

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Summary:

Long-term retrospective follow-up studies by Plakun (1991, in press) and McGlashan (1986) have studied outcome prediction in BPD. McGlashan has developed two prognostic scales for borderlines based on the Chestnut Lodge follow-up sample. Last year Aronoff and Plakun presented results of a correlation analysis testing the predictive value of McGlashan's scales on 33 BPD patients from the Riggs follow-up sample in an oral slide new research presentation. The current study extends that work, using a multiple regression analysis to extract the best predictors of outcome from the McGlashan prognostic scales as well as from among the Riggs predictors. Outcome was assessed along seven independent dimensions. For BPD, a core group of four predictors emerged, three from the McGlashan scales and one from the Riggs predictors (p ranges from .001 to .04). The three McGlashan predictors of good outcome were high IQ, the absence of depressed thinking, and a high quality of social relations. The Riggs predictor was the absence of a parental history of divorce. The BPD predictors were also tested on a sample of 16 narcissistic (NPD) patients. In NPD two items from the McGlashan scale were predictive of good

outcome, the absence of affective instability and of a tendency toward devaluation ($p = .008$ and .02, respectively). This lends further credence to the view of NPD and BPD as separate clinical entities.

NR304 Tuesday May 14, 12 noon-2:00 p.m.

Personality Disorder Overlap in a Community Survey

David P. Bernstein, Ph.D., Psychiatry, Mt. Sinai Hospital, 130 West Kingsbridge Road, Bronx, NY 10468; Patricia Cohen, Ph.D., Mary Schwab-Stone, M.D., C. Noemi Velez, Ph.D, Larry J. Siever, M.D., Lillian T. Shinsato, B.A.

Summary:

This study is the first to estimate Axis II comorbidity in a nonpatient sample that is representative of the general population. A stratified random sample of 776 children and adolescents aged 11 to 21 years was selected from two New York counties, and given a battery of structured interviews and self-report questionnaires, including the Diagnostic Interview Schedule for Children (DISC) and a modified form of the Personality Diagnostic Questionnaire (PDQ). Scales assessing the *DSM-III-R* personality disorders (PDs) were developed by matching interview and questionnaire items to *DSM-III-R* Axis II criteria, based on content validity; items were assigned exclusively to each PD scale, to minimize artifactual diagnostic overlap. Fifty percent of subjects with Axis II disorders received more than one Axis II diagnosis. Extensive overlap was found between many specific PDs, as indicated by conditional probabilities and risk ratios. Among the highest rates of comorbidity were: schizotypal with borderline, paranoid, and avoidant PDs; and narcissistic with histrionic and borderline PDs. Schizoid PD displayed low rates of overlap with other Axis II disorders. These findings suggest that extensive overlap among PDs is not limited to clinical settings, and supports dimensional approaches to PD assessment.

NR305 Tuesday May 14, 12 noon-2:00 p.m.

Characteristics of Autistic Children

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Summary:

The present study describes the characteristics of subjects that were identified in the course of a recent meta-analysis of the literature concerning the treatment of autism. The study focused on the children treated within single subject designs, thus allowing individual characteristics to be identified. The meta-analysis identified 329 individuals identified as "autistic" in the literature.

Results indicated that sex ratios of autistic subjects in the autism literature were almost identical to those found in the UCLA-Utah epidemiologic investigation showing overrepresentation of males; approximately 80 percent. However, children in the treatment literature had lower IQ scores than in the random sample obtained in the UCLA Utah study. The percentage of symptoms reported in the autism literature were then compared to symptoms reported in a study of *DSM-III-R* criteria for autism by Hertzig, Snow, New, and Shapiro (1990). Easily identifiable characteristics such as stereotyped behavior were equally prevalent in the two samples of autistic children. However, overrepresented in the treatment literature were reports of children without functional language. Underrepresented were reports of echolalia, oddities of speech production, insistence on sameness, social withdrawal, and gaze disturbance. Finally, implications for understanding the treatment of autism literature are discussed.

NR306 Tuesday May 14, 12 noon-2:00 p.m.

Pet and Personality Disorders

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Summary:

This study used positron emission tomography (PET) to examine cerebral metabolic rate of glucose (CMRg) in patients with *DSM-III-R* diagnoses of personality disorder. Within this series, there were three subgroups: borderline ($N = 6$), antisocial ($N = 8$), and other personality disorders ($N = 3$). Patients were administered an aggression rating scale, previously reported to inversely correlate with cerebrospinal fluid 5H1AA.

In the current study, global CMRg correlated inversely with rank on this aggression scale ($p < .05$). This global correlation was also significant in one of the five planes ($p < .02$ for the E plane). Using absolute scale values, inverse correlations were significant in the following E place regions: anterior medial frontal ($p < .02$), right anterior frontal ($p < .04$), left anterior frontal ($p < .04$), and right temporal ($p < .02$).

When each of the diagnostic groups was compared to a normal control group ($N = 43$), only the borderline group showed significant differences in CMRg. In this group, five regional CMRg's were significantly decreased in the frontal and parietal lobes of the B plane ($P < .02$ to .05, two tailed t) and three regional CMRg's were significantly increased in the frontal lobe of the D plane ($p < .01$ to .05, two tailed t).

To the authors' knowledge, these are the first findings to relate measures of impulse control to specific regions of brain metabolism.

NR307 Tuesday May 14, 12 noon-2:00 p.m.

Reliability Study of the Munich Diagnostic Checklists for the DSM-III-R Personality Disorders

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Summary:

Diagnostic checklists for the assessment of *DSM-III-R* Axis I diagnoses have been proven to be a reliable and feasible instrument in research and routine clinical care. A recently developed diagnostic checklist for the assessment of the *DSM-III-R* Personality Disorders (MDCL-P) has been tested for reliability in a test-retest design. Three out of four interviewers were not involved in the development of the MCDL-P and had never been engaged in personality research as well as in research with regard to diagnostic issues. Sixty patients were interviewed twice within a period of four days by two different psychiatrists. The average duration of the interview was 36 minutes. Forty-seven percent of the patients received a diagnosis of at least one personality disorder. The Kappa value concerning the distinction personality disorder as opposed to no personality disorder was 0.62. The range of Kappa values of personality disorders which were at least diagnosed five times was from 0.35 to 0.73. Furthermore, a comparison with a self-rating questionnaire also assessing the *DSM-III-R* personality disorders (PDQ-R) revealed considerable differences between these two instruments. An English version of the MDCL-P already exists.

NR308 Tuesday May 14, 12 noon-2:00 p.m.

Axis II Features and Social Impairment

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Summary:

DSM-III-R Axis II disorders were introduced in 1980 as personality features sufficiently maladaptive as to constitute mental disorders, i.e., conferring significant subjective distress and/or social and vocational impairment. Since many referred Axis II subjects have co-existent Axis I disorder at first treatment contact, the examination of the subjective and social correlates of Axis II disorders is confounded. We report here the rates of Axis II features and disorder in a sample of young adults (N = 182) unselected for treatment. These subjects are drawn from Sample A of the New York High-Risk Project, an ongoing longitudinal family study. Axis II assessments were made on the offspring in adulthood using the Personality Disorder Examination (PDE, Loranger et al., 1985). Results of an analysis of Global Assessment of Functioning (GAS scores) and the raw dimensional scores for Axis II categories indicate significant correlations between the expression of features and disorders from the odd cluster and GAS dysfunction for young adult offspring of parent index cases with schizophrenic disorder and no disorder (normal control parents). Features and disorders from the odd cluster, dramatic cluster, and the fearful cluster are significantly related to GAS dysfunction for young adult offspring of parental index cases with affective disorder.

NR309 Tuesday May 14, 12 noon-2:00 p.m.

Borderline Patients on Maintenance Fluoxetine

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Summary:

Several groups have reported preliminary data on the short-term benefits of fluoxetine in *DSM-III-R* borderline personality disorder (BPD). The effects of chronic treatment, however, may be more important both clinically and theoretically. Yet there appears to be no study to date reporting the chronic effects of any pharmacologic agent in PD.

This study is a two-year follow-up of BPD patients originally reported to respond acutely to fluoxetine (Norden, 1989). All 12 patients took fluoxetine over a period of at least one year, and ten continued over two years. Patients were rated on a seven-point global rating scale (following Cowdry and Gardner, 1988) and at endpoint all had improved, and all but one were assessed as much or very much improved. In the second year of fluoxetine treatment, most patients were able to be seen every four to eight weeks, in contrast to the weekly frequency typically required in the year preceding the trial.

All but one patient discontinued fluoxetine against advise at some point and the usual result was deterioration within five days and prompt recovery upon reinstatement. Treatment was generally very well tolerated, but dosage titration was critical in some patients. Daily doses ranged from 3 mg. to 80 mg. with a mean of 36 mg.

NR310 Tuesday May 14, 12 noon-2:00 p.m.

Elevation in Pain Thresholds in Bulimia Nervosa

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Summary:

Converging lines of evidence suggest that some component of antinociception and food intake may be subserved by common neurochemical/anatomical mechanisms. In particular, short-term satiety is known to involve peripheral responses to the ingestion of a meal which is mediated in part by afferent vagal fibers. The vagus nerve has also been implicated in mediating a portion of the analgesic response to peripherally administered opioids. Other neurotransmitters, e.g. CCK, are thought to function in both short term satiety and nociception. Thus, we hypothesize that bulimia nervosa involves disregulation of short-term satiety mechanisms that may also be accompanied by alterations in nociceptive processing.

We have investigated nociceptive and tactile responsivity in subjects fulfilling DSM-III-R criteria for either bulimia nervosa (n = 27), major depression (n = 10) and in normal volunteers (n = 31). Tactile thresholds were not found to differ between the groups (t = .237). Nociceptive thresholds were determined using a Ugo Basile pressure analgesiometer. Both pain detection (DT) and pain tolerance (TT) thresholds were found to be consistently elevated in bulimic subjects when compared to normal controls (p .004, DT; p .006, TT). In contrast, the depressed subjects did not show an increase in DT or TT compared to normal controls. In fact, there was an non-significant trend toward hyperalgesia.

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Long-Term Outcome in Bulimia Nervosa

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Summary:

Seventy subjects who completed a controlled treatment study for bulimia nervosa were interviewed 16 to 35 months after completion of the 12-week treatment phase. Of those, 51 (73 percent) were responders having had one or less binge eating and/or purging episode per week during the prior month. Subjects were subsequently categorized as responders (n = 43) and nonresponders (n = 27) to initial treatment, and further subdivided according to the course of their eating symptoms during the follow-up period. Twenty-one of the treatment responders maintained improvement, whereas 22 did not. Seventy-three percent of those who relapsed did so during the first three months of the follow-up period, supporting previous findings that relapse is highest early after treatment completion. However, 69 percent of these early relapsers regained control over their eating and were responders at the time of the follow-up interview. Of the treatment nonresponders, 15 recovered during the follow-up period and were responders at the time of the follow-up interview, whereas 12 remained chronically symptomatic. In this paper we will discuss pre- and post-treatment behavioral variables that predict the long-term outcome. A preliminary analysis revealed that permanent improvement without relapse in treatment responders was associated with a lower binge eating and vomiting frequency at baseline, an earlier response to initial treatment, and a complete cessation of eating symptoms during the last two weeks of treatment. In treatment nonresponders long-term success ("late" recovery) was also associated with a lower severity of eating pathology at baseline.

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Disordered Eating in Girls with Insulin Dependent Diabetes Mellitus

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Summary:

A growing literature describes patients with IDDM, typically females, who exhibit clinically significant symptoms of disordered eating. To date, epidemiological studies have produced conflicting results regarding the prevalence of dieting, binging, and purging in diabetic patients. Discrepant findings are largely due to methodological differences. Further, prior studies have used assessment instruments that do not permit a clear distinction between restrictive dieting for weight control and adherence to the diabetes regimen. This study sought to establish prevalence rates for eating disorders symptoms using state-of-the-art assessment methods. We evaluated 96 girls (ages eight to 18), recruited at the Yale Pediatric Endocrine clinic (IDDM subjects), and in local schools (age matched controls, response rates: 94 percent and 81 percent respectively.) Subjects participated in the Eating Disorders Examination interview and completed the Eating Disorders Inventory. Diabetic girls reported significantly more drive for thinness, shame about their bodies, anxiety about eating in public, and eating in secret, than controls. Interview responses suggest that these concerns arise in the context of diabetes and its management. The next step in our research will be to examine prospectively whether the presence of these symptoms put diabetic girls at greater risk for the development of more extensive eating pathology.

NR313 Tuesday May 14, 12 noon-2:00 p.m.

Resting Metabolic Rate in Bulimia Nervosa

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Summary:

Both dieters and bulimics have lowered metabolic rates, but bulimics are often tested during periods of abstinence in a hospital. We measured resting metabolic rate (RMR) by indirect calorimetry in 12 controls and 12 normal weight bulimic women during a week of bingeing and vomiting and during a period of abstinence in order to determine whether RMR normalizes during periods of active bingeing and vomiting. Thyroid hormone (T3), a major determinant of RMR was also measured. Weight of the bulimics was held stable during abstinence. RMR was significantly higher in the bulimics during the phase of active bingeing and vomiting compared to the abstinent phase. (1071 ± 68 kcal/day vs. 874 ± 32 kcal/day, $p = .003$). RMR of normals was 1002 ± 47 kcal/day which was significantly higher than abstinent bulimics ($p = .03$), but not different from active bulimics ($p = .41$). Similarly, T3 was higher during the active phase compared to abstinence (106 ± 8 ng/dl vs. 82 ± 5 ng/dl, $p = .02$). T3 in normals was 118 ± 6 ng/dl which was significantly higher than abstinent bulimics ($p = .0001$), but not different from normals ($p = .2$). In summary, RMR and T3 are elevated in bulimics during the active phase of bingeing and vomiting which may serve to counteract lowered RMR and T3 induced by dieting.

NR314 Tuesday May 14, 12 noon-2:00 p.m.

Four Treatments of Bulimia Nervosa

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Summary:

Behavioral treatment of bulimia nervosa (BN) consists primarily of cognitive therapy aimed at countering the dysfunctional thoughts that prompt bulimic behavior, and nutritional counseling aimed at correcting the chaotic food intake that leads to semi-starvation. Our study seeks to determine if a combined cognitive and nutritional approach is more effective than each component used alone, or attendance at a support group. Female patients fulfilling *DSM-III-R* criteria for BN were randomly assigned, stratified according to presence or absence of major depression, to one of four 14-week outpatient treatments: (1) Nutritional counseling ($N = 17$); (2) Cognitive therapy ($N = 21$); (3) Combined nutritional and cognitive treatment ($N = 15$); and (4) Support group attendance ($N = 18$). The first three treatments were conducted according to written manuals, the fourth, conducted by "lay" facilitators, had no fixed agenda. Assessments were made "blindly" at baseline and Week 6, 10, and 14. The superior efficacy of the combined treatment in decreasing bulimic episodes is indicated by: (1) an intent-to-treat analysis using a repeated measure analysis of variance with depression and baseline bulimic scores as covariates ($F = 4.96$; $df = 3$, $p = 0.0037$); (2) proportion of patients achieving abstinence (Fisher's exact test, $p = 0.019$, $df = 3$); (3) repeated measure analysis of variance with depression and baseline bulimic episodes as covariates between individual treatments found combined treatment to be superior to nutritional counseling ($F = 8.21$, $df = 1$, $p = 0.0078$) and support group ($F = 9.48$, $df = 1$, $p = 0.0045$), but not statistically different from cognitive therapy alone.

NR315 Tuesday May 14, 12 noon-2:00 p.m.

Bulimia Nervosa: Fluoxetine and Psychological Change

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Summary:

Numerous double-blind, placebo-controlled studies of antidepressants for bulimia nervosa have been reported. While they demonstrate antibulimic efficacy, they have been criticized for failure to evaluate change in associated psychological disturbance. Even psychotherapy studies have reported psychological change in ways that limit the clinical meaning of the data. An idiographic approach to the determination of clinically significant change (CSC) on measures of psychological function was applied to the largest reported drug trial for bulimia nervosa: the multicentre double-blind, placebo-controlled trial of fluoxetine at doses of 20 mg or 60 mg. Over the course of eight weeks of treatment, CSC in attitudes reflected by the Eating Disorder Inventory (EDI) and Eating Attitudes Test (EAT) occurred for some subjects and the prevalence of these changes was significantly associated with treatment condition ($p < .03$). Across the measures of associated attitudes and psychological function, CSC occurred among 23 percent - 51 percent of subjects who were treated with 60 mg of fluoxetine. The occurrence of CSC in all subjects was also significantly related to the degree of control of binge eating ($p < .014$), with subjects who had more control over their symptoms being more likely to display CSC in attitudes and psychological functioning. The findings will be compared to the CSC measured in other treatment approaches. The data contradict the idea that the pharmacotherapy of bulimia nervosa is irrelevant to its psychological disturbances.

NR316 Tuesday May 14, 12 noon-2:00 p.m.

Continued Open Trial of Fluoxetine in Anorexia

Theodore E. Weltzin, M.D., Psychiatry, Univ of Pittsburgh, RM E 735 3811 O'Hara Street, Pittsburgh, PA 15213; L.K. George Hsu, M.D., Walter H. Kaye, M.D.

Summary:

We extend and confirm an earlier report on the usefulness of an open trial of fluoxetine in patients with anorexia nervosa. We have now administered fluoxetine to 31 anorexia nervosa patients for 11 ± 6 months. The majority of anorexics were started on fluox-

etine after inpatient weight restoration and then discharged from the hospital and followed as outpatients. On fluoxetine, 29 of the 31 patients maintained their weight at or above 85 percent ABW (97 ± 13 percent ABW for the group). We judged response as good in ten partial in 17, and poor in four anorexics as measured by improvements in eating behavior, mood, and obsessional symptoms. Significantly more of the anorexics who had a good outcome were restricting anorexics (nine of 14 pure restrictors) compared to anorexics who binged and/or purged (one of 17).

Eighteen anorexics (n = 7 with good response and n = 11 with fair or poor response) were assessed at baseline (4 ± 6 days prior to treatment) and again while on fluoxetine for 145 ± 116 days. Those with a good response showed a significant reduction ($p < .05$) in obsessionality, core anorexic symptoms, depression, and anxiety. In comparison, the partial and poor response groups showed only a trend ($p < .1$) towards a reduction in core anorexic symptoms and were significantly more depressed at baseline.

In summary, this open trial suggests that fluoxetine helps most anorexics maintain weight. It is most effective in restrictor anorexics and, in that group, it not only helps weight maintenance but is associated with a global improvement in symptoms. While subjects in the partial and poor response groups maintained weight, they were more likely to binge or purge and have depression and anxiety. These findings remain preliminary pending a placebo-controlled, double-blind study.

NR317 Tuesday May 14, 12 noon-2:00 p.m.

Prevalence of Mental Disorders in the Morbidly Obese

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Summary:

Morbid obesity, defined as weight at least 100 percent or 100 pounds over ideal body weight, is a risk factor for many life threatening conditions. We systematically evaluated 88 morbidly obese subjects who had presented at a tertiary care center surgery clinic requesting vertical banded gastroplasty. The subjects were predominantly female, of low socioeconomic status, weighed over 300 pounds and had a history of obesity for nearly 20 years. Using the Diagnostic Interview Schedule, we found that the morbidly obese subjects were more likely than community controls to suffer from mood disorders, anxiety disorders, bulimia, and tobacco dependence. Using the Structured Interview for *DSM-III* for Personality Disorders, the obese subjects were also found to be more likely than community controls to meet criteria for one or more personality disorder diagnoses. We conclude that substantial psychopathology exists in morbidly obese persons presenting for gastroplasty. The clinical implications of these findings are discussed.

NR318 Tuesday May 14, 12 noon-2:00 p.m.

Alexithymia and Neuroticism in Anorexia Nervosa

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Summary:

Clinical observations suggest that in addition to high levels of psychoneurotic pathology, patients with anorexia nervosa manifest alexithymic features including difficulty identifying affects and a lack of psychological-mindedness. We report preliminary findings from a study of 48 female outpatients with anorexia nervosa who were assessed for alexithymia with the Toronto Alexithymia Scale (TAS) and for psychoneurotic pathology with the Crown-Crisp Experiential Index (CCEI). Seventy-seven percent of the anorexic patients were alexithymic, compared to 6.7 percent for a control group of normal women matched by age and education. Although the anorexic patients also showed significantly higher levels of neurotic pathology than the control subjects, there was a nonsignificant correlation between the TAS and CCEI ($r = 0.27$, $p > .05$). There were no significant differences in TAS scores between restricting anorexic patients (N = 30) and bulimic anorexic patients (N = 18), and between patients scoring high (≥9) on the CCEI Depression subscale (N = 24) and those scoring low (N = 18). In addition, alexithymia was unrelated to the duration of illness and extent of weight loss. The results suggest an independence of alexithymia and neuroticism, and that alexithymia is neither an adaptation to chronic illness nor an effect of starvation or depression.

NR319 Tuesday May 14, 12 noon-2:00 p.m.

Treatment Response in Obese Binge-Eaters

Detlev O. Nutzinger, M.D., Psychiatric Clinic, Vienna University, Waehringer Guertel 18-20, Vienna A 01090, Austria; Martina de Zwaan, M.D.

Summary:

The overall psychological adjustment of 62 obese females (BMI ≥ 27 kg/m²) was assessed before they entered a weight reduction program comprised of a cognitive behavior therapy and an antidepressant (Fluvoxamine). A rather difficult sample of treatment refractory subjects having in common a long-lasting history of fruitless attempts to lose weight was included into the study. At baseline a Structured Clinical Interview (SCID) for *DSM-III-R* diagnoses, the Diagnostic Survey of Eating Disorders (DSED) for gathering detailed information about subjects' eating behavior, and the Body Distortion Questionnaire (BDQ), a self-rating instrument assessing body image were carried out. In addition, subjects were asked about adverse emotional reactions during previous attempts to lose weight ("Dieting Depression"), as well as during the luteal phase (LLPDD, Late Luteal Phase Dysphoric Disorder). Sixty-eight percent fulfilled criteria for current or past depressive disorder, 39 percent for anxiety disorder or OCD, 42 percent presented a LLPDD, and 79 percent described emotional problems emerging during previous efforts of weight reduction. Twenty-one patients (33.9 percent) reported recurrent binge eating episodes. These subjects did not differ from their non binge eating counterparts with regard to depressive symptomatology, but they reported significantly more body image disturbances. The weight losses of those who completed the study did not differ, but binge eaters were more likely to drop out of treatment. These results suggest that obese subjects, who are refractory to usual weight reduction programs, might exhibit increased psychopathology, or might engage in binge eating behavior on a regular basis, possibly fulfilling criteria for binge eating disorder as proposed for the *DSM-IV*.

NR320 Tuesday May 14, 12 noon-2:00 p.m.

Eating Disorders in Women Who Misuse Alcohol

Robert C. Peveler, M.D., Psychiatry, Oxford University, Warneford Hospital, Oxford, England 0X3 7JX; Amanda Taylor, M.D.

Summary:

It has been suggested that eating disorders and alcohol use disorders co-occur more commonly than expected by chance. Preliminary studies indicate that eating disorders may be over-represented in women being treated for alcohol problems (1,2), but such studies have methodological limitations. Women attending an alcohol treatment unit were interviewed in detail about their eating habits and attitudes using the investigator-based interview, the Eating Disorder Examination (EDE). Fifty-two women aged 17-45 years (90

percent of the available subjects) were interviewed, and *DSM-III-R* diagnostic criteria applied. Three women (6 percent) met criteria for current bulimia nervosa (BN), and another 12 (23 percent) met operational criteria for "eating disorder not otherwise specified" (EDNOS). In a comparison group of 243 women recruited from general practice lists, the corresponding figures were: BN (2 percent) and EDNOS (15 percent). The EDE subscales (which provide continuous measures of eating disorder psychopathology) showed comparable significant differences between the samples. The eating disorders had been detected by the clinical team in only six out of 15 cases. We conclude that eating disorders are overrepresented in women receiving treatment for alcohol problems. Much of this morbidity remains undetected in routine clinical practice.

NR321 Tuesday May 14, 12 noon-2:00 p.m.

Prevalence of Eating Disorders in Diabetics

Robert C. Peveler, M.D., Psychiatry, Oxford University, Warneford Hospital, Oxford, England 0X3 7JX; Christopher Fairburn, M.D.

Summary:

It has been suggested that having diabetes may increase the risk of developing an eating disorder (1), but no previous studies have addressed this question using adequate methods (unbiased patient samples, interview assessment measures, and matched control groups). A representative sample of 175 insulin-dependent diabetic patients, aged 11-25 years, and age- and social class-matched control subjects were recruited, and assessed using a modified version of the Eating Disorder Examination (EDE) interview (2). No difference was found in the prevalence of *DSM-III-R* eating disorders among adult females with or without diabetes. EDE subscale scores did not differ between the samples. Glycaemic control was significantly worse in diabetic patients with disturbed eating habits. Insulin misuse for the purpose of weight and shape control was not restricted to patients with a clinical eating disorder. We conclude that women with diabetes do not exhibit more eating disorder psychopathology than nondiabetic women. A clinically significant disturbance of eating habits and attitudes is present in almost 10 percent of women aged 17-25 years, whether or not they have diabetes. Diabetic patients may omit or reduce their insulin dose to promote weight loss even if they do not have a clinical eating disorder.

NR322 Tuesday May 14, 12 noon-2:00 p.m.

Eating Disorder Pathology in Middle School Pupils

Ann C. Childress, M.D., Psychiatry, Medical Univ of SC., 171 Ashley Avenue, Charleston, SC 29425; Timothy D. Brewerton, M.D., Elizabeth L. Hodges, M.S.W.

Summary:

Bulimia nervosa occurs in approximately 1 percent - 3 percent of high school and college age females, while anorexia nervosa occurs much less frequently. Though eating disorders do occur in childhood, prevalence studies in younger samples are lacking. Therefore, we surveyed 3175 students (1610 females, 1565 males) enrolled in grades 5-8 in five public ($n = 2812$) and four private ($n = 363$) South Carolina middle schools using the Kids' Eating Disorder Survey (KEDS), a newly developed self-report instrument for children. A total of 88.3 percent respondents successfully completed the survey. Over 40 percent of the children reported feeling fat and/or the wish to lose weight. About 12.9 percent were below 85 percent of expected body weight. The following frequencies of weight control behaviors were reported, all of which were significantly greater in girls than boys ($p < 0.05$, Chi-square): dieting (31.4 percent); fasting (8.7 percent); vomiting (4.8 percent), diet pill use (2.4 percent); diuretic use (1.5 percent). Binge eating was reported by 16.2 percent of the sample and was more frequent in boys than girls ($p < 0.0001$). The effects of age, grade, weight, race, and type of school on responses will be presented. Results indicate that many pre-adolescents, especially girls, are overly concerned about appearance and engage in pathologic weight control methods to an alarming degree. The development of primary prevention programs aimed at recognizing suspicious eating behaviors in children is indicated.

NR323 Tuesday May 14, 12 noon-2:00 p.m.

Markers Linked to Eating Symptoms in School Girls

Howard Steiger, Ph.D., Eating Disorders, Douglas Hospital, 6875 LaSalle Blvd, Montreal Verdun PQ, Canada H4H 1R3; Freedom Leung, M.A., Guadalupe Puentes-Newman, M.A., L. Houle, B.A., J. Gulko, M.A.

Summary:

We used multiple markers to identify, among 924 high school girls, those thought to be "at-risk" for an eating disorder (ED). Seventy women with clinical ED's and 328 college females served as reference groups. Markers encompassed (a) the sense of "self", (b) family functioning, and (c) body-image concerns. Also measured were eating attitudes and behaviors, depression, mood lability, impulsivity, hostility, and obsessive-compulsive symptoms. In both nonclinical samples, canonical correlations among the "risk" and "symptom" variables indicated one dimension connecting multiple risk markers to all symptoms, another linking body image concerns to circumscribed eating symptoms alone. Comparisons across girls with different risk profiles also suggested "disturbed" and "intact" subgroups with eating symptoms. Only subjects with the broader risk pattern showed features consistent with clinical spectrum eating problems, according to (a) comparisons on self-reported symptoms across clinical and nonclinical groups, and (b) features detected in interviews in selected students. Findings indicate dimensions that may be useful in isolating subjects with genuine risk of an ED, from among a rather large group that will display benign eating anomalies.

NR324 Tuesday May 14, 3:00 p.m.-5:00 p.m.

The Low Dose DST in PTSD

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Summary:

Studies examining the cortisol response to the standard 1 mg dose of dexamethasone (DEX) in PTSD have all reported a normal cortisol suppression, which is consistent with our previous findings of lower 24-hr urinary cortisol excretion and increased numbers of lymphocyte glucocorticoid receptors (GR) in combat veterans with PTSD. To further characterize HPA dysregulation in PTSD we administered low doses of dexamethasone to combat veterans with PTSD and nonpsychiatric healthy males, in order to test the hypothesis of a "supersuppression" of cortisol to DEX in PTSD. All subjects were tested with both 0.5 mg and 0.25 mg DEX at least one week apart but within a five week period. PTSD patients suppressed cortisol to a greater extent than normals in response to both doses of DEX. The mean $\pm$ SD of the 8:00 a.m. post-DEX cortisol response to the 0.5 mg dose was 1.2 ± 0.5 ug/dl and 3.5 ± 2.9 in PTSD ($n = 8$) and normals ($n = 12$), respectively. Cortisol levels following the 0.25 mg dose were 4.0 ± 1.2 for PTSD and 9.6 ± 4.5 for normals. Cytosolic glucocorticoid receptors were also measured before and after DEX administration. Individuals showing the greatest suppression of cortisol in response to DEX

also showed the greatest reduction in lymphocyte GR following DEX, likely reflecting an enhanced translocation of the GR-DEX complex into the cell nucleus. The data support the hypothesis of an enhanced negative feedback sensitivity of the HPA axis in PTSD.

NR325 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Fluvoxamine, Fluoxetine and Frontal Lobe Function

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Summary:

Recently we reported apathy, indifference, and impulsivity occurring in some patients who received the selective serotonin reuptake blockers fluvoxamine or fluoxetine. These effects clinically resembled a frontal lobe syndrome and were dose dependent. To examine these effects in greater detail, we SPECT scanned six obsessive-compulsive disorder patients when free of medication and again after three to four months on fluoxetine 80 to 100 mg a day. On scan days, patients also underwent neuropsychological tests. As reported previously, regional cerebral blood flow showed a hyperfrontal pattern in drug free OCD patients. On fluoxetine, the hyperfrontality decreased significantly, indicating a lowering of frontal lobe blood flow. On fluoxetine, neuropsychological tests showed a significant decrease in patients' ability to organize material, but no signs of memory impairment. These results also suggest diminished frontal lobe function. Clinically, fluoxetine significantly lowered obsessive-compulsive and anxiety symptoms.

Our findings suggest that some effects of serotonin reuptake blockade, such as the decrease of obsessive-compulsive symptoms and of certain anxiety symptoms may also be attributed to an attenuation of frontal lobe activity. Recently reported disinhibitory effects of serotonin reuptake blocking medications may also be explained by excessive frontal lobe inhibition.

NR326 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Sex Differences in CSF Levels of CRF and TRH

Mark D. Fossey, M.D., Psychiatry, Medical Univ of S.C., 171 Ashley Avenue, Charleston, SC 29425; R. Bruce Lydiard, M.D., Michele T. Laraia, M.S.N., Garth Bissette, Ph.D., Charles B. Nemeroff, M.D., James C. Ballenger, M.D.

Summary:

Given the role that steroid hormones play in the regulation of gene expression and, thus, peptide formation, it is likely that neuropeptide quantities are affected by the sex of the subjects. To explore this hypothesis, CSF was obtained from 35 patients with anxiety disorders (PD and GAD) and 14 normal controls. The male sample consisted of nine normals, seven with GAD, and five with PD. The female sample consisted of five normals, five with GAD, and 18 with PD. ANOVA indicated no significant differences by sex across diagnostic groups. Female subjects had significantly higher CSF levels of CRF compared to males (46.02 ± 11.04 pg/ml vs 40.39 ± 5.90 pg/ml; $t = 2.28$; $p < .05$). In contrast, male subjects had significantly higher CSF levels of TRH compared to females ($2.29 \pm .95$ pg/ml vs $1.78 \pm .73$ pg/ml; $t = 2.02$; $p < .05$). No correlation between CSF CRF and TRH was noted in males; however, a positive correlation between CSF CRF and TRH was noted in females ($r = .46$; $p < .02$). These findings suggest that sex plays a more important role in determining quantities of CRF and TRH in the CSF than diagnosis in this sample. Larger samples might detect differences across diagnostic groups. Future studies examining the function of neuropeptides in neuropsychiatric disorders should take into account these sex differences to assure adequate numbers of sex-matched controls.

NR327 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Disruption of Sensory Gating by Yohimbine in NC's

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Summary:

Previous research using the auditory P50 response in a paired click paradigm has shown that schizophrenics have a chronic inability to regulate sensory stimuli. Other patient populations, including bipolar and PTSD patients, share this deficit. However, their disruption is transitory and reverts to normal with resolution of symptoms. Although amphetamine causes impaired auditory gating in normal subjects, it is unclear whether this is due to increasing CNS norepinephrine or dopamine. This pilot study was designed to assess the effects of a selective increase in central noradrenergic transmission on sensory gating, using yohimbine, a presynaptic alpha-2 adrenergic antagonist. Six normal subjects were studied in a double-blind comparison of yohimbine and placebo. Sensory gating of the P50 wave of the auditory evoked response showed significant disruption with yohimbine during the first 30 minutes post ingestion (CT ration 102.98 percent yohimbine, vs. 33.32 percent placebo), with rapid return to baseline levels. No changes were evident in the amplitude or latency of the P50 wave. The data suggest that increased noradrenergic neurotransmission, which characterizes a variety of psychiatric disorders, including mania and PTSD, may temporarily disrupt patients' ability to regulate sensory input. This mechanism may underlie similarities of symptoms during acute episodes.

NR328 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Buspirone Addiction in Fluvoxamine-Refractory OCD

Christopher J. McDougle, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Wayne K. Goodman, M.D., Lawrence H. Price, M.D., Jacob C. Holzer, M.D., Elinore F. McCance-Katz, M.D., George R. Heninger, M.D.

Summary:

The efficacy of primary treatment of OCD with serotonin (5-HT) reuptake inhibitors such as fluvoxamine (FVX) has been established. For OCD patients resistant to 5-HT reuptake inhibitor therapy, one approach has been to add agents such as tryptophan, fenfluramine, lithium, and buspirone, which may act by enhancing 5-HT neurotransmission, to ongoing treatment with antidepressants. To date, however, no controlled studies documenting the effectiveness of this treatment strategy have been published. This investigation examined the efficacy of adding the 5-HT 1A agonist, buspirone (BUS), to the regimens of OCD patients who were unresponsive to an eight-week trial of FVX. *METHODS:* To date, ten OCD patients (DSM-III-R) have completed a six-week randomized, double-blind placebo (PLA)-controlled trial of BUS addition to ongoing FVX treatment. All patients received and tolerated the maximum recommended doses of both FVX (300 mg/day) and BUS (60 mg/day). Criteria for treatment response were based on Y-BOCS scores and the global improvement item of the CGI. *RESULTS:* Neither active (ACT) BUS addition to FVX ($N = 6$) (-0.3 ± 1.2, $t = 0.7$, $df = 5$, $p < 0.53$) nor PLA BUS addition to FVX ($N = 4$) (-8.0 ± 13.6, $t = 1.2$, $df = 3$, $p < 0.33$) were associated with significant changes in Y-BOCS scores. Student's t-test demonstrated no significant difference between ACT and PLA BUS groups in change scores on the Y-BOCS ($t = 1.4$, $df = 8$, $p < 0.20$). On the basis of treatment response criteria, 0/6 patients who received ACT BUS were responders compared with 1/4 PLA BUS responders. *CONCLUSION:* These preliminary data suggest that BUS addition is not an effective combination strategy for OCD patients who are resistant to primary treatment with FVX, and perhaps other 5-HT

reuptake inhibitors. The continued investigation of other neurochemical systems (e.g., dopamine (DA)) and the interactions between systems (5-HT and DA) seem warranted in patients with OCD. Additional data derived from this ongoing study will be presented.

NR329 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Oral Idazoxan Versus Yohimbine in Healthy Subjects

Christopher J. McDougle, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; John H. Krystal, M.D., Scott W. Woods, M.D., Lawrence H. Price, M.D., Deborah A. Herbst, B.S., George R. Heninger, M.D., Dennis S. Charney, M.D.

Summary:

The primary purpose of this study was to investigate the effects of oral Idazoxan, an alpha-2 adrenoceptor antagonist, on behavior and norepinephrine (NE) turnover in healthy subjects. In addition, the study sought to determine if the biochemical and behavioral effects of Idazoxan are similar to those of the alpha-2 adrenoceptor antagonist yohimbine. *Methods*: Ten healthy male subjects received randomized, double-blind oral administration of placebo, 20 mg, 40 mg, and 80 mg of Idazoxan as well as yohimbine 20 mg, on five separate test days. Blood samples for plasma 3-methoxy-4-hydroxyphenylglycol (MHPG) (ng/mL) and cortisol (ug/dL), vital signs, and behavioral ratings were obtained at baseline and at intervals for up to four hrs following the oral study dose. *Results*: The 20 mg (1.31 ± 0.84, $p < .001$), 40 mg (1.21 ± 0.95, $p < .003$), and 80 mg (2.04 ± 1.34, $p < .002$) doses of Idazoxan resulted in consistent, significant increases in plasma free MHPG. The 20 mg dose of yohimbine also resulted in a significant increase in plasma free MHPG (1.76 ± 1.12, $p < .002$). Plasma cortisol levels were significantly increased following the 80 mg dose of Idazoxan (5.34 ± 7.35, $p < .05$) and following the 20 mg dose of yohimbine (4.61 ± 6.54, $p < .05$). Systolic and diastolic blood pressure (sitting and standing) increased significantly following all three idazoxan doses and following yohimbine. *Conclusion*: The robust increase in plasma MHPG following all three doses of oral Idazoxan demonstrates the Idazoxan increases NE turnover in human subjects. Although Idazoxan and yohimbine may differ in their selectivity for alpha-2 receptor subtypes, this study suggests that neuroendocrine and behavioral responses to these drugs are similar in human subjects. The measurement of the effect of Idazoxan on NE turnover and behavior may provide a means of assessing alpha-2 adrenoceptor function in human subjects.

NR330 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Yohimbine Potentiates Startle Reflex in Humans

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Summary:

Preclinical studies have suggested the acoustic startle reflex (ASR) may be a useful animal model to investigate the neurochemical basis of anxiety and fear states. This work has revealed that the anxiogenic alpha-2 receptor antagonist, yohimbine, increases the amplitude of the ASR in laboratory animals. The present investigation is evaluating the effects of yohimbine on the ASR in healthy subjects and patients with PTSD.

METHOD: 16 subjects (nine Vietnam veterans with PTSD, seven healthy subjects), received IV yohimbine (0.4mg/kg) or saline placebo on two separate days in a randomized double blind placebo control design. A trial of two tone frequencies with varied intensity (90, 96, 102, 108, 114 db) white noise, instantaneous rise time, was delivered binaurally through headphones connected to the San Diego Instruments Startle Machine (EMG-SR). Tones were delivered every 45-60 seconds, for a 30 ms duration, over a period of 15-20 minutes. The startle response was measured as the magnitude of the EMG activity of the blink response.

RESULTS: As previously reported, startle amplitude increased with decibel intensity compared to placebo. Yohimbine markedly increased ASR amplitude at decibel intensities 96 and greater in both the healthy subjects ($df = 4,24$; $f = 3.6$; $p \leq 0.020$ drug x intensity) and PTSD patients ($dr = 4,32$; $f = 2.7$; $p \leq 0.048$ drug x intensity). Preliminary observations suggest a different pattern of ASR response to yohimbine in the two groups with greater yohimbine effects in healthy subjects at lower decibel intensity and in the PTSD patients at higher decibel intensities ($df = 4,56$; $f = 2.5$; $p \leq 0.05$ 3-way ANOVA).

COMMENT: This is the first study in humans demonstrating specific neurochemical modulation of the ASR. Consistent with preclinical studies suggesting ASR as a model of anxiety and supporting the role of noradrenergic hyperactivity in anxiety states. Yohimbine had robust effects on ASR amplitude. Therefore, study of yohimbine induced changes in ASR may be a useful method to examine the neurophysiological and neurochemical modulation of human anxiety.

NR331 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Alprazolam Discontinuation in Panic Disorder

John C. Pecknold, M.D., Research, Douglas Hospital, 6875 LaSalle Blvd, Verdun PQ, Canada H3Z 2M3; Dennis Munjack, M.D., Paul Alexander, M.D., Lorenz Luthe, M.S.C.

Summary:

Choice of treatment and drug must seriously account for dependency and the difficulty of discontinuing medication. In recent long-term treatment studies with alprazolam, little evidence of tolerance was found; in fact, most patients decreased medication over time. The principal difficulty in the discontinuation of alprazolam appears to be the presence of rebound (anxiety and panic) and the withdrawal or abstinence syndrome. This is a study comparing slow release alprazolam, alprazolam and placebo on a six week efficacy trial followed by three discontinuation protocols. The first was a rapid four week taper, the second an intermediate 10-12 week taper and the last a prolonged taper over 18-20 weeks. Evaluation of rebound showed no anxiety or panic rebound in the prolonged taper. In the intermediate taper rebound for panic attacks occurred in 15 percent of the alprazolam patients and rebound for anxiety in 5 percent. In the short taper rebound panic attacks occurred in 39 percent of alprazolam patients and 13 percent had anxiety rebound. Evaluation of the abstinence syndrome revealed a moderate syndrome in 7 percent of the patients in the prolonged taper, 9.5 percent in the intermediate taper and in the short taper 7.8 percent for alprazolam and 13 percent for slow release alprazolam. These results indicate that rebound phenomena are particularly important in the difficult discontinuation and that a slower taper of medication will be virtually asymptomatic. The question of relapse must be considered from the perspective of length of treatment.

NR332 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Gepirone in Panic Disorder

John C. Pecknold, M.D., Research, Douglas Hospital, 6875 LaSalle Blvd, Verdun PQ, Canada H3Z 2M3; Lorenz Luthe, M.S.C., Stephen Jenkins, M.D.

Summary:

Gepirone, an azopirone, is a $5HT_{1A}$ agonist with a more potent serotonergic activity and a less powerful noradrenergic stimulation effect than buspirone. We report an uncontrolled six week study

in 15 patients (two males, 13 females, mean age 34.1) with a concurrent *DSM-III-R* axis 1 diagnosis of generalized anxiety disorder and panic disorder with agoraphobia. After a two week medication free period, patients were started on gepirone 2 mgs/day with increasing dosage over three weeks to 12 mgs/day. Of 15 patients in "intent-to-treat," three dropped out during the first week and two patients stopped the trial after four and five weeks as the medication was not efficacious. Thus 12 patients had a sufficient trial. Nine of these 12 (75 percent) had at least a 50 percent reduction in their panic attacks by week 6, seven of them by week 3. Seven patients had "0" panic attacks by week 6 (58 percent). On the Hamilton Anxiety Scale, 75 percent had a 50 percent or greater reduction in total score, mostly beginning in week 2. On global assessment by week 6, two patients were very much improved and seven were much improved. Adverse effects were rare and consisted of stomach upset, dizziness, or headaches. This preliminary study suggests possible efficacy of gepirone in panic disorder unlike buspirone. Further placebo and standard controlled studies are indicated.

NR333 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Low Iron Levels and Tricyclic-Induced Jitteriness

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Summary:

There is a phenomenological similarity between iron deficiency states, phenothiazine-induced akathisia, and tricyclic antidepressant-induced jitteriness. Previous reports suggest that patients who develop akathisia and panic patients who develop tricyclic antidepressant-induced jitteriness have low serum iron levels. In this prospective study, we obtained ratings of jitteriness in a double-blind, randomized treatment study of panic disorder patients treated with imipramine ($n = 16$), diazepam ($n = 18$), and placebo ($n = 18$).

While seven of 16 imipramine treated patients (44 percent) developed jitteriness as rated by the investigator, none of the patients in the diazepam or placebo groups developed jitteriness. Patients who had jitteriness during imipramine treatment had significantly lower levels of serum iron (65.7 ± 25.4 vs 119.7 ± 42.8 mcg/dl; $t = 2.94$; $df = 14$; $p < 0.01$), MCV (84.6 ± 4.0 vs 90.8 ± 3.4 cu-microns; $t = 3.4$; $df = 14$; $p < 0.005$) and MCH (28.8 ± 1.8 vs 31.1 ± 1.4 pg; $t = 2.91$; $df = 14$; $p < 0.02$) compared to those who did not have jitteriness. These findings may have both theoretical and practical implications and the above indices may help to identify those panic disorder patients who are at a higher risk to develop jitteriness. This may aid in treating such patients with very low doses of tricyclics in the initial stages of treatment.

NR334 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Clinician-Accompanied Exposure and Self-Exposure in Phobia Reduction: A Controlled Study

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Summary:

Exposure therapy is usually carried out both in the clinician's presence and alone as homework. Research suggests that self-exposure alone may be enough. The present large controlled study tested whether clinician-accompanied exposure (E) enhances self-exposure (e), whether e is more effective than self-relaxation (r) and whether these effects applied equally across agoraphobics, social and specific phobics.

A total of 99 phobic patients were randomized to and 80 completed one of three treatment conditions. In each condition 26-27 patients were treated individually over eight weeks and followed up to week 26. One condition was E + e (Ee); the second was e only, the third was r only. All patients had six treatment sessions, at weeks 0, 1, 2, 3, 4, and 6. In Ee, E was for 90' per session. In all three conditions each of six instruction sessions was 60' long, with patients being asked to practice either e or r for 90' daily up to week 14, and to keep a structured daily diary of e or r homework. Assessments were at weeks 0, 8, 14 and 26.

Results: Clinician-accompanied exposure was largely redundant, the self-exposure element being the main effective ingredient of treatment. Results were mostly consistent across agora-, social, and specific phobics, although in social phobics Ee was superior to e on a few measures.

This study's findings confirm the importance of systematic self-exposure for fear reduction, the therapist's role being mainly that of guide and monitor. Research is still needed to find out how to reduce the effort and discomfort that has to be incurred by the patient in order to improve, although most patients complete treatment successfully.

NR335 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Benzodiazepines Compared Using Three Mice Models

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Summary:

The respective clinical profiles of benzodiazepines are not well known and might differ among drugs. Thus, alprazolam, bromazepam, diazepam, and lorazepam were compared in mice using a stimulation-sedation test (Actimotor), a myorelaxation test (Rotarod), and an anxiolysis test (Four plates), after acute and chronic administrations (every half-life for seven half-lives), doses from 0.03 to 4mg/kg were used. Alprazolam showed stimulating and anxiolytic effects acutely which diminished after chronic administration. Lorazepam's sedative effect diminished but its anxiolytic action increased upon chronic administration. Except for lorazepam, all drug's myorelaxation properties increased with chronic treatment. These results obtained with animal model suggest that the effects of benzodiazepines might not be identical. These differences might be reflected clinically and require investigation in humans.

NR336 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Social Phobia: Behavioral Versus Drug Therapies

Cheryl Shea Gelernter, Ph.D., EPH Dept., Yale Univ Sch. of Med., 40 Temple Street. Lower Level, New Haven, CT 06510; T. Uhde, M.D., P. Cimbolic, Ph.D., D. Arnkoff, Ph.D., B.J. Vittone, M.D., M.E., Tancer, M.D., J.J. Bartko, Ph.D.

Summary:

Despite the prevalence of social phobia and its sometimes debilitating effects, little is known about the relative efficacy of currently available treatments. Previous studies of psychopharmacological and cognitive-behavioral treatments have suggested they may have some efficacy; specifically, studies of cognitive restructuring and exposure interventions suggest that both techniques can be effective in reducing social anxiety. There is also some evidence that phenelzine and alprazolam might be effective in the treatment of social phobia. No comparisons of these kinds of treatment have been published so far.

We report here the final results of our double-blind, placebo-controlled study comparing cognitive-behavioral group therapy to pharmacotherapy with alprazolam, phenelzine, or pill-placebo in the treatment of 65 social phobics. All groups also received instructions for self-directed exposure to phobic stimuli. Statistically sig-

nificant repeated-measures effects were shown on all measures, indicating that the treatments studied were associated with substantial improvements in severe and chronic social phobia. Patients treated with phenelzine were rated by clinicians as more improved on a measure of work and social disability than patients treated with alprazolam or placebo (patients in the cognitive-behavior therapy group were not rated on this measure). All subjects showed positive cognitive changes from before to after treatment, and there were no differences between treatment groups on the cognitive measure. These results demonstrate the efficacy of several modes of treatment for social phobia.

NR337 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Auditory Sensory Gating in PTSD and Depression

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Summary:

Gating of auditory sensory processing is defective in schizophrenic and manic patients. One defect is illustrated by the failure to gate the P50 auditory evoked potential in a conditioning-testing paradigm. In this paradigm, paired clicks are presented to the subject every ten seconds. Normal controls suppress the response to the second of the two paired stimuli, occurring 500 msec after the first. If the amplitude of the P50 response to the second stimulus is divided by the amplitude of the response to the first stimulus, the conditioning-testing ratio (C/T) can be calculated. This is usually less than 40 percent in normal controls. Schizophrenic patients, medicated or unmedicated, and acutely psychotic manic patients fail to suppress the second (test) response. Failure to do so has been related to the inability of such patients to filter out noise in the environment.

We studied a heterogeneous group of 11 male veteran patients with over 20 years of combat post-traumatic stress disorder and depression, before and after treatment with psychotherapy and therapeutic doses of tricyclic antidepressants for a mean of 178 days of treatment. Data analysis was done using paired t-tests, each patient as his own control. As a group, these patients had impaired P50 auditory sensory gating both before and after treatment with pretreatment C/T = 94.6 percent +/- 130.5 percent S.D., post-treatment 101.1 percent +/- 130.1 percent S.D. 8/11 subjects had P50 C/Ts >40 percent on either the pretreatment or post-treatment day. Fasting plasma MHPG, HVA, and VMA were measured on the day of recording. Plasma HVA increased from below normal pretreatment values to normal post-treatment values. Plasma MHPG and VMA did not change with treatment and were not different than a group of normal controls. Patients were rated on the Impact of Event Scale (IES), the Intrusion Subset of the Impact of Event Scale (IES-INT), the Brief Psychiatric Rating Scale (BPRS), and the Hamilton Depression Scale (HAM-D) Nine patients also completed the Presence of Mood State Scale (POMS) before and after treatment. Scores on the IES, BPRS, and HAM-D improved with treatment, as did POMS subscale scores for depression, fatigue and anxiety. There was no significant change in the IES-INT, which improved in only 3/11 subjects.

This study indicates that although patients with chronic severe PTSD may respond to treatment when assessed on a variety of psychological measures, they may demonstrate highly variable and intermittently impaired auditory sensory gating. These patients also tend to show little improvement on the IES-INT, even when improvement is demonstrated on other psychological measures.

NR338 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Progressive Withdrawal of Chronic Lorazepam Users

Marc M. Ansseau, M.D., Dept of Psychiatry, Univ of Liege, C.H.U. Du Sart Tilman, Liege, Belgium B-4000; Remy Von Frenckell, Ph.D.

Summary:

A total of 213 chronic lorazepam users (mean duration of chronic intake = five years and five months) accepted from their general practitioners to follow a progressive decrease in their daily intake while receiving a six-page booklet describing better ways to cope with everyday stress. During a maximal three-month period, the mean daily dose decreased by 49.0 percent from an initial level of 4.69 mg (SD = 2.95) to a final level of 2.30 mg (SD = 1.93 mg). The psychological condition of the patients, assessed by a visual analogue scale, improved throughout the study period. Withdrawal symptoms were seen in only 33.3 percent of the patients and were limited in duration and severity, except in one case of epileptic seizure. A total of 54.3 percent of the patients were moderately or very satisfied with the outcome. These results demonstrate the possibility for general practitioners without any specific training to significantly decrease the daily intake of long-term benzodiazepine users with an improvement in patient well-being.

NR339 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Withdrawal Phenomena of Suriclone and Diazepam

Marc M. Ansseau, M.D., Dept of Psychiatry, Univ of Liege, C.H.U. Du Sart Tilman, Liege, Belgium B-4000; Remy Von Frenckell, Ph.D., Philippe Guillet, M.D.

Summary:

Suriclone is a cyclopyrrolone derivative which binds with high affinity to a distinct site or to a special allosteric conformation of the GABA A-benzodiazepine-chloride ionophore receptor complex. Several clinical studies have demonstrated the anxiolytic activity of suriclone.

The purpose of this study was to compare the effects of gradual (half the dose during one week) and abrupt discontinuation on suriclone 0.4 mg tid and diazepam 5 mg tid following six weeks of treatment. A total of 120 outpatients with generalized anxiety disorder were included in the study and 80 entered the withdrawal phase clinical assessments were performed at baseline and after two, four, and six weeks (active phase) as well as after seven and eight weeks (withdrawal phase) and included Hamilton anxiety scale, the clinical global impressions, the Lader tranquilizer withdrawal scale, and the Ashton withdrawal scale.

Results show similar efficacy of diazepam and suriclone during the active phase without any significant difference in adverse events. Preliminary analysis of the withdrawal phenomena showed more worsening of the clinical condition following diazepam discontinuation.

NR340 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Trichotillomania: CSF Values and Treatment Response

Philip T. Ninan, M.D., Psychiatry, Emory University, 1365 Clifton Road NE, Atlanta, GA 30322; Mary Eccard, M.S., R.D. Jewart, Ph.D., Mark Stipetic, B.S., Richard J. Lewine, Ph.D., Craig S. Risch, M.D.

Summary:

Similarities between Trichotillomania (T) and obsessive compul-

sive disorder (OCD) exist in phenomenology, familial aggregation and pharmacological response, though differences exist in other areas (e.g., symptomatology, gender ratio). To explore the neurochemistry of T, we analyzed the first five patients with T who had drug free LPs as part of an ongoing study. There was a significant correlation between CSF 5HIAA and HVA ($r = .90$, $p = 0.038$), 5HIAA and cortisol ($r = -.92$, $p = 0.028$), and HVA and cortisol ($r = -.99$, $p = 0.002$). Age- and sex-matched normal controls also had a significant correlation between CSF 5HIAA and HVA ($r = .90$, $p = 0.038$). Comparison of the T patients with the controls failed to show a significant difference in 5HIAA, though a trend existed for MHPG and HVA to be higher in patients.

The demographic, history, phenomenology, co-morbidities, and pharmacological response in the first 12 T patients was also explored. All were female, with a mean age of 29, mean age of onset of 11. Seventy-five percent pulled scalp hair, 64 percent eyelashes and eyebrows, and 33 percent pubic hair. Seventy-three percent of patients responded to pharmacological treatment with potent serotonin uptake inhibitors. The value of baseline CSF measures in predicting treatment response will be presented.

NR341 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Effect of Imipramine Treatment on Lactate Anxiety

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Summary:

The purpose of this study was to determine if imipramine was more effective than diazepam and placebo in decreasing lactate-induced anxiety in a double-blind study. Forty-two panic disorder patients received both placebo and lactate infusions, eight weeks of treatment with imipramine, diazepam, or placebo, and were then reinfused.

Treatment with imipramine and diazepam were significantly better than placebo on a global improvement scale (ANOVA, $p = 0.04$). However, placebo was associated with a robust response, and there was no difference among treatment outcome measures on the CGI or in the frequency of panic attacks. After treatment, the severity of lactate-induced anxiety was significantly different among groups (ANOVA, $p < 0.0001$) as measured by the panic attack symptoms on the Panic Description Scale (PDS). Placebo patients became just as anxious after treatment as before. Both diazepam and imipramine decreased lactate-induced anxiety; imipramine's effect was especially pronounced, and greater than that of diazepam's (Bonferroni, $p < 0.05$).

In conclusion, imipramine greatly decreases lactate-induced anxiety while placebo has no effect, even though placebo is associated with a strong treatment response. This finding suggests that imipramine's effects on lactate-induced anxiety cannot be attributed to desensitization or a cognitive reinterpretation of the infusion experience.

NR342 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Buspirone Versus Diazepam in Reducing Anxiety

M.W. van Laar, M.D., NIDDR, Univ. of Utrecht, Vondellaan 14, 3521 GB, Utrecht, The Netherlands; E.R. Volkerts, A.P.P. von Willigenburg, T.A. Plomp, R.A.A. Maes.

Summary:

Buspirone is a non-benzodiazepine anxiolytic which appears to be equally effective as diazepam in the treatment of anxiety. It differs from the benzodiazepines in that it seems to be devoid of sedative side effects that can impair skilled performance such as automobile driving.

The present study was conducted to compare the therapeutic efficacy and the effects on actual driving performance of buspirone versus those of diazepam. Twenty-four outpatients (12 male and 12 female) with generalized anxiety disorder (*DSM-III-R* criteria) participated in this study, using a double-blind, randomized, two-arm, parallel group design. Subjects received placebo single-blind during seven days baseline, immediately followed by four consecutive weeks of double-blind drug treatment, ending again with seven days single blind placebo-washout. During the 1st week, buspirone 5 mg was administered three times a day. In week 2, 3 & 4, buspirone was administered in a 10 mg dosage in the morning, and 5 mg dosages in the afternoon and evening. Diazepam 5 mg was given three times a day during all drug treatment weeks.

Weekly assessments and measurements were performed on the evening of each seventh treatment day. These were the Hamilton Anxiety Scale and the Symptom Check List (90 items), followed by a driving test in actual traffic.

The main findings were that both buspirone and diazepam were effective in reducing overall anxiety symptoms. In addition, buspirone specifically reduced concomittant depressive symptoms and symptoms of interpersonal sensitivity and anger-hostility. Diazepam specifically reduced somatic symptoms and sleep disturbances. Abrupt discontinuation of buspirone did not produce rebound symptoms. In contrast, abrupt discontinuation of diazepam treatment resulted in a full relapse of psychic anxiety symptoms, and a partial relapse of somatic anxiety symptoms.

Driving performance was not affected by buspirone. However, diazepam seriously impaired driving performance in the first three weeks of treatment. There was no significant impairment in the fourth treatment week and placebo-washout week.

These results confirm that buspirone and diazepam are both effective in treating general anxiety. Yet, their profiles indicate that some patients may benefit more from buspirone and some more from diazepam, depending on the prevalence of specific associated on concomitant symptoms which are differently affected by the drugs. It is further concluded that buspirone in its therapeutic regimen can be safely used by ambulatory patients who continue their daily activities, including driving a motor vehicle. In contrast, patients using diazepam should be seriously warned of the possibility of severe impairment during the first weeks of treatment.

NR343 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Polydiagnostic Issues in Anxiety Disorders

Michael Bach, M.D. Psychiatry, University of Vienna, Waehringer Gurtel 18-20, A-1090 Vienna, Austria; Detlev O. Nutzinger, M.D., Martina de Zwaan, M.D., Lydia Hartl, M.D.

Summary:

Assessing only cross-sectional diagnoses in anxiety disorders entails a considerable loss of information and adds weight to hierarchical rules as probably the most weak diagnostic criteria. Using a semi-structured polydiagnostic interview (including St. Louis, RDC, *DSM-III, DSM-III-R* and ICD-10) we determined lifetime diagnoses in a sample of 82 outpatients with a *DSM-III-R* anxiety disorder. Seventy-three percent of patients with *DSM-III-R* panic disorder (PD) without agoraphobia (AP) at onset developed AG subsequently, whereas only 33 percent of patients with *DSM-III-R* AG at onset developed PD. In all classification systems more than 80 percent of patients had additional lifetime diagnoses, ranging from 1.29 mean additional diagnoses in St. Louis to 3.38 in *DSM-III*. Considering hierarchical rules did not substantially affect the overall number of lifetime diagnoses within each classification system, but it caused significant divergencies between the classification systems regarding the individual diagnoses (e.g. hypochondriasis was found in 14.6 percent of our sample according to *DSM-III* vs. in 51.2 percent according to *DSM-III-R*). Our results underline the importance of a polydiagnostic approach considering lifetime diagnoses in addition to cross-sectional classification especially for research purposes.

NR344 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Risk Assessment by Patients With Anxiety Disorders

Randolph M. Nesse, M.D., Psychiatry, Univ of Michigan, 1500 E. Med Ctr Med Inn C440, Ann Arbor, MI 48109; Richard Klaus, B.A.

Summary:

We compared risk assessments by patients in an anxiety disorders clinic (N = 122) to those of control subjects approached in public places (N = 152). Subjects estimated the likelihood that 22 possible events would happen to the average person in the U.S.A. during the next year on a 16-point scale keyed to absolute event frequency. They also rated their own relative chance of experiencing the event on a seven-point scale, and then completed demographic, mood, and anxiety items. The results for both groups match previous findings that normal people overestimate rare events and underestimate common events and those that may happen to the self. Contrary to our expectations, controls estimated dangers to be slightly more frequent than patients (6.22 vs. 5.88, repeated measures ANOVA with sex and age as covariates: $F = 2.64$, $p = .11$). Controls rated risks higher for each item except "Have a heart attack." Both groups were similar in their underestimation of relative risk for self ($F = 3.5$, $P = .06$). Accuracy of risk assessment, calculated for 15 items where objective data were available, was the same in both groups. These findings strongly challenge the hypothesis that anxiety patients assess risks differently from normal people.

NR345 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Somatization and Anxiety: Is There an Overlap?

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Summary:

Somatic symptoms figure prominently in the presentation of anxiety disorders. Substantial overlap between panic disorder (PD) and somatization disorder (SD) has been reported (1), as have differences in the rates of somatic symptoms between panic disorder and generalized anxiety disorder (GAD) patients (2). We report the results of a questionnaire on physical symptoms based upon *DSM-III-R* criteria for somatization disorder, given to a sample of 170 patients (PD, n = 79; GAD, n = 91) who were recruited for a multicenter drug trial.

GAD patients reported a significantly greater number of overall physical symptoms, and had a greater number of cardiac, pulmonary, and neurological symptoms than PD patients. Fifty-one percent of GAD patients reported greater than 13 symptoms (thus potentially qualifying for SD) compared to 41 percent of PD patients. However, when the other relevant diagnostic exclusion criteria from *DSM-III-R* were applied to each symptom, only three GAD patients continued to qualify for SD in terms of number of symptoms. The implications of these findings for the clinical management of anxiety disorder patients will be discussed.

NR346 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Non-Habituation of the Startle Response in PTSD

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Summary:

Exaggerated startle response is one of the *DSM-III-R* diagnostic criteria for post-traumatic stress disorder (PTSD). A recent study found increased magnitude of the eye blink response to auditory startle in PTSD. Autonomic dependent variables, and habituation, have not yet been measured in investigations of the startle response in this disorder. This project studied habituation of skin conductance (SC), heart rate (HR), and orbicularis oculi electromyogram (EMG) responses to 15 consecutive 1/2-sec., 95 dB, 1000 Hz, zero rise-time binaural tones in PTSD patients and three non-PTSD control groups: anxiety disorders (ANX), mentally healthy without a past history of trauma (NOTRA), and mentally healthy with a past history of trauma (TRA). As judged by a habituation criterion of two consecutive responses $\leq .05$ uS, SC response failed to habituate in 13 of 14 PTSD, but in only three of 14 ANX, seven of 19 NOTRA, and two of 15 TRA subjects; $x^2 = 22.8$, $df = 3$, $p < .001$. Mean transformed slopes of the habituation curves were: PTSD –.03 (sd .16), ANX –.15 (sd .10), NOTRA –.23 (sd .18), TRA –.15 (sd .18); $F = 3.9$, $df = 3,58$, $p = .01$. The HR and EMG data were in the same direction, although less dramatic, with regard to the difference of the PTSD from all the Control groups. To our knowledge, PTSD is the first mental disorder in which failure of habituation of the acoustic startle response has been demonstrated. It is suggested that this failure of habituation may be an important factor underlying the impaired recovery from the effects of overwhelming stressful experiences observed in PTSD.

NR347 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Psychophysiology of PTSD in Korean and WWII Veterans

Scott P. Orr, Ph.D., Research, VA Research Service, 228 Maple Street, Manchester, NH 03103; Roger K. Pitman, M.D., Lawrence R. Herz, M.D., Natasha B. Lasko, Ph.D.

Summary:

This study utilized a psychophysiologic procedure previously validated in Vietnam veterans to assess the responses of medication-free Korean and World War II combat veterans to imagery of their personal combat experiences. Subjects were classified on the basis of *DSM-III-R* criteria into post-traumatic stress disorder (PTSD, n = 10) and no mental disorder (Healthy, n = 10) groups. "Scripts" describing each individual's own combat experiences were recorded and played back in the laboratory. Subjects were instructed to imagine the events the scripts portrayed while physiologic reactivity was recorded. The groups' mean responses to imagery of the combat events were: heart rate (beats per minute), PTSD +6.9 (sd 6.4) vs. Healthy +1.7 (sd 1.4), $t = 2.5$, $df = 9.8$, $p = .03$; skin conductance (uS), PTSD +1.90 (sd 2.37) vs. Healthy +0.05 (sd 0.17), $t = 2.5$, $df = 9.1$, $p = .04$, frontalis electromyogram (uV), PTSD +0.8 (sd 1.6) vs. Healthy 0.00 (sd 1.1), $t = 1.4$, $df = 18$, $p = .18$. MANOVA yielded $F = 4.1$, $df = 3,16$, $p = .03$. These findings further replicate and extend the utility of physiologic responses to script-driven traumatic imagery in distinguishing PTSD from non-PTSD subjects. Remarkably, the physiologic responses of the Korean and World War II PTSD combat veterans studied here were as high as the responses found in two previously studied groups of PTSD Vietnam veterans, even though the combat events of the former occurred approximately 40 years ago. These results demonstrate the durability of the conditioned emotional responses of combat-related PTSD.

NR348 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Yohimbine and M-Chloro-Phenyl-Piperazine in PTSD

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Summary:

In a double-blind, placebo controlled study, we recently reported a marked increase in anxiety, panic attacks, and post-traumatic stress disorder (PTSD) specific symptoms to intravenous yohimbine infusion in Vietnam combat veterans with PTSD. A total of 62 percent of patients experienced a panic attack (PA) and 31 percent a flashback (FB). In conjunction with earlier psychophysiological, neuroendocrine, and peripheral receptor studies, these findings suggest that the noradrenergic system is dysregulated in chronic combat related PTSD. To determine the specificity of the yohimbine response and to evaluate potential serotonergic (5-HT) contributions to PTSD symptomatology we administered IV yohimbine (0.4 kg/mg), IV MCPP (1 mg/kg), and placebo on three separate test days to 14 Vietnam veterans with PTSD and to seven healthy controls in a randomized balanced design under double blind conditions. MCPP is a 5-HT agonist with predominant effects on 5-HT_2 and 5-HT_{1c} receptors. Six out of 14 (43 percent) of patients experienced a PA with yohimbine and 4 out of 14 (29 percent) had a FB. Five of 14 (36 percent) of patients had a panic attack and four of 14 (29 percent) a FB with MCPP. On placebo, no patients experienced a panic attack and one had a FB. One healthy control had a PA and none a FB with yohimbine. The fact that both yohimbine and MCPP induced PA and FB suggests that these complex behaviors are mediated by multiple neurotransmitter systems. Further, only one patient had a PA on both yohimbine and MCPP test days. In all cases, MCPP and yohimbine PA occurred in separate patients. These preliminary data suggest that traumatic stress can have long-lasting effects on responsivity of CNS noradrenergic and serotonergic systems and raises the possibility of pathophysiologic subtypes in PTSD.

NR349 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Comorbidity of Anxiety Disorders and PTSD

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Summary:

The Harvard/Brown Anxiety Research Project (HARP) is a large, prospective multicenter study of subjects with panic disorder, agoraphobia, social phobia, and/or generalized anxiety disorder as determined by *DSM-III-R*. Of 427 subjects, 119 (28 percent) reported a history of serious life trauma. Of these, 41 (10 percent of the total sample) met full *DSM-III-R* criteria for post-traumatic stress disorder (PTSD). Of the PTSD group, 29 (71 percent) gave a history of physical or sexual assault in adulthood or childhood. Of the remaining 78 trauma reporters (TR), 34 (44 percent) reported physical or sexual assault in childhood or adulthood. The rates for war-related trauma were comparable for both groups (20 percent PTSD vs. 15 percent TR). For the TR group, 44 of the 78 (56 percent) recalled witnessing violence, being injured in an accident, or other trauma, while 12 of the 41 (29 percent) of the PTSD group reported trauma in this category. A total of 27 percent of the PTSD group and 24 percent of the TR group experienced multiple trauma. Sex ratios were comparable for the entire sample (66 percent female), the PTSD group (73 percent female) and the TR group (67 percent female).

We found a high rate of serious trauma in subjects with anxiety disorders. The PTSD group was significantly more likely to have experienced personal assault than the TR group.

NR350 Tuesday May 14, 3:00 p.m.-5:00 p.m.

5HT Function and Neurology of Social Phobia

Eric Hollander, M.D., Psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; Concetta M. Decaria, M.S., Sari Trungold, B.A., Franklin Schneier, M.D., Brian Fallon, M.D., Larry Welkowitz, Ph.D., Michael R. Liebowitz, M.D.

Summary:

Agents such as buspirone and fluoxetine may have efficacy in the treatment of social phobia, suggesting that 5HT mechanisms may be involved in its pathophysiology. Six adult social phobic patients underwent pharmacological challenges with the 5HT agonist m-CPP (0.5 mg/kg p.o.) and with placebo. Four out of six (66 percent) had substantial increase in anxiety, as measured by API and SUDS ratings in response to m-CPP, but no increase in anxiety in response to placebo (peak delta t-test SUDS: $t = 2.627$, $p = .046$). Unlike OCD patients given m-CPP in prior studies, social phobics had no obsessional response. Prolactin response to m-CPP in social phobics was less blunted than that previously seen in OCD, and more similar to the response reported in normal controls. Social phobic patients had an intermediate number of neurological soft signs (mean = 3.2) when compared to OCD patients (mean = 5.3) and normal controls (mean = 1.4). Social phobic patients had a strong anxiety response to 5HT agonists, and had fewer neurological soft signs than OCD patients.

NR351 Tuesday May 14, 3:00 p.m.-5:00 p.m.

M-Chloro-Phenyl-Piperazine Activated Regional Cerebral Blood Flow in OCD

Eric Hollander, M.D., Psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; Isak Prohovnik, Ph.D., Concetta M. Decaria, M.S., Jihad B. Saoud, M.S., Sari Trungold, B.A., Dan J. Stein, M.D., Michael R. Liebowitz, M.D.

Summary:

This study measured the effect of the serotonin agonist m-CPP (0.5 mg p.o.) on 133-Xenon regional cerebral blood flow (rCBF) in ten OCD patients. There were no significant effects or interactions on BP P, Hct, or pCO2. There was a 42 percent peak increase in OCD severity following m-CPP. This corresponded with a decrease in flow to grey matter (fg) (80 to 64 ml/100g/min), but a significant increase in initial slope index (ISI) (47 to 51). Peak delta OCD following m-CPP correlated with peak delta ISI ($r = .61$), and the group x time effect was significant ($F = 15$, $p = .003$), suggesting that m-CPP responders had the greatest increase in cortical (ISI) blood flow. Regional hyperfrontality was also stronger in m-CPP responders. These findings are similar to Zohar et al of increased cortical blood flow during imaginal flooding in OCD.

NR352 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Predictors of Treatment Outcomes in OCD

Eric Hollander, M.D., Psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; Concetta M. Decaria, M.S., Jihad B. Saoud, M.S., Sari Trungold, B.A., Maxim Frenkel, M.D., Dan J. Stein, M.D., Michael R. Liebowitz, M.D.

Summary:

Serotonin reuptake blockers effectively treat approximately 60 percent of OCD patients, yet up to 40 percent of patients remain refractory. Prediction of poor response would be helpful. Thirty-one adult OCD patients, treated for more than 12 weeks with clomipramine or fluoxetine, previously participated in biological challenges with M-CPP and clonidine, and neurological soft-sign testing. Ten measures correlated with treatment outcome on CGI change score. Multiple regression analysis showed that these ten variables explained 69 percent of the total variance in outcome. Predictors of a poor response to clomipramine or fluoxetine included: old age; male sex; severe obsessions; severe depression; high number of neurological soft-signs; less-robust prolactin response, and less

behavioral exacerbation to M-CPP; low plasma M-CPP level; and less robust systolic BP response to clonidine. Implications will be discussed.

NR353 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Effect of the 5HT Agonist M-Chloro-Phenyl-Piperazine on Brain Metabolism

Chawki Benkelfat, Psychiatry, McGill University, 1033 Pine Ave Res & Trng Bldg, Montreal Quebec, Canada H3A 1A1; Paul Andreassen, M.D., Dennis L. Murphy, M.D., W. Semple, Ph.D., T.N. Nordahl, M.D., R.M. Cohen, M.D.

Summary:

Meta-chlorophenylpiperazine (m-CPP) is a $5HT_1$ receptor agonist widely used as a pharmacological probe of the serotonergic system in humans. When administered in normal volunteers, m-CPP induces a dose dependent anxiogenic effect, an evaluation in self-ratings of activation-euphoria, and a rise in oral temperature and plasma prolactin (Murphy et al, 1989). The recent report (Freo et al, 1990) of a relationship between the m-CPP induced hypomotility in rodents and a widespread regional reduction in brain glucose metabolism suggests that some of the m-CPP induced behavioral effects observed in humans might be mediated via specific regional brain changes, which can be detected using functional brain imaging techniques.

We report here a study systematically exploring local cerebral glucose metabolic rate (LCGMR) changes measured by positron emission tomography with [^{18}F]-2-deoxyglucose (FDG) following the administration of a single dose of 0.5 mg/kg m-CPP, po, 75 mn prior to FDG, in seven normal volunteers. The same normal volunteers had an identical PET study on a separate day without m-CPP administration.

Despite mild but measurable activating behavioral effects, resulting in an increase in various NIMH-self rating subscores, including altered-self reality ($p = .04$), functional deficit ($p = .04$) and activation/euphoria ($p = .12$), m-CPP had only a minimal or no effect on regional brain metabolism: LCGM increased significantly in only one of sixty regions of interest examined, the anterior medial prefrontal cortex (A plane, 94 mm above cantho-meatal line; $p = .009$). Other trends were observed, in particular, a decreased LCGM in the left medial temporal cortex ($p < .06$) and right caudate nucleus ($p < .1$). All subjects had demonstrable m-CPP plasma levels at the time of scan and exhibited a significant increase in oral temperature ($p < .002$) and plasma prolactin ($p < .03$). These essentially negative FDG results will be discussed in terms of the various effects of m-CPP on brain serotonergic systems.

NR354 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Behavioral Responses to Methylphenidate in OCD

Delbert G. Robinson, M.D., Research, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004; Carmen Z. Lemus, M.D., Michael H. Kronig, M.D., Gail Lerner, M.S.

Summary:

Although serotonin is considered to be the neurotransmitter most associated with obsessive-compulsive disorder (OCD), several indirect lines of evidence suggest a possible involvement of dopamine (DA) in OCD. To assess the role of DA in OCD, 12 subjects with OCD (three men, nine women; 31.9 ± 8.7 years old) were given 0.5mg/kg of intravenous methylphenidate. Before and after methylphenidate administration, subjects were assessed with the SADS-C, SADS-PD, Y-BOCS and visual self-rating scales. Comparing baseline with post-infusion SADS-C ratings, subjects had a significant decrease in global obsessive-compulsive symptoms (4.0 ± 1.2 versus 2.9 ± 2.2, $t = 2.14$, $df = 10$, $p = 0.05$) as well as an overall activating/euphoric effect. No subject had a psychotogenic response to the infusions. Results of other analysis included a comparison of OCD subjects' responses to those of normal control subjects will be presented at the meeting.

NR355 Tuesday May 14, 3:00 p.m.-5:00 p.m.

A Time-Limited Behavioral Group Treatment for OCD

Barbara Van Noppen, A.C.S.W., Bulter Hospital, 345 Blackstone Blvd, Providence, RI 02906; Steven A. Rasmussen, M.D., Jane L. Eisen, M.D.

Summary:

In vivo exposure with response prevention is an effective treatment for OCD either alone or in combination with pharmacotherapy. Widespread application of this technique has been limited due to lack of trained therapists and expense of intensive individual therapy. We have developed a time limited ten-session behavioral group therapy for OCD whose key elements includes participant and therapist modeling and in vivo exposure with response prevention. One hundred probands meeting *DSM-III-R* criteria for OCD have completed the ten-session group. Yale Brown OC scores at baseline were 21.2 ± 5.9. By the end of the ten-week treatment, scores had decreased to 16.9 ± 6.1 (p .0001). Improvement was sustained at one-year follow-up with a YBOCS of 17.2 ± 5.8. A descriptive analysis of the therapeutic elements of the group and its advantages over individual behavioral treatments will be presented.

NR356 WITHDRAWN

NR357 Tuesday May 14, 3:00 p.m.-5:00 p.m.

OCD and Compulsive Traits: Phenomenology and Outcome

Jane Eisen, M.D., Butler Hospital, 345 Blackstone Blvd., Providence, RI 02906; Steven A. Rasmussen, M.D., Brandon Krupp, M.D.

Summary:

Obsessive-compulsive disorder (OCD) and compulsive personality disorder (OCPD) have been viewed as related on a continuum of severity. However, recent literature has questioned the validity of conceptually linking these two syndromes. We analyzed the frequencies of individual compulsive personality traits in 114 OCD probans participating in a multicenter five-site clomipramine trial. Probands were assessed with two different instruments: a clinician rated structured interview (SID-P), and a self-report questionnaire (the WISPI). A total of 22 patients (19 percent) met criteria for OCPD using the SID-P compared to 2 percent in a nonpatient population. This is considerably higher than the 6 percent found by Bear et al in a recent study using the same instrument. The majority of patients had difficulty with perfectionism and indecisiveness (82 percent and 68 percent respectively). In contrast, a minority of patients had difficulty with the other traits making up the criteria for OCPD: emotional expressiveness (32 percent), flexibility (32 percent), and overinvolvement with work (18 percent). The presence of these traits was not correlated with outcome as measured by the Yale Brown Obsessive Compulsive Scale. No significant change in WISPI compulsive personality trait scores before and after improvement of OCD symptoms were noted. Finally, we found no correlation between the two instruments in establishing the diagnosis of OCPD. In summary, over one fifth of the patients with OCD met criteria for OCDP. Only certain OCPD traits were seen frequently in OCD probands.

NR358 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Symptoms in OCD With and Without TIC Disorder

Jacob C. Holzer, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Lawrence H. Price, M.D., Christopher J. McDougle, M.D., Beth K. Boyarsky, M.S.N., Wayne K. Goodman, M.D.

Summary:

Previous studies suggest clinically and biologically important relationships between obsessive-compulsive disorder (OCD) and chronic tic disorders. In this study the types of obsessive-compulsive (OC) sxs were compared in OCD pts with and without a tic disorder. *Methods:* OCD pts (*DSM-III-R*) were evaluated for a lifetime h/o chronic motor and/or phonic tics. Thirty-five pts in the OCD tic group (M = 27, F = 8; mean ± age SD = 29.9 ± 8.7 yrs) were age- and sex-matched to the OCD non-tic pts (M = 27, F = 8; mean age = 30.5 ± 8.3 yrs). OC sxs were determined using the Y-BOCS clinician-rated inventory of 74 types of obsessions and compulsions. The Y-BOCS and HAM-D measured sx severity. *Results:* No differences were found between the two groups in ages of onset of OC symptoms or baseline Y-BOCS and HAM-D scores. The age of onset of tic sxs occurred significantly earlier than the age of onset of OC sxs in the OCD tic group. Comparison of sxs between groups revealed the OCD tic group had more obsessions and compulsions involving numbers ($p < .05$), checking ($p < .005$), repeating ($p < .01$), touching/tapping/rubbing ($p < .001$), blinking/staring ($p < .005$), and less compulsions with cleaning ($p < .05$) and contaminations ($p < .05$). *Conclusions:* Results indicate that these two groups differ with respect to particular obsessions and compulsions. This suggests that differences between the two putative subgroups of OCD (with tic sxs and without tic sxs) may be reflected, in part, as differences in the clinical expression of OC sxs. The possible neurobiological and ethological implications will be discussed.

NR359 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Family Study of OCD

Donald W. Black, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; Russell Noyes, M.D., Rise Goldstein, M.P.H., Nancee Blum, M.S.W.

Summary:

First-degree relatives of obsessive-compulsive disorder probands (n = 32) and psychiatrically normal controls (n = 33) were blindly interviewed using the Diagnostic Interview Schedule (DIS). The morbidity risk for anxiety disorders was increased among the relatives of obsessionals compared with the relatives of controls, but the risk for obsessive-compulsive disorder (OCD) was not. Risk for a more broadly defined OCD (including relatives with obsessions and compulsions not meeting criteria for OCD) was increased among the parents of obsessionals but not the parents of controls (16 percent vs 3 percent). The findings suggest that an anxiety disorder diathesis is transmitted in OCD families, but that its expression within these families is variable. The findings also support the current practice of classifying OCD as an anxiety disorder.

NR360 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Cholecystokinin and Octapeptid Concentrations in Panic Disorder and Normal Controls

R. Bruce Lydiard, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; James C. Ballenger, M.D., Michele T. Laraia, R.N., Mark D. Fossey, M.D., Margerie C. Beinfeld, Ph.D.

Summary:

Cholecystokinin is a neuroactive peptide found both in the central nervous system and gut. Predominant CNS forms include the octapeptide (CCK-8) and tetrapeptide (CCK-4) forms. In light of recent reports that intravenous administration of the CCK-4 is a potent panicogenic agent, we measured CSF concentrations of CCK-8 in CSF from panic disorder patients and normal volunteers. After four days of a low monoamine diet and nine hours of bedrest, lumbar CSF was obtained from panic disorder patients (n = 25, 20 females, five males) and controls (n = 16, eight females, eight males), frozen at -70 degrees centigrade and stored until assay, 200ul aliquots were assayed by radioimmunoassay (MB) in duplicate. Results are expressed as pq/ml, mean ± SD. Panic patients' CSF concentration of CCK-8 (16.2 ± 5.9 pq/ml) were significantly ($p < 0.05$) lower than normal volunteers (20.6 ± 7.7 pq/ml). Normal controls showed no sex differences in CCK values. CCK-8 values were normally distributed. Theoretical and practical implications of these findings will be discussed.

NR361 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Psychoeducation/Reflective Listening Compared to Cognitive-Behavioral Treatment in Panic Disorder

M. Katherine Shear, M.D., Psychiatry, New York Hospital, 525 East 68th Street, New York, NY 10021; Andrew C. Leon, Ph.D., Laura Portera, B.A., Janet Klosko, Ph.D., Marylene Cloitre, Ph.D.

Summary:

Recently developed cognitive-behavioral treatment techniques appear to be effective in blocking panic. We report here preliminary results of a study comparing CBT with a control treatment consisting of a combination of psycho-education and reflective listening (PERT). *Methods*: Patients who met *DSM-III-R* criteria for panic disorder were randomly assigned to 15-week treatment with CBT (n = 23) or PERT (n = 22). Outcome was assessed two weeks post-treatment and at six-month follow-up.

Results: Both treatments showed significant treatment effects on panic and associated symptomatology. Panic attacks were blocked in 70 percent of the patients in both groups. Significant improvement also occurred in anticipatory anxiety, phobic avoidance, and overall symptom measures (SCL90). There was no difference in outcome between the two treatment groups at post-treatment or six-month follow-up. Power analyses indicated that the lack of difference we found was not due to the relatively small sample size. *Conclusion*: A short-term psychotherapy treatment with elements of both intensive psychoeducation and empathic listening appears to be effective in the acute treatment of panic disorder. Further studies are needed to dissect the active ingredient(s) of this approach.

NR362 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Comorbidity of Social and Simple Phobia in Generalized Anxiety Disorder and Panic Disorder

Andrzej R. Kuczmierczyk, Ph.D., Psychiatry, LSU Med. Center, 1542 Tulane Avenue, New Orleans, LA 70112; James G. Barbee, M.D., Donna M. Mancuso, M.D., Richard Maddock, M.D., Cameron Carter, M.B., Barbara Kennedy, M.D.

Summary:

Increasing attention has been focused on the importance of evaluating psychiatric comorbidity in anxiety and mood disorders. The present study examined the prevalence rates for social and simple phobias in a cohort of 92 patients with generalized anxiety disorder (GAD) and in a sample of 91 patients with panic disorder

(PD) matched on a number of demographic variables. Patients were recruited as part of a multicenter medication treatment study of GAD and panic disorder and were screened utilizing the Structured Clinical Interview for *DSM-III-R* (SCID). Prevalence rates for social phobia and simple phobia in the GAD sample were 27 percent and 16.3 percent respectively, and for the panic disorder group prevalence rates for social phobia and simple phobia were 19.8 percent and 30.8 percent respectively. The prevalence rate for social phobia was five times higher for females than for males in the panic disorder group and twice as high for females compared to males in the GAD group. The rates of social phobia, in particular, are far higher in these two patient samples than rates which have been reported by other authors (DiNardo and Barlow, 1990). A specific behavioral model, based upon increased autonomic reactivity of anxious patients exposed to fear relevant stimulus situations will be proposed to explain these findings (Barlow, 1988). Clinical, diagnostic, and treatment implications will also be discussed.

NR363 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Doxapram: A Novel Panicogenic Probe

Yue-Joe Lee, M.D., Psychiatry, University of Michigan, Med. Inn 444 1400 E Med Ctr Dr, Ann Arbor, MI 48109; George C. Curtis, M.D., John G. Weg, M.D., James L. Abelson, M.D., Jack Modell, M.D.

Summary:

Doxapram is a respiratory stimulant, apparently acting on peripheral carotid oxygen receptors and on the respiratory center of the medulla oblongata. For these reasons doxapram might provide a useful probe for investigating the hypotheses that hyperventilation and/or hypersensitive medullary chemoreceptors are important pathophysiologic mechanisms in panic disorder. To explore this possibility, saline placebo and doxapram 0.5 mg/kg were administered intravenously in successive bolus doses under single-blind conditions to five panic disorder patients and seven normal controls. Following doxapram but not placebo, all subjects exhibited increased minute volume and tachycardia, and all reported a warm flushing sensation in the head and trunk. No panic attacks occurred following the placebo injection, but four patients and one control reported panic attacks meeting *DSM-III-R* criteria following doxapram ($p = .000$). Following doxapram but not placebo, patients as compared to controls developed significantly higher minute volume, lower end tidal pCO2, and required approximately twice as long for these measures to return to baseline. The results are consistent with a role for hyperventilation and/or respiratory center hypersensitivity in panic disorder. Doxapram appears to be a potentially useful probe for investigating the pathophysiology of panic disorder.

NR364 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Panic in Balance Disorder Patients

Duncan B. Clark, M.D., WPIC, Univ of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213; Rolf G. Jacob, M.D., Martha Leslie

Summary:

Vestibular abnormalities have been documented in panic disorder patients (Jacob, et al., 1985). The purpose of this study was to assess symptoms of panic, agoraphobia, and depression by questionnaire in 100 patients presenting to a dizziness and balance disorder self-help group. The majority of these patients (55 percent) reported panic attacks, and 23 percent met *DSM-III-R* criteria for panic disorder. Like patients with agoraphobia, most avoided boats, airplanes, buses, and high places. Compared to balance disorder patients without panic, balance disorder patients with panic disorder had an earlier age of onset of vestibular disorder symptoms (33 yrs. v. 51 yrs.; $t = 3.67$, $p < .001$), more avoidance (Mobility Inventory: 2.7 v. 1.5; $t = 4.67$, $p < .0001$), and higher levels of anxiety (Beck Anxiety Inventory: mean = 18.0 v. 9.3; $t = 3.70$, $p < .001$). The results suggest that many patients presenting with vestibular disorder symptoms have a subtype of panic disorder characterized by vestibular, as opposed to cardiac, symptoms and space/motion phobia (Jacob, et al, 1989).

NR365 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Long-term Alprazolam Therapy in Panic Disorder

Richard C. Shelton, M.D., Psychiatry, Vanderbilt University, TVC RM 3942 22nd Avenue, South, Nashville, TN 37232; Phyleen Stewart, Shawn Harvey, Peter T. Loosen, M.D.

Summary:

Alprazolam has been established to be effective in the treatment of panic disorder in short-term trials but information regarding its long-term efficacy is lacking. The charts of 78 outpatients with panic disorder treated with alprazolam (mean dose 4.30 mg/day, mean duration 31.86 months) were reviewed. Moderate to significant improvement was found in 76.9 percent of patients. Alprazolam had been tapered in 67 (85.9 percent) patients and discontinued in 48 (61.5 percent), though 18 had been switched to clonazepam. Subjects with comorbid major depression (41 percent) were significantly more likely to have a diagnosis of panic disorder with agoraphobia (30/32, 93.8 percent) than those without depression (34/46, 73.9 percent) (Fisher's Exact = 5.04, $df = 1$, $p < 0.03$). In addition, seven (21.9 percent) of depressives had a history of alcohol abuse, compared to two (4.3 percent) of non-depressives (Fisher's Exact = 5.68, $df = 1$, $p < 0.02$). There was no *DSM-III-R* anxiolytic abuse, but 11.5 percent showed misuse of the alprazolam, all by regularly increasing the dose of drug. Alprazolam misusers were much more likely than non-misusers to have a history of drug abuse (three [33.3 percent] vs. seven [10.1 percent]) (Fisher's Exact = 3.83, $df = 1$, $p = 0.05$). The results indicate that alprazolam is effective in long-term treatment, but raise concerns about indiscriminate use in treating panic disorder.

NR366 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Effects of Intravenous Diazepam on Lactate-Induced Panic

Michael R. Liebowitz, M.D., Psychiatry, NYS Psychiatric Inst., 722 West 168th Street, New York, NY 10032; Jeremy D. Coplan, M.D., Jack M. Gorman, M.D., Abby J. Fyer, M.D., Jose Martinez, M.A., Donald F. Klein, M.D.

Summary:

To assess the role of prelactate anxiety levels on subsequent lactate responsivity, ten patients with panic disorder who panicked during a standard sodium lactate infusion underwent a repeat infusion modified by prelactate intravenous diazepam (5mg) treatment. Despite significant reductions of prelactate anxiety by diazepam, only three of ten patients experienced panic blockade during the second trial, a nonsignificant effect. Diazepam treatment did, however, significantly increase infusion duration when compared to the first trial. The findings of the current study therefore suggest that although reductions of prelactate anxiety by diazepam delays the onset of lactate panic, it does not alter its intrinsic panicogenic effects. A similar partial attenuation of lactate panicogenesis by acute administration of intravenous clonidine suggests that production of lactate panic may occur through the interaction of several neurochemical systems.

NR367 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Replication of Action of Cholecystokinin-Tetrapeptide-4 in Panic Disordered Patients

Jacques Bradwejn, M.D., Psychiatry, St. Marys Hospital, 3830 Lacombe Avenue, Montreal PQ, Canada H3T 1M5; Diana Koszycki, M.A., Richard Payeur, M.D., Heather Borthwick, M.D.

Summary:

CCK-4 induces panic attacks more often in panic disorder patients (PD) than normal controls. In order to study the effect of antipanic agents on CCK-4 induced panic attacks, it is important to determine whether the action of CCK-4 is reproducible upon repeated administration (test-retest effect). We studied whether the effects of CCK-4 were reproducible in PD. Patients (n = 10) received single-blind i.v. placebo and CCK-4 (25 ug) on two separate days. The onset of CCK-4 induced symptoms was more abrupt on day II ($P < .05$), but no significant test-retest differences were noted for the mean number and sum intensity of symptoms, or the frequency and intensity of individual symptoms. The rate of panic attacks was 90 percent on Day I and 80 percent on Day II. The data suggest that the effects of CCK-4 are reproducible within a given patient and that CCK-4 is a viable model to study whether antipanic agents can block CCK-4 induced panic attacks. The potential for this paradigm as a screening test for the antipanic activity of new drugs should be studied.

NR368 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Fluoxetine Augments Tricyclics in Panic Disorder

Indu M. Varia, M.D., Psychiatry, Duke University, Duke Med Ctr P.O. Box 3889, Durham, NC 27710; Craig L. Donnelly, M.D.

Summary:

BACKGROUND: We report the use of fluoxetine with low doses of tricyclic antidepressants to augment their therapeutic efficacy and to minimize the side effects of antidepressants associated with their standard doses in the treatment of panic disorder.

METHOD: Sixteen consecutive patients (age 19-56) who met the *DSM-III-R* criteria for panic disorder were given fluoxetine 20 mg and the tricyclic antidepressants 25-50mg. SCL-90 was measured before and after the treatment. Tricyclic antidepressant plasma levels were measured after two to three weeks of augmentation therapy. Minimum follow-up period is three months.

RESULTS: In 14 out of the 16 patients, clinical assessment as well as SCL-90 demonstrated significant improvement in control of their panic disorder. One patient could not tolerate desipramine. Although minor side effects were seen in most patients, no major adverse effects were observed.

CONCLUSION: These data suggest that fluoxetine may have a role in augmenting *low* dose tricyclic antidepressant treatment for therapeutic effectiveness with minimal adverse effects in panic disorder.

NR369 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Follow-up Study of Alprazolam Treated Panic Disorder

James L. Abelson, M.D., Psychiatry, Univ of Michigan, Med Inn 405 1500 E Med Ctr Dr., Ann Arbor, MI 48109; George C. Curtis, M.D., Oliver G. Cameron, M.D., Pamela B. Schweitzer, B.S.N.

Summary:

Alprazolam is now an "approved" treatment for panic disorder, but there are concerns about the long-term course of alprazolam-treated patients since its use may be complicated by tolerance, withdrawal, and excessive relapse rates upon discontinuation. Available outcome data may lack relevance to clinical practice, since drug taper rates are dictated by protocol and are more rapid than those used in many clinical settings. In order to obtain naturalistic data on the long-term course of alprazolam treatment of panic, we obtained follow-up data on 18 of 20 patients who had been enrolled 12 to 24 months earlier in a study of alprazolam effects on hypothalamic-pituitary-adrenal (HPA) axis functioning. The HPA protocol provided measures of symptom severity, biological markers, and short-term treatment response (three months). Routine clinical care was then provided, with dosage adjustments dictated by individual clinical needs. The follow-up study repeated clinical measures 11 to 26 months (mean = 21) after initiation of treatment. Patients were treated with alprazolam for 4.5 to >22 months. Drug tapers lasted from one to 18 months (mean = 5.2) and led to successful discontinuation in 78 percent of patients. Relapse occurred in 36 percent of these, an average of 6.4 months after drug discontinuation. At follow-up, 61 percent were medication-free. No one who discontinued alprazolam restarted it. All patients remaining on alprazolam were on substantially reduced doses. The total group showed significant improvement on all clinical measures during the short-term protocol. Non-relapsing patients showed a further reduction in disability at follow-up; and the total group had improved values on all clinical measures at follow-up despite the presence of the five relapsers. HPA axis activity did not predict dose requirements, discontinuation difficulties, or relapse. Implications for the clinical management and biology of panic disorder will be discussed.

NR370 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Thyroid Activity in Depression with Panic Symptoms

Gary M. Hasey, M.D., Psychiatry, Clarke Institute, 250 College Street, Toronto, ON, Canada M5T1R8; Robert G. Cooke, M.D., Jerry J. Warsh, M.D., David Koczerginski, M.D., A. Bonello, B.A., T. Jorna, B.Sc.

Summary:

Sympathetic overdrive is seen in hyperthyroidism and panic disorder (PD), and both conditions may be associated with major depression (MD). Thyroid function and psychopathology were retrospectively compared in 31 lithium free patients who met *DSM-III* criteria for MD and PD (MD-PD) and in 57 who had MD only (MDO). Diagnoses were made using the Diagnostic Interview Schedule. The MD-PD group had higher T4 ($p < .001$) and free T4 index ($p < .0003$) but similar TSH and T3RU. Including patients on lithium, the MD-PD group (38) had higher depression rating scale scores ($p < .0002$), more depressive symptoms ($p < .0007$), longer hospital stay ($p < .032$), and greater prevalence of alcohol abuse ($p < .05$), obsessive compulsive symptoms ($p < .02$) than MDO patients (82). PD was much more common in unipolar than in bipolar patients ($p < .003$). These preliminary data suggest that MD-PD patients are sicker, less responsive to treatment, and have higher thyroid activity than MDO patients. Some of these symptom differences may be the result of thyroid effects upon adrenergic functioning in the brain.

NR371 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Explaining Impairment in Panic Patients

Andrew C. Leon, Ph.D., Psychiatry, New York Hospital, 525 East 68th Street, New York, NY 10021; M. Katherine Shear, M.D., Laura Portera, M.A.

Summary:

A guiding principle in the development of the *DSM-IV* is the empirical validation of the diagnostic criteria. As a contribution to that

process, this study set out to determine aspects of panic-related impairment that are not reflected in the *DSM-III-R* criteria for panic disorder. An examination of *DSM-III*, *DSM-III-R* and other hypothesized correlates of panic disorder impairment was conducted. The study sample consisted of 71 outpatients being treated for panic disorder. The relationship between each of the criteria and a composite measure of social, family, and vocational impairment was examined. Two current criteria, frequency of attacks and anticipatory anxiety, along with comorbid diagnosis of dysthymia and a more general nonpanic symptomatology were significantly related to impairment. Neither the number of symptoms in an attack, nor other comorbid diagnoses, added to the predictive validity of the explanatory variables. These results from a clinical sample are contrasted with those from an epidemiologic sample.

NR372 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Child Abuse in Panic Disorder: Hypnotic Findings

Ambrogio Pennati, M.D., Dept. of Psychiatry, Ospedale S. Paolo, Via A. Di Rudini 8, 20142 Milano, Italy; Emilio Sacchetti, M.D.

Summary:

Child abuse (CA) seems to be a significant risk factor for several psychiatric disorders (1) but no data exist about CA in panic disorder (DAP). Therefore, 21, DAP *DSM-III-R* criteria; 13 with and eight without agoraphobia patients were asked to report about sexual and/or physical abuse before age of 15. In order to avoid possible post-traumatic amnesia (1) we used the hypnotic technique of age regression (2). CA was reported by 11 patients (52 percent), and nine of the abused subjects were completing amnesic about CA before the hypnotic inquire. All abused patients described a strict similarity between feelings during CA and panic attacks. No association was found between CA and agoraphobia. Revivification of CA led to a significant reduction of frequence and severity of attacks. The high rate of CA and the symptomatological improvement following its revivification suggest, although preliminary, a possible pathogenetical relevance for CA in DAP.

References:

1) VanderKolk B: Psychological Trauma, APA Press, 1987.
2) Spiegel H, Spiegel D: Trance and treatment, APA Press, 1978.

NR373 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Panic Disorder in an Inner-City Psychiatric Outpatient Department: Results of a Structured Interview

Cheryl M. Paradis, Psy.D., Psychiatry, SUNY HSCB, 450 Clarkson Avenue Box 1203, Brooklyn, NY 11203; Steven Friedman, Ph.D., Ronald M. Lazar, Ph.D., John Grubea, M.D., Martin Kesselman, M.D.

Summary:

One hundred psychiatric outpatients at a municipal hospital were screened with the Anxiety Disorder Interview Schedule — Revised (ADIS-R) to assess the presence of anxiety symptoms meeting *DSM-III-R* criteria for panic disorder, obsessive-compulsive disorder, post-traumatic stress disorder, and simple phobia. These patients were primarily black and low in socioeconomic status. The structured interview identified seven patients with primary panic disorder, three with post-traumatic stress disorder, and one with obsessive-compulsive disorder. Sixteen additional patients had an anxiety disorder as a secondary diagnosis. The outpatient clinical staff, however, did not diagnose any of these patients with a primary diagnosis of anxiety disorder. We conclude that a structured interview is an effective means in identifying panic disorder, which is underdiagnosed in this patient population.

NR374 Tuesday May 14, 3:00 p.m.-5:00 p.m.

HLA and Panic Disorder

Jose L. Ayuso-Gutierrez, M.D., Psychiatry, Hospital San Carlos, Isaac Peral sn., Madrid 28040, Spain; Leopoldo J. Llorente Perez, M.D., Carmen Ponce De Leon, M.D., Jose L. Ayuso-Mateos, M.D.

Summary:

We used the HLA system to evaluate the distribution of different antigens in the members of a family with high morbidity of panic disorder. Our aim was to look for HLA haplotype sharing among the affected subjects. All members of the family were interviewed with the SCID interview to detect any psychiatric disorder. Third generation members under 18 were evaluated with a structured interview especially designed to identify separation anxiety disorder. In all cases we assessed 11 HLA-A, 16 HLA-B and 5 HLA-Cw antigens.

The result suggest a genetic component for panic disorder, based on the presence of the same haplotype (A3B18) in the six members of the family suffering from panic disorder and agoraphobia, compared with its absence in the others who were free of such disorders.

NR375 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Mental Health Intervention Programs in Primary Care: Their Scientific Basis

Wim van den Brink, M.D., Psychiatry, Univ of Groningen Social, Oostersingel 59, Groningen 59 RB 09700, The Netherlands; Johan Ormel, Ph.D.

Summary:

This study examines the scientific basis for mental health intervention programs in primary care. The validity of five underlying assumptions is evaluated, using the results of a naturalistic follow-up study covering 1450 GP attenders from a representative sample of 25 GPs. Our findings corroborate the validity of these assumptions. Firstly, our study indicates that mental disorders are indeed very prevalent in primary care settings (10-30 percent depending on case-definition). Secondly, it is shown that a substantial proportion of mental disorders is not recognized by the GP. Thirdly, our data show that mean episode duration after index-consultation is about nine months and that approximately 50 percent of the mental disorders in primary care have an unfavorable course. Fourthly, we find that only half of the GP attenders with a mental disorder received some form of mental health treatment in the 14 months after index-consultation. Anxiolytics were the most frequently prescribed drugs for almost any mental disorder. GPs were very reluctant to prescribe antidepressants. Finally, our data suggest that mental disorders, when identified, can be treated effectively in primary care. Future training programs for general practitioners should be directed at improving recognition and diagnosis and at enhancing the availability and quality of mental health interventions. The effectiveness of these programs have to be tested in randomized trials.

NR376 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Effects of Aging on Somatization in Panic Disorder

Javaid I. Sheikh, M.D., Psychiatry, Stanford University, TD-114 Stanford Sch of Med, Stanford, CA 94305; Gregory R. Bail, B.A., Gregory C. Sazima, M.D., Roy J. King, M.D.

Summary:

Studies suggest the presence of higher somatization in panic disorder patients compared to normal controls [1]. No investigation has looked at the possibility that somatization may increase

with age in such patients. The purpose of the present study was to inquire into the possible differences in somatization between young and older panic disorder patients.

Our sample consisted of 64 females who were participating in studies of psychopharmacological treatments for panic disorder. All subjects met the *DSM-III-R* criteria for panic disorder, were in good physical health, and intact cognitively. They were evaluated using the Self-Report Inventory for Somatic Symptoms (SSIS) [2] before the start of treatment. Older subjects ages 55 and above (n = 22; age range 55-72, mean age = 60.2) were compared to younger subjects (n = 42; age range 21-54, mean age = 34.6). The older subjects showed a significantly higher Total Somatization Disorder Scores (TSDS) than younger patients (mean = 11.54, sd = 7.45 vs. mean = 8.07, sd = 4.77; $p < .05$). Implications of these findings for diagnosis, therapeutic strategies, and future research will be discussed.

NR377 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Panic Disorder and Chest Pain in the Coronary Care Unit

Cameron S. Carter, M.D., Psychiatry, UC Davis, 4430 V. Street, Sacramento, CA 95817; Richard M. Maddock, M.D., Steven McCormick, Ph.D., C. Waters, M.D., J. Billett, M.D., E. Amsterdam, M.D.

Summary:

Consecutive admissions to the UCD Medical Center C.C.U. to rule out myocardial infarction were evaluated using the SCID by interviewers blind to the patients cardiac status. Of a total N = 71 62 (87.3 percent) consented and gave reliable histories. A total of (30.6 percent) patients evaluated met criteria for panic disorder. Thirteen (20 percent) ruled in for myocardial infarction; 35 (56 percent) had at least one positive cardiac finding. Two patients with panic disorder ruled in for myocardial infarction (10.5 percent of total P.D.) Eleven subjects without panic disorder ruled in for MI (25.6 percent non P.D.). Four patients with panic disorder had a positive cardiac workup (21 percent of total P.D.). Thirty-one patients without P.D. had a positive cardiac workup (72.1 percent of non P.D. group). Of the 27 patients with a negative cardiac workup 15 had panic disorder (55.5 percent). Overall 79 percent of those with panic disorder had a negative cardiac workup, compared with 28 percent of those without panic disorder. These findings suggest that while the presence of panic disorder in no way rules out the presence of an acute myocardial event in patients with acute chest pain it is associated with a decreased likelihood of positive cardiac findings overall. They also emphasize the strikingly high prevalence of panic disorder among patients with acute chest pain and no cardiac findings, a finding consistent with previous studies of chest pain patients in other settings. Demographic and other patient characteristics will be reviewed including their clinical course. The presence of other psychiatric disorders and their relevance to these findings above will be discussed.

NR378 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Co-Segregation of Alcoholism, Anxiety and Depression

Wolfgang Maier, M.D., Psychiatry, University of Mainz, Untere Zahlbacher Strasse 8, 6500 Mainz, Germany; Dirk Lichtermann.

Summary:

Combination of alcoholism and/or panic disorder and/or unipolar depression have been frequently observed in treated and non-treated populations. Controlled family studies including probands with all three disorders and their combinations may help clarify the mechanisms of those associations (1,2): if the individual disorders are breeding true there is no overlap of etiological compounds; if they are congregating, a sharing of etiological factors is likely. Unfortunately, no family of this kind is published.

Data of a family study conducted in Mainz/FRG in 240 probands (in/out-patients) with unipolar major depression or alcoholism or panic disorder/agoraphobia and 80 healthy control probands (recruited in the general population) are presented; 80 percent of the living first-degree relatives were interviewed directly (SADS-LA).

All three disorders were found to be familial. Panic disorder was breeding true; alcoholism was also more common in relatives of probands with agoraphobia; no direct association between alcoholism and depression was found; the risk of depression was increased in families of panic disorder probands. The variation of the transmission of major depression and of alcoholism was mediated by panic disorder.

NR379 Tuesday May 14, 3:00 p.m.-5:00 p.m.

The Effects of Single-Dose Anxiolytics Upon Memory

James G. Barbee, M.D., Psychiatry, LSU Medical Center, 1542 Tulane Avenue, New Orleans, LA 70112; William F. Black, Ph.D., Catherine E. Kehoe, M.Ed, Alexandre A. Todorov, M.Ed.

Summary:

The cognitive and psychomotor effects of alprazolam (in dosages of 1.0 mg and 0.5 mg) and buspirone (in dosages of 10 mg and 5 mg) were compared to placebo in a study sample of 125 young, healthy students, utilizing a single-dose, double-blind design. In dosages which were not sedating and did not significantly impair visuomotor reaction time, alprazolam 1.0 mg did result in significant impairments on two of the subtests of a modified version of the Randt Memory Test. Alprazolam .5 mg showed similar non-significant trends. Buspirone 5 mg showed a (nonsignificant) trend toward improvement of memory function.

The data from this experiment will be reviewed in the context of recent efforts to utilize the effects of the benzodiazepines as a neuropharmacological model for organic-induced amnesias (1). A hypothetical mechanism for these results, based upon the effects of the benzodiazepines upon the phenomenon of long-term potentiation (2), as mediated through the NMDA receptor, will be described. The clinical implications of these findings in the treatment of anxiety will also be discussed.

NR380 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Discontinuation of Fluoxetine in Trichotillomania

Cesar L. Benarroche, M.D., Fair Oaks Hospital, 5440 Linton Blvd., Delray Beach, FL 33484

Summary:

This study is part of an ongoing open investigation of the responsiveness of trichotillomania patients to long-term, high dose (80 mgs.), fluoxetine treatment. Last year we reported that 80 percent of our subjects and a ≥60 percent reduction of hair pulling behavior after completion of a three-month open trial of fluoxetine 80 mgs./day as measured by Y-BOCS-C, (compulsions), Trichotillomania Impairment Scale (TIS). NIMH global and hair counts.

Ten patients who were still responders after 12 months of treatment with 80 mgs. of fluoxetine were gradually withdrawn from the drug at a rate of 20 mgs./month. By month 4 all patients had relapsed (NIMH global, TIS or Y-BOCS-C ≥baseline). Comorbid syndromes = panic disorder (N = 2), major depression (N = 3), and OCD (N = 2) as well as associated oral behaviors (lip touching or trichophagia) remained either in remission or improved from baseline after discontinuation.

We conclude that trichotillomania is a chronic disorder with a strikingly rapid rate of relapse after fluoxetine discontinuation. It is possible that this syndrome has different response/relapse patterns compared to comorbid disorders and associated oral behaviors.

NR381 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Comparison of Two Flexible Drug Schedules for Panic

Sergio Gloger, M.D., Psychiatry, Catholic Univ-Chile, Casilla 114-D, Santiago, Chile; Francisco O'Ryan, M.D., Alexei Franulic, M.D., Fernando Pizarro, M.T., Mario Barahona, R.N.

Summary:

In a previous trial we found that low doses of clomipramine (CMI) were significantly more effective than diazepam for panic disorder patients. Alprazolam (ALP) has been found equally effective to standard doses of imipramine. Fixed doses have been used in most studies; few have evaluated the effectiveness of individual dose responses. This 16-week, randomized double-blind study compares the treatment outcome of CMI and ALP, in 60 *DSM-III-R* (300.21-300.01) panic patients. After two placebo wash-out weeks, drug schedule slowly increased to target doses by week 8 (CMI 150 mg, ALP 6mg). Nevertheless, dose augmentation was stopped when clear clinical improvement was achieved. Forty-two subjects (ALP 22, CMI 20) completed the trial, 31 women and 11 men (two placebo responders, nine wash-out dropouts, seven active drug phase). A daily panic inventory, C.G.I. and six other monthly rating scales were administered.

Both drug treatments were equally effective according to all measurements (p N.S). Mean doses were CMI: 78 mg and ALP: 2.9 mg. Ten CMI subjects received 10-75 mg (mean 41.5) and the other half got 100-150 mg; Nine ALP patients received 0.75-2.5 mg and 13 received 3-6 mg. Higher mean doses of ALP were required in the agoraphobics compared to the pure panic patients (3.3 vs 1.8 mg). CMI and ALP higher doses were not more effective than lower doses. This study suggests that both drugs are effective and comparable treatments for panic and that individual dosage should be considered for good clinical practice. Supported by FONDECYT grant 472-89.

NR382 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Social Phobia in Panic Patients

Jean-Michel Chignon, M.D., Dept. of Psychiatry, Hopital Bichat, 46 Rue Henri-Hochard, Paris 75877, France Cedex18; Mardjane Teherani, R.A., Elie Hantouche, M.D., J. Pierre Lepine, M.D.

Summary:

Patients with anxiety disorders often have features of multiple disorders. In an ongoing clinical study among panic patients, we assessed the comorbidity between social phobia and other anxiety and mood disorders.

We studied 155 patients fulfilling panic disorder (PD) criteria *(DSM-III-R)*, 50 males and 105 females, who were consecutive referrals in the anxiety clinic. All of them were interviewed with a modified version of the SADS-LA. Lifetime comorbidity with agoraphobia, obsessive-compulsive disorder (OCD), major depressive episode (MDE) and/or alcohol abuse was very frequent in this population. Only 16.8 percent of these patients were suffering from PD alone, 41.3 percent had another lifetime diagnostic, and 41.9 percent had at least two other diagnoses.

Fifty patients, 18 males and 32 females, had a lifetime diagnostic of social phobia. Age at the time of referral, age of the first panic and age of onset of PD were similar in patients who suffered from social phobia and those who did not. Lifetime comorbidity was higher in social phobics than in other PD patients ($p<.01$). We found an association between social phobia and OCD ($p<.01$) but not with either agoraphobia or alcohol abuse. Although the rates were not statistically significant, panic patients with social phobia had more often a history of MDE ($p<.06$). Such pattern of comorbidity in panic social phobics differs from the usual comorbidity of primary social phobics with depression and alcoholism.

NR383 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Panic Disorder: Which Diagnostic Criteria?

Jean-Pierre Lepine, M.D., Dept. of Psychiatry, Hopital Bichat, 46 Rue Henri-Hochard, Paris 75877, France Cedex18; Joseph Lellouch, Ph.D.

Summary:

The *DSM-III* and *DSM-III-R* panic disorder (PD) definitions differ in several ways, mostly on the recurrence of panic attacks. As precised in the *DSM-III-R*, PD patients must have experienced either four attacks in a four-week period or "one or most attacks have been followed by a period of at least a month of persistent fear of having another attack". As far as the *DSM-IV* process is ongoing, more research data are needed to evaluate the influence of revisions and modifications of criteria.

In order to compare different criteria sets for PD, we reanalyzed a database obtained from an epidemiological survey in the general population including 1787 subjects. This study investigates the prevalence and risk factors of anxiety and depressive disorders assessed by modified sections of the DIS/CIDI. We added some new questions on the recurrence of panic attacks, the presence of a "persistent fear of having another attack" and the occurrence of acute somatic anxiety symptoms which are very often labelled by french general practitioners "spasmophilia."

First, the inclusion of the anticipatory anxiety criterion lead to a two-fold increase of the rate of PD. Secondly, many subjects denying any history of an acute anxiety attack reported they "ever had a dizzy spell, palpitations, tetany or spasmophilia." After probing, as required by the CIDI, and applying the same algorithms than for the *DSM-III-R* PD, we found another subgroup suffering from what may be called "recurrent acute somatic symptoms."

In an attempt to validate these different definitions of PD we compared the different subgroups according comorbidity, global well-being, and psychotropic drug use at the time of the interview. Results of these analyses are presented.

NR384 Tuesday May 14, 3:00 p.m.-5:00 p.m.

PTSD in Combat Veterans of WWII, Korea and Vietnam

Robert Rosenheck, M.D., NEPEC., VA Medical Center, 950 Campbell Avenue, West Haven, CT 06516; Alan Fontana, Ph.D

Summary:

Introduction: Combat veterans of World War II, the Korean conflict, and the Vietnam conflict were systematically evaluated in the national, Department of Veterans Affairs PTSD Clinical Teams Program (N = 1,734). This study compared: 1) combat trauma, 2) PTSD symptomatology, 3) course of illness, 4) non PTSD psychiatric symptomatology and 6) social adjustment among veterans of these wars. *Results*: Veterans of the three wars scored similarly on measures of combat exposure, but Korean and Vietnam veterans more frequently reported participation in abusive violence and feelings of alienation after their return home. Vietnam veterans more often met *DSM-III* criteria for PTSD (74.5 percent) than World War II (54.7 percent) or Korean veterans (64.8 percent). Frequencies of individual PTSD symptoms were similar with the exception of numbing/avoidance symptoms which were highest among Vietnam veterans. Vietnam veterans more often experienced a delay in recognition of the war-related nature of their symptoms than veterans of other wars. Psychiatric symptomatology, history of suicidal behavior, substance abuse, and social isolation, were highest amoung Vietnam veterans. *Conclusions*: PTSD is identified among treatment seeking combat veterans of all three major 20th century American wars but clinical differences are noted and may be explained by differences in combat experience, generational cohort phenomena, and the aging process.

NR385 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Diagnosis Related Group Based-Budgeting and the VA Psychiatric Care

Robert Rosenheck, M.D., NEPEC, VA Medical Center, 950 Campbell Avenue, West Haven, CT 06516; Louis Massari, M.P.H.

Summary:

Introduction: This study examined the impact of both the *implementation* (in 1984) and *suspension* (in 1988) of Diagnosis Related Group (DRG)-based budgeting on inpatient psychiatric care in VA Medical Centers. *Methods:* Computerized discharge abstracts were reviewed for all episodes of VA inpatient care occurring nationally from 1980 though 1989. Various measure of inpatient care were determined for psychiatric and nonpsychiatric (i.e. medical and surgical) care before, during, and after DRG-based budgeting was in effect. *Results*: In the case of VA psychiatric care, implementation of DRG-based budgeting was associated with increased episodes of care (+7.2 percent/year), shortened lengths of stay (–9.2 percent/year), higher re-admission rates (+8.7 percent/year) and a greater number of episodes of care per occupied bed (+13.1 percent/year). DRG-based budgeting had similar effects on medical-surgical care, although an increase in episodes of care was not observed. Changes in both psychiatric and medical-surgical care that were related to DRG-based budgeting were slowed, and in some cases reversed, during the first year after this funding mechanism was suspended.

Conclusions: Psychiatric inpatient care in the VA have been shown to be sensitive to changes in funding mechanisms. These changes were generally similar to those observed in VA medical-surgical care and in psychiatric care provided by non-VA hospitals reimbursed under Medicare's DRG-based prospective payment system.

NR386 Tuesday May 14, 3:00 p.m.-5:00 p.m.

The Multidimensionality of Grief: A New Measure

Susan D. Cunningham, M.D., Psychiatry, Michigan State Univ., B-117 West Fee Hall, East Lansing, MI 48824.

Summary:

Studies suggest differences in bereavement between those suffering an unexpected loss from those experiencing an expected loss. This investigation involved a retrospective survey of 150 subjects who had experienced the loss of a relative or close friend in a variety of ways. These losses were classified into expected and unexpected categories. A 52-item self-report Grief Dimension Scale (GDS), developed for the study indicated those experiencing unexpected losses reported significantly more distress than those experiencing an expected loss, as reflected by the total GDS score, ($p < .0001$). A step-wise multiple regression analysis revealed the younger age (i.e. 45 or less) of the decreased ($p < .00001$), shorter time (less than five years) since the death, and unexpected death ($p < .004$) all contributed significantly and independently in predicting the total GDS score prediction (multiple $R = .71$). Whether or not the body of the deceased was viewed by the bereaved and whether the death was by trauma rather than illness, were not independent predictors of the total GDS score.

This poster will provide details on the reliability of the measure and information on items characterizing the distinctive bereavement experiences of individuals who have undergone different types of losses.

NR387 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Stress and Coping Within Couples Forced to Relocate

Frederick S. Wamboldt, M.D., Medicine, National Jewish Center, 1400 Jackson Street, Denver, CO 80206; Peter Steinglass, M.D., Atara Kaplan-Denour, M.D.

Summary:

Is our understanding of how individuals adjust to stressful life events increased when we analyze their adjustment in ways that recognize that these individuals are also married couples? This question is addressed using data from a unique "natural experiment" occasioned by the forced evacuation of the Israeli settlement of Ophira under the terms of the Camp David Accords. Resource (coping skills and perceived social support) and adjustment (psychological and social) variables were collected from 36 individuals compromising 18 married couples prior to the involuntary relocation and again two years post-relocation. Three important results were found. First, adjustment in the vast majority of couples became more similar across the relocation, i.e., couples adapted as a "family system." Second, the increased similarity resulted because one member's prerelocation resources, specifically the member with the best coping skills, predicted the adjustment for both individuals in the couple. If one member had good coping skills, both members benefitted. Finally, although most couples became more similar, a small number showed a second, "polarized" pattern of adjustment, with one spouse getting better, the other worse across the relocation. This "polarized" outcome appeared related to preexisting longstanding individual and marital psychopathology. The implications of these findings for the theory and practice of psychiatry will be discussed.

NR388 Tuesday May 14, 3:00 p.m.-5:00 p.m.

1988 Spitak Earthquake: Child PTSD Reactions

Robert S. Pynoos, M.D., Psychiatry, UCLA NPI&H, 300 UCLA Medical Plaza, Los Angeles, CA 90024; Armen K. Goenjian, M.D., Meline Karakashyan, Ed.S., Raffi Manjikian, C.A.S., Madlene S. Tashjian, R.N., Setrak Setryian, Ph.D.

Summary:

On December 7, 1988, a devastating earthquake struck Soviet Armenia causing widespread destruction, injury, and death. The Armenian Relief Society's Earthquake Relief Fund established an extensive outreach mental health program. In collaboration with the UCLA Program in Trauma, Violence and Sudden Bereavement, the Armenian teams conducted a one-year post-earthquake screening of school age children in three cities–Spitak, Gumayri (Leninagan) and Yerevan, which were at increasing distances from the epicenter of the earthquake. A child post-traumatic stress disorder reaction index (PTSDRI) was administered to 237 children. In a subgroup, there was a .98 correlation between scores on the Armenian and English versions of the PTSDRI. There was a direct relationship between the intensity and destructive impact of the earthquake and the mean reaction index scores (Spitak, 52.6; Gumayri, 43.6; and Yerevan, 35.2; $F = 42.3$, $df = 2, 234$, $p < .001$). Ninety-two percent of the children in Spitak suffered from severe or very severe PTSD reactions, 69 percent in Gumayri and 32 percent in Yerevan. In a subgroup, there was a high level of agreement between severity categories and *DSM-III-R* PTSD by clinical assessment.

NR389 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Course of Psychological Symptoms After Lawsuits

Renee L. Binder, M.D., 401 Parnassus Avenue, San Francisco, CA 94143; Michael R. Trimble, M.B., Dale E. McNiel, Ph.D.

Summary:

Although psychiatrists are frequently asked by attorneys to evaluate the extent of psychological damage and prognosis for psycho-

logical symptoms suffered by accident victims, few follow-up studies have been conducted of litigants whose lawsuits claim that they have suffered psychological symptoms from accidents. This study followed up 18 such accident victims after their lawsuits had been settled (mean = 2.5 years, SD = 1.69, range, 0.1 to 5.7), using standardized measures of diagnosis (Structured Clinical Interview for *DSM-III-R*), symptoms of post-traumatic stress disorder (Impact of Event Scale), general psychological distress (SCL-90R), and overall severity of psychiatric impairment (Global Assessment of Functioning scale). From the time of the accident to the time of the interview (mean = 7.2 years), the proportion of subjects with one or more *DSM-III-R* diagnoses decreased significantly, from 78 percent to 44 percent ($p < .02$, Fisher's Exact Test). Correlation analyses showed that better psychological outcome, as indicated by the GAF, was associated with a shorter time between the accident and settlement of the lawsuit ($r = -.50$, $p < .04$), a longer time after lawsuit resolution ($r = .55$, $p < .03$), and less severe initial psychiatric symptomatology. Long-term psychological outcome was not significantly correlated with age, gender, marital status, current employment status, extent of physical injury, or amount of compensation awarded.

NR390 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Dopamine in Acute and Chronic Stress

Mark B. Hamner, M.D., Psychiatry, VAMC and MUSC, 109 Bee Street 116A VAMC, Charleston, SC 29403; John I. Entrekin, B.S., Bruce I. Diamond, Ph.D.

Summary:

The role of dopamine (DA) in response to acute or chronic stress is unclear. The forced swim (FS) test may be a model for stress-response. In this test, animals develop increased immobility on repeat exposure to swimming in an inescapable container. We hypothesized that if DA is involved differentially in response to acute versus repeated stress then dopaminergic drugs would alter immobility responses as a function of acute vs chronic stress. We studied male Sprague-Dawley rats (160-180 g) undergoing acute FS (AFS) or chronic FS (CFS). Animals received ip haloperidol (HAL) 0.2 mg/kg, apomorphine (APO) 0.25 mg/kg, or water (CONT) 15 min prior to timing their immobility responses. They were tested on days 1, 7, and 14 after the final FS. APO increased immobility in the AFS group on day 7 (APO 290 $\pm$ 4.6 sec vs CONT 271 + 8.7 sec, $p < 0.005$) but not days 1 or 14. In the CFS group, APO increased immobility at day 14 (APO 292 $\pm$ 4.4 sec vs CONT 278 $\pm$ 15.5 sec, $p < 0.004$). HAL also increased immobility on day 14 in the CS group only (HAL 290 $\pm$ 3.3 2sec vs CONT, $p < 0.007$). These data support a role for DA in stress-response. The delayed effects of these DA agents on immobility and the similar effects of HAL and APO in chronic stress implicate alterations in DA receptor function.

NR391 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Perceived Stress, Sleep and Natural Killer Function in Medical School

Steven E. Keller, Ph.D., Psychiatry, UMD-NJ Medical School, 185 South Orange Avenue, Newark, NJ 07103; David F. Dinges, Ph.D., Emily Carota-Orne, Nancy Bauer-Manley, M.S.S., Wayne G. Whitehouse, Ph.D., Martin T. Orne, Ph.D.

Summary:

To assess the relationship between stress and immune function, we recorded Natural Killer (NK) cell function of 37 students during their fist semester in medical school, at weeks 1, 14, 16 (acute exam stress), and week 19 (post semester recess). Perceived stress varied across the semester ($F = 5.4$, $p < .002$), peaking at week 16, relative to low post-recess. NK activity (% cytotoxicity) paralleled these ratings (F-19.3, $p < .0005$), with lows at weeks 1 and 19, and highs at weeks 14 and 15. Similarly, average weekday total sleep time was significantly lower during weeks 14 and 16 relative to weeks 1 and 19. The correlation between mean weekday stress and sleep across all 19 weeks was $rho = -.70$ ($p < .005$); when stress was perceived as high, sleep was reduced. These covariations suggest that changes in perceived stress, sleep, and NK activity may reflect a common psychobiological process mobilized at times of high performance demand.

NR392 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Physician Pregnancy: Colleagues' Attitudes

Marijo B. Tamburrino, M.D., Psychiatry, Medical College of OH, 3000 Arlington P.O. Box 10008, Toledo, OH 43699; Cynthia L. Evans, M.D., Kathleen Franco, M.D., Nancy Campbell, M.D.

Summary:

As more women enter the field of medicine and the percentage of female medical students and physicians having children increases, the impact of pregnancy on one's colleagues deserves attention. This is of special interest due to the overlap of childbearing years with those of medical training and career building.

A total of 833 survey questionnaires were sent to medical students, residents, and faculty with a return rate of 47 percent ($N = 372$). Females comprised 32 percent ($N = 121$) of the sample and men 68 percent ($N = 251$).

More women than men felt that pregnant physicians maintain job performance and interest in patient care, departmental affairs, and chosen field of medicine. Women were more likely than men to endorse flexible scheduling, maternity leave, and reduced on call for pregnant physicians. Men considered women of childbearing years as being a risk to optimal functioning of the department; women did not.

Thus, there were significant gender differences in attitudes toward physician pregnancy, indicating that underlying conflicts do exist. Open discussion of this topic with written maternity/paternity policies may help to reduce these conflicts by careful planning.

Providing a less stressful and more nurturing environment for pregnant physicians may enable these caregivers to more easily combine their roles of mother and professional.

NR393 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Effects of Disasters on Emergency Workers

J. Lachenmeyer, Ph.D., North Shore Univ Hosp., 300 Community Drive, Manhasset, NY 11030; M. Gibbs, Ph.D., A. Dillonma, L. Lodico, M.D., R. Deucher, M.D., T. Vandersall, M.D.

Summary:

Little research exists on the psychological effects of emergency work for the personnel involved, Taylor and Frazer (1982) found that emergency workers at the Mt. Erebus crash reported signs of stress up to 20 months after the crash. Jones (1985) found youth, lack of experience, lower rank, and degree of exposure were all related to each other and were associated with emotional stress in the military men and women who recovered bodies following the mass suicides by members of the People's Temple at Georgetown, Guyana, 1978. The present study assessed reactions of 77 emergency workers, nurses, physicians, and security personnel to the Avianca airliner crash on Long Island, NY, 1990. The questionnaires were distributed approximately two months following the disaster. Group contrasts were performed. Nurses reported significantly more changes in energy levels, depression, confused, and angry feelings than the other three groups. Emergency workers and nurses reported significantly more worried feelings and the greatest

desire to be around others. Several variables are likely to be important: the exposure to the disaster scene including triaging of victims, direct exposure to large number of victims, and direct or perceived impact on survival. Implications of these findings by the emergency function performed will be discussed.

NR394 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Psychiatric Predictors of Length of Hospital Stay in Hip Fracture Patients

John S. Lyons, Ph.D., Psychiatry, Northwestern Univ Hosp, 303 E Chicago Ave Ward 12-138, Chicago, IL 60601; James J. Strain, M.D., Marianne Fahs, Ph.D., Jeffrey S. Hammer, M.D.

Summary:

Introduction: Fulop et al. observed a relationship between medical and psychiatric morbidity and length of stay (LOS). This prospection denominator study examines elderly patients hospitalized for an acute hip fracture to understand the relationship between their admission psychiatric status and LOS at two university hospitals: Mount Sinai (MSH) (NYC) and Northwestern Memorial (NMH) (Chicago). *Findings:* At admission, all elderly acutely fractured hip patients (1987-1989) were administered the Geriatric Depression Scale (GDS), the Spielberg Trait/State Anxiety Inventory (STAI), and the Mini-Mental Status (MMS). The correlation between depression and LOS was: MSH - $r = .33$ ($p = < .01$, $N = 73$); NMH - $r = .32$ ($p = < .01$, $N = 91$). Correlations between anxiety and LOS were: MSH - $r. = 37$ ($p = < .01$, $N = 71$); NMH - $r = .17$ $p = < .1$, $N = 94$). No significant relationship was observed between the MMS and LOS at either hospital. At MSH psychiatric liaison intervention was more effective with cognitive impairment and at NMH with depression, both of which were associated with decreased LOS. *Conclusion:* This is one of the first prospective "denominator" studies to demonstrate an increased LOS associated with psychiatric morbidity. Analyses will examine the relationship of improvement in psychiatric morbidity post treatment and LOS.

NR395 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Psychopathology and Treatment of 30,344 Swedish Twins

Christer T. Allgulander, M.D., Karolinska Institute, Department of Psychiatry, M56 Hugginge Hospital, Hugginge Sweden 14186; John P. Rice, Ph.D., Justyna Nowak, M.Sc.

Summary:

We studied whether regular treatment with tranquilizing and hypnotic drugs among 30,344 twins in Sweden was associated with robust indicators of poor health. Longitudinal psychiatric diagnoses and subsequent suicides were analyzed with data from cross-sectional health questionnaires. The problem of potentially interacting variables in multiple domains was solved by creating severity scales within each of four survey domains, and analyzing them separate from the registry psychiatric diagnoses and suicides. We found that within each of mental, somatic, and lifestyle domains, medication was more frequent among those with multiple problems. We also found a genetic contribution to treatment and diagnosis, independent of sex and shared environment. We conclude that treatment was largely in agreement with current peer guidelines, although the reasons why women were more often treated than men require further study.

NR396 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Heatwave Deaths in Psychiatric Patients

Nigel M. Bark, M.D., Psychiatry B.P.C., Albert Einstein Col Med., 1500 Waters Place, Bronx, NY 10461; Anne Brebbia, M.A.

Summary:

This poster presents the results of a study of mortality during heat waves compared with control periods in psychiatric hospitals in and near New York City and in the general population of the city over 15 years, 1970 - 1984. There was a 38 percent increase in deaths during heat waves in the psychiatric hospitals compared with 17 percent in the general population. In the psychiatric hospitals there was not a significant difference in risk in different age groups although the elderly in the general population were at greater risk. Sex and race did not significantly affect the risk although younger female patients were at slightly increased risk whereas older females in the general populations were at increased risk. Diagnosis did not greatly alter the risk except that those with dementia were surprisingly at decreased risk. The greatest risk was in those in their first month of hospitalization. (The majority had been in hospital 10-20 years!)

There was a greatly decreased risk in the hospitals in the most recent five year period presumably a result of preventive measures taken within the hospitals. However, patients outside of hospital - especially the poor - are probably at much greater risk than those in hospital.

NR397 Tuesday May 14, 3:00 p.m.-5:00 p.m.

PTSD Symptoms in a Community Sample of WWII Veterans

Bruce A. Kaup, M.D., Psychiatry, Baltimore DVAMC, 3900 Loch Raven Blvd., Baltimore, MD 21218; Joseph Liberto, M.D., Paul E. Ruskin, M.D.

Summary:

To study prevalence of chronic symptoms of PTSD in a community sample of WWII veterans, subjects were randomly selected from a WWII discharge list of Maryland residents. Twenty-five male veterans (mean age-69.6, average length of WWII service-35.9 months) with a current listing in the Baltimore telephone directory were recruited. The Brief Symptom Inventory, Combat Scale, PTSD section of the SCID, Mississippi Scale, and questions concerning demographics and military history were administered. Twenty-four percent of the veterans had been in direct combat, and 32 percent in combat support with variable combat exposure. The most common PTSD symptoms currently present among veterans scoring in the moderate/heavy combat range ($N = 14$) were difficulty sleeping (29 percent) and exaggerated startle response (29 percent). Survivor guilt was present in 71 percent. On the Mississippi Scale, the difference between group means of moderate/heavy combat vs. no/low combat (66.0 vs. 54.3) was statistically significant (1-tailed, $t = 2.43$, $df = 23$, $p < .025$), suggesting veterans with moderate/heavy combat experience exhibit chronic mild PTSD symptomatology. The difference between group means on the General Severity Index of the BSI (0.54 vs. 0.29) was statistically significant (1-tailed, $t = 2.18$, $df = 23$, $p < .025$), suggesting exposure to combat results in a higher level of chronic psychologic symptomatology. Thus, WWII combat veterans may continue to experience mild PTSD symptomatology 45-50 years after the original stressful experiences.

NR398 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Establishing Reliability and Validity for Axis IV

Carolyn M. Mazure, Psychiatry, Yale School of Medicine, Yale New Haven Hosp MU 10-5, New Haven, CT 06504.

Summary:

Axis IV is part of the *DSM-III-R* multiaxial system because stress remains implicated in the development and exacerbation of psychopathology. However, Axis IV interrater reliability has not been assessed in adults since the *DSM-III* field trials. *DSM-III* validity

studies have found that Axis IV scores have correlated with some yet not other patient variables thought to be associated with stress. But, it is unknown if a clinician's rating of how stressors affect an "average" person (i.e. Axis IV) reflects the patient's own perception of stress. The current work studied Axis IV (1) interrater reliability, and (2) validity in terms of the correlation of clinician Axis IV ratings with patients' own ratings on Axis IV. Study 1: Interrater reliability was excellent (N = 40 consecutive inpatients; weighted kappa = .76). Study 2: Patients were interviewed about stressors and then rated themselves on Axis IV. Patients rated their stress as significantly more severe than did clinicians (N = 31; McNemar chi square = 11.1, p = .001). This work indicates that despite interclinician reliability in rating Axis IV, clinician ratings based on the experience of an "average person" do not reflect patients' reports. Also, patients' scores were not correlated with illness severity (r = .06) indicating that patients' stress ratings are not simply a measure of patient psychopathology. Results further suggest that studies of validity must address whether clinician or patient ratings better serve the purpose of this axis.

NR399 Tuesday May 14, 3:00 p.m.-5:00 p.m.

Admission Decisions Using Artificial Neural Nets

Eugene C. Somoza, M.D., Psychiatry, VA Medical Center, 3200 Vine Street, Cincinnati, OH 45220; John Somoza, B.A.

Summary:

The purpose of this research is to study the decision-making process involved in admitting patients from a psychiatric evaluation center (PEC). Such a process involves the recognition of complex patterns that cannot easily be broken down into a set of separate non-interacting parameters. Instead, a "gestalt" approach is necessary. Such an approach is now possible with artificial neural networks. A 53-input-node neural net was trained to discriminate between patients needing admission and those who could be treated as outpatients. All walk-in patients arriving at our PEC during normal working hours during a 12 month period were included in this study. The network was trained to predict admission on half of them (N = 339), and tested on the other half (N = 319). Ten characteristics were presented to the network for each patient, including total BPRS score, GAF, diagnosis, etc. There was substantial agreement between the network's admission decision and that of the therapists (kappa coefficient = 0.66, sensitivity = 0.75, specificity = 0.92, accuracy = 0.91). Due to its high negative predictive power (0.95), such a neural net may have some value as a screening instrument in psychiatric emergency rooms. Methods for further improving its diagnostic performance will be discussed.

NR400 Wednesday May 15, 9:00 a.m.-10:30 a.m.

Sequelae of Birth Problems: The Vancouver Study

G. William MacEwan, M.D., Riverview Hospital, 500 Lougheed Highway, Port Coquitlam, BC Canada V3C 4J2; Geoffrey N. Smith, Ph.D., Raymond J. Ancill, M.B., Henry G. Dunn, M.B.

Educational Objectives:

The learner will be made aware of the evidence of increased obstetric complications in the history of schizophrenics.

Summary:

The Vancouver study involved the identification and prospective assessment of 501 low birth weight and 203 full birth weight infants. (Dunn, 1986) Comprehensive assessments were completed at birth and at regular intervals for seven to 15 years. These included detailed medical, social, psychological, and educational measures. This cohort is now 27 to 32 years of age and we are in the process of tracing each of the initial participants. There is clear evidence for increased number of obstetric complications in the history of schizophrenics (McNeil, 1988). A preliminary search through hospital records in one Vancouver hospital has identified seven psychotic patients and ten people with nonpsychotic psychiatric problems. Preliminary data on the obstetric and developmental histories of these individuals will be discussed.

References:

1. Dunn H.G. *Sequelae of Low Birthweight: The Vancouver Study.* Oxford, Blackwell, 1986.
2. McNeil T.F. *Obstetric Factors and Perinatal Injuries,* in Handbook of Schizophrenia. Vol. 3: Nosology, Epidemiology and Genetics. Edited by Tsuang M.T., Simpson J.R., New York, Elsevier 1988.

NR401 Wednesday May 15, 9:00 a.m.-10:30 a.m.

MRI in Schizophrenics and Their Siblings

Stephen C. Olson, M.D., Ohio State Univ, 473 West 12th Ave RM 065 Upham, Columbus, OH 43210; Henry A. Nasrallah, M.D., Steven B. Schwarzkopf, M.D., Mary B. Lynn, M.S.

Educational Objectives:

1) To understand how a study design utilizing siblings of schizophrenics can provide useful to understanding genetic *vs.* environmental etiologies. 2) To learn results of a MRI study using this design.

Summary:

Family members of persons with schizophrenia (SZ) provide an interesting control group for marker studies since both genetic and environmental influences can be studied while nonspecific factors such as ethnic and early nutritional differences are controlled. We report here results from a MRI study of SZ and their same-sex siblings (SIB) and pairs of normal siblings (CTL). SZ-SIB pairs (N = 14 pairs; 8 M, 6 F) were divided on the basis of spectrum disorder in the sib, as determined by Kendler's SISS interview, into spectrum pairs (SZ-SP, n = 6) and pairs with a normal sibling (SZ-NL, n = 8). Control pairs (n = 9 pairs, 4 M, 5 F) were free of major psychopathology in all 1° family members by FH-RDC. Lateral and third ventricle volumes (LVV,3VV) were measured by summing area measures calculated by post-processing digital data on a Sun/PIXAR system, using a series of 5mm coronal inversion recovery magnetic resonance images obtained on a GE 1.5 tesla MRI device. Analysis of LVV in the three groups showed a significant difference ($F = 4.849$, $p = .013$) between SZ and CTL (LVV mean $\pm$ SD: SZ = 19.8 ± 10.3 mL *vs.* CTL = 11.5 ± 5.8 mL; Scheffe post hoc $p = .02$) with the SIB group (LVV = 12.5 ± 7.6 mL) similar to CTL. Within the SZ-SIB pairs, a significant diagnosis (SZ *vs.* SIB) by SIB diagnosis (SP *vs.* NL) interaction was found ($F = 11.1$, $p = .002$). Spectrum siblings had larger LVV than NL siblings (LVV = 16.1 ± 9.4 mL *vs.* 9.7 ± 4.9 mL), but the SZ with NL sibs had greatly enlarged ventricles (LVV = 24.8 ± 10.3 mL) compared to SZ with spectrum sibs (13.1 ± 5.5 mL). In contrast, 3VV was found to be larger in SZ than SIBs (3VV = $0.422 \pm .29$ *vs.* $0.273 \pm .14$ mL, paired $t = 2.30$, 2 tailed $p = .0389$), regardless of SIB diagnosis.

These results provide support for the familial-sporadic distinction as regards its effect on VE, and may account for some of the discrepancy in the small literature on VE in SZ and their siblings, suggesting that spectrum disorders should be assessed to avoid misclassifying families with SP as sporadic. The results will be presented with attention to the implications for interpretation of recent studies of MRI in identical twins discordant for schizophrenia.

References:

1. DeLisi LE, Goldin LR, Hamovit JR, Maxwell ME, Kurtz D, Gershon ES: A family study of the association of increased ventricular size with schizophrenia. *Arch. Gen. Psychiatry* 43: 148-153, 1986.
2. Weinberger DR, DeLisi LE, Neophytides AN, Wyatt RJ: Familial aspects of CT scan abnormalities in chronic schizophrenic patients. *Psychiatry Res.* 4:65-71, 1981.

NR402 Wednesday May 15, 9:00 a.m.-10:30 a.m.

Follow-Up MRI Study in First Episode Schizophrenia

Gustav Degreef, M.D., Psychiatry, Albert Einstein Col Med, Hillside Hospital P.O. Box 38, Glen Oaks, NY 11004; Manzar Ashtari, Ph.D., Howard Wu, B.M.D., Michael Borenstein, Ph.D., Stephen Geisler, M.D., Jeffrey A. Lieberman, M.D.

Educational Objectives:

To examine the evidence for and against progressive brain changes in schizophrenia. Data will be presented from an ongoing prospective MR study and from the literature.

Summary:

We obtained MR scans in 32 first episode schizophrenic patients (RDC) and eight controls at baseline and 18 months as well as MR scans at 36 months in ten of 32 patients. Psychopathology and treatment response were also prospectively assessed.

MR scans were acquired on a Siemens (1 Telsa). Coronal sections were collected with a 3-D gradient echo 50° FLASH sequence with TR 40msec, TE 15msec. The sequence acquires 63 contiguous 3.1mm thick sections of the whole brain. Total ventricular volume (TVV) and cortical volumes (TCV) were determined using a computerized system.

The mean decrease in TCV and TVV in eight controls was 1.5 percent (max. change 6.7 percent) and 0.9 percent (max. change 10.1 percent) respectively. The mean increase in TCV and mean decrease in TVV in 13 schizophrenics was 0.25 percent (max. change 9.3 percent) and 5.5 percent (max. change 19.4 percent) respectively. Correlations were seen with weight change ($r = -.51$, NS) and age ($r = -.39$, $P = .07$) and percent change in TVV (but not TCV) in schizophrenics.

The results give little evidence for progressive brain changes in schizophrenia. The greater variability of change in brain structures seen in the schizophrenics may be related to nutritional factors and age. The baseline TVV but not TCV were correlated to prognosis, outcome, and course ($r = .63$ to $r = .48$, $P < .03$ to $P < .10$). We will present data on the larger sample.

References:

1. Nasrallah HA, Olson SC, McCalley-Whitters M, Chapman S, Jacoby CG. Cerebral ventricular enlargement in schizophrenia: A preliminary follow-up study. *Arch Gen Psychiatry.* 43:157-159, 1986
2. Kemali D, Maj M, Galderisi S, Milici N, Salvati A. Ventricle-to-brain ratio in schizophrenia: A controlled follow-up study. *Biol Psychiatry.* 26:753-756, 1989

NR403 Wednesday May 15, 9:00 a.m.-10:30 a.m.

Changes in Plasma HVA Concentrations and Neuroleptic Treatment Response

Rene S. Kahn, M.D., Psychiatry, Bronx VAMC, 130 W. Kingsbridge Road, Bronx, NY 10468; Michael Davidson, M.D., Robert G. Stern, M.D., Peter Knott, M.D., Farooq Amin, M.D., Kim Dumont, B.A., Seth Apter, M.A., Kenneth Davis, M.D., Michelle Duffelmeyer, B.S.

Educational Objectives:

To provide new data suggesting a possible biological basis for treatment response and non-response to neuroleptic treatment in schizophrenic patients

Summary:

Measurements of pHVA concentrations during neuroleptic treatment are an indirect method to estimate in clinical studies, these drugs effects on dopamine (DA) turnover. It is hypothesized neuroleptics reduce DA activity and ameliorate schizophrenic symptoms in parallel. The study presented here postulate that pHVA concentrations will decrease in those patients who showed a clinically meaningful response to neuroleptic treatment but not in those who did not benefit from the treatment. Following a minimum of two weeks drug-free period, 20 RDC schizophrenic inpatients were treated with neuroleptic for five weeks and maintained on a low monoamine diet. Blood for pHVA was drawn under controlled conditions at baseline (the last drug-free day) and twice a week during five weeks of neuroleptic administration. Samples were assayed by HPLC, blind to treatment outcome. BPRS and CGI were rated once a week. A reduction from baseline at week 5 of 1 or greater in CGI scores was defined a-priori as *"treatment response"* while lack of such change was defined as *"treatment non-response"*. Seven patients responded to neuroleptic treatment, while 13 did not. The two groups did not differ in age or drug-free period. Change from baseline pHVA was significantly different for the two groups with a decline present in the patients who improved but not in the patients who did not (main effect for group: $F = 7.85$, $df = 1,18$, $p < 0.02$). Decline in pHVA, CGI and BPRS scores coincided in time. Change scores in CGI and change in pHVA correlated significantly at week 3 ($r = 0.54$) and week 5 ($r = 0.52$). Results of this study, which are consistent with other similar studies, suggest that during neuroleptic administration pHVA concentrations gradually decline in patients who experienced drug related improvements but not in patients who are refractory to treatment.

References:

1. Davidson M, Kahn RS, et al. Changes in plasma homovanillic acid concentrations in schizophrenic patients following neuroleptic discontinuation. *Arch Gen Psychiatry,* 48:73-76, 1991
2. Davidson M, Kahn RS, et al. Effects of neuroleptic treatment on schizophrenic symptoms and plasma homovanillic acid concentrations. Submitted to *Arch Gen Psychiatry*, 1991.

NR404 Wednesday May 15, 9:00 a.m.-10:30 a.m.

Catecholamine Metabolites and Clozapine Response

Alan I. Green, M.D., Psychiatry, Harvard Med. School, Mass Men Hlth Ctr 74 Fenwood Rd., Boston, MA 02115; Mohammed Y. Alam, M.D., Kathleen M. Pappalardo, B.S., Carl Salzman, M.D., Alan F. Schatzberg, M.D., Joseph J. Schildkraut, M.D.

Educational Objectives:

To acquaint the listener with recent research suggesting that plasma measures of catecholamines and their metabolites change during administration of clozapine to schizophrenic patients, and that baseline values of these biochemical measures (especially HVA) may predict clinical response to clozapine, and changes in plasma HVA may correlate with that response.

Summary:

Clozapine was administered to nine schizophrenic or schizoaffective patients resistant to or intolerant of typical neuroleptics. After a prolonged neuroleptic-free period (median >6 wks), clozapine was administered for 13 weeks, with doses increased as tolerated to 500 mg/day. The Brief Psychiatric Rating Scale (BPRS) was administered weekly, and plasma levels of norepinephrine (NE), 3-methoxy-4-hydroxyphenylglycol (MHPG), and homovanillic acid (HVA) were measured weekly. During clozapine treatment, plasma levels of NE increased, while plasma levels of MHPG and HVA decreased (particularly in responders). At neuroleptic-free baseline, BPRS was strongly correlated with HVA ($r = .81$; $p < .008$). Clinical response to clozapine at the end of the study (week 13) was strongly correlated with baseline HVA ($r = .88$; $p < .002$) and with percent decreases in HVA from baseline during weeks 3-9 ($r = .64$ to $.88$; $p = .08$ to $.002$), but not thereafter. Less robust but statistically significant correlations were also observed between clinical response and baseline values of NE and the NE/MHPG ratio. These preliminary data suggest that after a neuroleptic-free period, baseline levels of HVA (and possibly NE and the NE/MHPG ratio) may predict clinical response to clozapine, and that early changes in plasma HVA may correlate with that response. Further analyses

are in progress to explore the relationships between clinical response and changes in plasma NE and MHPG levels during treatment with clozapine.

References:

1. Kane J, Honigfeld G, Singer J, et al: Clozapine for the treatment-resistant schizophrenic. *Arch Gen Psychiatry* 45:789-796, 1988.
2. Pickar D, Labarca R, Doran AR, et al: Longitudinal measurement of plasma homovanillic acid levels in schizophrenic patients. *Arch Gen Psychiatry* 43:669-676, 1986.

NR405 Wednesday May 15, 9:00 a.m.-10:30 a.m.

Dementia in Elderly Schizophrenics: Clinical Features

Michael Davidson, M.D., Psychiatry, Bronx VA Hospital, 130 W. Kingsbridge Road, Bronx, NY 10468; Peter Powchik, M.D., Miklos F. Losonczy, M.D., Shlomit Katz, M.D., Michael Parrella, Ph.D., Marvin Goldstein, Ph.D., Janice McCrystal, R.N., Kenneth L. Davis, M.D., Danya Vardi, M.A.

Educational Objectives:

To examine the clinical and neuropathological correlates of dementia in elderly schizophrenic patients and to discuss the practical implications.

Summary:

Clinical observation indicates that many elderly, institutionalized schizophrenic patients are affected by severe cognitive dysfunction resembling "dementia." This study examines a) if the Clinical Dementia Rating Scale (CDR), Alzheimer's Disease Assessment Scale (ADAS) and the Mini-Mental Status Exam (MMSE) can be utilized to assess dementia in elderly schizophrenic patients b) what is the prevalence of dementia in elderly schizophrenic patients c) the differences and the similarities between demented schizophrenic patients and AD patients of comparable degree of dementia. Correlations between the CDR, ADAS, and the MMSE are above .80 indicating internal validity. Based on a sample of 35 elderly schizophrenic patients, the correlation between two raters observing the same interview and utilizing the scales mentioned above was also above .80 indicating good interrater reliability. The prevalence of dementia in a subsample of 154 schizophrenic patients of mean age 79 years was above 66 percent. Similar to AD patients, schizophrenic patients who achieved a lower level of education appear to be more demented than patients who achieved higher levels of education. These data indicate that the instruments used to assess dementia in elderly, institutionalized schizophrenic patients are adequate and the prevalence of dementia is high. Additional data characterizing the dementia in elderly schizophrenic patients will be presented.

References:

1. Buhl, Boisen-Moller. Frequency of Alzheimer's disease in a postmortem study of psychiatric patients. *Dan Med Bull;* 35:288-290, 1988.
2. Angst J. European Long Term Follow-up Studies of Schiz. *Schizophrenia Bulletin;* 14:501-573, 188.

NR406 Wednesday May 15, 9:00 a.m.-10:30 a.m.

Limbic Plaque/Tangles in Patients With Alzheimer's Disease and Psychosis

Alan J. Waldman, M.D., Psychiatry, Univ of Florida, Box J256 J Hills Miller H.C., Gainesville, FL 32610; William Ballinger, M.D.

Educational Objectives:

The learner should be aware of the high prevalence of Alzheimer's with psychosis. He/she should recognize the pathologic lesions of Alzheimer's disease. He/she should increase knowledge of the anatomy — function of the hippocampus and amydgala and understand why damage of these structures could cause impaired reality testing.

Summary:

A significant percentage of Alzheimer's disease patients suffer from psychotic symptoms. Our hypothesis is that those patients with Alzheimer's and psychosis will have a higher density of the neuritic plaques and neurofibrillary tangles, in the information processing structures, the hippocampal formation and amygdala, than those Alzheimer patients without psychosis. Out of 206 postmortum records of Alzheimer's patients screened, 12 subjects with Alzheimer's and psychosis and eight subjects with Alzheimer's without psychosis met inclusion criteria. Plaque and tangle densities were calculated for the amygdala and the regions of the hippocampal formation. There were significantly greater tangle densities in the parahippocampal gyrus and plaque densities in the amygdalas of patients with Alzheimer's and psychosis. This is the first study, to our knowledge, which demonstrates a relationship between the degree of Alzheimer pathology in specific structures and the development of psychotic symptoms. This degree of pathology would essentially disconnect the majority of inputs into hippocampus and renders the amygdala dysfunctional. The psychotic symptoms may be due to impaired information processing of the damaged structures. Through a better understanding of the function and dysfunction of these structures, a better understanding of other impaired reality testing illnesses (e.g., schizophrenia) may be gained.

References:

1. Wragg RE, Jeste DJ: Overview of depression and psychosis in Alzheimer's disease. *Am J. Psychiatry,* 146:577-587, 1989
2. Miller FD, Hicks SP, D'Amato CJ: A descriptive study of neuritic plaques and neurofibrillary tangles in an autopsy population. *Am J. of Epidemiology,* 120:331-341, 1984.

NR407 Wednesday May 15, 9:00 a.m.-10:30 a.m.

Velnacrine Raises Brain Metabolism in Alzheimer's Disease

Richard A. Margolin, M.D., Psychiatry, Vanderbilt University, 3945 TVC 22nd Avenue South, Nashville, TN 37232; Lon S. Schneider, M.D., Yaorong Ge, M.S.

Educational Objectives:

This presentation aims to inform attendees about a new finding in drug treatment in Alzheimer's disease. An important method for assessing brain changes in response to pharmacotherapy will be explained and the results of a preliminary study presented.

Summary:

Intense interest exists in the potential therapeutic efficacy of cholinergic agonist drugs for the treatment of Alzheimer's disease (AD), and several large multicenter trials of such agents are underway. A biological index of CNS drug action would be useful in evaluating patients' response to these agents. One promising measure is regional cerebral glucose metabolism ($rCMR_{glu}$), which can be determined by the positron emission tomography (PET)/^{18}F-fluorodeoxyglucose (FDG) method. Both regional and global decreases in CMR_{glu} occur in AD; the most common pattern being bilateral parietal lobe decrements.

In order to assess CMR_{glu} correlates of cholinergic drug treatment, several patients with probable AD enrolled in a therapeutic trial of an acetylcholinesterase inhibitor (velnacrine maleate [HP 029], Hoechst-Roussel) were studied before and after chronic drug administration (three months) by the PET/FDG method. CMR_{glu} was assessed in multiple brain regions. Substantial increases in $rCMR_{glu}$ (mean = 37 percent) were noted in most regions examined; the largest increases (58%) occurred in the posterior parietal lobe.

These findings demonstrate that major CMR_{glu} increases occur

with prolonged cholinergic drug treatment in AD, and suggest that the PET/FDG method can be used to assess biological response. Clinical correlation of these changes is being studied.

References:

1. Duara R, Grady C, Haxby J, et al.: Positron emission tomography in Alzheimer's disease. *Neurology 36:*879-887, 1986.
2. Davis KL, Mohs RC: Enhancement of memory processes in Alzheimer's disease with multiple-dose intravenous physostigmine. *Am J. Psychiatry 139:*1421-1424, 1982.

NR408 Wednesday May 15, 9:00 a.m.-10:30 a.m.

Bright Light Treatment of Sleep Disturbances in Alzheimer's Disease

Andrew Satlin, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Ladislav Volicer, M.D., Virginia Ross, Ph.D., Lawrence Herz, M.D., Scott Campbell, Ph.D.

Educational Objectives:

Attendees will be able to (1) identify common behavioral problems in Alzheimer's disease; (2) understand the possible role of circadian rhythm disturbances in these behavioral disorders in AD; (3) cite evidence for the possible benefit of bright light treatment for these disturbances.

Summary:

Sleep-wake disturbances and "sundowning" suggest that circadian rhythms may be disrupted in AD patients. We previously reported decreased amplitude and delayed acrophase of the circadian locomotor activity rhythm in AD. In this study, we tested the hypothesis that bright light pulses would reduce agitation and improve sleep in AD. Ten subjects were studied for three weeks. During each evening of week 2 subjects received 2 h of exposure to 10,000 lux (1900-2100h). Nurses performed daily ratings each shift for agitation and sleep-wakefulness. Subjects were activity-monitored for 48 h at the end of each study week.

The degree of sundowning at baseline correlated with lower relative amplitudes of the locomotor activity cycle ($r = 0.742$; $p = 0.02$), and with the degree of improvement on clinical measures during the evening shift from baseline to treatment week ($r = 0.646$, $p = 0.02$) and from baseline to post-treatment ($r = 0.774$; $p = 0.004$). Sleep-wake measurements on the evening shift improved with treatment ($p = 0.03$); agitation did not change. Percent nocturnal activity declined with treatment ($t = 2.84$; $p = 0.02$) and relative circadian amplitude increased ($t = 2.69$; $p = 0.03$). These results suggest that evening bright light pulses may ameliorate sleep-wake cycle disturbances in some AD patients.

References:

1. Satlin A. et al.: Circadian locomotor activity rhythms in Alzheimer's disease. *Neuropsychopharmacology,* in press, 1991.
2. Czeisler CA et al.: Bright light resets the human circadian pacemaker independent of the timing of the sleep-wake cycle. *Science* 233: 667-671, 1986.

NR409 Wednesday 15, 9:00 a.m.-10:30 a.m.

Aging, Sleep Disorders and Sexual Function

Raul C. Schiavi, M.D., Psychiatry, Mt. Sinai School of Med., 19 East 98th Street Box 1084, New York, NY 10029; John Mandeli, Ph.D., Patricia Schreiner-Engel, Ph.D., Anthony Chambers, B.S.

Educational Objectives:

The relation between sleep disorders and sexual function in older men is not known. We have recently reported a significant negative relation between age, sexual behavior, and erectile capacity in healthy married men between the ages of 45 and 74. The educational objective is to examine and discuss the possible role of sleep disorders on the age-related variation in sexual function.

Summary:

Several authors have noted an association between sleep apnea and erectile impotence, but this relation has not been systematically studied in older men. We have assessed sleep disorders, sexual behavior, and nocturnal penile tumescence (NPT) in relation to age in 70 healthy married men 45 to 74 years old. The subjects had an extensive psychosexual interview, a medical and SADS-L evaluation, and, after completion of several psychological tests, were studied in the sleep laboratory for four nights. There was a marked age-related increase in sleep disordered breathing but no significant changes in periodic leg movements (PLM) with age. Respiratory distress and PLM indices were mostly unrelated with sexual behavior dimensions, as well as with NPT measures when age was taken into account in the analysis of results. Men who met criteria for erectile impotence did not differ significantly in degree of respiratory or PLM disturbances or in the prevalence of sleep disorders when compared to an aged-matched sexually nondysfunctional group. The overall results did not support the notion that sleep disorders are involved in the decrease in sexual desire, arousal and activity associated with aging, or in the pathogenesis of erectile impotence in non-diseased individuals.

References:

1. Schiavi RC, Schreiner-Engel P, Mandeli J, Schanzer H, Cohen E: Healthy aging and male sexual function. *Am. J. Psychiatry* 147:766, 1990.
2. Hirshkowitz M, Karacan I, Gurakar A, Williams RL: Hypertension, erectile dysfunction and occult sleep apnea. *Sleep* 12:223, 1989.

NR410 Wednesday May 15, 9:00 a.m.-10:30 a.m.

Psychiatric Epidemiology and the Homeless

Louise Fournier, Ph.D., Research, Douglas Hospital, 6875 LaSalle Blvd, Verdun QC, Canada H4H 1R3; Vivianne Kovess, Ph.D., Cecile Rousseau, M.D.

Educational Objectives:

At the end of the presentation, the participant should be able to recognize the impact of certain methodological choices on prevalence rates of mental disorders among the homeless. Also, they will learn how a very meticulous comparison between studies may contribute to a better comprehensive of the homeless mentally ill.

Summary:

The notable variability in the prevalence of mental disorders among the homeless as reported in the recent literature appears to stem largely from differences in methodology. To determine the impact of these differences, the authors describe the methodology used in their study of 299 homeless subjects in Montreal and compare their findings with those obtained in seven other studies selected for methodological similarity: random sampling of shelter users, *DSM-III* mental disorders criteria, measure of mental disorders through a standardized instrument or clinical examination. With methodological differences eliminated or controlled, the studies compared showed considerable concurrence regarding lifetime prevalence of organic disorder (3.3 percent to 5 percent), bipolar disorder (about 5 percent), alcohol-related disorder (65 percent) and drug-related disorder (22 percent to 30 percent). Prevalence rates for schizophrenia and major depression were largely influenced by the type of measure used: compared with standardized instruments, clinical examinations tended to yield higher rates for schizophrenia and lower rates for major depression. Finally, real local differences were identified between the homeless population of Los Angeles and Montreal owing to the very similar methodologies used in the studies conducted in these cities. The authors propose reasons for these differences.

References:

1. Fischer PJ: Estimating the prevalence of alcohol, drug and mental health problems in the contemporary homeless population: a review of the literature. *Contemporary Drug Problems,* Fall: 333-389, 1989.
2. Koegel P, Burnam MA, Farr RK: The prevalence of specific psychiatric disorders among homeless individuals in the inner city of Los Angeles. *Arch Gen Psychiatry,* 45: 1085-1092, 1988.

NR411 Wednesday May 15, 9:00 a.m.-10:30 a.m.

Psychopathology Among Homeless Female Veterans

Catherine A. Leda, M.P.H., NEPEC, VA Medical Center, 950 Campbell Avenue, West Haven, CT 06516; Robert Rosenheck, M.D., Peggy Gallup, Ph.D.

Educational Objectives:

To identify psychiatric problems found among homeless female veterans.

Summary:

Introduction/Methods: Previous studies have suggested that homeless female adults have a significantly higher prevalence of chronic mental illness (CMI) in comparison to homeless males. In 1987 the VA established a 43-site national program for homeless chronically mentally ill veterans (HCMI Program). This study reviewed clinical assessment data on 17,026 veterans assessed by the program over two years. *Results.* Altogether 1.7 percent (N = 287) of these veterans were female (compared to 2.5 percent females in the general veteran population). When compared to male homeless veterans in the HCMI program, female veterans were younger, had been homeless for slightly shorter periods of time, and were more likely to be married. These women had higher prevalences of schizophrenia (16 percent vs. 12 percent), affective disorders (36 percent vs. 22 percent) and other psychotic disorders (9.4 percent vs. 7 percent) when compared to their male counterparts. Female veterans, however, had notably lower prevalences of alcohol abuse/dependence (35 percent vs. 64 percent) and drug abuse/dependence (23 percent vs. 32 percent) than males. *Conclusions.* Although women constitute only a small proportion of homeless veterans, our findings are consistent with studies of females in the general homeless population. Homeless female veterans show high levels of psychopathology and a great need for psychiatric treatment services.

References:

1. Breakey WR, Fischer PJ, Kramer M, Nestadt G, Romanoski AJ, Ross A, Royall RM and Stine OC. Health and mental health problems of homeless men and women in Baltimore. *JAMA,* 262:10,1352-1357, 1989
2. Wright R. *Address Unknown: The Homeless in America,* New York: Aldine Degruyter, 1989.

NR412 Wednesday May 15, 12 noon-2:00 p.m.

Third Ventricle and Cognitive Deficit in Schizophrenia

Robert A. Bornstein, Ph.D., Psychiatry, Ohio State University, 473 West 12th Avenue, Columbus, OH 43210; Henry A. Nasrallah, M.D., Stephen C. Olson, M.D., Steven B. Schwarzkopf, M.D.

Summary:

Enlargement of the lateral and third ventricles is not a uniform finding in schizophrenia, but there is evidence of a subgroup of patients with this abnormality. Studies of the relationship of lateral ventricle enlargement and cognitive deficit have yielded inconsistent results. To our knowledge, the relationship of third ventricle enlargement with cognitive deficit has not been explored. This would appear to be a promising area of inquiry because of our previous studies that suggest that MRI demonstrated third ventricle enlargement discriminates schizophrenic patients more clearly that lateral ventricle changes. To explore this question we studied 31 controls and 72 schizophrenic subjects meeting DSM-III-R criteria for diagnosis and confirmed by research psychiatrists. All subjects underwent an MRI scan and a complete neuropsychological examination including WAIS-R, Wechsler Memory Scale Revised, and the Halstead Reitan Battery. The neuropsychological examination yielded 35 variables. Twenty-six of these measures were significantly correlated with third ventricle volume, most at the .01 level of significance or better, and all suggesting greater volume related to greater deficit. In contrast fewer than five variables were related to lateral ventricle volumes. These data strongly suggest that third ventricle volume may be more predictive of cognitive deficit in schizophrenia. In combination with previous data, these findings suggest that enlargement of the third ventricle (rather than lateral ventricle) may be more directly linked to the neuropathology of schizophrenia.

NR413 Wednesday May 15, 12 noon-2:00 p.m.

Asymmetric Frontal Horns in Kraepelinian Psychosis

Miklos F. Losonczy, M.D., Pilgrim Psych. Center, Box A, Brentwood, NY 11717; Ede Frecska, M.D., Michael Davidson, M.D., Richard Keefe, Ph.D., Kenneth L. Davis, M.D.

Summary:

Numerous studies have reported enlarged lateral ventricles in neuroleptic-treatment-resistant schizophrenics. Previously, we have reported various characteristics differentiating "poor prognosis" (or Kraepelinian (K)) schizophrenics from other schizophrenics (non-Kraepelinian (NK)), including the presence of significantly asymmetric enlargement of the left relative to the right lateral ventricles. In this study, we examined 22 K, 52 NK schizophrenics and 32 normal controls (NC). We found a significant correlation of the left lateral ventricle with age ($r = .41$, $p < .05$) in K, but not in NK or NC subjects, and no significant increase with age for the right lateral ventricle in any group. Significant age-dependent increases were noted, however, for all three groups in the frontal horn ventricle brain ratio (VBR) (K: $r = .70$, $p < .0005$; NK: $r = .43$, $p < .002$; NC $r = .42$, $p < .02$) with the most marked increase noted in the K group. The slope of the age-frontal horn VBR regression line was significantly greater for the left frontal horn in the K compared the NC individuals ($t = 2.69$, $p = .01$). Finally, the frontal horn left to right ratio was significantly greater for K (1.20 +/- .29 (SD)) than NK (1.02 +/- .23 (SD)) ($t = 2.84$, $p < .01$). These findings implicate an asymmetric and accelerated tissue destruction predominantly in the left frontal lobe in poor prognosis schizophrenic individuals and suggest the need for neuropathological and MRI studies focused on asymmetric frontal lobe tissue loss in this population.

NR414 Wednesday May 15, 12 noon-2:00 p.m.

Hemispheric Activation Treatment for Schizophrenia

Bruce E. Wexler, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Erika Navarro, M.D., Keith Hawkins, Ph.D., Terry Halwes, Ph.D.

Summary:

Dysfunction of the left hemisphere (LH) in schizophrenia has been reported in multiple studies. Two studies suggest that increased LH function may accompany recovery. In normal subjects it is possible to selectively activate the LH by presenting stimuli to the right hemi-sensory space or by presenting tasks that require specialized LH processing. This pilot study ($n = 7$) examined the possibility that giving schizophrenic patients tasks that engage LH processors would lead to improved LH functioning, and thereby

to clinical improvement. Auditory, visual, motor and tactile tasks were used. Subjects followed a training schedule with tasks gradually increasing in difficulty and duration. Dichotic listening tests before and after training indicated greater change in hemispheric balance in schizophrenic patients receiving training than in normal controls ($p < .005$) or schizophrenic patients ($p = .04$) not receiving training. All seven patients receiving the training showed clinical improvement ($p = .01$). Both the dichotic tests and an independently administered battery of neuropsychological tests indicated that the five patients with predominantly negative symptoms had a relative increase in LH function. The same measures indicated that the two patients with predominantly positive symptoms had a relative increase in right hemisphere function. These findings suggest that it may be possible to develop physiotherapies for psychiatric illness based on understanding pathophysiological processes.

NR415 Wednesday May 15, 12 noon-2:00 p.m.

Comparison of the Positive and Negative Syndrome Scale with the Brief Psychiatric Rating Scale

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Summary:

In a psychiatric rehabilitation study, 154 concurrent ratings were performed using the 30-item Positive and Negative Syndrome Scale (PANSS) and the 18-item Brief Psychiatric Rating Scale (BPRS). Although both instruments had excellent inter-rater reliability, the PANSS was consistently better: on the 18 symptoms the two instruments share, the PANSS had higher intra-class r's on 14; for the syndromes, PANSS was better than the BPRS on Positive (.93 versus .87); Negative (.94 versus .80) and Total (.91 versus .87). Weighted Kappa's comparing shared items revealed most were not interchangeable, with only three symptoms in the excellent range (>.75). Symptoms with poorest weighted Kappa's tended to be those with poor inter-rater reliabilities. Ten of 12 items of the PANSS not included in the BPRS had low first-order correlations with BPRS items suggesting they measure symptoms distinct from those measured by the BPRS and should add to clinical predictive power. This proved true in our study of rehabilitation of schizophrenic patients. PANSS symptom ratings explained up to 50% of the variance on seven measures of work performance while the BPRS had lower predictive power on six of seven measures. We conclude that the PANSS maybe superior to the BPRS in clinical research and that most BPRS items are not interchangeable with identically named PANSS items.

NR416 Wednesday May 15, 12 noon-2:00 p.m.

Schizophrenic Premorbid Adjustment

James J. Levitt, M.D., Psychiatry, Harvard Med. School, VAMC 940 Belmont Street, Brockton, MA 02401; Martha E. Shenton, Ph.D., Robert W. McCarley, M.D., Amy S. Ludwig, B.A., Robert S. Smith, B.A.

Summary:

Premorbid adjustment may predict current schizophrenic pathology and course, but its measurement is subject to problems of reliability and validity. To address this problem we interviewed 12 chronic schizophrenic (SZ) male veterans plus 12 normal controls (NCLs) matched for age and social class, and their respective first-degree relatives. We also obtained, as objective data, school records. We used the Cannon-Spoor et. al. Premorbid Adjustment Scale (PAS; reliability for two interviewers for SZs was, Spearman's rho = .97, $p < .001$ 2 tail); this included four developmental periods. Results showed SZ PAS scores were significantly poorer than NCL scores overall for all informants ($t(22) = 5.30$, $p < .001$ 2 tail), with marked divergence of SZ-NCL scores in late adolescence (16-18) and adulthood. We found premorbid adjustment predicted: 1) current clinical state (GAS, Spearman's rho = −.50, $p = .05$ 1 tail); 2) specific clinical symptomatology (SANS, rho = .585, $p = .02$ 1 tail; but not SAPS); 3) current functional status (degree of independent living, rho = .653, $p = .01$ 1 tail; duration of hospitalization, rho = .607, $p < .02$ 1 tail). Also, lower premorbid IQ and worse childhood school performance were associated with worse premorbid adjustment (rho = −.821, $P < .05$ 1 tail; rho = .680, $p < .02$ 1 tail). In addition, independently of age, lower premorbid IQ predicted larger corrected lateral ventricular volume as measured by MRI (rho = −.949, $p = .05$ 2 tail). In summary, premorbid adjustment has been reliably evaluated by objective measures and by information obtained from first-degree relatives; these premorbid adjustment measures differentiate SZs from NCLs and predict SZ pathology and course.

NR417 Wednesday May 15, 12 noon-2:00 p.m.

Systematic Reduction of High-Dose Neuroleptics in Chronic Treatment Refractory Schizophrenia

Linda Bowen, Ph.D., Psychiatry, UCLA Camarillo Res Ctr, P.O. Box 6022, Camarillo, CA 93010; B.D. Marshall, Jr., M.D., R.P. Liberman, M.D., Timothy G. Kuehnel, Ph.D., Joel Kelsch, L.C.S.W., Jeffery Hayden, B.S.

Summary:

The benefit/risk ratio of neuroleptic therapy for chronic treatment refractory schizophrenics was empirically studied in a systematic, double-blind, step-wise, decremental dosage study of haloperidol. Reduction from initial doses of 80 mg/day or more occurred at five-week intervals unless patients were determined to be significantly worse by consensus of ratings on the CGI by the Interdisciplinary Treatment Team after a review of data from an assessment battery. When significant deterioration was present, the patient's dose was restored to the previous effective level. While two patients tolerated only modest reduction of 15-25 mg haloperidol, the remaining patients achieved mean dosage reductions of 67%, down to 20 mg per day or less. Over 70% of the patients' dosage reduction resulted in serum haloperidol levels between 4.4 and 12 ng/ml, which are within the putative "therapeutic window" for acute schizophrenia. Despite the substantial decreases in maintenance haloperidol doses, patients demonstrated improvements in their psychopathology as measured by total BPRS and all symptom subscales. In addition, akathisia and EPS significantly declined, while tardive dyskinesia showed slight increases. Subsequent to dosage reduction, patients became more accessible to psychosocial treatments aimed at their residual negative and positive symptoms. The study replicates findings from outpatient schizophrenics exposed to low-dose neuroleptic maintenance treatment and suggests that many treatment refractory, institutionalized patients can benefit from significant reductions in their neuroleptic dose.

NR418 Wednesday May 15, 12 noon-2:00 p.m.

Trazodone as Adjunctive Treatment of Negative Symptoms in Chronic Schizophrenia

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Summary:

Effects of adjunctive treatment with trazodone on "negative" symptoms and psychosis were examined in 48 DSM-III-R chronic schizophrenic inpatients during a six-week, double-blind, placebo-controlled random assignment study. Trazodone was started at 50 mg bid, and increased up to 300 mg/day over the first three weeks,

with blind dose adjustments permitted thereafter. Negative symptoms were measured using the SANS, and the BPRS withdrawal-retardation factor (WRF), and psychosis with the BPRS thinking disturbance factor (TDF). Baseline assessments were completed after two weeks of placebo, and one-week anticholinergic (trihexylphenidyl) trial.

Repeated measures ANOVAs revealed significant main effects of time, and interactions between treatment modality and time on negative symptom measures (all p's $\leq .02$). Trazodone was better than placebo in reducing the WRF score (11.5 to 9.7 vs. 11.8 to 12.1), as well as affective flattening (18.8 to 15.8 vs. 19.6 to 19.6) and alogia (8.1 to 6.5 vs. 8.7 to 8.8) scores of the SANS. Neither treatment had an effect on TDF scores (all p's $\geq .20$). We conclude that adjunctive treatment with trazodone is effective in treating negative symptoms in chronic schizophrenia without worsening the psychosis.

NR419 Wednesday May 15, 12 noon-2:00 p.m.

Genetic Linkage Studies in Schizophrenia Using the (CA)N Repeat Polymorphisms

Mihael H. Polymeropoulus, M.D., NIMH Neurosci Ctr., Lab of Biochem Genetics, 2700 Martin Luther King Ave., Washington, DC 20032; Hong Xiao, Denise S. Rath, Angela Boccio, Timothy Crow, James L. Weber, Lynn Delisi, Carl R. Merrill

Summary:

The search for a genetic factor in schizophrenia has been hampered by the absence of any specific biological markers. Genetic linkage studies, so far, have been limited to the study of candidate genes or candidate chromosomal loci, mainly because of the inability to screen the whole genome in a cost effective manner. A recently discovered class of DNA polymorphisms offers the potential for whole genome screening. These polymorphisms are based on tandem dinucleotide repeats of the (dCA)n. (dGT)n type. Such polymorphisms may be studied using the polymerase chain reaction to amplify short 100-200 b.p. DNA fragments containing the repeated sequences, followed by analysis on 6% PAGE sequencing gels. Alleles generally differ in size in multiples of two bases. These (CA)n repeat polymorphisms are highly informative with average PIC values of 0.60. It is estimated that 7,000 to 12,000 informative markers of this type may be available. They appear to be distributed throughout the genome. Our study of four families with schizophrenia with 40 such markers has confirmed the efficiency of this approach and the high degree of informativeness of these markers. Results on the linkage analysis with these markers will be presented.

NR420 Wednesday May 15, 12 noon-2:00 p.m.

Continued Medication Trials in Borderline Personality

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Summary:

We report the first double-blind, placebo-controlled, *continuation* study of a neuroleptic (haloperidol up to 4 mg) with an MAOI antidepressant (phenelzine up to 60 mg) in 54 randomly assigned borderline inpatients defined by DIB and DSM-III-R criteria. The continuation trials lasted 16 weeks following a five-week acute treatment trial (reported elsewhere involving the same medications). Weekly self and observer ratings were made, with monthly plasma drug level determinations. Haloperidol demonstrated within group efficacy on paired t-tests for the treatment of hostility. However, no significant within-group improvement was noted for measures of depression, atypical depression, hysteroid dysphoria, borderline psychopathology, global symptom severity, anxiety, impulsivity, or schizotypal symptoms for phenelzine, haloperidol, or placebo. Three way comparisons (ANCOVA) indicated superior efficacy for phenelzine and placebo over haloperidol in the treatment of depression, and for phenelzine and haldol over placebo in the treatment of irritability, and surprisingly for placebo over both phenelzine and haldol in the treatment of atypical depression. Pairwise comparisons demonstrated therapeutic superiority for haloperidol vs. placebo and for phenelzine vs. placebo in treating irritability, but showed superiority for placebo over haloperidol in treating depression and atypical depression. In treating depression, pairwise comparisons demonstrated superiority for phenelzine vs. haloperidol, but not for phenelzine vs. placebo. These data demonstrate efficacy for phenelzine and haloperidol only in the treatment of irritability in continuation therapy of BPD patients.

NR421 Wednesday May 15, 12 noon-2:00 p.m.

Predictors of Subjective Stress in Schizophrenic Patients

Ross M. G. Norman, Ph.D., Psychiatry, Victoria Hospital, 375 South Street, London Ontario, Canada N6A 4G5; Ashok K. Malla, M.D.

Summary:

Although many clinicians and researchers believe that stress influences the course of schizophrenia, there is very little evidence to support this assumption. One of the problems with research in this area has been the exclusive reliance on major life events as the index of stress to be related to symptomatology. It could be that minor life stressors or "hassles" are a far more important influence on levels of stress among patients with schizophrenia. This possibility is consistent with: (a) clinical impression; (b) vulnerability or diathesis-stress models of schizophrenia; and (c) findings in other areas of research that indicate that minor stressors are a more important predictor of physical and psychological symptomatology than are major life events. The results to be reported in this paper are from an ongoing prospective study of symptomatology in schizophrenia. Standardized and reliable measures of major life events, minor life stressors, and subjective stress were obtained on 100 patients diagnosed as schizophrenic using DSM-III-R criteria. Both cross-sectional and longitudinal data from this study using multiple regression show that comparatively minor life events are significantly more predictive of subjective stress in schizophrenic patients than are major life events. The implications of this finding for future research on stress and schizophrenia are discussed.

NR422 Wednesday May 15, 12 noon-2:00 p.m.

A Prospective Study of Stress and Schizophrenia

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Summary:

There is considerable uncertainty and controversy concerning the influence of psychological stress on symptomatology in schizophrenia. Although many clinicians and researchers believe that stress influences the course of schizophrenia, there is, in fact, little strong evidence to support this assumption. Much of the confusion concerning this issue results from an almost exclusive reliance in the past on the use of retrospective and cross-sectional studies. In this paper we present the results of a prospective study of 40 schizophrenic patients who were assessed monthly using standardized and reliable measures of stress and symptomatology. This study is an improvement on much past research in this area not only because of its prospective design, but also because:

(a) it assessed stress and symptomatology as continuous as opposed to categorical variables; (b) measures of psychosocial stress included daily hassles and subjective stress as well as major life events; and (c) an effort was made to systematically assess the possible effect of stress on not only positive symptoms, but also on negative and possible prodromal symptoms of schizophrenia. Data are presented concerning the relationship of each type of stress to each type of symptomatology, while controlling for the possible effects of prior symptomatology.

NR423 Wednesday May 15, 12 noon - 2:00 p.m.

Schizophrenics' Views of Relatives Predict Outcome

Malca B. Lebell, Ph.D., Psychiatry, Brentwood VAMC/UCLA Rm 15, 11301 Wilshire Blvd Bldg 210, Los Angeles, CA 90073; Stephen R. Marder, M.D., Jim Mintz, Ph.D., Lois Mintz, Ph.D., Martha Tompson, M.A.

Summary:

Schizophrenic patients with close relatives who express critical or emotionally overinvolved attitudes — high Expressed Emotion (EE) — have been found to be more vulnerable to relapse. EE is based on relatives' attitudes elicited in a semi-structured interview. However, the degree to which patients recognize these attitudes has not been assessed. To address this issue, we studied a sample of 39 chronic schizophrenic outpatients and their key relatives. Soon after entry in a low-dose-neuroleptic treatment program, patients and relatives independently rated the quality of their relationship, their own attitudes toward the other, as well as their perceptions of others' attitudes toward themselves on a number of scales (Feelings & Thoughts Scale, Contact Scale, Patient Rejection Scale). Using survival analyses, three measures — patients' perceptions of the relatives' attitudes toward them, patients' own attitude toward the relative, and patients' views regarding their relationship — predicted relapse ($p < .01$) during a two-year follow-up. However, relatives' reported measures did not significantly predict outcome, despite the fact that the correlations between relative and patient-based measures were high ($r = .60$, $p < .0001$). Patients' negative attitudes toward their relatives were also significantly correlated with BPRS ratings of psychosis ($r = .37$, $p < .02$). Implications of the findings for family process research and treatment will be discussed.

NR424 Wednesday May 15, 12 noon-2:00 p.m.

Schizophrenia: P3 Asymmetries Vary With Handedness

Dorothy P. Holinger, Ph.D., MMHC, Harvard Med. School, 74 Fenwood Road, Boston, MA 02115; Nicholas S. Sokol, Robert W. McCarley, M.D., Steven F. Faux, Ph.D.

Summary:

Although handedness-linked studies/postulates of abnormalities are prominent in some domains *of* schizophrenia work, we are not aware of any previous study of P300. We studied topographic differences in the auditory P300 in medicated schizophrenic males who were left-handed ($n = 9$) and right-handed ($n = 9$), and in normal males who were left-handed ($n = 8$) and right-handed ($n = 8$). Oldfield's Edinburgh Inventory was used to assess magnitude and direction of handedness; schizophrenics were SADS diagnosed, and normal controls were MMPI assessed. Differences in P300 topography (within an integrated 300-400 ms time window) were evident in color maps and grand-averaged waveforms. Right-handed schizophrenic males showed an asymmetry with a right-handed shift in P300 amplitude compared to a symmetry in the right- and left-handed normal male groups. In contrast, left-handed schizophrenic males showed a reversed asymmetry with a left-sided shift in P300 amplitude. Statistically significant differences between right-handed schizophrenic and right-handed normal males were present at T3 and T4 electrodes (Mann Whitney-U, $p < .05$), and between left-handed schizophrenics and left-handed normals at T4 (MW-U, $p = .01$). These data underline the importance of segregating schizophrenics according to handedness. When the left- and right-handed schizophrenic groups are combined, the distinctive left and right asymmetries disappear, resulting in a symmetric topography. Based on the assumption that topographic differences in P300 reflect activation of different/altered neural generators, these preliminary results suggest that left- and right-handed schizophrenics have abnormalities in different neural generators whose laterality is associated with handedness.

NR425 Wednesday May 15, 12 noon-2:00 p.m.

Mazindol in Negative Symptoms Schizophrenics

John P. Seibyl, M.D., Psychiatry, Yale University VAMC, West Haven 950 Campbell Avenue, West Haven, CT 06516; John H. Krystal, M.D., Robin Johnson, M.D., Dennis S. Charney, M.D.

Summary:

Recent work suggests mesofrontal dopamine (DA) deficits may be involved in negative schizophrenic symptoms. Consistent with this, most schizophrenics experience minimal negative symptom improvement or even worsening with standard neuroleptic treatment. Pharmacological strategies that enhance mesofrontal dopamine function may be useful in negative symptom patients. Mazindol is a long-acting agent that blocks DA reuptake at the dopamine transporter site. We tested the responses of positive and negative symptoms to mazindol augmentation of neuroleptic in partially refractory, stable outpatient schizophrenics. *Methods:* In an ongoing study, outpatients stabilized on neuroleptic medication were enrolled in a double-blind, placebo-controlled trial of mazindol (2 mg/day) augmentation of typical neuroleptic agents. Weekly Brief Psychiatric Rating Scale, Positive and Negative Symptom Scale, AIMS, Webster's ratings, and fasting serum neurohormones and HVA were obtained for four weeks prior to mazindol/placebo augmentation and for six weeks after randomization. *Results:* The first six patients receiving active mazindol demonstrated approximately 30% reduction of PANSS and BPRS negative symptoms ratings. No changes in positive symptom scores were noted. There was reduction of extrapyramidal symptoms in five of six patients and increases in AIMS scores in one of six after mazindol treatment. Subjectively, five of six patients experienced increased mood and energy and correctly guessed the identity of the randomized medication. *Conclusions:* Preliminary data suggest mazindol may be effective for treatment of refractory negative symptoms in otherwise stable outpatient schizophrenics. There was no worsening of positive psychotic symptoms and minimal effects on tardive dyskinesia with mazindol. Most patients experienced fewer extrapyramidal side effects after mazindol augmentation.

NR426 Wednesday May 15, 12 noon-2:00 p.m.

Rat Entorhinal Neuron Physiology and Morphology

David M. Finch, Ph.D., Brain Res Ins., Univ of California, 73-364 CHS, Los Angeles, CA 90024; Thomas D. White, Ph.D., Kurt Lingenhohl, B.A., Aiko M. Tan, B.S.

Summary:

Results from several studies have suggested that the hippocampal formation, including the entorhinal cortex, is involved in schizophrenia. We used *in vivo* intracellular recording techniques to provide information on the physiological relationships of the entorhinal cortex and the prefrontal cortex. The most salient synaptic response was inhibition, as shown by the presence of IPSPs in 48% of the cells sampled. Responsive fast-spiking cells (candidate inhibitory neurons) and EPSPs in a few principal neurons

provided evidence for a local source of inhibition via a feedforward inhibitory circuit. We have also studied entorhinal neurons morphologically. Twenty-four entorhinal neurons were labeled and showed extensive dendritic domains, with total dendritic lengths averaging 9.8 mm ± 3.8 (SD). The dendrites of layer II neurons were largely restricted to layers I and II or layers I-III, while the dendrites of deeper cells could extend through all cortical layers. Axonal processes showed patterns varying from rope-like projects with few axonal collaterals to net-like projections with extensive collaterals. By providing a more complete understanding of the physiology and morphology of normal entorhinal neurons, our work contributes to the normative base that may be useful in evaluating pathological changes occurring in schizophrenia.

NR427 Wednesday May 15, 12 noon-2:00 p.m.

Cyproheptadine Treatment for Tardive Dyskinesia

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Summary:

Neuroleptic-induced movement disorders, like tardive dyskinesia (TD), represent a significant complicating side effect of treatment with antipsychotic medications. Despite numerous attempts at developing pharmacologic therapies for TD, no drugs have yet been clearly established to provide therapeutic benefit. At present, the usual recourse for treating severe TD is to increase the dose of neuroleptic (at the risk of worsening the underlying dyskinetic process) or to discontinue antipsychotic medication (at the risk of increasing psychosis). However, several reports suggest that serotonin (5HT) antagonists may be useful in treating TD.

This study reports results of treatment with cyproheptadine, a mixed 5HT and histamine antagonist, in 13 patients with TD. Patients were maintained on stable doses of psychotropic medications and treated in an open study design with cyproheptadine. Doses of cyproheptadine were titrated up to 16-32 mg daily. Dyskinesia scores obtained after six to nine weeks of treatment at these doses were significantly improved over baseline (See Table). These results support previous evidence that cyproheptadine, like several other 5HT antagonists, may be useful in the treatment of TD and indicate that cyproheptadine may confer 'atypical' characteristics to treatment with typical antipsychotic drugs.

Effect of Cyproheptadine on Dyskinesia

Severity Measure	Baseline	6-8 Weeks' Treatment	t (paired)	p
AIMS Total	10.0 ± 4.80	7.0 ± 5.8	2.85	<0.012
AIMS Severity	2.65 ± 0.70	1.65 ± 0.93	5.22	<0.001

NR428 Wednesday May 15, 12 noon-2:00 p.m.

Reliability of a Depression Scale for Schizophrenia

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Summary:

The reliability and validity of a new scale, the Calgary Depression Scale (CDS), are reported. The CDS is compared with three established measures: the Hamilton Depression Rating Scale (HDRS), the Beck, and a scale derived from three items of the Brief Psychiatric Rating Scale (BPRS). The four measures were administered to a sample of 100 outpatients and 50 inpatients with schizophrenia. Confirmatory factor analysis on the CDS using LISREL showed a coefficient of determination of .96 indicating a single latent factor explaining a significant portion of the scale. Interrater reliability for the CDS, measured using intra-class correlations was .895. Validation that the CDS was a measure of depression was provided by significant correlations (p.001) with the other measures of depression. The CDS was compared with HDRS, Beck and BPRS on measures of internal reliability and potential for predicting the presence of a major depressive episode. The CDS had higher internal consistency (.79) across both inpatients and outpatients than all but the Beck scale, which, however, was difficult to administer. In conclusion, the CDS is a parsimonious reliable scale that is superior to the other scales for assessing depression across both acute and residual stages of schizophrenia.

NR429 Wednesday May 15, 12 noon-2:00 p.m.

Blood-Brain Barrier Permeability in Schizophrenia

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Summary:

The analysis of cerebrospinal fluid (CSF) is one of the primary methods used to study neuropsychiatric illnesses. The ratio of albumin in CSF to serum is an accurate measure of blood-brain barrier (BBB) permeability. Increases in this rate indicate functional BBB pathology. The ratio of immunoglobin G (IgG) in the CSF to serum (corrected for the albumin ratio) is an index of endogenous IgG production in the central nervous system (CNS). Increased CNS IgG production is associated with infectious and/or autoimmune processes that stimulate central IgG synthesis. Simultaneously collected CSF and serum samples from 46 schizophrenic patients and 20 normal controls were analyzed for evidence of BBB pathology and CNS IgG production. Eight of the schizophrenic subjects were studied both on and off neuroleptic treatment. When compared with established normal ranges, the data indicated modest increases in BBB permeability in 22% of schizophrenic patients and 5% of the control group, and increased CNS IgG production in 20% of the schizophrenic patients and none of the control subjects. Only three patients showed elevations in both indices. Comparison of values on and off neuroleptics indicated no significant effects of drug treatment.

NR430 Wednesday May 15, 12 noon-2:00 p.m.

Central Interleukin-2 in Unmedicated Schizophrenics

Julio Licinio, M.D., Psychiatry, West Haven VAMC, 950 Campbell Avenue, West Haven, CT 06516; John Seibyl, M.D., Margaret Altemus, M.D., Dennis S. Charney, M.D., John Krystal, M.D.

Summary:

Cytokines and growth factors contribute to cell growth and differentiation. Schizophrenia has been hypothesized to be a disorder of brain growth and differentiation (Crow TJ et al., 1989; 46:1145). Autoimmunity and viral factors may also be implicated in the pathophysiology of schizophrenia. It is therefore important to assess cytokine and growth factor levels in schizophrenic patients. Interleukin-2 (IL-2) is both a brain cell growth factor and an immunomediator, which is elevated in chronic autoimmune disorders. In this study we measure cerebrospinal fluid (CSF) levels of IL-2 and IL-1 in eight drug-free schizophrenics, meeting DSM-III-R diagnostic criteria, and eight normal controls. CSF was collected by spinal tap at 9:00 a.m. IL-1 and IL-2 were measured by enzyme-linked assays. CSF IL-1 levels were 553.5 ± 82.9 pg/ml in schizophrenics and 395.5 ± 58.9 pg/ml in controls (nonsignificant); CSF IL-2 levels in 852.1 ± 26.3 pg/ml in schizophrenics and 555.4 ± 33.4 pg/ml in controls ($p<0.0001$; unpaired t test), with

no overlap between the two groups. These results suggest that IL-2, but not IL-1, is centrally elevated in schizophrenia. Further studies are necessary to determine whether past history of neuroleptic treatment affects central IL-2 levels.

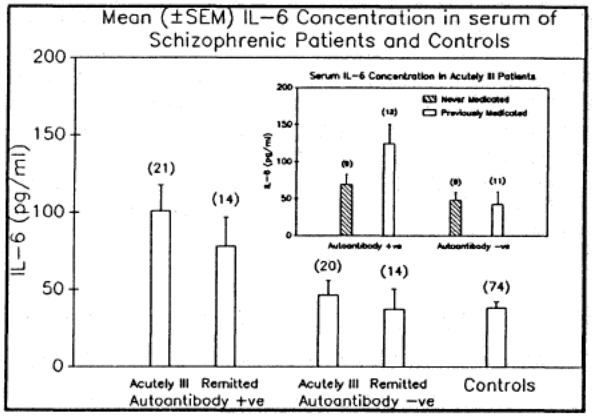
NR431 Wednesday May 15, 12 noon-2:00 p.m.

Alterations in Interleukins in Schizophrenics

Rohan Ganguli, M.D., WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213; Cathy G. McAllister, Ph.D., B.S. Rabin, M.D., W. Solomon, J.S. Brar, M.D., T. Rehn, M.S.

Summary:

We have previously reported that some schizophrenics have decreased IL-2 production and that this is largely confined to subjects with other immunologic alterations suggestive of autoimmunity such as the production of autoantibodies. In this sample of 69 RDC schizophrenics and 74 matched controls, in addition to PHA stimulated IL-1 and IL-2 production, we also measured serum IL-2, IL-6 and IL-4. Simultaneously, lymphocyte subsets were quantitated including T helper (CD4+), T suppressor (CD8+), true suppressors (Leu 15+), inducers of help (4B4+), inducer of suppression (2H4+), B cells and CD5+ B cells. Stimulated IL-2 production was significantly *reduced* in acutely ill patients who also had autoantibodies. IL-6 was *increased* (figure) in autoantibody positive cases including drug-naive patients (inset). Of the lymphocyte subsets significant changes included an increase in CD4+ (T helper) with a specific increase in the helper subpopulation designated as the inducer of suppression (2H4+). This is the largest multidimensional investigation of immune function in schizophrenia so far attempted, and the findings are in accord with what would be predicted if some schizophrenics suffer from an autoimmune disease.



NR432 Wednesday May 15, 12 noon-2:00 p.m.

Cognitive Deficits in Sporadic Schizophrenia

Frederic J. Sautter, Ph.D., Psychiatry, Tulane University, 1415 Tulane Avenue, New Orleans, LA 70112; Barbara E. McDermott, Ph.D., F. William Black, Ph.D., Patrick O'Neill, M.D.

Summary:

A number of studies have suggested a positive relationship between ventricular enlargement and a lack of family history of psychosis in schizophrenic patients. In an ongoing study of recent-onset schizophrenia, 14 Family History Positive (FH-P) and 13 Family History Negative (FH-N) RDC schizophrenics were administered the Rey Auditory-Verbal Learning Test, the Rey Osterrieth Complex Figures Test, the Grooved Pegboard Test, the Verbal Fluency Test, the Symbol Digit Modalities Test and the Wisconsin Card Sort. The relationship between test performance and four dimensions of functioning (positive and negative symptoms, interpersonal and occupational role functioning) was assessed separately for the two groups. Patient functioning was strongly associated with the presence of neuropsychological deficits in the FH-N group; there was no relationship between neuropsychological test scores and patient functioning for the FH-P group. Impaired functioning in the FH-N patients was significantly associated with deficits on the Grooved Pegboard Test ($p < .05$), the Symbol Digit Modalities test ($p < .05$), the Verbal Fluency Test ($p < .008$) and perseverative errors on the Wisconsin Card Sort ($p < .03$). The data suggest that subtyping on the basis of family history represents a valid strategy for reducing the heterogeneity of schizophrenia.

NR433 Wednesday May 15, 12 noon-2:00 p.m.

Cognitive Deficits and Loss of Role Functioning

Frederic J. Sautter, Ph.D., Psychiatry, Tulane University, 1415 Tulane Avenue, New Orleans, LA 70112; Barbara E. McDermott, Ph.D., F. William Black, Ph.D., Tammy Sobrapena, M.A.

Summary:

The impairment of occupational role functioning represents one of the most debilitating aspects of the schizophrenic deficit state. The current study is designed to identify precisely those neuropsychological deficits that are associated with occupational role impairment in 27 recent-onset RDC schizophrenics. Patients were administered the Quality of Life Scale to quantify occupational role functioning, and the following neuropsychological tests were also administered: (1) Verbal Fluency Test, (2) Auditory Verbal Learning Test, (3) Grooved Pegboard Test, (4) Symbol Digit Modalities Test, (5) Rey Complex Figure Test, and (6) the Wisconsin Card Sort. Patients who showed marked impairments in occupational role functioning showed significantly more perseverative errors on the Wisconsin Card Sort ($p < .03$). Occupational role functioning was negatively correlated with scores on the Grooved Pegboard ($p < .03$), Symbol Digit Modalities ($p < .05$) and the Wisconsin Card Sort ($p < .04$). The data also demonstrate that the cognitive impairments that are associated with the loss of occupational role functioning are often evidenced in the early phases of the patient's illness. These data have strong implications for neuropsychiatric rehabilitation and the importance of early intervention.

NR434 Wednesday May 15, 12 noon-2:00 p.m.

Natural Auto-Antibodies in Schizophrenia

A. Galinowski, M.D., Centre Hospitalier St-Ann, 1 Rue Cabanis 75674, Paris, France; P. Levy-Soussan, R. Barbouche, H.F. Poirier, F. Hartmann, H. Loo, S. Avrameas

Summary:

Antinuclear and anti-DNA autoantibodies have been described in schizophrenia. Autoantibodies reacting with most other self constituents have not yet been reported. Using a panel of self and nonself antigen (actin, DNA, dopamine, serotonin, myosin, thyroglobulin, trinitrophenyl, tubulin). We examined the sera of 14 schizophrenic patients (DSM-III-R) prior to and after one month of haloperidol treatment (6 to 45 mg/day). Patients were drug naive or neuroleptic drug free for at least three months. When studying relationships between autoantibody levels and clinical parameters (Andreassen's SANS and SAPS) we observed: 1) A significant increase of IgG actine and IMP autoantibodies in schizophrenic patients at day 0 versus healthy volunteers; 2) No modification of total autoantibody levels during neuroleptic treatment, but an increase of IgM antidopamine antibodies in drug free compared with naive patients; 3) A significant decrease of some initial IgG autoantibodies (DNA, thyroglobulin, dopamine) in nonresponders versus responders (30% of SANS scores).

In conclusion, the presence of autoantibodies reacting with dopamine and serotonin was evidenced in our study. Level of some autoantibodies seem to predict a positive response of negative symptoms to neuroleptic treatment.

NR435 Wednesday May 15, 12 noon-2:00 p.m.

Postpartum Psychosis and Neuroleptic Dosage

John A. Baker, M.D., Psychiatry, Michigan State University, B101 West Fee Hall, East Lansing, MI 48824; Dale D'Mello, M.D., Melpomeni Kavadella, M.D.

Summary:

The postpartum period is one of particular vulnerability for women with coexistent psychiatric disorders. Hormonal and neuroreceptor changes are compounded by complex psychodynamic conflicts, particularly in unmarried women who anticipate losing custody of their newborn infants. A retrospective review was completed on patients who were treated for postpartum psychosis on a 30-bed inpatient psychiatric unit between 1981 and 1990. Eleven patients were identified, ranging in age from 19 to 35 years, with a mean age of 27 years. The mean duration of postpartum admission was 61 days (S.D. $\pm$ 44.7 d.) and was longer than any antepartum admission, the average of which was 31 days (S.D. $\pm$ 36.4 d.). ($Z = 1.65$, $p < 0.01$). The mean discharge neuroleptic dosage for the postpartum admission (1153 chlorpromazine (CPZ) equiv.) was significantly greater than that of the antepartum admission (555 CPZ equiv.) ($Z = 2.7$, $p < 0.01$). If longer duration of hospitalization and greater neuroleptic dosage requirement can be interpreted as paralleling more severe psychopathology, then women prone to psychosis are likely to suffer a more severe disturbance postpartum than at other periods of the life cycle.

NR436 Wednesday May 15, 12 noon-2:00 p.m.

Hyponatremia in a State Hospital: 31 New Cases

Pritesh J. Shah, M.D., Psychiatry, Bergen Pines Hospital, East Ridgewood Avenue, Paramus, NJ 07652; William M. Greenberg, M.D.

Summary:

The poorly understood syndrome of hyponatremia associated with polydipsia in psychiatric patients is dangerous and usually difficult to manage. We undertook to identify and examine these individuals in a state hospital. Nursing staff identified patients who were water-restricted or drank water excessively; we reviewed charts and interviewed the patients. We identified 31 patients of 635 (4.9%) who had a recently documented serum sodium of 125 or less, including several in whom hyponatremia had not been suspected. We verified several previous findings: our hyponatremic patients were predominantly schizophrenic (84%), smokers (94%), and often had alcoholic histories (48%). Thirty-two percent had seizures and 10% urological abnormalities related to polydipsia. Their average age was 43 years, duration of psychiatric illness 23.2 years. Contrary to previous reports, 87% were male ($p < .05$). We were particularly interested in patients' explanations for their polydipsia. Many couldn't clearly respond, but at least 11 had hydrophilic delusions, two had command hallucinations to drink water, three explicitly cited boredom, four indicated that they were seeking pleasure and one was trying to relieve hunger. We believe that addressing patients' internal experiences, besides behaviors, history, and diagnosis, should lead to better individualized treatments.

NR437 Wednesday May 15, 12 noon-2:00 p.m.

Structural Abnormalities in Schizophrenic Patients with Hyponatremia

William B. Lawson, M.D., Psychiatry, Vanderbilt University, A-2215 Medical Center North, Nashville, TN 37232; Darrell Kirch, M.D., Richard Shelton, M.D., David Daniels, M.D., Andrei Lager, M.D., Gary Robertson, M.D., Larry Welch, Ed.D.

Summary:

Polydipsia with hyponatremia is often seen in schizophrenia, but the etiology remains unknown. CT scans were done on 19 physically healthy schizophrenic patients meeting DSM-III-R criteria. Brain areas were rated blindly and independently, with concordance of .9 or better. Hyponatremic patients (serum sodium < 135mEq/1 on two occasions) were more likely to show prefrontal atrophy (PFA) (6/6 vs. 6/13, Fishers $< .05$), or increased ventricular to brain ration (VBR). No significant differences were seen for general atrophy or third ventricle size. Sixteen of these patients after three weeks of medication withdrawal, were given 30mg/kg water loads. Plasma osmolality, and vasopressin were measured hourly. Patients with PFA showed significant, transiently lower osmolality. Patients with enlarged VBR showed significantly lower osmolality that persisted. They also displayed significantly lower thresholds for vasopressin release. Another group of hyponatremic schizophrenic patients showed poorer performance on the Wisconsin Card Sort, which can detect prefrontal pathology ($N = 4$, errors $= 71.2 \pm 17.2$ vs. $N = 5$, 33 ± 25 $p < .05$). Schizophrenic patients with structural brain abnormalities, supported by CT findings and neuropsychological testing, are at risk for hyponatremia.

NR438 Wednesday May 15, 12 noon-2:00 p.m.

Depot Neuroleptics and Negative Symptoms

Susanne Steinberg, M.D., Psychiatry, St. Mary's Hospital, 3830 Lacombe Avenue, Montreal PQ, Canada H3T 1M5; Lawrence Annable, D.S.

Summary:

The negative symptoms of schizophrenia are associated with poor adjustment in social and work areas. There is some suggestion from clinical studies that flupenthixol decanoate may be advantageous in patients with marked negative symptoms. We carried out an open clinical trial of six months duration comparing flupenthixol decanoate and haloperidol decanoate in the treatment of eight chronic schizophrenic (*DSM-III*) patients manifesting significant negative symptomatology. The patients were evaluated on the SANS, SAPS, and Beck Depression Inventory at baseline and at monthly intervals. At endpoint, both treatment groups showed a significant ($p < 0.001$) reduction in mean scores for negative symptoms on the SANS, with a trend ($p = 0.12$, two-tailed) for greater improvement with flupenthixol than haloperidol. On the other hand, haloperidol showed a trend ($p = 0.13$, two-tailed) to be superior to flupenthixol in reducing the total score for the Beck Depression Inventory, although depressive symptoms were not a prominent feature of these patients. Specific criteria distinguishing negative symptoms from depression will facilitate the search for a treatment of choice.

NR439 Wednesday May 15, 12 noon-2:00 p.m.

Plasma HVA in Psychotic and Non Psychotic Disorders

Giovanni Muscettola, M.D., Psychiatry, 2nd Univ. Med. School, Via Pansini 5, Napoli 80131, Italy; Andrea de Bartolomeis, M.D., Giuseppe Barbato, M.D., Dina Nerozzi, M.D.

Summary:

Increased levels of plasma homovanillic acid (pHVA) have been associated with the severity of schizophrenic symptoms, although neuroleptic (NL) treatment and phase of the illness are potential confounding factors. To better elucidate the role of such factors, pHVA was measured by HPLC in 87 hospitalized chronic schizophrenic patients (after neuroleptic withdrawal for a mean of 32 months and on stable NL treatment with mean 388 CPZ mg eq./day

dose) and in two samples of hospitalized male draftees, never medicated with neuroleptics and diagnosed as schizophreniform disorder or adjustment disorder. Controls were chosen from staff personnel of the hospital. pHVA levels in pmol/m1 ± SD were: drug free chronic schizophrenia (n = 41) = 80.5 ± 26.0, NL treated chronic schizophrenia (n = 46) = 83.5 ± 28.5, schizophreniform disorder (n = 29) = 75.5 ± 29.2, adjustment disorder (n = 15) = 40.2 ± 19.5, normal controls (n = 16) 53.3 ± 13.1. The elevated pHVA levels could be related to an augmented central dopamine turnover in patients with psychotic symptoms regardless of the phase of the illness or the NL treatment. The preliminary finding of reduced pHVA levels in patients under stressful conditions, albeit not psychotic will be discussed in terms of "acute" altered dopaminergic plasticity and compared to the "chronic" reduced dopamine function found in patients with tardive dyskinesia.

NR440 Wednesday May 15, 12 noon-2:00 p.m.

Clozapine Treatment of Borderline Patients

Frances R. Frankenburg, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Mary C. Zanarini, Ed.D, Joan H. Glutting, B.A.

Summary:

Neuroleptic medications are frequently prescribed for patients with borderline personality disorder (BPD) who experience psychotic or psychotic-like symptoms. Eight patients with BPD and pronounced but atypical psychotic symptoms (five female, three male with a mean age = 28.3 ± 6.2 years) who had failed to benefit from three or more conventional neuroleptics were entered into a long-term prospective study of clozapine. At entry into the study, they were rated on the BPRS (Brief Psychiatric Rating Scale), CGI (Clinical Global Impression), and GAS (Global Assessment Scale). They were rerated, blind to their baseline status, two to 12 months after beginning clozapine treatment. Average dose was 298 ± 167 mg/day. Patients complained of side-effects (chiefly sedation and weight gain), but they showed significant improvements on all scales: BPRS baseline score = 56.6 ± 8.2, follow-up score = 32.9 ± 7.6, t = 9.91, p = .001; CGI baseline score = 4.9 ± 1.0, follow-up score = 3.6 ± 0.9, t = 7.6, p = .001; and GAS baseline score = 32.9 ± 5.5, follow-up score = 46.6 ± 9.0, t = 4.20, p = .004. While double-blind, placebo controlled trials are needed to confirm these results, they suggest that clozapine may be a useful agent for these difficult patients with BPD and treatment-refractory psychotic symptoms.

NR441 Wednesday May 15, 12 noon-2:00 p.m.

The Heterogeneity of Schizophrenia: Season of Birth

Ann E. Pulver, Sc.D., Psychiatry, Johns Hopkins University, 1615 Thames Street, Baltimore, MD 21231; John J. McGrath, M.D., Paula S. Wolyniec, M.A., Doreen Tam, B.S.

Summary:

Risk for schizophrenia among first-degree relatives of schizophrenic probands obtained from an epidemiologic sample using family history methods were examined using the Cox proportional hazards model to determine whether month of birth of the proband was associated with familial risk. The results of this study of the relatives of 106 female schizophrenics and 275 male schizophrenics suggested that the relatives of probands born February through March had the highest risk. The relationship between month of birth and familial risk for schizophrenia was the greatest for the relatives of female probands. The relatives of female schizophrenic probands born February through May had seven times the risk than the relatives of female probands born during November through January and three times the risk for the relatives born in June through September.

NR442 Wednesday May 15, 12 noon-2:00 p.m.

Premorbid Functioning and Outcome in Schizophrenia

Jean M. Addington, Ph.D., Holy Cross Hospital, Univ of Calgary, 2210 2nd St. SW, Calgary Alta, Canada T2S 1S6; Donald E. Addington, M.D.

Summary:

In this study, we examined longitudinally, the relationships between premorbid functioning and (i) positive and negative symptoms of schizophrenia (using the SANS & SAPS) and (ii) performance on 15 measures of cognitive functioning, in a sample of *DSM-III* schizophrenics (14 females, 24 males). Subjects were assessed at hospitalization and six months later during a period of relative remission. Pre-morbid functioning was significantly associated with negative symptoms but not positive symptoms at both time 1 and time 2. The majority of the cognitive measures were not significantly associated with premorbid functioning. The exceptions were that at both time 1 and 2 poor premorbid functioning was related to poor performance on the Wisconsin Card Sort Test and to a measure of verbal fluency at time 1. Males and females did not differ significantly in terms of levels of symptoms or cognitive functioning, but they showed significant differences in premorbid functioning. Males had poorer premorbid functioning. These findings suggest that, although the dimensions of premorbid functioning and negative symptoms are reliably associated, there is no evidence that these dimensions are interchangeable and such dimensions must be examined separately in future research.

NR443 Wednesday May 15, 12 noon-2:00 p.m.

Gender Differences and Schizophrenic Symptoms

Jean M. Addington, Ph.D., Psychiatry, University of Calgary, Holy Cross Hosp. 2210 2nd St., SW Calgary AB, Canada T2S1S6; Donald E. Addington, M.D.

Summary:

Cognitive functioning and positive symptoms were examined longitudinally in a sample of *DSM-III* schizophrenics (15 females, 27 males). Subjects were assessed at hospitalization and six months later during a period of relative remission. There were few differences between men and women on ratings of positive and negative symptoms and on performance on the cognitive tests. Compared to females, males had significantly more flat affect and anhedonia and more deficits on the Wisconsin Card Sort Test. Males also had poorer premorbid functioning. An examination of the relationship between symptoms and cognitive functioning revealed that in the male group there were significant relationships between negative symptoms and poor cognitive functioning at both stages of the illness; whereas in the female group there were no significant associations between symptoms and cognitive functioning at hospitalization but there were significant relationships at follow-up between poor cognitive functioning and positive symptoms. These results are discussed in the context of other known gender differences in schizophrenia.

NR444 Wednesday May 15, 12 noon-2:00 p.m.

CSF Diazepam-Binding Inhibitor in Schizophrenia On and Off Haloperidol

Daniel P. van Kammen, M.D., Chief of Staff, Dept of VAMC, Highland Drive, Pittsburgh, PA 15206; Alessandro Guidotti, Ph.D., John A. Gurklis, Jr., M.D., Mark W. Gilbertson, Ph.D., Jeffrey Yao, Ph.D., Erminio Costa, M.D.

Summary:

Diazepam-binding inhibitor (DBI) is a novel neuropeptide purified

from rodent, mammalian, and human brain. Diazepam-binding inhibitor-like immunoreactivity (DBI-LI) was measured in CSF of 67 drug-free male chronic schizophrenic patients, 53 of whom were also tested prior to haloperidol withdrawal. Following withdrawal from haloperidol treatment, CSF DBI-LI increased significantly. CSF DBI-LI in the drug-free patients was not significantly different from the ten normal controls. A diagnosis of paranoid schizophrenia, however, was associated with higher levels of CSF DBI-LI. CSF DBI-LI correlated significantly with the age of onset of the illness but not with age. Negative relationships between DBI-LI and schizophrenic behavior, i.e., positive and negative symptoms, were observed in the drug-free state but not during haloperidol maintenance treatment. The present findings indicate that CSF DBI-LI may play a role in the pathophysiology of schizophrenia.

NR445 Wednesday May 15, 12 noon-2:00 p.m.

Schizophrenia: Gender and Familial Risk

Paula S. Wolyniec, M.A., Psychiatry, Johns Hopkins Univ, 1615 Thames Street, Baltimore, MD 21231; Ann E. Pulver, Sc.D., John J. McGrath, M.A., Doreen Tam, B.S.

Summary:

The morbid risks for schizophrenia and other psychiatric disorders in the first-degree relatives of male and female schizophrenic probands were compared utilizing Cox Proportional Hazards Models. The schizophrenic probands (275 male; 106 female) were drawn from a larger sample of hospitalized patients obtained by systematically screening all psychiatric admissions to 15 facilities over a six-year period. Proband diagnoses (*DSM-III*) were made by a psychiatrist six months following the patient's index admission and were based on results of a structured interview, medical records, and a conversation with the patient or an informant. The family history method was used to obtain information about the first-degree relatives of the probands. Cox Proportional Hazards models were adjusted for duration of illness of the proband and gender of the relatives. First-degree relatives of female probands had a significantly higher morbid risk of nonaffective psychotic illness (i.e., schizophrenia and unspecified functional psychosis) than relatives of male probands. There were no differences in risk to relatives for any affective disorders. Although male relatives of both male and female probands were at higher risk for alcohol and drug use disorders than female relatives, the effect was more salient among relatives of male probands.

NR446 Wednesday May 15, 12 noon-2:00 p.m.

Treatment of Schizophrenia in the Mentally Retarded

Michael B. Sheikman, M.D., Psychiatry, Univ of Mass MC WSH, P.O. Box 528 Main Office, Shrewsbury, MA 01545

Summary:

The prevalence of psychiatric disorders among people with mental retardation (PWMR) is estimated to be three to four times higher than that of the general population. In many cases maladaptive behavior is the presenting complaint of such a disorder. The behavior associated with acute psychosis should be differentiated from that associated with chronic brain disfunction. Psychosis in PWMR is usually overdiagnosed because there are certain difficulties in using *DSM-III-R* criteria in patients with severe developmental disability due to difficulties in communication. Pharmacotherapy of schizophrenia is the same in PWMR as it is for the patients without mental retardation. In eight hospitalized patients with mental retardation who met *DSM-III-R* criteria for schizophrenia (delusions, prominent hallucinations, loosening of associations, flat and in some patients inappropriate affect) treatment with neuroleptics significantly reduced the severity of psychotic symptoms. The use of neuroleptics for the treatment of maladaptive behavior in the absence of neuroleptic-responsive psychiatric disorders was less effective or not effective. All patients with mental retardation in this study were adults. Of eight cases with coexisting schizophrenia, five were male and three were female. Three patients with coexisting schizophrenia received haloperidol in doses 5-15 mg/d, two patients received fluphenazine 10-25 mg/d, two patients received thioridazine 50-400 mg/d, and one patient received chlorpromazine 200-300 mg/d. PWMR were found more likely to have central anticholinergic syndrome. Routine screening for tardive dyskinesia must be a part of the treatment plan.

NR447 Wednesday May 15, 12 noon-2:00 p.m.

Cognition and Social Functioning in Schizophrenia

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Summary:

In schizophrenic patients, information processing and intellectual deficits along with positive and negative symptoms significantly interfere with (1) interpersonal problem solving and (2) skill learning. To investigate relationships between deficits in cognitive, symptom, and social domains, 30 schizophrenic patients (meeting *DSM-III-R*) criteria as assessed on the PSE) and 15 normal control subjects completed measures that assessed each of these areas. Results showed that schizophrenic patients scored significantly below normals on interpersonal problem solving and skill learning variables. Significant correlations were found between interpersonal problem solving and measures of verbal intelligence and short term recall. Similarly, skill learning was significantly related to verbal and nonverbal measures of intelligence, early visual processing, short-term recall, and cognitive flexibility. *NO* significant correlations were found between positive and negative symptoms and either interpersonal problem solving or skill learning. Subsequent regression analyses showed that intellectual and information processing variables were highly intercorrelated and that intellectual functioning accounted for the greatest amount of the variance when predicting either social functioning variable. These findings suggest that rehabilitative programs that wish to incorporate cognitive interventions to remediate social (information) functioning should target intellectual processes.

NR448 Wednesday May 15, 12 noon-2:00 p.m.

Impact of Clozapine on Chronically State Hospitalized Treatment-Refractory Schizophrenic Patients

Jeffery Grace, M.D., Buffalo Psych. Center, 400 Forest Avenue, Buffalo, NY 14213; Marvin Herz, M.D., John Treanor, M.D., Kerry Donnelly, Ph.D., Stephen B. Bellus, Ph.D., Patricia Smith, R.N., Susan Gunn, R.N., Thomas Hays, M.D., Margaret Paroski, M.D.

Summary:

The treatment efficacy of clozapine was evaluated in an open trial of 31 hospitalized chronically treatment-refractory schizophrenic patients, for a six-month period (mean current hospitalization 41 months, mean clozapine dose at three months = 600mg./day, and six months = 740mg./day). Scheduled evaluations were carried out using the BPRS (Brief Psychiatric Rating Scale), the CGI (Clinical Global Impression Scale), and a neuropsychological cognitive battery. Weekly patient supportive therapy groups and family support group were offered. Comparing base-line BPRS Scores (Mean = 52.9) with scores at three (Mean = 38.6) and six (Mean = 38.2) months, significant improvement occurred in 67 percent and 72 percent of patients, respectively. Similar improvements were noted on the CGI (Mean scores at baseline = 6.04, at three months = 5.13,

and at six months = 5.09). Nine of the 16 measures of cognitive functioning showed significant improvement at six months. Ten patients were discharged due to marked improvement. These data suggest that clozapine in higher than previously reported dosages, is an effective medication for these treatment-refractory patients. Virtually all of the clinical improvement occurred in the first 12 weeks. The greater than 60 percent BPRS response rate is considerably higher than results reported in other studies.

NR449 Wednesday May 15, 12 noon-2:00 p.m.

P3 and Thought Disorder Index Scores in Families of Schizophrenics

Brian F. O'Donnell, Ph.D., Psychiatry 116A, Harvard Med. School., BVAMC 116A 940 Belmont Street, Brockton, MA 02401; Martha E. Shenton, Ph.D., Robert W. McCarley, M.D., Seth D. Pollak, M.E.D., Steven F. Faux, Ph.D., Robert S. Smith, B.A.

Summary:

The amplitude of the auditory P3 response is usually reduced in schizophrenia (SZ). We report initial findings of P3 responses and Thought Disorder Index (TDI) scores recorded from six patients with SZ (by *DSM-III-R* and RDC criteria) and from four of their nonschizophrenic family members (NON-SZ) drawn from three families. The P3 responses of these two groups were compared with six control subjects who were matched for age (mean = 41) and handedness (Right) to the family members. P3 responses were recorded using an auditory oddball paradigm, and P3 amplitude from the target tones were integrated over a 300-400 ms window using a coronal electrode chain (T3, C3, Cz, C4, and T4). Groups were compared using ANOVAs followed by planned comparisons. The ANOVAs indicated group differences at all electrode sites ($p < .025$, one tailed test). More specifically, the SZ group showed reduced P3 amplitude compared to controls at *all* electrode sites ($p < .025$, one tail; mean difference across electrodes = 6.9 uv). In addition, NON-SZ family members showed reduced P3 amplitude vs. controls at C3, CZ, C4, and T4 ($p < .05$, one tail; mean difference across electrodes = 2.5 uv). Using the 2 uv cut-off at the T3 electrode site used in our previous studies, none of the controls but 25 percent of the NON-SZ members and 67 percent of the SZ members had abnormally low amplitudes. Among SZ and NON-SZ family members, TDI scores were inversely correlated with P3 amplitude at T3, C3, Cz, and T4 ($r = -.79$ to $-.88$, $p < .05$). Among nonpsychotic family members there was also an inverse, though nonsignificant, relationship between P3 amplitude and the TDI scores. These findings suggest that severity of thought disorder is reflected by diminished P3 amplitude, and that abnormal P3 amplitudes may occur in family members who are not psychotic.

NR450 Wednesday May 15, 12 noon-2:00 p.m.

M-Chloro-Phenyl-Piperazine in Schizophrenia: Typical Versus Atypical Neuroleptic Effects

John H. Krystal, M.D., Psychiatry, Yale Univ Sch of Med., West Haven VA Medical Center, West Haven, CT 06516; John Seibyl, M.D., Lawrence H. Price, M.D., Scott W. Woods, M.D., George R. Heninger, M.D., Dennis S. Charney, M.D.

Summary:

We have previously showed that MCPP appears to exacerbate psychosis in schizophrenic patients but not healthy subjects or other patient groups. This presentation will attempt to further characterize MCPP effects in unmedicated schizophrenic patients. It will also present recent data attempting to link the MCPP effect to the serotonin-1C (5-HT_{1C}) receptors by evaluating the capacity of pretreatments that have high (clozapine, ritanserin) or low (haloperidol) affinity for the 5-HT_{1C} receptor to block MCPP effects. *Method*: In an ongoing study, schizophrenic patients off neuroleptics for at least two weeks (N = 12) and healthy subjects (N = 14) completed MCPP (0.1 mg/kg, i.v. over 20 min.) and placebo test days in a randomized double-blind fashion. Repeat MCPP and placebo tests were performed in patients treated for four weeks with haloperidol (20 mg/d, N = 10) or clozapine (800 mg/d, N = 3). Additional unmedicated patients (N = 4) completed four test days (MCPP, MCPP + ritanserin 10 mg, p.o., ritanserin, or placebo). *Results:* MCPP significantly increased the combined score of the 4 Key BPRS Schizophrenia Items (Hallucinatory Behavior, Unusual Thought Content, Suspiciousness, and Conceptual Disorganization) in unmedicated schizophrenics, but not healthy subjects. The increase in four key symptoms correlated with increases in prolactin and growth hormone, but not cortisol or self-rated measures of anxiety. Patients and healthy subjects experienced comparable increases in anxiety after MCPP administration. Haloperidol treatment nonsignificantly reduced MCPP effects on positive symptoms or anxiety in patients. Preliminary data on clozapine and ritanserin effects will be presented at the meeting. *Implications:* MCPP-induced exacerbations of schizophrenia symptoms suggest a modulatory role for 5-HT systems in this disorder. Differential blockade of MCPP effects by typical and atypical neuroleptics may implicate the 5-HT_{1C} receptor may provide a clue to the increased efficacy of clozapine in treatment-resistant schizophrenia.

NR451 Wednesday May 15, 12 noon-2:00 p.m.

Factor Analysis of MRI Volumes in Schizophrenia

Allen Y. Tien, M.D., Mental Hyg., Johns Hopkins University, 624 North Broadway Street, Baltimore, MD 21205; Godfrey D. Pearlson, M.B., Pat Barta, M.D., Richard Powers, M.D., Gary Chase, Ph.D.

Summary:

Many brain structure abnormalities have been reported in schizophrenia, generally in terms of smaller size for a given brain structure compared to a nonschizophrenic group. As the number of structures examined in this way increases, concerns about chance findings can arise. Conflicting reports from different researchers may partly reflect this problem. In addition, relationships between different brain structures may be difficult to appreciate.

An alternative approach is the use of latent structure analyses to test for patterns of brain structure size abnormality. We examined MRI volume measures of amygdala, hippocampus, parahippocampal gyrus, superior temporal gyrus, entorhinal cortex, and third ventricle. As these measures were normally distributed, ordinary factor analysis was suitable. There were 44 schizophrenic and 55 normal subjects.

Both groups produced 5-factor models. Factor 1 was the strongest for both groups. (Differences are underlined). In normals Factor 1 loaded on left and right hippocampus and *left superior temporal gyrus* (STG). Factor 1 for schizophrenia loaded on left and right hippocampus and *right parahippocampus* with a moderate loadings on *right STG*, *third ventricle*, and *left parahippocampus*. With the relatively small sample size comparison of the other factors is limited. The results with Factor 1 suggest possible systematic differences in brain structure in schizophrenia.

NR452 Wednesday May 15, 12 noon-2:00 p.m.

Hallucinations in a State Hospital Population

Kenneth N. Sokolski, M.D., Psychiatry, VA Med Ctr Long Beach, 5901 E. 7th Street, Long Beach, CA 90822; Edward M. Demet, Ph.D., Bruce I. Abrams, M.D., Jerome F. Costa, M.D., Christopher Reist, M.D., Jeffrey L. Cummings, M.D.

Summary:

In order to assess the frequency and diagnostic usefulness of

hallucinations in a chronic psychiatric population, 113 consecutive cooperative admissions to a state psychiatric hospital were administered the SCID-R, a demographic interview, BPRS, MMSE, and an 80-question Hallucination Interview developed by the authors (K.S,J.C.). The incidence of past auditory hallucinations (AH) approached 90 percent in schizophrenics (SCZ) and 53 percent in bipolar manics (BPM). Past visual hallucinations (VH) were reported in 75.6 percent of chronic paranoid schizophrenics (CPS), 56.7 percent of chronic undifferentiated schizophrenics, and 47.6 percent of BPM. Tactile, olfactory, and gustatory hallucinations were less common. Compared to BPM, AH of SCZ were two to three times as likely to be treatment resistant, perceived as real, and to include non-voice symptoms. Seventy-percent of SCZ and 55 percent BPM hallucinators reported commands. More than half of these patients followed orders. All groups perceived AH as unpleasant. In contrast only BPM reported VH as mostly unpleasant. While AH did not lateralize, right hemifield VH predominated. VH of SCZ occurred significantly earlier, were more often Lilliputian, and more frequently in color than BPM. The present data suggest that a more detailed description of hallucinations may provide a means of discriminating between otherwise similar diagnostic groups.

NR453 Wednesday May 15, 12 noon-2:00 p.m.

Family Intervention for Schizophrenia Among Hispanics

Cynthia Telles, Ph.D., Psychiatry, UCLA School of Med., 300 UCLA Medical Plaza, Los Angeles, CA 90024; Marvin Karno, M.D., George Paz, M.D., Miguel Arias, M.D., Douglas Tucker, M.D., Jim Mintz, Ph.D.

Summary:

Recent studies have demonstrated that a structured behavioral family intervention along with optimal neuroleptic medication have significantly reduced clinical morbidity among patients with schizophrenia (Falloon, et al, 1982). In this presentation, we will discuss an ongoing controlled study which sought to replicate and extend these findings to a population of unacculturated Hispanics. Behavioral Family Management (BFM) provided over a one-year period was compared through random case assignment to an individual case management (CM) approach. Forty patients were recruited from local psychiatric hospitals and clinics and administered the Present State Examination (PSE) and the *DSM-III* checklist to determine the diagnosis. Ratings of expressed emotion were obtained from the Camberwell Family Interview. Clinical status was monitored using the Brief Psychiatric Rating Scale and other measures. Significant findings will be discussed, including the extremely low rate of high "expressed emotion" among unacculturated immigrant Hispanics, which are consistent with results from developing countries (International Pilot Study of Schizophrenia). The results of analysis covariance examining the relationship of intervention modality to outcome, adjusting for medication compliance and expressed emotion, will be presented. Implications for appropriate intervention with severely mentally ill persons from a culturally diverse background will be discussed. The results presented will be based on a nearly completed sample.

NR454 Wednesday May 15, 12 noon-2:00 p.m.

A Carbamazepine Augmentation Trial in Chronic Schizophrenics

Kurt Meszaros, M.D., Psychiatry, Univ of Clinic Vienna, Waehringer Guertel 18-20, Vienna 01090, Austria; Christian Simhandl, M.D., Elisabeth Denk, M.D., A. Liechtenstein, M.D., A. Topitz, M.D., K. Thau, M.D.

Summary:

A significant group of schizophrenics are poorly responsive to neuroleptics (NLs) or can't maintain their initial treatment improvement. In an attempt to examine the role of augmented CBZ in these patients, we designed a double-blind, randomized, placebo-controlled study. After patients have been examined physically, demographic and biological characterization of patients for inclusion have to be done. Patients have to fulfill specific criterias for NL nonresponse and have to be diagnosed according to *DSM-III-R*. During a six week period either CBZ or placebo have been added to NLs; between the following two weeks only placebo has been added in both groups. Patients were assessed at baseline, and then bi-weekly blood taking and ratings have to be done up to the end of the trial at week 8. Twelve patients were randomized to CBZ-group, 10 patients to the placebo group (16 male, 6 female). For statistical analysis we used the Friedman rank variance analysis. At the BPRS CBZ-treated patients statistically improved between baseline and week 6 in the "anxiety-depression"-subscore. In the SANS we noted statistically improvements in the "affective flattening" and "alogia"-items. Comparing schizophrenic symptoms between both groups with the -adjusted U-test we noted improvements for the CBZ-group in two items of the SANS, namely for "affective flattening" at week 8 ($p = 0.0500$) and for "attention" at week 8 ($p = 0.0163$). In our opinion in appears that there is continued promise for the use of CBZ in nonresponsive schizophrenics.

NR455 Wednesday May 15, 12 noon-2:00 p.m.

Role of Serum Serotonin Assay in Schizophrenia

Anand K. Pandurangi, M.D., Psychiatry, Medical College of VA, Box 710 MCV Station, Richmond, VA 23298; Anthony L. Pelonero, M.D., Nedathur Narasimhachari, Ph.D.

Summary

Serotonergic abnormalities have long been postulated but not proven in schizophrenia (1). Reports of high 5-HT in blood and serotonin antagonism by clozapine have renewed interest in the role of 5-HT. We report two studies of how serotonin relates to clinical and structural measures in schizophrenia. We use HPLC and measure serum 5-HT which in our lab shows high correlation with platelet 5-HT, the main reservoir of 5-HT in blood (2). *Methods*: 55 subjects with schizophrenia *(DSM-III* & RDC), and 35 normal controls were recruited. Premorbid adjustment (scale by Canon-Spoor et al), positive and negative symptoms (by BPRS and SANS, respectively) were blindly rated. Ten ml blood was drawn, centrifuged and stored at –70. In Study A, 36 schizophrenics underwent MRI to assess frontal lobe volume, corpus callosum area, and cortical atrophy. Treatment response was retrospectively assessed. In study B, 19 subjects underwent CT to assess VBR and cortical atrophy and amphetamine challenge test (ACT) under double-blind conditions. Serum serotonin was measured at three time points during the test. Treatment response was assessed prospectively. *Results*: There was no difference in serotonin levels between schizophrenics and controls (mean + S.D = 131 + 71 and 120 + 63, respectively). In the first cohort serotonin had a weakly significant relation with treatment response ($r = 0.30, p < .07$). This was replicated in the second cohort with a robust relation of serotonin with treatment response ($r = 0.58$, $p < 0.03$). Further 5-HT from the ACT correlated significantly with negative symptoms ($r = .48, p < .06$). No correlation was evident between 5-HT and other variables including VBR, frontal lobe volume, and cortical atrophy. *Discussion*: Our findings do not support the notion of increased serotonin in schizophrenia. This conclusion is subject to limitations imposed by medication status, assay of serum rather than platelets, and sample heterogeneity. Baseline 5-HT and amphetamine induced increase in 5-HT had interesting relations with treatment response and negative symptoms suggesting 5-HT as a potential measure of illness plasticity. Further implications and limitations will be discussed in the presentation.

NR456 Wednesday May 15, 12 noon-2:00 p.m.

Cessation of Polydipsia in Schizophrenia Following Clozapine Administration

John C. Kluznik, M.D., Clinical Director, Minnesota Security Hosp, 300 Sheppard Drive, Saint Peter, MN 56082

Summary:

Polydipsia is a serious and potentially fatal complication of the course and treatment of schizophrenia in some patients. During the course of treatment with clozapine nine of ten chronically and severely ill inpatient schizophrenics with polydipsia had a substantial or complete remission of polydipsia following administration of clozapine. One had no change after six weeks of treatment and one woman who had never had polydipsia developed it four weeks after beginning clozapine. All met *DSM III-R* criteria for schizophrenia. Their age range is 28-78 years. Eight of 11 were men. The average duration of hospitalization is over ten years. None was taking carbamazapine. None had a history of significant brain injury. The remission occurred early, in one case following a single dose of 25 mg. This patient had been capable of gaining 17 pounds of water weight in one hour. These findings have important implications for treatment of schizophrenic patients with polydipsia, for the monitoring of polydipsia in patients starting to take clozapine and for whom it had not previously been present, and for the understanding of the pharmacology of clozapine and the underlying mechanisms of polydipsia in schizophrenia.

NR457 Wednesday May 15, 12 noon-2:00 p.m.

Indicators of Vulnerability to Schizophrenia

Wolfgang Maier, M.D., Psychiatry, University of Mainz, Untere Zahlbacher Strasse 8, 6500 Mainz, Germany; Christoph Hain, Peter Franke, Thomas Klingler, Dirk Lichtermann.

Summary:

It is generally recognized that schizophrenia is transmitted in families; yet its penetrance (about 50 percent) is far from being perfect. Therefore, healthy relatives of schizophrenics might carry the genes without showing the psychopathologically defend phenotype, but might reveal other disturbances indicating the vulnerability to schizophrenia. Several neuropsychological measures have been proposed as such indicators of vulnerability. As the results are controversial or limited to particular settings (e.g. continuous performance test in high risk samples), the following neuropsychological indicators were compared among drug-free schizophrenics ($n = 50$) and healthy siblings of schizophrenics ($n = 50$) matched to the patients' siblings ($n = 56$): *reaction time paradigms* as the crossover and the modality-shift reaction time, *selective attention paradigms* as continuous performance test (identical pair and single target versions) and span of apprehension test, and *indicators of cognitive flexibility* as the Wisconsin Card Sorting Test. The crossover *paradigm* turned out to be an ideal indicator of the transmitted vulnerability identifying a substantial number of healthy siblings of schizophrenics by a deviant pattern of neuropsychological functioning independently of age.

NR458 Wednesday May 15, 12 noon-2:00 p.m.

Patterns of Substance Use in New Onset Psychosis

Beatrice Kovasznay, M.D., Psychiatry, Suny Stony Brook, HSC T-10, Stony Brook, NY 11794; Ranganatha Ram, M.D., Joseph E. Schwartz, Ph.D., Evelyn Bromet, Ph.D

Summary:

Most longitudinal studies of psychotic populations have excluded patients with considerable drug or alcohol use from their samples. Therefore, our understanding of the relationship between drug and alcohol problems and the early course of psychosis has been incomplete. We shall present here the methodology and preliminary results from an on-going county-wide (population 1.3 million) epidemiologic prospective study of newly diagnosed psychotic patients. Three questions are addressed in 59 male and 52 female patients entering treatment (hospital or outpatient clinic) for a psychotic disorder:

1. What are the lifetime patterns of drug and alcohol use in patients with onset of psychotic symptoms?
2. Is the age of onset of psychotic symptoms influenced by differing intensities of drug and alcohol use?
3. Is there a specific relationship between the specific class of substance use and individual psychotic symptoms?

The results indicate that only 15 percent of subjects did not use drugs or drink regularly. Differences in symptomatology in relation to the patterns of substance use will be discussed.

NR459 Wednesday May 15, 12 noon-2:00 p.m.

The DST and Psychosis: An Eight-Year Follow-Up

William H. Coryell, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; Debby Tsuang, M.D.

Summary:

Ninety-two inpatients with nonorganic, nonmanic psychoses had dexamethasone suppression tests during their hospitalization. Raters who were blind to DST results and to baseline chart and research diagnoses conducted personal interviews with 71 of these patients eight years later. Patients who had been DST nonsuppressors were five times more likely than those who had been suppressors to be free of psychotic features and to exhibit insight at the follow-up interview (42 percent vs. 8 percent; $X^2 = 10.3$, $df = 1$, $p = .001$). Baseline diagnoses also strongly predicted outcome in the expected directions, even among DST nonsuppressors. DST results had no prognostic significance among patients with a baseline diagnosis of schizophrenia. These data replicate those of an earlier follow-up. Both studies suggest that, among patients with a functional psychosis, DST nonsuppression may be prognostically meaningful, particularly after the exclusion of those who meet narrow criteria for schizophrenia.

NR460 Wednesday May 15, 12 noon-2:00 p.m.

Symptoms and Work Performance in Patients with Schizophrenia

Robert Milstein, M.D., Psychiatry, Yale University, YNHH 20 York St. MU-10-805A, New Haven, CT 06504; Morris Bell, Ph.D, Paul Lysaker, Ph.D., Gary Bryson, B.S., Joseph L. Goulet, M.S.

Summary:

Anthony and Jansen reviewed psychiatric rehabilitation outcome and reached the counter-intuitive conclusion that symptoms and employment are unrelated. In a psychiatric rehabilitation study, 30 *DSM-III-R*-diagnosed schizophrenic patients received first and third week ratings of symptoms (Positive and Negative Syndrome Scale [PANSS], Brief Psychiatric Rating Scale [BPRS] and work performance (Work Personality Profile [WPP], Minnesota Satisfactoriness Scale [MSS]) using on-site observation and interview. Multivariate regressions revealed a) significant relationships between symptoms and work performance, with PANSS ratings providing more powerful predictions than BPRS; b) PANSS negative and general symptoms were the best predictors, accounting for up to 50 percent of the variance on several dimensions of work performance; c) stepwise procedures yielded an optimal predictive model relating symptoms to seven measures of work performance in the first week of work; d) a replication study using coefficients from this model applied to symptoms and work ratings in the third week of work

proved the model to be robust on four of seven work measures; e) for the three work measures where the model failed to replicate, work measures themselves were poorly correlated from the first to third week. Results underscore the importance of symptoms in psychiatric vocational rehabilitation.

NR461 Wednesday May 15, 12 noon-2:00 p.m.

Relationship Between Depression/Anxiety and Positive and Negative Symptoms in Schizophrenia

Ashok K. Malla, Psychiatry, Victoria Hospital, 375 South Street, London Ontario, Canada N6A 4G5; Ross M.G. Norman, Ph.D.

Summary:

Ninety-five outpatients with a diagnosis of *DSM-III-R* (SCID) schizophrenia were examined to assess the relationship between depression, anxiety, and positive and negative symptoms of schizophrenia. Self-report instruments (Beck Depression Inventory, Spielberger, et al Self Evaluation Questionnaire and 28-Item General Health Questionnaire) were used to evaluate anxiety and depression, while positive and negative symptoms of schizophrenia were assessed through the use of Scale for Assessment of Positive Symptoms (SAPS) and Scale for Assessment of Negative Symptoms (SANS), respectively. Positive and negative symptoms were assessed by raters who were not aware of patients' self-reported level of anxiety or depression, thus avoiding the risk of bias contained in much previous research in this area. The measures of depression and anxiety showed a pattern of interrelationships (x $r = .68$), which suggested that they were measuring a general state of dysphoria. Both depression and anxiety, as well as a composite measure of dysphoria were found to be more reliably related to the level of positive symptoms ($r = .38$) than to negative symptoms ($r = .14$, n.s.).

NR462 Wednesday May 15, 12 noon-2:00 p.m.

Third and Lateral Ventricular Volumes in Schizophrenia

Steven B. Schwarzkopf, M.D., Psychiatry, The Ohio State University, 473 West 12th Avenue, Columbus, OH 43210; Henry A. Nasrallah, M.D., Stephen C. Olson, M.D, Mary B. Lynn, M.S., Tanmoy Mitra, M.S.

Summary:

Ventricular enlargement is present in a subgroup of schizophrenic patients. Some studies show a high correlation between lateral and third ventricular measures, possibly indicating a process affecting the entire ventricular system. In a previous study, we found significantly greater lateral to third ventricular volume correlations in patients than controls (Schwarzkopf, 1990). In the present report, ventricular volumes were examined in a new sample of schizophrenic patients.

Seventy-one schizophrenics (53 males, 18 females) and 39 controls (18 males, 21 females) underwent magnetic resonance imaging (GE 1.5 tesla scanner, inversion recovery sequence). Total ventricular volumes were obtained (direct postprocessing of MRI slice data, complete coronal set of scans, inter-rater reliability $>.95$) Lateral (LVENT) and third (3VENT) ventricular volumes were analyzed.

Patients had significantly larger 3VENT volumes ($P<.01$) and LVENT volumes ($P<.05$) than controls. Correlation analyses (Spearman r) showed a very high association between (LVENT) and (3VENT) in patients ($r = +.58$, $p<.0001$). Controls showed a much less robust relationship between the measures ($r = +.27$, $p = .097$). Although 3VENT enlargement was more specific pathologic finding, this was due to lack of specificity LVENT enlargement rather than limited 3VENT involvement. These findings indicate a nonfocal pathological process in schizophrenic patients with ventriculomegaly.

NR463 Wednesday May 15, 12 noon-2:00 p.m.

Symptom Profile in First Episode Schizophrenia

Derri Shtasel, M.D., Psychiatry, Univ of Pennsylvania., 202 Piersol Bldg 36 Spruce Sts, Philadelphia, PA 19104; Rachel E. Gur, M.D, Carolyn Heimberg, M.D., David Mozley, M.D., Fiona Gallacher, B.A., Jeff Richards, B.A., Ruben C. Gur, M.D.

Summary:

Hypotheses concerning the course of schizophrenia suggest that positive symptoms appear earlier and are more treatment responsive, whereas negative symptoms herald chronicity and are more resistant to treatment. Examining the phenomenologic differences between first-episode (FE) patients and those who have been ill can help clarify the clinical profile before the effects of intervention and chronicity take place. We have administered standard clinical scales (BPRS, Sans-Saps, and others) to a sample of 96 patients with schizophrenia (*DSM-III-R*), of whom 27 had been evaluated at first presentation. On BPRS factors, FE patients did not differ in overall severity, but had lower scores on the thought disorder and higher on the hostility factors ($p<.05$). FE patients did not differ in overall SANS or SAPS. They had less severe scores on the affect and attention subscales of the SANS and the thought disorder subscale of SAPS ($p<.05$), but higher scores on the delusions subscale of the SAPS ($p<.001$). These results do not support the hypotheses. Instead they suggest that some symptoms may be phase specific, but that symptom fluctuation over time is a complex process. Whether these changes in overt symptoms represent progression of illness, adaptation to illness, or both, warrants further study.

NR464 WITHDRAWN

NR465 Wednesday May 15, 12 noon-2:00 p.m.

Can Clinical Response to Clozaril be Predicted?

Wayne S. Fenton, M.D., Research Inst., Chestnut Lodge, 500 West Montgomery Avenue, Rockville, MD 20850; Beth Lee R.N.

Summary:

Although many treatment-resistant schizophrenic patients derive significant clinical benefit from clozapine, potentially serious side effects compel a careful weighing of risks and benefits for individual patients (1). Identifying predictors of drug response might usefully inform these deliberations. This pilot study explores predictors of clinical benefit among 27 refractory *DSM-III-R* schizophrenic patients treated with clozapine (mean 545mg/d) for an average of 12 months (range 1-26) in a clinical setting. Potential predictors rated from clinical records included premorbid functioning, age and type of illness, onset and early course, indices of chronicity, schizophrenia subtype, prognostic scale score (2), and pre-clozapine clinical signs and symptoms (BPRS, SANS, SAPS). Improvement in positive symptoms, negative symptoms, and global functioning was independently rated by three members of each patient's clinical team. RESULTS: Agreement across independent ratings of clinical response was excellent (mean correlation 0.88). Golbal clinical ratings of improvement was positively correlated with prehospitalization independent living ($r = 0.38$, $p<.03$) and negatively correlated with pre-clozapine blunted/inappropriate affect ($r = -.41$, $p<.02$). A simple two-item predictive index including these two variables, correlated 0.52 ($p<.003$) with global clinical improvement. Illness course, indices of chronicity, and pre-treatment symptom severity were not predictive. Patients with good prognostic features

had a high likelihood of clinical benefit, but in defiance of prediction, several patients with poor prognostic features also experienced substantial improvement.

NR466 Wednesday May 15, 12 noon-2:00 p.m.

Self-Appraisal Deficits in Schizophrenia

Xavier F. Amador, Ph.D., Dept. of Clinical Psych., Columbia University, 722 W. 168th ST. Box 2, New York, NY 10012; D.H. Strauss, M.D., S. Yale, M.S.W., K. Gimmestad, O.T.R., A.E. Rundquist, R.N., H. Deutsch, R.N., P. Stern, M.A., C. Kaufmann, M.D., J.M. Gorman, M.D.

Summary:

Between 81 percent and 89 percent of patients with the diagnosis of schizophrenia believe they do not have a mental disorder[1,2]. A comprehensive examination of the meaning, treatment, etiology, and pathophysiology of unawareness of illness (UOI) in schizophrenia has been difficult due to conceptual ambiguities and the lack of a standardized measure. For this reason, we have recently proposed guidelines for the measurement of UOI in the interest of increasing comparability between studies[2]. Also, we have developed a scale and questionnaire to assess UOI. Reliability and validity data for these instruments will be presented (from N = 30 *DSM-III-R* schizophrenics). Preliminary data from a subgroup of the total sample (N = 12) indicate that increased UOI is unrelated to both level of delusions (SAPS score) suggesting that UOI is not simply a measure of severity of delusions. Level of unawareness was stable over time, and predictive of poorer course of illness (i.e. greater severity of symptoms of psychosis, poorer social functioning, and increasing occupational dysfunction). In addition, psychological defensiveness subscale items from the aforementioned scale were strongly related to daily ratings of medication compliance in the expected direction of higher ratings being associated with poorer compliance.

NR467 Wednesday May 15, 12 noon-2:00 p.m.

Are Neurological Soft Signs a Marker of Perinatal Brain Damage?

Michael Linden, M.D., Psychiatrie, Ereie Universitat, Eschenallee 3, D-1000 Berlin 19, Germany; Albert Diefenbacher, M.D.

Summary:

The pathoplastic implications of pre- and perinatal brain damage as to course and outcome of psychiatric disorders are controversial. On the one hand, an earlier age at the manifestation of disease as well as a more chronic course were found in combination with anamnestic indications of early brain damage (VOGES 1975). On the other hand, the benefit of such information has been disputed because of its little specifity, especially with regard to the low reliability of such anamnestic data (ESSER/SCHMIDT 1987). Therefore, it should be of interest to look for objective markers indicative of early brain damage that can be easily to be detected.

Method: We examined 102 consecutively admitted inpatients of the Psychiatric Hospital of the Free University of Berlin with a 67-item soft-sign list. The patients were not medicated. Psychopathological state and frequency of the anamnestic attribute of 'early brain damage' were documented by the AMDP-System (Arbeitsgemeinschaft fur Methodik und Dokumentation in der Psychiatrie 1979).

Results: Patients with anamnestic reference to pre- and/or perinatal complications showed significantly more neurological soft signs as compared to those without such a history, irrespective of their psychiatric diagnosis (according to ICD-9). We conclude that neurological soft signs in adults could be an objective marker of early brain damage, what furthermore is underlined by their frequent occurrence in countries with poor obstetrical care (GUREJE 1988). We suggest that a neurological examination on basis of a soft-sign set would provide an easily to be performed bedside test to detect the anamnestic risk factor of 'early brain damage' in adults.

NR468 Wednesday May 15, 12 noon-2:00 p.m.

Delusions of Parasitosis: An Entomologist's View

Donald J. Kushon, M.D., Psychiatry, Hahnemann University, Broad and Vine St. MS 535, Philadelphia, PA 19102; Jean Helz, M.D., Kendrick Lau, Michael Williams, Ph.D.

Summary:

Delusions of Parasitosis is a nonspecific syndrome referring to a conviction that live organisms such as insects or mites are infesting the body. A postal survey of a random sample of 86 entomologists from throughout the United States identified 170 cases with a presumptive diagnosis of DOP which were seen within a one-year period. An estimate of incidence of DOP in the United States ranged from 7,100 to 19,800 new cases per year. The data provided on 93 cases which met the study criteria were examined in more detail.

The age at presentation varied widely. Females predominated with a female to male ratio of 2.6:1. Eighty-nine percent of the cases were Caucasians. Most were married, living with family, employed, and at a lower middle-class socio-economic level. Abnormal personality traits were commonly identified, especially the paranoid type. Symptoms were more commonly nonbizarre. Thirty-six percent of the cases involved a group outbreak in which co-workers at an office setting were most frequently involved. The cases presented mostly of short duration, less than six months. Eighty-six percent of the cases received an inspection by the entomologist and 39 percent of the cases revealed a causal or contributory environmental factor; 16 percent of the cases revealed a true infestation. Most of the cases were seen by the entomologist prior to a physicians's evaluation. A total of 70 percent of the cases were referred, mostly to dermatologists. Only three cases were referred to psychiatrists. A total of 93 percent of the entomologists indicated that there was a need for a multidisciplinary approach.

NR469 Wednesday May 15, 12 noon-2:00 p.m.

The Use of ECT in Neuroleptic Malignant Syndrome

John M. Davis, M.D., Research, Il. State Psych. Center, 1601 West Taylor Street, Chicago, IL 60612; Philip Janicak, M.D., Cindy K. Gilmore, Psy.D., Paul Sakas, M.D., Zhengu Wang.

Summary:

In review of 734 cases of Neuroleptic Malignant Syndrome (NMS), we found a 21 percent mortality rate and 665 cases with sufficient data to allow for statistical analyses. Fifty-four had received ECT either during or subsequent to an episode of NMS and were compared to those with no specific treatment for their episode of NMS. We also analyzed the data available comparing three drugs (i.e., amantadine, bromocriptine, and dantrolene) to no specific treatment. In comparison to no treatment, we found that treatment with bromocriptine ($x^2 = 6.44$, $p < .01$), amantadine ($x^2 = 5.23$, $p < .02$), or dantrolene ($X^2 = 7.44$, $p < .006$) led to a significantly better outcome when we applied the Mantel-Haenszel statistical method on this retrospective, case controlled data. The results of our second analysis revealed a substantially better outcome (i.e., mortality rate of 9 percent) in the specific drug or ECT treated groups versus the no treatment group ($X^2 = 15.0$, $p < .0001$). The safety and possible benefits of earlier intervention with ECT for NMS are discussed in the context of the case controlled analysis, keeping in mind certain methodological limitations.

NR470 Wednesday May 15, 12 noon-2:00 p.m.

Early Response to Neuroleptic Treatment by Schizophrenics

David B. Glovinsky, M.D., NSC at St. Elizabeth, 2700 King Avenue SE, Washington, DC 20032; Richard Jed Wyatt, M.D., Darrell G. Kirch, M.D.

Summary:

Psychiatric and pharmacology texts often state that it takes three or more weeks for neuroleptics to produce their antipsychotic effects. In order to clarify this important clinical and pharmacological issue, a systematic study of the response of 45 chronic schizophrenic inpatients to remedication with 0.4mg/kg haloperidol was performed in a double-blind, placebo-controlled setting. Patients were rated daily using the Psychiatric Symptom Assessment Scale (PSAS) to monitor symptom change during a drug-free interval which was followed by six weeks of neuroleptic treatment. Statistically significant improvement in Total PSAS scores (31.05, $p<0.05^*$), Verbal Positive/Paranoia (9.4, $p<0.05^*$), and Behavior Positive (12.9, $p<0.05^*$) subscales were evident within seven days after remedication. The Total PSAS score fell by 10.55 units during the first week of haloperidol treatment, a 25 percent decrease from baseline; this constituted more than 50 percent of the total change. We conclude that haloperidol demonstrated significant antipsychotic effects in our chronic schizophrenic patients within the first week of treatment with more than 50 percent of the total measured improvement occurring during that time.

NR471 Wednesday May 15, 12 noon-2:00 p.m.

Outpatients Assess Treatment Involvement and Satisfaction

Kishor Sangani, M.D., Dir. Com. Serv., Mohawk Valley Psychiatry, 1400 Noyes at York, Utica, NY 13502; Charles Sheppard, M.D.

Summary:

Consumer satisfaction assessment of mental health programs began a decade (1964) after satisfaction assessment of primary medical care (1953). Consumer satisfaction monitoring is supported by: government policy, standards of review bodies, societal expectations, and changing attitudes of some administrative and clinical staff. A complementary pull is emerging from data needed for: program development, planning, implementation, and assessment; patient designated service needs, and, treatment compliance issues. Sophisticated measurement lags behind the need for useful scales. The concept of satisfaction remains ambiguous being measured in different ways. Few studies provide standard reliability and validity measures. Analyses are based on inadequately drawn samples of insufficient size to offer normative data. Data fail to differentiate satisfaction levels among program types. This study meets the weakness of earlier reports. This presentation will familiarize attendees with the Mohawk Valley Psychiatric Center Patient Satisfaction Inventory (MVPC-PSI). The (MVPC-PSI) consists of (28) Likert scaled items paralleling a successful treatment course. Empirical validity, internal consistency reliability, item and factor normative data, based on responses from (500) outpatients are provided. Responses discriminate satisfaction levels among patients by: program type, treatment willingness, number of hospitalizations, education, age, and, gender. Copies of the scale, standardization data, and norms will be provided to facilitate use and interpretation of the scale.

NR472 Wednesday May 15, 12 noon-2:00 p.m.

Effects of a Smoking Ban on a Psychiatry Unit

Noel E. Taylor, M.D., Psychiatry, Beth Israel Med. Center, First Ave. at 16th Street, New York, NY 10003; Richard N. Rosenthal, M.D., Brent Chabus, M.D., Stewart Levine, M.D., Amy Hoffman, M.D.

Summary:

The authors conducted a prospective study on two inpatient psychiatry units in response to staff concerns about the effects of a proposed hospital-wide smoking ban. Data were gathered on the two units during the smoking-permitted phase, a wash-out phase, and the no-smoking phase. Patients were given a four-item smoking attitudes questionnaire at admission and discharge. Demographic information, smoking history, and psychiatric diagnoses were obtained on 340 patients. Chi-square analysis of these data revealed no significant patient differences between the units. A log of prn medication, seclusion, restraint, elopement, incident reports, and smoking-related discharge against medical advice was kept for each patient. The log totals were used to compute each patient's relative contribution to unit stress, and scores were pooled to look at unit disruption. Analysis of variance comparing unit disruption by phase showed no significant differences. Fifty staff members answered pre-and post-ban questionnaires about the smoking ban. Paired t-test analysis demonstrated a significant change in staff attitude toward supporting the ban. These data indicated that smoking can be stopped on inpatient psychiatry units without adverse effects on patient care or staff morale.

NR473 Wednesday May 15, 12 noon-2:00 p.m.

The incidence of Tardive Dyskinesia in Chronic Outpatients

William M. Glazer, M.D., Psychiatry, Yale University, CMHC 34 Park Street, New Haven, CT 06519; Hal Morgenstern, Ph.D

Summary:

The Yale TD Study is an ongoing prospective cohort investigation of 400 psychiatric outpatients maintained on neuroleptic medications at one facility and without any history of TD at baseline. Patients are examined every six months for TD symptoms, using the Abnormal Involuntary Movement Scale. This presentation reports incidence rates and risks as well as risk factors pertaining to demographic and neuroleptic exposure characteristics of the population.

The mean age of patients at baseline was 42 years, and the median duration of previous neuroleptic use was 6.1 years. Between 1985 and 1990, the average incidence rate of TD in the total sample was 0.053/year, and the cumulative five-year risk was about 20 percent. Additionally, the rate of TD in this population decreases steadily after a few years of neuroleptic use, but new cases continue to occur even after ten years of exposure. The most important predictors of TD incidence are age, race, and duration of previous neuroleptic exposure at baseline. The rate also appears to be greater for patients treated with higher doses. We will report other effects of clinical variables such as type of medications, diagnosis, age at first neuroleptic exposure, etc.

NR474 Wednesday May 15, 12 noon-2:00 p.m.

Laterality of Tardive Dyskinesia and Parkinsonism

Thomas E. Hansen, M.D., Psychiatry, VAMC Portland 116AP, 3710 SW US Veterans Hosp Road, Portland, OR 97201; George A. Keepers, M.D., William F. Hoffman, M.D., Melinda K. Lowe, B.S., Daniel E. Casey, M.D.

Summary:

Asymmetry of tardive dyskinesia (TD) and drug-induced parkinsonism (DIP) could suggest lateralization of neurochemical activity, but reports vary in finding this asymmetry. In this study, psychotic inpatients were examined for TD with the Abnormal Involuntary

Movement Scale (AIMS) and for DIP with the Sct. Hans Scale. Items subject to lateralization (upper and lower extremity dyskinesia, bradykinesia, tremor, rigidity, arm swing) were scored for right (+) and left (-) sides and added together to yield TD and DIP laterality scores. Only patients with at least one body part symptom score of mild severity were analyzed.

Thirty-two right-handed patients were evaluated. TD lateralized in 14 (70 percent) of the 20 TD patients, to the right in nine (64 percent). DIP lateralized in nine (75 percent) of the 12 DIP patients, to the right in six (67 percent). TD and DIP did not consistently lateralize to either the same or opposite side for the 23 patients with either/or both disorders (chi-square not significant). Higher total DIP scores correlated with higher DIP laterality scores (Pearson's $r = 0.7$, $p = .01$, $n = 12$), but total AIMS scores did not influence TD laterality ($r = -0.3$, $p = .2$, $n = 20$). At final rating (mean 17 days), nine patients no longer had lateralized TD, five new patients did, leaving four right and four left-sided cases. Five patients shifted from lateralized DIP to not lateralized, but four new cases emerged (seven patients had left, and four right-sided DIP on final rating).

These findings have important implications for underlying psychopathology, the coexistence of TD and DIP, and methodologic approaches to study in this area.

NR475 Wednesday May 15, 12 noon-2:00 p.m.

Does the N-Methyl-D-Aspartate Receptor Mediate the Effects of PCP?

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Summary:

The psychotomimetic drug phencyclidine (PCP) has been demonstrated in interact potently with the ion channel associated with the N-methyl-d-aspartate (NMDA) subtype of glutamate receptor (1). It has therefore been postulated that this NMDA binding site may mediate the psychotomimetic actions of PCP. We therefore investigated the effects of a PCP antagonist on PCP-induced behaviors and PCP binding sites in rat brain. PCP competition for the specific binding of [^{3}H]TCP to rat brain membranes demonstrated multiple sites. The affinity of PCP for the high and low affinity components (K_H and K_L, respectively) of the [^{3}H]TCP binding were: K_H 2nM and % R_H 30 percent; K_L 200 nM and % R_L 70 percent. MK801 competition for [^{3}H]TCP binding also demonstrated multiple binding sites: K_H 10nM, %R_H 70 percent K_L 1uM, %R_L 30 percent. The site representing 70 percent of the binding of [^{3}H]TCP with high affinity for MK801 and relatively low affinity for PCP represents the ion channel associated with the NMDA receptor. Metaphit is an irreversible antagonist of PCP-induced behaviors (2) and irreversibly inhibits a population of [^{3}H]TCP binding sites. Brain tissue from rats treated with dose of metaphit (2 umol i.c.v.) which inhibits PCP-induced behaviors demonstrated an irreversible 30 percent decrease in specific [^{3}H]TCP binding. Competition of PCP and MK801 for the remaining [^{3}H]TCP binding sites were essentially monophasic with the high affinity component of PCP competition absent and the high affinity component of MK801 competition intact. Furthermore, the binding of [^{3}H]MK801 to brain tissue was not significantly affected by metaphit. Therefore a dose of metaphit which produces a loss of PCP-induced behavior was without effect on the NMDA receptor. These data indicate that the NMDA associated site may not mediate the psychotomimetic actions of PCP.

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Reliability of Rating Extrapyramidal Side Effects

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Summary:

Quantitative assessment of drug-induced extrapyramidal syndromes, such as tardive dyskinesia (TD) and drug-induced parkinsonism (DIP) relies heavily on the use of clinical rating scales. The reliability of rating TD has been previously investigated, but the reliability of DIP assessment has received less attention.

Ratings of TD and DIP were obtained on 175 psychiatric inpatients receiving treatment with neuroleptic drugs. Eleven raters in various combinations simultaneously rated each patient to produce a total of 715 ratings. Instruments used to rate TD were the Abnormal Involuntary Movement Scale and the Sct. Hans Rating Scale for Extrapyramidal Syndromes. DIP was rated using the SCT. Hans, the Simpson-Angus Scale, the Unified Rating Scale for Parkinsonism, and a scale under development by our group. Items and total scores were compared by averaging the correlations across raters for each item. Reliability coefficients for pairs of individual raters ranged from -.87 to .85, while averages across raters ranged from .02 to .85. Low or negative inter-rater correlations tended to be specific to specific pairs of raters on specific items, indicating a lack of consensus on specific rating criteria rather than a global effect of rater training or skill. Items with the lowest average reliabilities were all items that had low rates of occurrence (e.g. trunkal dyskinesia), although some items with low rates had adequate reliability. Implications for scale refinement, clinical research, and training of raters are discussed.

NR477 Wednesday May 15, 12 noon-2:00 p.m.

Neuroleptics Obscure the Correlation of Tardive Dyskinesia and Ventricular Brain Ratio

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Summary:

Efforts at elucidating anatomical correlates of tardive dyskinesia (TD) have yielded equivocal results. We investigated the hypothesis that suppression of TD by neuroleptic treatment obscured the relationship between TD and ventricular brain ratio (VBR) in patients with chronic schizophrenia.

Thirty-eight stable outpatients over age 40 with a *DSM-III-R* diagnosis of schizophrenia were randomly assigned, in a double-blind fashion, to neuroleptic withdrawal ($n = 19$) or control ($n = 19$) groups. In the withdrawal group, neuroleptics were tapered by 10 percent per day. After withdrawal was complete, subjects were maintained drug free for 21 days. TD was assessed three times weekly with the Abnormal Involuntary Movement Scale (AIMS). Neuroleptic doses were converted to chlorpromazine equivalents. CT scans were obtained on a GE 88000 scanner and VBR was determined using a semi-automated technique developed in our laboratory. Seven patients did not complete the study: five were withdrawn because of psychotic relapse and two withdrew for personal reasons. Only data on patients who completed the protocol were entered into further analysis.

The withdrawal group experienced a significant increase in total AIMS (repeated measures analysis of variance : significant group by time interaction, $F(13,5434) = 54$, $p < .001$). Further analysis (controlled for age) revealed that VBR was significantly ($p < .05$) associated with the magnitude of the increase in AIMS in the patients withdrawn from neuroleptics. There was no significant relationship of VBR to total AIMS in the control group. Future imaging studies of TD should endeavor to examine the subjects in a neuroleptic free state.

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Endocrine Effects of Antipsychotic Drugs in Patients

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Summary:

We studied prolactin (PRL) and growth hormone (GH) levels before and after apomorphine test (APO, 0.75 mg subcutaneous) - a dopaminergic receptors agonist (DA) - after washout and after one month of treatment in *DSM-III-R* schizophrenic inpatients. Patients received either amisulpride (n = 15), clozapine (n = 6), SDZ HDC 912 (n = 11), OPC 4392 (n = 10), or 52028 RP (n = 7). Amisulpride, a D-2 DA receptors antagonist caused a large increase in baseline PRL ($p < 0.005$), and a decrease in APO-induced PRL inhibition ($p < 0.005$), without modifying GH secretion. Clozapine, an atypical neuroleptic, induced a weak increase in baseline PRL ($p < 0.05$) but no change in PRL and GH responses to APO test. SDZ HDC 912, a DA D-2 partial agonist, induced a decrease in baseline PRL ($p < 0.06$), a blunting in APO-induced PRL suppression ($p < 0.02$), and a blunting in APO-induced GH stimulation ($p < 0.04$). OPC 4392, a DA autoreceptor agonist, induced a decrease in baseline PRL ($p < 0.02$), and a decrease in APO-induced PRL suppression ($p < 0.05$), without modifying GH levels. 52028 RP, a peripheral benzodiazepine receptor antagonist, did not significantly modify PRL or GH secretion. These results suggest that neuroendocrine responses differentiate atypical from typical antipsychotic agents.

NR479 Wednesday May 15, 12 noon-2:00 p.m.

Adrenocorticotropic and Ovine Corticotropin Releasing Hormone Effects on Dopamine Activity in Man

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Summary:

Interactions between the hypothalamic-pituitary-adrenal (HPA) axis and dopamine systems have important implications for psychiatry, but questions remain concerning their sites and mechanisms. We have hypothesized that the development of delusions in depressed patients is due to cortisol induced increases in mesocorticolimbic dopamine (DA) activity. This hypothesis was based on a number of observations: delusionally depressed patients demonstrated marked elevated cortisol levels; the administration of dexamethasone to healthy controls increases plasma free DA and homovanillic acid (HVA); and the administration of glucocorticoids (GC) increases central DA activity in the rat. Recently, one group has reported that the use of a GC synthesis blocker increased plasma HVA in healthy controls, suggesting ACTH, and not cortisol, controls DA synthesis or activity. This paper elucidates the effects on dopamine by stimulating different levels of the HPA axis. Seven healthy volunteers without personal or family psychiatric history were studied. On Day 1, 0.25 mg. synthetic Adrenocorticotropic hormone (ACTH) was administered at 0835, and plasma DA, cortisol, HVA and ACTH were measured at 30 minute intervals until 1200. On Day 2 or later, 1 mcg./kg of ovine Corticotropin Releasing Hormone (oCRH) was administered at 1900, and plasma cortisol, ACTH and HVA were measured at 15-30 minute intervals until 2300. The results will help determine the relative effects of ACTH and oCRH on DA in man.

NR480 Wednesday May 15, 12 noon-2:00 p.m.

Fetal Alcohol Exposure, Schizophrenia and Pervasive Developmental Disorders

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Summary:

A growing body of evidence suggests that subtle fetal insults may increase risk for schizophrenia and related disorders. In a group of 17 psychiatrically hospitalized prepubertal children whose mothers had alcohol abuse/dependence by FH-RDC, nine had fetal alcohol exposure and eight did not. Four of nine with FAE and none without had a pervasive developmental (N = 3) or schizophrenic (N = 1) disorder. A fifth FAE child had psychosis by projective testing but not clinical diagnosis. None of the PDD/schizophrenic children had a family history of schizophrenia spectrum disorders. EEGs were ordered on clinical grounds in 7/9 FAE and 2/8 non-FAE children ($chisq = 4.23$, $df = 1$, $p = .04$) and showed both paroxysms (N = 2) and excess slow waves (N = 5). FAE has previously been shown to be associated with cognitive difficulties and behavior disorders. Rigorous studies in larger samples from psychiatric and other populations will identify more clearly the potential contribution of FAE as an etiologic factor in psychotic and pervasive developmental disorders.

NR481 Wednesday May 15, 12 noon-2:00 p.m.

Controlled Study of Intravenous Amobarbital in Relieving Catatonic Mutism

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Summary:

Although intravenous amobarbital is believed to relieve catatonic symptoms, no rigorous studies exist. Previous reports either were not blinded and randomly assigned[1] or did not examine the proper population.[2] This is the first rigorously controlled study of amobarbital in catatonia.

Method: Twenty patients with acute catatonic mutism were randomly assigned in a balanced design to receive either intravenous saline or 5 percent amobarbital solution at one cc/minute for ten minutes. Drug identity was blinded for the patient, and for the physicians administering the drug, performing the interview, and rating outcome. The interview was structured, and standardized criteria designated patients as either responders or nonresponders. Interviews were videotaped to test reliability by additional blind raters.

Results: Six of ten patients' mutism was relieved by amobarbital, and none of ten patients' mutism was relieved by saline ($p = 0.005$ Fisher's exact). Of the ten nonresponders to saline, four responded when blindly crossed to amobarbital. Inter-rater reliability of 11 videotaped interviews demonstrated 100 percent concordance.

Discussion: Intravenous amobarbital is superior to placebo in relieving catatonic mutism, yet all patients do not respond. Responsivity is not related to age, sex, or dose.

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Imaging of Extrastriatal Dopamine Receptors in Man

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21st Avenue S. & Garland Ave., Nashville, TN 37232; William O. Whetsell, M.D., Mohammad S. Ansari, M.S., John R. Votaw, Ph.D., Tomas dePaulis, Ph.D., Robert Bell, M.D., Dennis Schmidt, Ph.D., N. Scott Mason, Ph.D., Ronald G. Manning, Ph.D., Michael H. Ebert, M.D.

Summary:

It has been proposed that the mesolimbic and mesocortical dopaminergic systems may mediate the antipsychotic effects of neuroleptics. We have previously reported that epidepride is an extremely potent (K_D = 24 pM) and selective ligand for the D2 receptor. A high resolution SPECT study in man using this ligand and a three-headed camera has revealed not only a very high striatal:cerebellar uptake ratio (<200:1 at 18 h after injection), but also uptake in the hypothalamus, thalamus, medial temporal lobes, and temporal cortex. While extrastriatal D2 receptors have been reported in the hypothalamus and temporal lobes in human postmortem studies, dopamine D2 receptors in the thalamus have not been previously reported. Fresh autopsy specimens were obtained from two subjects without evidence of significant brain disease. In vitro binding studies reveal the presence of dopamine D2 receptors in several brain regions (Bmax in pmol/g brain tissue) as follows: putamen (17.4), caudate (16.2), globus pallidus (3.65), hypothalamus (1.8) ventral nucleus of thalamus (0.88) anterior nucleus of thalamus (0.77), dorsomedial nucleus of thalamus (0.70), pulvinar (0.55), uncal cortex (0.41). Competitive binding studies to ventral thalamic, uncal cortical and hypothalamic homogenates using D1, D2, adrenergic, GABAergic cholinergic, serotonergic, and opiate ligands failed to show significant inhibition of binding for any but dopamine D2 ligands; this demonstrates that the uptake seen in these regions represents binding to a D2 site. This study identifies a previously unreported site of dopamine D2 receptors in man, the thalamus, and demonstrates the feasibility of using emission tomography for the study of extrastriatal D2 receptors in man.

NR483 Wednesday May 15, 12 noon-2:00 p.m.

MRI Volume in Late-Life Onset Schizophrenia

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Summary:

Late life onset schizophrenia (LOS) bears phenomenologic similarities to early-life onset cases. We hypothesized that MRI and neuropathologic changes reported in early onset schizophrenia would be observed in LOS.

Volumes of medial and lateral temporal lobe structures and control regions were assessed using magnetic resonance imaging (MRI) in 11 patients with LOS (onset >age 55 years), 18 normal elderly controls, and 12 patients with moderate cognitive impairment due to Alzheimer's disease (AD), matched on age and sex.

Both patient groups had significantly smaller volumes of medial temporal regions (hippocampus, amygdala, entorhinal cortex). LOS had significantly smaller superior temporal gyri (STG) than both normal controls *and* AD patients. Most of these significant volume changes were not accounted for by overall brain shrinkage.

We have previously demonstrated STG volume to be reduced in more typical cases of early life onset schizophrenia. This preliminary report suggests that similar morphologic changes occur in LOS, but not AD.

NR484 Wednesday May 15, 12 noon-2:00 p.m.

Computer Automated Magnetic Resonance Brain Volume Measures in Schizophrenics

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Summary:

Using automated image processing techniques, we performed volumetric measurements of MR whole brain and CSF spaces in a sample of 15 male, right-handed, chronic medicated schizophrenics (SZs; *DSM-III-R* diagnosed) and 15 normal controls (NCLs) matched for age (mean = 38 years), sex, handedness, social class of origin, and verbal I.Q. MR data from entire brain were acquired axially using conventional spin echo sequences (TR = 3000, TE = 30/80, matrix = 256X192/0.5NEX, FOV = 24cm, slice thickness = 3mm, #slices = 108) on a Signa GE 1.5T MR Scanner. New image processing techniques allowed intracranial cavity (ICC) identification; ICC segmentation into CSF and tissue classes; calculation of absolute/relative volumes for ICC components; and 3D reconstructions. Results showed significant differences between NCLs and SZs on left lateral ventricle where SZs showed greater variance ($F_{max/min} = 14.18$, df = 1,28, $p < 0.001$). Correlational data for relative volumes showed that total SANS score was negatively correlated with grey matter (n = 9, rho = -.79, $p < 0.011$) and positively correlated with white matter (n = 9, rho = .711, $p < 0.032$); Thought Disorder Index scores were also correlated negatively with grey matter (n = 13, rho = -.709, $p < 0.007$) and positively with white matter (rho = .671, $p < 0.012$). In contrast, P300 amplitude for the T4 electrode site was correlated positively with grey matter (n = 15, rho = .570, $p < 0.025$) and negatively with white matter (rho = -.518, $p < 0.048$). These initial findings are undergoing additional analyses, including examination of smaller anatomical regions such as temporal horn and hippocampus.

NR485 Wednesday May 15, 12 noon-2:00 p.m.

Fractal Dimension of Schizophrenic Brains

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Summary:

Qualitative studies of gross anatomical features of the brains of schizophrenic patients suggest that the illness may be associated with sulcal-gyral abnormalities. Although this hypothesis is straightforward, previous studies have been handicapped by limited means for quantitative analysis of these findings as well as lack of attention to control groups.

The mathematical study of statistically self-similar objects (fractals) suggests that the brain's fractal dimension, a quantity which is related to the complexity of the brain's convolutions, might be altered in schizophrenic patients.

Fourteen pairs of schizophrenic and control subjects were matched pairwise on age, gender, race, parental SES, and years of education. MRIs of subjects were obtained, and brain surface contours in 3 mm coronal sections at the level of the mammillary bodies were traced using a computerized image processing system.

There was no significant difference in brain area at the chosen location between normals and schizophrenics (t = 2.0, df = 13, p = N.S.). However, estimates of the fractal dimension of the brain were significantly different (t = 2.92, df = 13, p .02). Work in progress is investigating the specificity of this finding relative to other diseases such as affective disorder.

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Basal Ganglia MRI Volumes in Schizophrenia

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Summary:

Previous neuropathological investigations of basal ganglia in schizophrenia have failed to demonstrate consistent differences from normal controls. However, there is evidence to associate basal ganglia dysfunction with several clinical features of schizophrenia, particularly negative symptoms. Recent PET studies in schizophrenia report basal ganglia changes; one report specifically implicates the left globus pallidus.

This MRI investigation addressed methodological issues in assessing volumes of caudate, putamen, and globus pallidus, using standardized atlases for region finding, and a realistic anatomic phantom for validation. Subjects were 15 schizophrenics and 15 screened normal controls, blindly rated. After individual matching on age, sex, race, years of education, and parental SES, there was a significant inverse correlation ($r = -0.69$) between negative schizophrenic symptoms and total basal ganglia volume. More specifically, a strong negative correlation ($r = -0.74$, $p < 0.001$) between left globus pallidus volume and ratings of affective flattening on the Scale for the Assessment of Negative Symptoms is reported, which remained significant after Bonferroni correction.

NR487 Wednesday May 15, 12 noon-2:00 p.m.

Brain Iron and Oxidative Stress Increase Extrapyramidal System Risk

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Summary:

This paper will present MRI data that is consistent with a *hypothetical* model of the pathogenesis of tardive dyskinesia (TD). The model focuses on a neurotoxic process involving brain iron interacting with products of oxidative metabolism and lipid membranes and leading to hydroxyl radical production and lipid peroxidation as common CNS damaging mechanisms. The model asserts that this destructive iron-dependant process occurs primarily in the extrapyramidal system, causes cell dysfunction and death, and manifests itself as choreoathetoid movements. Bartzokis et al (1990) used MRI to investigate whether increased iron levels (as reflected in shortened T2 relaxation time) is involved in the pathophysiology of TD and observed that patients with TD had significantly shortened caudate T2. Based on this pilot study and the above model, caudate T_2 values (average of left and right) were evaluated in a sample of 40 *DSM-III* male schizophrenic patients. Preliminary analysis reveals that consistent with the a priori hypothesis, T_2 values were highest in the non-TD group ($N = 20$, mean = 67.5, SD = 4.6) intermediate in the probable TD group ($N = 8$, mean = 64.2, SD = 2.7), and lowest in the subjects with persistent TD ($N = 12$, mean = 63.5, SD = 3.5), and the planned linear contrast was highly significant ($F = 7.98$, $df = 1$, one-tailed $p = .004$). After adjustment for the effects of age, the linear contrast across the three groups remained significant (contrast $F = 4.30$, $df = 1,36$, one-tailed $p = .022$) as did the pairwise t-test between the non-TD and persistent TD groups (one-tailed $p = .022$, Bonferroni-adjusted $p = .066$)

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Support Program Influence on Daily Activity Pattern

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Summary:

A first group of 47 chronic patients living in a small city of Northwest Quebec harboring a comprehensive support program was matched to a similar group living in a nearby city lacking such a program. The Activity Pattern Inventory was used, four times within a year frame. This questionnaire collects 125 items on ten daily activity categories.

Groups were matched for sex distribution, marital status, financial level, and residential settings. Though the first group has a lower GAS level of functioning (54.1 percent) with almost twice hospitalizations (mean # of 8.5). Most of the patients from both cities have a *DSM-III-R* diagnosis of schizophrenia (79.3 percent of total sample) and a median dose of 250 mg/24hrs of CPZ equivalent antipsychotic medication.

Significantly the first group is performing more activities related to rehabilitation but less self-care tasks. Vocational or educational activities take only 5 percent of their time and during 50 percent of the daytime they rest. Nevertheless they are satisfied with their life in general.

From these results we can suggest that to evaluate the benefits of a support program one has to consider both variations of activity patterns and subjective perceptions of the clients.

NR489 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Impaired Perception of Emotion in Neuropsychiatry

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Summary:

Impaired perception of facially expressed emotion has been associated with focal lesions in nondominant parietal cortex. We studied 20 consecutive admissions to a specialized neuropsychiatric facility using the standardized battery of Ekman Slides for recognition of facial emotions to classify subjects as impaired (<80% correct responses, $n = 11$) or unimpaired (<80% correct responses, $n = 9$). Patients were 11 males and nine females, aged 17-71 (mean +/- s.d. = 39 +/-13 years), including five left-handed subjects (three male/two female), with subacute or chronic psychiatric syndromes following vascular, traumatic or postsurgical brain injuries, who met DSM-III-R criteria for Organic Mood Disorder ($n = 11$) or Organic Personality Disorder ($n = 9$). All had brain imaging by SPECT *and* MRI or CT and results evaluated by radiologists unaware of Ekman performance.

Groups of subjects with impaired vs. unimpaired Ekman performance did not differ by frequency of abnormalities localized to either parietal cortex, nor by psychiatric diagnosis. Of patients with lateralized lesions, eight of nine with left-hemisphere involvement had impaired Ekman performance vs. one of four with right-hemisphere involvement ($p < .02$). Impaired Ekman performance was significantly more frequent ($p < .01$) in males (10 of 11 males: seven of eight right-handed, three of three left-handed) vs. females (one of nine females; one of seven right-handed, none of two left-handed). Additional findings will be discussed and indicate impaired perception of facially expressed emotions can occur following brain injury regardless of location of lesion, and is neither sensitive nor specific to parietal lobe damage.

NR490 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Risk Factors for Delirium in Psychiatric Inpatients

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Summary:

Delirium is a significant problem in medically ill patients, but little is known about it in hospitalized psychiatric patients. Identified risk factors include aging, malnutrition, polypharmacy, anticholinergic medication, fatigue, psychological stress and CNS pathology,

most of which are seen in psychiatric patients on admission. To examine the incidence and etiology of delirium in hospitalized psychiatric patients, a retrospective chart review was conducted of 268 consecutive admissions to the psychiatric service of a general care hospital. Patients with delirium on, or within 48 hours of, admission and those admitted for substance abuse were excluded. Age, sex, diagnosis, length of stay and all medications were recorded for each patient. The total incidence of delirium was 14.6%. Patients with bipolar disorder represented 14.6% of all patients but 34.4% of all patients with delirium. By contrast, schizophrenia accounted for 38.6% of all patients and 37.9% of cases with delirium. The odds ratio for bipolar disorder compared with schizophrenia was 9.31 (8.27, 10.35). Analysis of all variables by backward and stepwise logistic regression showed a diagnosis of bipolar disorder to be most significantly related to development of delirium ($p < .0001$); age and peak dose of antiparkinsonian agents were also significantly related ($p < .05$). Lithium was reanalyzed and found not to be independently associated with the development of delirium. In summary, psychiatric patients have been found to be as much at risk for delirium as are medically ill patients, with bipolar patients being at highest risk.

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Distinguishing the Organic Psychoses

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Summary:

A research task force of the NIMH found that of all psychiatric illnesses, organic psychosis has been the most severely neglected by researchers. To address this problem, the subsequently issued DSM-III and DSM-III-R included the new diagnostic categories of organic delusional syndrome (ODS) and organic hallucinosis (OH). No published date currently exist that compare the clinical features of theses syndromes. Spitzer, et al. have recently proposed major changes in the diagnostic system for organic psychoses. Evaluation of these proposals will be difficult until the distinctions between these syndromes are better characterized.

A total of 39 cases of ODS and 11 cases of OH presented at our institution out of 14,889 patients evaluated between 1/1/83 and 12/31/87. ODS patients were significantly older that OH patients ($X = 61.8$ yrs. vs. $X = 43.2$ yrs.). ODS patients demonstrated significantly more suspiciousness, acquired intellectual impairment, and lack of insight on the Initial Evaluation Form (1981), while OH patients had more visual hallucinations, dissociative symptoms, depersonalization, and "other visual hallucinations." The most common symptoms were noted for both these syndromes and compared with those from a group of schizophrenics. The most common treatments, the level of functioning, and the most common medical diagnoses of these two patient groups were also noted.

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The Effects of Nicotinic Blockade on Cognition

Paul A. Newhouse, M.D., Psychiatry, Univ of Vermont, 1 South Prospect Street, Burlington, VT 05401; Kathryn Pedersen, M.S., Robert Lenox, M.D.

Summary:

The finding that central nicotinic cholinergic receptors decline substantially in Alzheimer's disease (DAT) and Parkinson's disease (PD) compared with age-matched normals strongly suggests that the central nicotinic cholinergic system may be important in the generation of the cognitive symptoms of DAT and PD. As part of an investigation of the role of this system in cognitive functioning, we produced a temporary blockade of central nicotinic receptors with the drug mecamylamine, a centrally and peripherally active ganglionic blocking agent that produces an antagonism of function at C6 (ganglionic) type nicotinic receptors. Subjects were administered a single dose of 5, 10, and 20 mg of mecamylamine and placebo in a double-blind fashion on different days. Vital signs were monitored at regular intervals, and subjects completed a computer battery of cognitive tests including tests of reaction time, spatial rotation, sustained attention, repeated acquisition of behavioral chains, recognition memory, and the Buschke selective reminding task. Behavioral effects were assessed by having subjects complete the POMS, visual analog scales, and physical symptoms scale, as well as having the observer complete the BPRS and visual analog ratings. Twelve young normal volunteers (mean age 24, range 18-36) and seven elderly volunteers (mean 62, range 55-70) have completed the study to date. Preliminary results from the young normals show a significant ($p < .05$) effect on response bias in the recognition memory task. Analysis of the selected reminding task showed little effect of drug. Behavioral effects were modest. Effects in older subjects to date appear enhanced, with greater effects on vital signs, memory, and psychomotor speed. Further results will be presented. These findings have implications for the source of some cognitive deficits in DAT and PD and for the role of central nicotinic systems in age-related changes in human cognition. (Supported by NIMH grant R29-46625 to P.N.)

NR493 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Memory and Serotonergic/Cholinergic Interactions

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Summary:

Profound impairments of forebrain cholinergic and serotonergic systems are among the characteristic deficits of Alzheimer's disease (AD). The present studies aimed to determine the degree to which the serotonergic deficits contribute to the cognitive impairments and how forebrain serotonergic deficits may interact with forebrain cholinergic lesions. In several different experiments, serotonergic deficits were induced in rats ($Ns = 8$-9) by the systemic administration of 2.5mg/kg/PCA. Rats were then tested for the acquisition and retention of passive avoidance and a water maze task. Administration of PCA led to profound cortical 5-HT depletion (52%, $P < 0.001$) and significant deficits on the performance of both cognitive tasks ($ps < 0.01$). When PCA treatments were combined with NMDA-induced lesions of basal forebrain (nbM), PCA administration blocked the passive avoidance memory enhancing effects of physostigmine (0.06mg/kg) and exaggerated the cortical cholinergic marker deficits induced by nbM lesions ($ps < 0.05$). Subsequent studies with combined PCA treatment and 5-7-DHT lesions of the nbM demonstrated that the memory impairing effects of PCA were a result of the actions of PCA at extra-cortical sites. These studies suggest that the serotonergic disturbances seen in AD may contribute to the cognitive deficits and possibly attenuate responsivity to cholinomimetic therapy.

NR494 Wednesday May 15, 3:00 p.m.-5:00 p.m.

MRI High Intensity Signals in Alzheimer's Disease

Anand Kumar, M.D., Ger. Psychiatry, Univ of Pennsylvania, Ralston-Penn Ctr 3615 Chestnut St., Philadelphia, PA 19104; David Yousem, M.D., Elaine Souder, Ph.D., David Miller, M.D., Gary Gottlieb, M.D., Abass Alavi, M.D.

Summary:

The purpose of this study was to clarify the relationship between dementia of the Alzheimer type (DAT) and periventricular (PVWH),

deep white matter (DWH) and subcortical high-intensity signals (SCH) on magnetic resonance imaging (MRI). We studied 16 subjects with DAT (9F, 7M) mean age ± SD = 67 ± 7.6 and 23 healthy age-matched controls (12F, 11M), mean age ± SD = 68 ± 7.8. DAT subjects met NINCDS-ADRDA criteria for probable DAT, had a mean MMSE score of 24 ± 3 and were free of significant medical illness such as hypertension. DAT subjects and controls were scanned on a 1.5 Tesla signa GE scanner with head coil (TR = 3000, TE = 30 and 80 msec), and 5 mm thick contiguous slices were obtained. Transaxial T2 weighted and proton density images were examined by a neuroradiologist blind to the clinical diagnosis. PVWH, DWH, and SCH were rated on a 0-3 severity scale (Fazekas et al, AJNR 1987; Coffey et al, AJP 1990). There were no statistically significant differences in the prevalence of PVWH, DWH or SCH between the DAT and control groups (Robust rank order test). These data demonstrate that in the absence of vascular risk factors, DAT is not associated with an increased prevalence of high-intensity signals on MRI.

NR495 Wednesday May 15, 3:00 p.m.-5:00 p.m.

The Relationship of Apathy and Depression

Robert S. Marin, M.D., Psychiatry, Univ of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213; Ruth C. Biedrzycki, M.E.D., I. Firinciogullar, M.S.

Summary:

The objectives of this presentation are to describe the development and validation of the Apathy Evaluation Scale (AES), discuss the discrimination of apathy from depression and indicate the relationship between apathy, depression and related neuropsychiatric concepts including psychomotor retardation, bradyphrenia, psychic akinesia, emotional blunting, flat affect, and aprosodia. Clinician, informant, and self-rated versions of the AES were evaluated in 123 subjects with major depression, probable Alzheimer's disease (AD), hemispheric stroke (HS), and normal aging. Multiple forms of reliability (internal consistency, inter-rater, test-retest) were evaluated. Following the criteria of the multitrait multimethod matrix procedure, convergent and discriminant validity of the AES were evaluated vis à vis the Hamilton and Zung depression rating scales. Regarding predictive validity, measures of apathy, but not depression, predicted freely initiated behavior, as measured by subjects' play at video games and their use of novelty toys and games in a waiting room. Correlational analyses indicate that the overlap between AES and depression measures in AD and HS is due to a subset of items (psychomotor retardation, agitation, and loss of insight) that appear to have diagnosis-specific relationship to AES scores. On the other hand, discriminant function analyses using items from the Hamilton rating scale, clearly indicate the discriminability of a syndrome of apathy and a syndrome of depression.

NR496 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Diagnostic Markers in Alzheimer's Disease

Larry D. Altstiel, M.D., Psychiatry, Mount Sinai Hospital, One Gustave Levy Place, New York, NY 10029; Brian A. Lawlor, M.D.

Summary:

A variety of recent studies indicate that alterations in both immune and inflammatory responses may be involved in the pathogenesis of Alzheimer's disease (AD). We have tested a series of patients with AD, patients without dementia having a variety of neurologic and psychiatric disorders, and first-degree relatives of AD patients for antibodies against neuronal cell antigens, glial cell antigens, and levels of the acute phase reactants a_1-antichymotrypsin and C-reactive protein (CRP). Our preliminary results with 107 age-matched patients indicate that patients with AD have elevated titers of both anitneuronal and antiglial antibodies when compared with non-affected (NA) patients (Mean titer(AD)–16.44, mean titer(NA) –5.1; $p < 0.022$ for antineuronal antibodies. Mean titer (AD)–23.8, mean titer (NA)–16.06 $p < 0.0004$ for antiglial antibodies). In addition our results show that levels of a_1-antichymotrypsin and CRP are elevated in AD patients when compared with non-affected patients (Mean (AD)-95.3 mg/dL, mean (NA)-16.4 mg/dL; $p < 0.00012$ for a_1-antichymotrypsin. Mean (AD)–458.3 ug/dL, mean (NA)-63.4; $p < 0.0007$ for CRP). Approximately 50% of non-affected first-degree relatives also have elevated levels of both a_1-antichymotrypsin and CRP. There is approximately 80% concordance between elevated levels of acute phase reactants and clinical diagnosis of AD.

NR497 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Optic Nerve in Alzheimer's Disease Patients

Michael Davidson, M.D., Psychiatry, Bronx Va Hospital, 130 W. Kingsbridge Road, Bronx, NY 10468; Jacqueline Lustgarten, M.D., Pamela Rizzuto, M.A., Robert Massini, M.S., James Schmeidler, Ph.D., Brian A. Lawlor, M.D.

Summary:

Postmortem investigations of brain specimens from AD patients have revealed axonal degeneration of the optic nerve and of cell bodies in the ganglion cell layer of the retina, suggesting that the neuronal degeneration of AD may extend to the optic nerve. Although visual impairment is not a consistent finding in AD, degeneration of the optic nerve may be present in the absence of visual impairment. This study examined the optic nerve in 19 NINCDS probable AD patients and 20 age-matched normal controls utilizing the Humphrey Retinal Analyzer, which is a device that takes stereoscopic pictures of the optic nerve head. Computerized reconstructed images were assessed blindly and assigned a diagnosis of AD or normal control. Thirty of 39 cases were classified correctly with two false positives and seven false negatives (Chi-square analysis $x^2 = 11.97$, $df = 1$, $p < .001$). The implications of these results will be discussed.

NR498 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Correlation Between CBF and Cognitive Tests

Philippe H. Robert, M.D., Pavillon J., Hospital Pasteur, 30 AV Voie Romaine, Nice 06002, France; Octave Migneco, M.D., Valerie Aubin, M.D, J. Darcourt, M.D., O. Ricq, M.D., G. Darcourt, M.D.

Summary:

Fourteen Alzheimer's disease patients (AD) satisfying DSM-III-R criteria for primary degenerative dementia (mean age 75 years, mean MMSE:11,6) and eight controls (mean age 80 years, mean MMSE:27,7) were studied using Tc^{99m}HMPAO. All subjects were right handed. The following psychological tests were performed: Mini Mental State Examination (MMSE), Hierarchic Dementia Scale (HDS). This scale was built with 20 subtests that covered the entire range of cognitive functions. Each subtest was hierarchically organized so that success in an item implied success in inferior items. HMPAO was injected in an I.V. line previously placed. After reconstitution, the slices are analyzed, using a computed approach. Five symmetrical regions of interest (ROI) were delineated by the computer using reference of a brain atlas automatically adapted for each subject. The saggital cuts are computed and added together for each hemisphere. This leads to two lateral views of the cortical uptake on which the five ROIs are positioned (F frontal, P parietal, T temporal, TPO temporo-parieto-occipital, O occipital). For each ROI, a cortex/cerebellum ratio was calculated. Results revealed:1) The AD group had significantly lower activity bilaterally in T and TPO than controls group (t-test); 2) For whole population (AD + controls) correlations between - right TPO and : MMSE,

subtests 1 (concentration), 7 (remind test), 9 (visual exploration), 11 (denomination), 12 (gnosia), 15 (constructional praxis), 16 (figures), 17 (ideo-motor praxis), 18 (ideo-praxis). - right T and MMSE, subtests 1, 9, 11, 15, 17.- left TPO and : MMSE, subtests 1, 7, 11, 12, 15, 17.

NR499 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Mini Mental State Examination: A Discrimination of Alzheimer's Disease?

Jane C. Wells, M.D., Mental Hygiene, Johns Hopkins University, 624 N. Broadway, Baltimore, MD 21205; Penelope M. Keyl, Ph.D., Gary A. Chase, Ph.D., Ahmed Aboraya, M.D., Marshal F. Folstein, M.D., James C. Anthony, Ph.D.

Summary:

Linear discriminant analysis was used to construct a series of discriminant functions including subsets of demographic variables and the Mini Mental State Examination item responses for a case series and a population sample. The two samples consisted of: 1) 181 patients meeting National Institute of Neurological and Communicative Disorders and Stroke — Alzheimer's Disease and Related Disorders Association criteria for probable Alzheimer's disease (AD), and 55 volunteer controls, and 2) 22 elderly subjects with dementia and 82 normal community controls who were identified in the National Institute of Mental Health Epidemiologic Catchment Area study in Baltimore using the Diagnostic Interview Schedule. Accuracy of the classification of cases and controls was assessed in terms of sensitivity, specificity, positive predictive value and negative predictive value. A nine-item discriminant function, which included the variables for time orientation, recall, calculation, copying a figure, age writing, 3-step command, naming, and race, distinguished demented subjects from community controls with 90.9% sensitivity and 87.8% specificity. This discriminate function has been cross-validated as a potent screening instrument for Alzheimer's Disease in a community based sample. The same discriminant function classified AD patients and controls with 95.5% sensitivity and 98.2% specificity.

NR500 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Variable HLA Association in Alzheimer's Disease

Gary W. Small, M.D., Psychiatry, UCLA/NPI, 760 Westwood Plaza, Los Angeles, CA 90024; Steven S. Matsuyama, Ph.D., Albert Heyman, M.D., Emily G. Reisner, Ph.D., Edward B. Renvoize, M.D., Raimo Sulkava, M.D.

Summary:

In a previous study, Small and Matsuyama (1986) reported the presence of the HLA antigen A2 in all 10 men with clinically diagnosed early-onset ($\leq$ 60 years) Alzheimer's disease (AD), a significantly ($p < .001$) higher frequency than that found in other patient groups (late-onset men and early- and late-onset women; 40% to 44%) or in age-matched cognitively intact controls (30% for men; 53% for women). Because of small samples sizes, we attempted to replicate the association by reanalyzing prior HLA/AD findings from other laboratories, according to age at dementia onset and sex. All patients had a clinical diagnosis of AD, and HLA typing techniques were standardized.

Data on 165 patients from three geographic regions (North Carolina, Great Britain, and Finland) indicated an HLA-A2 frequency of 41% in early-onset men, not significantly different from other patient groups and controls. Although this study failed to replicate the association, Payami et al (1990) found A2 to be present in all eight men with early-onset dementia, which was significantly higher than the expected 49% (relative risk = 17.4, $p < .01$), and A2 appeared to be primarily associated with sporadic, rather than familial, AD. Thus, two laboratories from the west coast of North America (Oregon, California) have confirmed the finding. These results indicate a variable association with some other contributing factor, such as geographic region or disease familiality.

NR501 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Course of Major Depression in the Elderly

Gregory A. Hinrichsen, Ph.D., Psychiatry, Hillside Hospital, P.O. Box 38, Glen Oaks, NY 11004

Summary:

Outcome data and clinical impression suggest that depression in the elderly has a bleaker prognosis than in younger individuals. However, direct comparison of rates of recovery from major depression between old and young are lacking, and cross-study comparisons are complicated by inconsistent methodologies. This study employed identical diagnostic (SADS/RDC) and follow-up (the Longitudinal Interval Follow-up Evaluation) methods in an older depressed population as was utilized in the NIMH Collaborative Study of Depression in younger adults. A total of 127 elderly psychiatric inpatients meeting RDC criteria for major depression and clinical/demographic/family predictors of one year course were evaluated. We found that 72% of elderly major depressives remitted from index episode of depression. This rate parallels NIMH Collaborative Study findings for younger depressives (Keller & Shapiro, 1981). In contrast, 18% of remitted geriatric depressives relapsed during the follow-up period, as compared with 36% of younger Collaborative Study participants. No demographic or clinical variables related to older patients' one-year course. However, symptoms of depression in the patient's primary family caregiver at patient admission predicted course of depression. Taken together, these data suggest that: 1) remission rates of acute major depression are similar between younger and older age groups, 2) relapse rates in elderly depressives are less than in younger counterparts, 3) importance of family intervention at admission of geriatric depression may be underrecognized.

NR502 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Psychogeriatric Delirium

Raymond J. Ancill, M.B., Riverview Hospital, 500 Lougheed Highway, Port Coquitlam BC, Canada V3C 4J2; Leslie J. Sheldon, M.B., Nelson Collins, M.D., William Carlyle, M.D., Nagi Youssef, M.D.

Summary:

Delirium is common in the elderly (Lipowski Z., 1989). Sepsis and congestive heart failure are the most frequent causes on admission to general medicine wards (Rockwood K., 1989). This is a retrospective review of 100 consecutive admissions during 1989 to a psychogeriatric service. After a comprehensive, standardized two-week assessment, 23 patients were diagnosed as delirious on admission by DSM-III-R criteria. The mean age of all patients was 76.9 years. Fifty-five were female and 45 male. Of the delirious patients, 14 were female (60.9%) and nine male (39.1%). Twenty-two received concurrent Axis I and Axis III diagnoses. The causes were medication related in 15 (65.2%), medical illness related in four (17.4%), mixed in three (13.1%), and unknown in one (4.3%). After intervention all cases of delirium resolved. Of the 23 cases of delirium, 18 were discharged (78.3%), two died (8.7%), and three remain admitted (13.0%). Of 77 nondelirious patients, 56 were discharged (72.7%), 10 died (13.0%) and 11 remain admitted (14.3%). These differences are not statistically significant. These data demonstrate that delirium in this population is unique in terms of its drug-related etiology and better outcome.

NR503 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Physical Restraints in Dementia With Agitation

Elisse Kramer, Ph.D., Psychiatry, Hillside Hospital, P.O. Box 38, Glen Oaks, NY 11004; Blaine S. Greenwald, M.D., Susan Abraham, M.D., Jacob Reingold, M.S., Helene Grossman, M.S.

Summary:

Although frequently employed, physical restraints are controversial devices in nursing homes, since an increasing data base suggests that adverse consequences may outweigh potential benefits. A key question is whether or not physical restraint use is associated with specific clinical/diagnostic features. If so, these patients could be targeted for alternative lower-morbidity management approaches. A total of 96 residents of two dementia units were screened by treatment staff for presence of agitation; 42% ($n = 40$) were identified as agitated. All patients met DSM-III-R criteria for "dementia." Agitated patients were comprehensively evaluated in terms of behaviors, falls, and physical illness by medical/nursing staff employing standardized rating instruments. Independently, underlying dementia diagnosis was established by a research geropsychologist. Patients were then classified according to use ($n = 25$) or non-use ($n = 15$) of physical restraints and compared. Restrained patients were distinguished by greater medical illness ratings ($p = .01$), cardiovascular illness ($p < .01$), frequency and severity of falling ($p < .05$), and Hachinski Ischemic index ($p < .01$). All of agitated, multi-infarct dementia (MID) patients were restrained, as compared with 60% of Alzheimer patients ($p < .01$). Data suggest that the confluence of agitation and physical (especially cardio- and cerebrovascular) illness relate to physical restraint use. MID patients with agitation appear to be particularly at risk.

NR504 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Increased Synthesis and Accumulation of Heat Shock 70 Proteins in Alzheimer's Disease Brain

William Wallace, Ph.D., Psychiatry, Mount Sinai Hospital, One Gustave Levy Place, New York, NY 10029; Nancy Perez, B.A., Carol Merril, M.D., J. Sugar, B.S., L. Bierer, M.D., V. Haroutunian, Ph.D.

Summary:

We have examined postmortem tissues from Alzheimer's disease (AD) for alterations of gene expression. Cortical tissues were found to contain significantly elevated levels of two heat shock proteins of 72 and 73 kD (hsp 72/73) ($128 + 56$ vs $259 + 142$ units, $n = 8$ for each group; $p < 0.05$). This elevation was associated specifically with the disease pathology in that AD cerebella (which do not exhibit the neuropathology of AD) do not show increased levels of these proteins ($275 + 66$ vs $302 + 48$, $n = 4$ for each group). In addition, there was no correlation of hsp 72/73 levels with any perimortem characteristic of the cases, including immediate cause of death. The increase of mature hsp 72/73 was reflected in an increase in the synthesis of the proteins as determined by immunoprecipitation of translation products from control and AD polysomes. Consistent with their proposed role in cotranslational processing of nascent proteins, many other newly synthesized proteins were found to coprecipitate with the hsp 72/73 antibodies, which indicates that hsp 72/73 remains permanently associated with these nascent proteins. This permanent association most likely accounts for the earlier observation of hsp 72/73 in senile plaques and neurofibrillary tangles and suggests a role in their formation. These results indicate that the AD brain exhibits a well-characterized cellular and molecular response to stress. This stress response may interact with the initial pathological events to cause the neuropathology of AD.

NR505 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Dyskinesia and Neuroleptic Use in Elderly Inpatients

Robert A. Sweet, M.D., Univ of Pitts. Psychiatry, Geriatric Health Service, 3811 O'Hara Street, Pittsburgh, PA 15213; Benoit H. Mulsant, M.D., Aicha H. Rifai, M.D., George S. Zubenko, M.D.

Summary:

Previous studies have identified an increase in prevalence of tardive dyskinesia and spontaneous orofacial dyskinesia with age. We studied a series of 50 psychiatric patients, over the age of 60, admitted consecutively to an acute psychiatric inpatient unit. Patients were examined and rated by one author (RS) according to the Abnormal Involuntary Movement Scale (AIMS). Thirty-three patients (73%) had a history of neuroleptic use. Mean AIMS severity scores for this group were significantly higher than for those patients without neuroleptic exposure ($t = -1.79$, $df = 38$, $p = 0.04$, 1-tailed). Seven patients (16%) met severity criteria for possible tardive dyskinesia, as described by Schooler & Kane (1982). All seven patients with tardive dyskinesia had a history of neuroleptic exposure, as compared with 38 (79%) of the nonaffected individuals. This trend approached significance ($p = 0.09$, Fisher's exact test, 1-tailed). No case of spontaneous orofacial dyskinesia was identified. These findings differ from the current literature, which reports higher prevalences of both tardive dyskinesia (42%-56%) and spontaneous orofacial dyskinesia (8%-16%) in the elderly. This may reflect differences in the severity criteria for diagnosis of dyskinesia, or the inclusion of chronically hospitalized and nursing home populations in previous studies. Finally, our results suggest that published rates of tardive and spontaneous dyskinesia in the elderly may over-estimate the prevalence of these disorders, especially among geriatric patients with acute psychiatric presentations.

NR506 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Suicide and Aging: Psychological Autopsy Findings

Yeates Conwell, M.D., Psychiatry, Univ of Rochester, 300 Crittenden Blvd, Rochester, NY 14642; Eric D. Caine, M.D., Robin E. Henderson, Ph.D., Catherine J. Flannery, M.D., Nicholas T. Forbes, M.D.

Summary:

The clinical profile of elderly suicides differs from that of younger victims. We report preliminary findings of an ongoing psychological autopsy study of completed suicides in Monroe County, New York. Seventy-two cases between the ages of 21 and 92 years have been examined thus far. With increasing age, victims were more often widowed and living alone. Firearms were the most common method for all ages. The elderly, however, had greater lethality of intent, and more often revealed their suicidality to others during the last month of life. Older victims less often had histories of suicide attempts or psychiatric contact, but physical illness and contact with a primary care physician in the month before death were far more common. In victims aged 75 and over, single episode, unipolar major depression was the predominant diagnosis, and substance abuse as a single or comorbid diagnosis was unusual. In marked contrast, substance use disorders and schizophrenia were the most common psychopathologies of young adult suicides. These date provide further evidence that suicide in late life is associated with treatable psychopathology. Those elderly at higher risk, however, often go unrecognized in primary care settings, to which they more commonly present than to mental health providers.

NR507 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Mortality and Psychotropics in Long-Term Care of Elderly Patients

Ira R. Katz, M.D., Psychiatry, Medial College of PA, 3200 Henry Avenue, Phildelaphia, PA 19129; Paul Thuras, Ph.D., Patricia Parmelee, Ph.D., Patricia Beaston-Wimmer, Ph.D.

Summary:

To investigate the impact of psychopathology and/or drug treatment on frail elderly patients in long-term care, we evaluated the association between psychotropic medications and mortality using survival analysis in 625 patients, mean age 84, living in a nursing home or congregate housing facility. Of these patients, 10.9% were receiving antidepressants at the time of record review; two-1 year survival in these patients was .750 compared with .741 in the remainder (n.s.) we also found that 7.4% were taking antipsychotics on a regular basis, 3.5% prn; survival was .652 and .591 compared with .755 (Mantel-Cox Statistic 5.54; $p = .06$). Twenty percent were taking benzodiazepines on a regular basis, 17.3% prn; survival was .776 and .657 compared with .755 (Mantel-Cox Statistic 5.10; $p = .08$). Also, 10.9% were taking hypnotics on a regular basis, 13.6% prn; survival was .750 and .624 compared with .763 (Mantel-Cox Statistic 7.08; $p = .03$). The increased mortality associated with prn use of hypnotic agents could be due to selective prescription of prn medications in more frail patients or to adverse effects of drug withdrawal associated with irregular use. In general, these findings demonstrate the need for further research on the risks and benefits of psychotropic drugs in these vulnerable patients to refine practice and inform the development of regulatory guidelines.

NR508 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Predictors of Mild Postoperative Psychopathology

Marion Zucker Goldstein, M.D., Psychiatry, SUNY Buffalo-ECMC, 462 Grider, Buffalo, NY 14215; Barry Fogel, M.D.

Summary:

The following hypotheses were tested for the first 88 patients of NIMH grant #1R01MH45048 01: a) Incidence of delirium following elective noncardiac surgery in elderly patients carefully screened for preoperative psychopathology is very low; b) Transient psychopathologic symptoms not constituting the full syndrome of delirium are common in this population and are associated with similar risk factors as delirium is in a more vulnerable population.

Method: Patients aged 55 and over who were scheduled for selected orthopedic or general elective surgeries, were given a structured psychosocial questionnaire, BPRS, MMSE, GDS, SAS prior to hospital admission. The same tests were administered one month post-operatively. A Delirium Rating Scale was administered three days post-operatively. Occurrence, predictors and sequela of mild psychopathology were studied using the Chi square test, Wilcoxon rank sum test and a logistic regression model. *Results:* Forty-two percent were found to have new post-operative psychopathology. The logistic regression model identified depression, cardiac condition and length of time in recovery room as associated with increased risk. No residual symptoms were found one month post-operatively. *Conclusion:* Predictors for mild post-operative psychopathology and delirium are similar to those that predict delirium in a more vulnerable population.

NR509 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Major Depression in Severe Dementia

Blaine S. Greenwald, M.D., Psychiatry, Hillside Hospital, P.O. Box 38, Glen Oaks, NY 11004; Elisse Kramer, Ph.D.

Summary:

Major depression complicating *advanced* dementia has received minimal attention, yet may represent a treatment-responsive element in an otherwise hopeless clinical deterioration. This study investigated prevalence of and diagnostic markers reflecting major depression in nursing home dementia patients with advanced disease—a subgroup that is typically neglected in terms of depression assessment. Seventy-four subjects meeting DSM-III-R criteria for "severe dementia" were evaluated by two psycogeriatricians for DSM-III-R and an operationalized "Gestalt Rating" for major depression. Kappa coefficients for interrater reliability were .78 for DSM-III-R depression and .88 for "Gestalt depression". Nurses independently rated depressive phenomena. On consensus assessment, 51% and 8% of subjects were unratable employing DSM-III-R and "Gestalt" ratings, respectively. Twenty-three percent were diagnosed with major depression. Concordance between DSM-III-R and "Gestalt" ratings was 0.93. Comparisons between depressed and nondepressed groups on nurse-rated clinical variables revealed greater depressed appearance ($p = .02$), physical agitation ($p = .06$), and paranoia ($p = .07$); and shorter duration of dementia ($p = .01$) amongst depressed patients. Results suggested that (1) depression can be reliably assessed in advanced dements; (2) DSM-III-R criteria are applicable in just 50% of such patients; (3) only nurse ratings of "depressed appearance" associated with clinician diagnosis of depression; (4) physical agitation recommends depression evaluation; and (5) "Gestalt" ratings merit further validation.

NR510 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Appropriate Terminal Care for End-Stage Dementia

Daniel J. Luchins, M.D., Psychiatry, Univ of Chicago, 5841 S. Maryland Avenue, Chicago, IL 60637; Patricia Hanrahan, Ph.D.

Summary:

No consensus exists on the appropriate level of terminal care for end-stage dementia. Since these patients can't express their own preferences, this uncertainty increases the stress experienced by their family and professional caregivers. To address the issue of appropriate care, we sought informed opinions from geriatricians ($N = 819$), other gerontologists ($N = 1{,}000$); and from families of dementia patients ($N = 550$). Response rates were: professionals, 68%; families, 49%. Five levels of terminal care were described from most aggressive to most palliative (Volicer, et al., 1986A, 1986B); 56% of the professionals and 71% of the families chose least aggressive care. Physicians chose less aggressive care than other professionals, $p < .004$. In view of the Curzon decision, it is distressing that 57% of the families never discussed terminal care preferences with their demented relatives. Across all samples, 90% considered hospice care an appropriate alternative for end-stage dementia. The majority of professionals preferred home hospice care, but over half of the families preferred institutional hospice care, $p < .001$. Despite the desirability of hospice care, only 21% knew of hospice programs for end-stage dementia patients, suggesting problems in access to this important service.

NR511 Wednesday May 15, 3:00 p.m.-5:00 p.m.

ALZ50 Binding in the Brains of Demented Elderly Psychiatric Patients is Identical to That of Nondemented Nonpsychiatric Controls

Peter Powchik, M.D., Psychiatry, Mount Sinai Hospital, 1 Gustave Levy Place, New York, NY 10029; D. Purohit, Charles B. Nemeroff, M.D., M. Davidson, M.D., V. Haroutunian, Ph.D., D. Perl, M.D., K.L. Davis, M.D.

Summary:

A decline in cognitive functioning occurs is common in hospital-

ized psychiatric patients. When viewed cross-sectionally, this dementia may be indistinguishable from the dementia characteristic of Alzheimer's disease (AD). The ultimate diagnosis of AD is made by both a clinical history of dementia coupled with the presence neuritic plaques (NP) and neurofibrillary tangles (NFT). Schizophrenia has been considered to be an illness characterized by a functional dementia. Other severe and persistent mental illnesses may have similar functional impairment. The present study was conducted to determine whether the neuropathological and neurochemical characteristics of AD were present in a group of demented, elderly psychiatric patients.

Post-mortem cortical tissue (Brodman areas 10 and 38) from persons with Alzheimer's disease, 15 demented hospitalized psychiatric patients, and twelve normal persons were stained with Alz50 antibody. Two psychiatric patients had neuropathological changes similar to AD (one with a clinical diagnosis of AD, and one with Down's syndrome). No other psychiatric patients had neuropathology of AD, multi-infarct dementia or any other histopathologically common forms of dementia. Alz50 staining in demented psychiatric patients was virtually identical to that of non-demented normals (0.3104 for AD, 0.0109 for normals, and 0.0092 for psychiatric patients). Thus no classical histopathological abnormalities associated with dementia were found in these severely demented individuals.

NR512 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Efficacy and Side Effects of Nortriptyline Versus Desipramine in Geriatric Inpatients With Major Depression

Lawrence W. Lazarus, M.D., Psychiatry, Rush- Pres- St. Luke's, 1653 West Congress Parkway, Chicago, IL 60612; David Winemiller, B.S., Lesley Blake, M.D., Carolyn Hartman, M.D., Mehrdad Abbassian, M.D., Usha Kartan, M.D., Pauline Langsley, M.D., Andrew Ripeckyj, M.D., Virginia Markvart, R.N., Jan Fawcett, M.D.

Summary:

Although secondary amine tricyclic antidepressants have fewer anticholinergic and cardiovascular side effects than tertiary amine antidepressants, there have not been double-blind studies comparing the efficacy and side effects of two of the more commonly used antidepressants -- nortriptyline and desipramine.

Nortriptyline and desipramine were studied for safety and efficacy in the treatment of elderly depressed patients at Rush-Presbyterian-St. Luke's Medical Center in Chicago. Eighteen elderly inpatients with a DSM-III-R diagnosis of major depressive disorder, a minimum Hamilton Depression Rating Scale score of 15, and a minimum Mini Mental Status score of 14 were treated and studied for three weeks.

Subjects from each treatment group experienced similar incidences of anticholinergic and cardiovascular side effects. Seven subjects, six on desipramine and one on nortriptyline (a statistically significant difference), were discontinued from the study due to intolerable orthostatic hypotension. Of those subjects completing the study, significant Hamilton score reductions (greater than 50%) were found in a significantly greater number of nortriptyline subjects (six or seven) than desipramine subjects (none of two). While side effects were evident in both groups, desipramine produced more clinically significant side effects than did nortriptyline. Nortriptyline was also more efficacious than desipramine in alleviating depression. Double-blind studies are needed to compare the efficacy and side effects of these and other antidepressants in elderly subjects.

NR513 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Efficacy and Side Effects of Methylphenidate (Ritalin) for Post-Stroke Depression

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Summary:

Large numbers of stroke victims suffer significant depression within the first two years following stroke. Use of tricyclic antidepressants among elderly patients is often complicated by side effects such as orthostatic hypotension. Methylphenidate has been shown to be a rapid, safe, and effective treatment for depressed geriatric patients.

Methylphenidate was studied for safety and efficacy in the treatment of post-stroke depression at Rush-Presbyterian-St. Luke's Medical Center in Chicago. Ten elderly stroke patients with a DSM-III-R diagnosis of major depressive disorder, a minimum Hamilton Depression Rating Scale score of 15, and a minimum Mini Mental Status score of 14 were treated with methylphenidate and studied for three weeks.

Four of the 10 subjects showed Hamilton score reductions of 50% or greater. An additional four subjects showed Hamilton score reductions of at least 25%. No subject had adverse side effects necessitating discontinuation from the study. Five of the 10 subjects reported between one and three individual side effects.

Methylphenidate appears to be a safe and effective treatment for elderly patients with post-stroke depression. Its rapid onset of action and relatively low side effect profile may offer advantages over tricyclic antidepressants, particularly in a rehabilitation or acute medical hospital setting.

NR514 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Learning and Memory Impairment in Elderly Detoxified Benzodiazepine Dependent Patients

Teresa A. Rummans, M.D., Psychiatry, Mayo Clinic, 200 First Street Southwest, Rochester, MN 55905; Leo J. Davis, Ph.D., Robert M. Morse, M.D.

Summary:

Twenty-two elderly detoxified benzodiazepine-dependent patients in a drug-dependence rehabilitation program were studied to determine the prolonged effects of benzodiazepine dependence on their ability to learn and remember new material using the Auditory-Verbal Learning Test. These patients were matched for age, sex, and Wechsler Adult Intelligence Scale-Revised full scale I.Q., with 22 elderly detoxified alcohol-dependent patients in the same drug dependence rehabilitation program and 22 elderly controls obtained from a community sample. The neuropsychological testing was performed in both drug-dependent groups one to two weeks after the patients had been completely detoxified from the addicting substance. On the critical test of delayed recall in the Auditory-Verbal Learning Test, the controls scored better than both of the other groups; and the controls and alcohol-dependent patients were significantly superior to the benzodiazepine-dependent patients. These results suggest that addictive use of benzodiazepines in the elderly may produced memory impairment even after the drugs have been discontinued.

NR515 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Anticholinergic Effects of Common Medications

Larry E. Tune, M.D., Psychiatry, Johns Hopkins Hospital, 600 N. Wolfe St. Meyer 3-166, Baltimore, MD 21205

Summary:

Anticholinergic medications have long been known to induce confusional states and, in toxic doses, frank delirium in a wide range of clinical settings. The risk of toxicity from anticholinergic medications is particularly great in elderly patients. This is presumably due to age-related decreases in acetylcholine neurotransmission. In the current investigation we hypothesize that cholinergic toxicity is unappreciated for at least two reasons. First, many parent compounds and their metabolites have not been studied for their effects on cholinergic neurotransmission. Particularly with "older drugs" the cholinergic effects are unknown. Second, the cumulative toxicity to acetylcholine neurotransmission of multiple drug combinations is poorly understood. It is possible that a number of drugs with modest anticholinergic effects, taken together, could result in significant toxicity. We have investigated the 25 most commonly prescribed drugs in the elderly. These drugs were studied with an antimuscarinic acetylcholine radioreceptor assay. Of the 25 most commonly prescribed drugs, twelve produced detectable anticholinergic drug levels. Eight drugs: ranitidine, codeine, dipyridamole, coumadin, isosorbide, nifedipine, digoxin, and prednisone, produced anticholinergic levels which have been found in other studies to result in cognitive impairments in normal elderly patients. The results of this study will be discussed.

NR516 Wednesday May 15, 3:00 p.m.-5:00 p.m.

10-OH-Nortriptyline and Hypotension in the Elderly

Robert C. Young, M.D., Psychiatry, NY Hospital Cornell, 21 Bloomingdale Road, White Plains, NY 10605; George S. Alexopoulos, M.D., Barnett S. Meyers, M.D., Richard Shindledecker, M.A., Gabriel Tsuboyama, M.D., Amiya K. Dhar, D.S.C.

Summary:

Emergent orthostatic hypotension is of particular concern in elderly patients treated with antidepressants because of potential complications including hip fracture. While nortriptyline (NT) is particularly low in orthostatic hypotensive effect, elderly patients differ in their cardiovascular response to treatment. We tested the hypothesis that orthostatic hypotensive changes during NT treatment are positively associated with plasma drug concentrations.

In geriatric patients with major depression ($n = 30$), lying and standing blood pressure (BP) and pulse were monitored before and weekly during six weeks of treatment at a target dose of 75 mg daily. Total plasma NT and unconjugated E- and Z-10-hydroxynortriptyline (10-OH-NT) were determined weekly.

Repeated measures ANOVA indicated that orthostatic differences in systolic BP increased significantly during treatment ($F = 8.18$; $p < .01$). BP changes were not related to dose. Plasma 10-OH-NT exceeded NT by more than 2.5-fold on average. Multiple regression analysis revealed that emergent orthostatic differences in systolic BP were associated with increased plasma E-10-OH-NT/NT ratio ($t = 2.75$; $p < .01$) but were not associated with plasma NT alone or with plasma Z-10-OH-NT. The findings are consistent with the hypothesis and suggest that monitoring plasma 10-OH-NT during NT treatment in the elderly may contribute to the identification of patients at increased risk for hypotensive changes.

NR517 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Hospitalization of the Elderly: Canadian Trends

Alex Richman, M.D., Psychiatry, Dalhousie University, 5849 University Avenue, Halifax NS, Canada B3H 4H7; Rod Riley, B.Sc.

Summary:

Aims: How have recent changes in demography, attitudes and treatment affected hospitalization of the mentally ill? Are hospitalization episode rates for the elderly increasing or decreasing? *Methods:* We analyzed the Statistics Canada national data base on psychiatric hospital episodes (mental hospitals, general hospital units, scatter-beds) in Canada between 1971 and 1986. *Results:* The elderly showed progressively increasing rates during the 15-year period. The increases were higher for the old-old (75+) than for the young-old (65-74). At the same time the rates decreased for younger persons. *Conclusions:* These data show the effect of increased recognition of mental illness in the elderly. However, we must consider the possible role of medication side effects, the lack of community alternatives and physical comorbidity on increasing hospital episodes for the elderly.

NR518 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Low-Dose Neuroleptic Treatment for AIDS Delirium

William Breitbart, M.D., Psychiatry, Memorial Hospital, 1275 York Avenue, New York, NY 10021; Meredith Platt, Ph.D., Rocco Marotta, M.D., Kathy Corbera, M.D., Carmen Grau, M.D., Susan Raymond, B.S., Henry Weisman, M.D., Maria Derevenco, Psy.D.

Summary:

A total of 125 medically hospitalized AIDS patients with capacity to sign informed consent agreed to participate in a double-blind, randomized study comparing the efficacy and safety of three drug interventions for the treatment of delirium: haloperidol, chlorpromazine, and lorazepam. Twelve (9.6%) patients became delirious and entered the treatment phase ($n = 4$ for each drug) of the study. Instruments used to rate efficacy and side effects included the Delirium Rating Scale (DRS), the Mini-Mental State Examination (MMSE), the Extrapyramidal Symptom Rating Scale, and the Symptom Side Effects Checklist. Both neuroleptic drugs, in low dosages (mean dose first 24 hrs. = 1.75 mg of haloperidol, or 80 mg chlorpromazine; mean maintenance dose = 0.875 mg haloperidol or 40 mg chlorpromazine a day) were highly effective in the treatment of delirium. Resolution of delirious symptoms was rapid (three to six hours), often prior to medical intervention. Analysis of variance (ANOVA) showed significant improvement from day 1 to day 2 on the DRS ($p = .026$) and the MMSE (ANCOVA, $p = .026$), when comparing neuroleptics with lorazepam. The benzodiazepine group had significantly more side effects than the neuroleptic groups ($p > .002$, chi square). All patients on lorazepam developed treatment-limiting side effects requiring discontinuation of drug. No patients receiving neuroleptics developed clinically significant extrapyramidal or other side effects. Low-dose neuroleptics are effective and safe in the management of delirium in AIDS.

NR519 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Methylphenidate's Antidepressant Effect in HIV

Francisco Fernandez, M.D., Psychiatry, Baylor College Medicine, One Baylor Plaza, Houston, TX 77030; Joel K. Levy, Ph.D., Francis Pirozzolo, Ph.D., Becky Viscuso, R.N.

Summary:

It was previously found that methylphenidate qualitatively and quantitatively improved mood and cognitive functioning in HIV patients. In this randomized, six-week, double-blind, placebo-controlled study, the effectiveness on mood and cognition of methylphenidate (30 mg/day) versus desipramine (150 mg/day) in depressed, minimally symptomatic HIV patients was assessed upon mood and cognitive functioning.

Twenty-five males, 20 to 50 years old, with major depression and either PGL or ARC with limited symptomatology, were enrolled. Subjects were excluded for having a history of major psychiatric or neurologic disorder, severe cognitive impairment (MMSE $\leq$ 25), or suicidal ideation.

Results indicated none of the subjects appeared, at entry, to have any significant cognitive impairment. Neuropsychological markers indicated no significant improvement with the treatment of depression, regardless of agent. There were no significant correlations of high transmission risk behaviors with scores of depression measures or treatment.

There were no significant differences between the two drug groups on depression measures by repeated measures analysis of variance, with both drugs appearing equally effective against depression. The placebo group had no such amelioration of depression.

Our results indicate that methylphenidate may be recommended equally as an antidepressant treatment in noncognitively impaired, depressed HIV-infected patients.

NR520 Wednesday May 15, 3:00 p.m.-5:00 p.m.

HIV Infection, Psychiatric Symptoms and Risk Taking

David S. Metzger, Ph.D., Psychiatry, University of Penn, Addict. Res Ctr 3900 Chestnut, Philadelphia, PA 19104; George E. Woody, M.D., A.T. McLellan, Ph.D., Charles P. O'Brien, M.D.

Summary:

The Risk Assessment Project completed serologic assessments on 150 *in treatment* and 100 *out of treatment* IVDUs at baseline, six and 12 months. Ninety percent of patients were contacted at all points and screened for HIV, HTLV I-II and high-risk behaviors. The HIV infection rate for the in-treatment sample increased from 9%, to 12%, to 14% across these points. The out-of-treatment sample had a substantially higher infection rate at baseline (16%). This increased to 22% at six months. We project 28% will be HIV positive at 12 months. The differences in both the baseline infection and conversion rates help to verify protective function of methadone treatment.

Behavioral data from this study provided an opportunity to examine correlates of AIDS risk taking behaviors. Using a new assessment tool, the Risk for AIDS Behavior (RAB), we confirmed that needle sharing was strongly associated with elevated levels of psychiatric symptoms. We also examined changes in risk behaviors following notification of HIV status. While there was a general decline in needle sharing, the most pronounced risk reductions took place among the HIV positive. This suggests that comprehensive testing programs can be important risk-reduction interventions.

NR521 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Peptide T for Cognitively Impaired HIV Positive Patients

Marc I. Rosen, M.D., Psychiatry, Yale University, 34 Park Street CHMC 4th Floor, New Haven, CT 06508; Mikel Thomas, M.D., H. Rowland Pearsall, M.D., Christopher H. van Dyck, M.D., Scott W. Woods, M.D., Thomas R. Kosten, M.D.

Summary:

Peptide T, an analogue of Vasoactive Intestinal Peptide, has improved cognitive function in patients with AIDS Dementia Complex in open clinical trials. We treated five methadone-maintained, cognitively impaired, HIV positive patients in a double-blind crossover study for four weeks with Peptide T, 5 mg intranasally tid, and with placebo for four weeks. The five patients were impaired on at least two tests of neuropsychological function, and had been treated with AZT for at least one month prior to enrollment. The sample was 80% male, with a mean age of 37 and baseline WAIS of 84, verbal IQ of 86, performance IQ of 83. Our patients did not show any statistically significant trends toward improvement with Peptide T on Trails B, the Parker Verbal Learning Test, Grooved Pegboard, Stroop Interference Test, and the Paced Auditory Serial Addition Test (Paired t-tests, $t > .25$). Nor was there a significantly greater change on Peptide T than placebo ($t > .23$ on all tests). Pre- and post-treatment SPECT rCBF data will be presented. Methodologic differences between our study and the previous open-label trials include different doses of Peptide T, different routes of administration (IN vs IV), concurrent administration of AZT; and subject population (methadone-maintained substance abusers vs. homosexual men). Further studies will be necessary to determine optimal parameters for Peptide T administration and selection of patients likely to respond to Peptide T.

NR522 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Suicidal Ideation After HIV Testing

Samuel W. Perry, III, M.D., Psychiatry, Cornell Medical Center, 525 East 68th Street, New York, NY 10021; Lawrence B. Jacobsberg, M.D., Baruch F. Fishman, Ph.D.

Summary:

Objective: To examine the reported suggestion that HIV serological notification is associated with suicide. *Method:* Item #9 of the Beck Depression Inventory (BDI) was used to measure longitudinally over 12 months the suicidal ideation among 501 physically asymptomatic adults at perceived risk for AIDS. The scale consisted of four points: 0 = no suicidal ideation, 1 = suicidal thoughts, 2 = suicidal wishes, 3 = suicidal intent. *Results:* Among 326 seronegatives and 68 newly tested seropositives, rates of suicidal thoughts remained low relative to pre-testing. Suicidal ideation was not associated with serological status, but rather with depression as measured by a modified BDI score (excluding item #9): $r = .36$–$.52$. Further, mean modified BDI score among subjects with suicidal wishes or intent (2%–4% of sample) were in the range associated with clinical depression (modified BDI = 17 to 22). Rates of suicidal ideation among 107 subjects who previously tested seropositive elsewhere and sought further counselling with us also did not increase over 12 months relative to rates at entry. *Conclusions:* In this sample, suicidal ideation is associated with depression and not with HIV testing or serological status.

NR523 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Health Attributions Mediate Distress in HIV Seropositives

Baruch F. Fishman, Ph.D., Psychiatry, Cornell University, 445 East 65th Street #3K, New York, NY 10021; Samuel W. Perry, III, M.D., Lawrence B. Jacobsberg, M.D.

Summary:

Aim: Examine the mediating role of Health Attributional Style (HAS) in emotional distress and response to Stress Prevention Training (SPT) in HIV-infected patients (HIV+). *Method:* 140 asymptomatic subjects who tested HIV+ were counseled by a psychiatric nurse. Then, 53 were randomly assigned to six weekly sessions of SPT, and 87 received only additional videotaped or printed information (NO-SPT). SPT is based on cognitive behavioral principles, is designed to enhance sense of personal control and optimism, and to train active-rational coping skills. Subjects also completed the Health Attributional Style Questionnaire (HASQ) and the Brief Symptom Inventory (BSI), among other measures, two weeks before and 10 weeks after HIV+ notification. The HASQ measures attributions of personal control and optimism in health-related situations. *Results:* low scores on HASQ were strongly correlated with higher initial ($r = .53$) and follow-up ($r = .58$) emotional

distress (BSI score). Change in BSI score was associated with change in HASQ score (r = .42). Mean improvement on BSI was greater for subjects who received SPT than for those who did not [21.8 vs. 5.9; F(1,137) = 4.7, p = .03]. This effect was substantially reduced when HASQ score was added the ANOVA as a covariate [F(1,133) = 3.6, p < .06]. *Conclusion:* 1) Seropositives with dysfunctional HAS are vulnerable to emotional distress after HIV antibody testing. 2) SPT is effective for reducing their distress during the first few weeks following notification. 3) Improved HAS mediates the effect of SPT on distress.

NR524 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Denial in Self-Report of Cognitive Function in HIV

Robert A. Stern, Ph.D., Psychiatry, Univ of North Carolina, Campus Box 7160, Chapel Hill, NC 27599; Naomi G. Singer, B.A., Jane Leserman, Ph.D., Susan G. Silva, M.A., Dwight L. Evans, M.D.

Summary:

Diagnosis of dementia has a profound impact on HIV-infected patients and is frequently made on the basis of self-report of cognitive disturbance. We studied the relationship between self-report and objective neuropsychological test results in 25 asymptomatic, HIV seropositive, gay men and 34 seronegative controls. Strict exclusion criteria were used to preclude confounding effects of substance abuse, head injury, learning disability, or zidovudine use. Controlling for education, objective test measures revealed significant group differences only in the area of motor functioning ($p < .05$), with seropositive subjects performing more slowly than controls. In contrast, the seropositives self-reported significantly better functioning than controls in all areas except motor, for which the groups did not differ. In fact, among seropositives, self-report of cognitive abilities correlated *negatively* with objective test scores. We hypothesized that this discrepancy between self-report and objective test data was an attempt on the part of the seropositives to deny neurocognitive difficulties. To assess the role of denial as a coping strategy, a brief measure was adapted from the COPE scale (Carver et al., 1989). Controlling for education, a trend existed (p = .15), with seropositives exhibiting greater denial than controls. These results suggest that self-report of cognitive functioning in HIV seropositive individuals may not be reliable, and should not serve as criteria for diagnosis of dementia. Rather, neuropsychological testing appears warranted to detect cognitive deficits in early HIV infection.

NR525 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Psychosocial Predictors of HIV High-Risk Behavior

Diana O. Perkins, M.D., Psychiatry, Univ of North Carolina, Campus Box 7160, Chapel Hill, NC 27599; Jane Leserman, Ph.D., Duanping Liao, M.D., John Boucvalt, B.S., Dwight L. Evans, M.D.

Summary:

Despite general awareness that HIV is sexually transmitted, people continue to engage in high-risk behavior. We examined the role of psychosocial factors (e.g., personality, mood, and gay self-acceptance) in sexual risk-taking behaviors. As part of a larger HIV project, the Coping in Health and Illness Project (CHIP), we studied 41 HIV-negative gay men. Mean education was 16 years, mean age was 32 and 95% were white.

Risk behavior was measured on a three-point scale taking into account condom use, number of sexual partners, and type of sexual activity (adapted from Multicenter AIDS Cohort Study-MACS). The scale indicated that 61% of the subjects practiced low-risk, 19.5% practiced moderate-risk and 19.5% practiced high-risk behavior. Using multiple regression, we found that risk behavior was positively correlated with optimism (Life Orientation Test) (p = .0004), and anger (POMS)(p = .007). Risk Behavior was negatively correlated with emotional control (Courtauld)(p = .007), gay self-acceptance (adapted from the MACS)(p = .0004), self-esteem (Rosenberg)(p = .01) and loneliness (UCLA) (p = .004). These six variables accounted for 54% of the variance in taking risk. Our findings held when controlling for education, income, age and race. The results indicate that risk-taking behavior may be reduced by enhancing gay self-esteem, increased understanding and adaptive use of anger, and modifying overly optimistic attitudes to increase realism. Understanding these factors may help improve the success of risk-reduction interventions.

NR526 Wednesday May 15, 3:00 p.m.-5:00 p.m.

HIV Seroprevalence in Psychiatric Inpatients

Michael H. Sacks, M.D., Cornell University, 525 East 68th Street, New York, NY 10021; Helen Dermatis, Ph.D., Salome Looser-Ott, M.A., William Burton, M.A., Samuel W. Perry III, M.D.

Summary:

Aim: To determine HIV seroprevalence and risk behaviors in acute psychiatric inpatients during a five-year period. *Method:* Consecutive psychiatric admissions are being tested for HIV in an unlinked design using bloods remaining from admission screening tests. Information regarding patients' HIV antibody status and risk factors as recorded in the physician's admission note was obtained. *Results:* The patient sample assessed during the first two months of the second year of the study (N = 81) was comparable to the first year's sample (N = 350) with respect to seroprevalence rate (7.4% vs. 7.14%) and rate of HIV risk factors in seropositive (HIV +)(100% vs. 88%) and seronegative (HIV-) patients (17% vs. 16%). In contrast to the findings obtained in the first year's sample, in which 60% of the HIV + patients were noted on admission to be HIV +, all HIV + patients admitted during the second year of the study were know to be HIV + on admission. These second year results are preliminary pending the assessment of the entire two-year sample. *Conclusion:* These findings suggest: (1)rates of HIV seroprevalence and risk factors in psychiatric admissions are stable over a two-year period, and (2)HIV + patients who are admitted to a psychiatric hospital are increasingly aware of their HIV status and report it to the admitting psychiatrist. These findings underscore the need for clinicians to provide HIV-related services.

NR527 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Two Clinical Service Delivery Models for HIV Patients

Marianne C. Fahs, Ph.D., Psychiatry, Mt. Sinai Sch of Medicine, 1 Gustave Levy Place Box 1228, New York, NY 10029; George Fulop, M.D., James J. Strain, M.D., Henry S. Sacks, Ph.D., Charlotte Muller, Ph.D., Paul D. Cleary, Ph.D., James Schmeidler, Ph.D., Barbara Turner, M.D.

Summary:

Two health delivery models were compared for general hospital HIV patients: Traditional scatter beds on a medical service, and a dedicated cluster unit for HIV patients only, and with a dedicated staff. The analysis estimates whether the two models differ with regard to: patient selection, length of stay (LOS), charges, nursing staff turnover rate, and inpatient mortality. Psychiatric services were of the liaison mode on the cluster unit, and of the consultation/referral mode in general inpatient placement model ("scatter beds").

Mean age (older) (p = < .05), sex (female) (p = < .05), race (black) (p < .05) were significantly greater in the scatter bed model. Deaths (p < .05), LOS (p < .01), total charges (p = < .01) were greater on the cluster unit until severity of illness was controlled for. Severity

of illness was the major predictor of admission to the AIDS cluster unit. There was no difference between the units in the rate of detection of psychiatric disorders (17%). The findings did not support greater stigmatization, higher costs, or excessive staff burnout in the cluster unit. Lower proportions of older, black, and female patients admitted to the AIDS cluster unit raise the issue regarding access to AIDS units for minorities.

NR528 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Early Neuropsychiatric Morbidity in HIV Disease

Rifaat S. El-Mallakh, M.D., Neuropsychiatry, Neuropsych. Res. Hosp., 2700 Martin L. King Jr. Ave SE, Washington, DC 20032; David J. Ligay, M.S.W.

Summary:

Although it is clear that advanced human immunodeficiency virus (HIV-1) disease causes severe neuropsychiatric dysfunction, the effects of early, otherwise asymptomatic HIV-1 infection are far less clear. In order to examine this question we performed neuropsychiatric evaluations on patients specifically referred for evaluation (Indication Group [IG]: $n = 22$; male = 17; mean age = 33) and on asymptomatic individuals as part of baseline work-up (Routine Group [RG]: $n = 40$; male = 24; mean age = 35), at a Prince George's County, Maryland, AIDS outpatient clinic. The IG had more individuals with AIDS (40.9%) than the RG (17.5%; $z = 2.93$; $p < 0.002$). With the exception of current adjustment disorder (IG 10, RG 8; $z = 3.18$; $p = 0.0007$) and AIDS-dementia-related psychiatric problems (IG 4, RG 0), there were no other significant differences in demographic variables, other psychiatric diagnoses, or Mini Mental State scores (IG 26.7 ± 3.7 [SD]; RG 27.9 ± 2.3 [SD]; $t = 1.4$, $df = 60$; $p = 0.16$). Although preliminary, our results support other studies that have found early, otherwise asymptomatic HIV-1 infection does not appear to greatly increase neuropsychiatric morbidity.

NR529 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Psychiatric Disorders in 100 HIV-Infected IV Drug Users

Steven L. Batki, M.D., Psychiatry, UC-San Francisco, San Francisco General Hosp., San Francisco, CA 94110; Julie A. London, Ph.D., Stephen Ferrando, M.D., Jerry Pattillo, Ph.D., Craig J. Abbott, B.A., Rochelle Hartwig, B.A.

Summary:

Method: A chart review examined psychiatric consultation in all 100 HIV-infected patients in methadone maintenance treatment (MMT) at SFGH during March, 1990. Forty percent of patients were males, mean age 40. Approximately two-thirds were minorities.

Outcome: Sixty-six percent of patients had a psychiatric contact. The most prevalent diagnoses were psychoactive substance dependence disorders: cocaine in 22 (33.3%), alcohol in 14 (21.2%), and sedative-hypnotic in nine (13.6%). Anxiety disorders were seen in 13 patients (19.7%), mood disorders in 11 (16.7%), dementia in 10 (15.2%), disorders with psychosis in 10 (15.2%), sleep disorders in nine (13.6%), and adjustment disorders in five (7.6%). Organic disorders were predominant. Medications were used in 51 (77.3%) patients: antidepressants in 29 (43.9%), nonbenzodiazepine antianxiety agents in 13 (19.7%), benzodiazepines in 13 (19.7%), antipsychotics in nine (13.7%) and disulfiram in seven (10.6%). Patients with psychiatric contacts had 35% dirty urines, contrasted with only 25% in those without psychiatric contact.

Conclusion: Psychiatric disorders are common and predominantly organic in this sample of HIV-infected IVDUs. They require medication, and may be associated with a higher prevalence of illicit drug use while in treatment.

NR530 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Depression in HIV Infected men

Patricia Rosenberger, Ph.D., Psychiatry, Ohio State University, 151 Upham Hall 473 W 12th Ave, Columbus, OH 43210; Robert A. Borenstein, Ph.D., Henry A. Nasrallah, M.D., Michael F. Para, M.D., Robert J. Fass, M.D., Robert R. Rice, Jr., Ph.D.

Summary:

Objective: The study investigated the presence of depressive disorders in HIV+ asymptomatic and symptomatic males.

Method: Eighty-four HIV+ asymptomatic males (group 1) and 49 ARC/AIDS males (group 2) participated in structured diagnostic interviews assessing lifetime and current DSM-III-R diagnoses (SCID) and current depressive symptomatology (Hamilton). Self-reports including the Beck Depression Inventory were also completed.

Results/Discussion: Major depressive disorder (MDD) was the most common depressive diagnosis in this population, with 37% of group 1 and 60% of group 2 reporting past episodes ($p = .02$), and 7% (group 1) and 8% (group 2) reporting current episodes. The next most commonly diagnosed depressive disorder in both groups was depressive disorder not otherwise specified, followed by dysthymia, adjustment disorder with depressed mood, and bipolar disorder. No differences in rate of these disorders were found between groups. ARC/AIDS subjects had significantly higher mean Hamilton depression scores ($p = .02$) and Beck scores ($p = .03$) than asymptomatic subjects. Results indicate that depressive disorders, particularly MDD, are prevalent in HIV-infected homosexuals, with rate of MDD diagnosis significantly higher in ARC/AIDS subjects. Consistent across interview and self-report measures of depression, men who have progressed to later stages of infection report higher levels of depression. Diagnostic problems encountered in this population will be discussed.

NR531 Wednesday May 15, 3:00 p.m.-5:00 p.m.

The Use of Fluoxetine in Patients on Hemodialysis

Michael Blumenfield, M.D., Psychiatry, MY Medical College, RM. B006 Psych Inst WCMC, Valhalla, NY 10595; Norman B. Levy, M.D., Anjani Dubey, M.D., Richard Solomon, M.D., Alvin Goodman, M.D.

Summary:

Nine patients with normal renal function (NRF) and seven on hemodialysis (HD) were studied. All were between 18 and 70 years, had a diagnosis of major depressive disorder and a score of at least 16 on the first 17 items on the Hamilton Depression Scale (HDS). All received 20mgs. of fluoxetine daily, weekly psychiatric evaluations and assessments for adverse reactions to this medication. Psychological tests were performed prior to, during and upon completion of the study: HDS, Beck Depression Inventory, Montgomery Test for Depression, Brief Symptom Inventory, Global Well-Being Scale and the Electronic Visual Analog Scale Assessment. Serum levels for fluoxetine and its active metabolite norfluoxetine were taken three times the first week, during each weekly evaluation, and six times during the final 24 hours of this study.

Six NRF patients and six on HD completed the eight-week study. All tolerated the medicine well. Five HD patients and all with NRF had a moderate to marked improvement in their depression as measured by psychological tests and clinical evaluations. The blood levels of fluoxetine and norfluoxetine of those on HD were similar over the nine-week period to those with NRF and well below toxic levels.

These results suggest that fluoxetine is well tolerated and efficacious for depressed patients on HD.

NR532 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Nonpsychiatric Physicians Frequently Misdiagnose Delirium and Other Conditions as Major Depression

Russell L. Margolis, M.D., Bio Psychiatry, NIMH Bldg 10 3N212, 9000 Rockville Pike, Bethesda, MD 20892

Summary:

The extensive prescription of antidepressants by nonpsychiatrists emphasizes the need for correct diagnosis of major depression. To evaluate this skill, nonpsychiatric house staff referring inpatients to a psychiatric consultation service at a large teaching hospital were asked to make a psychiatric diagnosis (in DSM-III-R terms) before their patients were evaluated by the consultants. In a consecutive series of 100 patients, supplemented by an additional series of 30 patients, the referring physicians identified 27 cases of major depression. The psychiatric consultants agreed with this diagnosis in only six (22%) of these cases. The psychiatrists identified 10 cases (37%) of delirium, seven cases (26%) of adjustment disorder, and four cases (16%) of various other conditions. Age, race, and sex did not distinguish between the groups identified by the consulting psychiatrists as having and not having major depression. The rate of agreement with the final psychiatric diagnosis differed by the specialty service of the referring physician, ranging from 100% (2/2) for neurologists to 13% (2/15) for internists. These results suggest that nonpsychiatric house staff frequently misidentify other psychiatric conditions as major depression. A simple protocol is proposed to enable health care providers to distinguish among delirium, major depression, and adjustment disorder.

NR533 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Somatization and Recognition of Psychiatric Distress

Laurence J. Kirmayer, M.D., Psychiatry, Jewish General Hospital, 4333 Cote Ste Catherine Road, Montreal PQ, Canada H3T 1E4; J. Robbins, Ph.D., M. Dworkind, M.D., M. Yaffe, M.D.

Summary:

We examined the effect of patients' style of clinical presentation on physicians' recognition of depression and anxiety in 685 patients attending family medicine clinics. Subjects completed a structured interview for presenting complaints, symptom self-report measures and the Diagnostic Interview Schedule (DIS). Physician recognition was determined by any notation of psychiatric diagnosis in the medical chart over the ensuing 12 months. Of 202 patients with Center for Epidemiologic Studies-Depression (CES-D) scale ≥ 16, 85% made somatic presentations, while of 70 patients with DIS major depression or anxiety disorder, 79% made somatic presentations. We identified three gradations of progressively more persistent forms of somatic presentation, termed *initial, facultative* and *true* somatizers. Among patients with CES-D ≥ 16, somatization reduced physician recognition from 74% for psychosocial presenters, to 51% for initial, 39% for facultative, and 30% for true somatizers ($p < .001$). The same trend was found for patients with DIS depression or anxiety ($p = .06$). Somatized presentation remained a predictor of recognition in logistic regression models including sociodemographic variables, symptomatology and history. Rate of recognition was unaffected by patients' age, sex, education, income, seriousness of illness, history of medically unexplained symptoms, current level of somatic symptomatology or recent life events. Factors that increased recognition of a psychosocial problem were high levels on the CES-D, hypochondriasis, worry about having an emotional problem, and a past history of psychiatric disorder. We conclude that somatized presentations reduce the detection of depression and anxiety in primary care by up to 50%. However, most patients' tendency to somatize is easily countered by specific questions about symptom attribution, so underrecognition must ultimately be attributed to physicians' reluctance to diagnose and treat psychiatric comorbidity.

NR534 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Chronic Fatigue Syndrome and Psychiatric Illness

Grant E. Mitchell, M.D., Psychiatry, NY Medical College, 295 Hayward Street, Yonkers, NY 10704; Steven B. Friedenthal, M.D., Michael Blumenfield, M.D., Barbara Orlowski, Ph.D., Louis Raimondo, M.D.

Summary:

Chronic Fatigue Syndrome (CFS) is a debilitating disease that remains a diagnosis of exclusion, since routine laboratory studies and physical examination are usually normal. However, many CFS patients report depression and cognitive disturbances, suggesting that CFS may be a variant of major depressive disorder. This study was designed to examine the presence of depressive symptoms in CFS patients.

One thousand members of the National CFS Association were randomly selected and queried about CFS symptomatology as well as about their own and family history of psychiatric illness. Subjects also completed the Symptom Checklist-90-R (SCL-90-R).

A total of 720 questionnaires were returned (response rate of 72%). Results from the first 405 questionnaires revealed that 59% (238) met the Centers for Disease Control criteria for CFS. Fourteen percent (34) of the 238 CFS patients reported being treated for depression prior to the onset of CFS and 17.6% (42) reported a family history of depression. While 95% (226) of the CFS patients reported periods of depression, 78% of these depressions were seven days or less in duration. At least five of the self-report symptoms that comprise the DSM-III-R criteria for major depression were present in 16% (38) of CFS patients. The entire symptom profile of the CFS patients from the SCL-90-R will also be presented.

NR535 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Cognitive and Emotional Findings in Intensive Care Unit Ventilator Patients

Kathleen Franco, M.D., Psychiatry, University of Vermont, Burlington, VT 05401; Laurie Verbosky, M.B.A., John McSweeney, Ph.D., Keith Freeman, M.S., James Tita, D.O.

Summary:

There are few data about the cognitive or emotional state of chronic ventilator patients. We compared 20 patients (Group 1) requiring chronic ventilation ($x = 67.9$ days) with 20 of similar age and illness severity (APACHE II) non-ventilator ICU patients (Group 2). Group 1 patients were evaluated after five to seven days of ventilation and approximately one week after weaning, and Group 2 once after five or more days in the ICU. Both groups were assessed using the Mattis Dementia Rating Scale and Profile of Mood States. Laboratory parameters known to be associated with organic mental deficits and those used in APACHE II calculation were collected. Memory ($p = .028$) and concept performance ($p = .019$) were more impaired in Group 1 than Group 2. Post ventilation, Group 1 patients showed improved scores for total cognitive ($p = .000$), attention ($p = .0015$), concepts ($p = .003$), memory ($p = .0015$), and improved abstraction ($p = .027$), total mood scores ($p = .0185$), tension ($p = .035$), and anger ($p = .039$). Both groups demonstrated significant cognitive and emotional deficits associated with higher APACHE II scores, sepsis, age, and other variables. Patient age had mixed influence on ventilator patients' moods. The data suggested that ventilator patients have higher levels of cognitive and emotional impairment than other ICU patients. Factors involved may include hypoxia, hypotension, or medications. The ability of critically ill patients to participate effectively in treatment planning should be carefully assessed.

NR536 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Interictal Psychiatric Morbidity and Focus of Epilepsy in Treatment Refractory Subjects

Dr. Rahul Manchanda, Psychiatry, University Hospital, 339 Windermere Road, London Ontario, Canada N6A 5A5; Betsy Schaefer, Dr. Richard S. McLachlan, Warren T. Blume

Summary:

Seventy-one patients were admitted to an epilepsy unit during a 20-month period. All patients had seizures refractory to medical treatment and were admitted for an assessment for neurosurgical intervention. There were 36 males and 35 females. Majority of the patients were single, with a mean age of 29 years. Average age of onset of epilepsy was 12.2 years; mean duration 16.8 years; average number of seizures 9.6 per week. A definite focus of seizure was determined by EEG recording with telemetry and subdural electrode placement wherever necessary. Forty-seven (66%) patients had a temporal lobe focus of seizures: left temporal (N = 19), right temporal (N = 20), and bitemporal (N = 8). Using the 60-item General Health Questionnaire with a cut-off score of 11, 32 (45.1%) patients emerged as psychiatric cases. When either total GHQ scores or caseness status was used for comparison, no differences were evident either between temporal an nontemporal lobe focus or in the laterality of seizure focus. The increased prevalence of interictal psychiatric morbidity is in keeping with other studies, but this study fails to support a specific relationship to the type or focus of epilepsy.

NR537 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Chronic Pain and Suicide Death

David A. Fishbain, M.D., Psychiatry, Univ Miami School of Med., South Shore Hosp. 600 Alton Rd, Miami Beach, Fl 33139; Myron Goldberg, Ph.D., Hubert Rosomoff, M.D., R. Steele-Rosomoff, R.N., M. Jorge, M.A., E. Abdel-Moty, Ph.D.

Summary:

Aim: Convergent lines of evidence indicate that one can expect a high rate of suicide death for chronic pain patients. This problem has not been previously examined.

Methods: From our patient follow-up data, we became aware of three chronic pain patients (two males and one female) who completed suicide. The sequential nature of our data enabled us to calculate suicide rates (number of suicides per 100,000 patients per year) for a subsample of our chronic pain population.

Results: These suicide rates are as follows: 16.5 females per year; 29.3 males per year; 57.1 white males aged 35-64 per year, and 78.6 white worker-compensation males age range 35-64 per year. These results indicate chronic pain white males and chronic pain white worker-compensation males aged 35-64 years are twice and three times as likely, respectively, as their counterparts in the USA general population to die by suicide.

Conclusion: Chronic pain and worker's compensation status in 35- 64-year-old white males may be suicide death risk factors. These results indicate a need for future research in this area and careful psychiatric evaluation for suicide potential with all chronic pain patients.

NR538 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Clonazepam Open Clinical Trial for Chronic Pain of Myofascial Pain Syndrome Origin Refractory to Pain Unit Treatment

David A. Fishbain, M.D., Psychiatry, Univ Miami School of Med., South Shore Hosp. 600 Alton Rd, Miami Beach, FL 33139; Myron Goldberg, Ph.D., Hubert Rosomoff, M.D., R. Steele-Rosomoff, R.N., M. Jorge, M.A., E. Abdel-Moty, Ph.D.

Summary:

Clonazepam (CL) has shown efficacy in noncontrolled, open clinical trials for treatment of lancinating chronic pain, but has not been utilized for treatment of chronic pain secondary to MPS.

Methods: Consecutive MPS patients refractory to pain-unit treatment were recruited into an open clinical trial of CL. CL was titrated upwards at 0.5 mgs. per day until the patient had pain relief or intolerable side effects. Pain relief was rated by the patient as none, partial or total. Serum drug levels were determined on those patients with a positive response. No other psychotrophic or analgesic drugs were used.

Results: Of 40 patients, 85% had partial relief, 15% developed sedation before pain relief, 0% had total pain relief. For patients with partial relief, average CL dose was 2.24 mgs. per day. Average serum levels were 19.6 mcg/L; 44% of the responders had a DSM-III diagnosis of generalized anxiety disorder.

Conclusions: CL may be useful for MPS patients refractory to pain-unit treatment, and warrants controlled trials that need to separate the pain effects of CL from its antianxiety effect.

NR539 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Magnesium Levels in Chronic Pain Patients

David A. Fishbain, M.D., Psychiatry, Univ Miami School of Med., South Shore Hosp. 600 Alton Rd, Miami Beach, FL 33139; Myron Goldberg, Ph.D., Hubert Rosomoff, M.D., R. Steele-Rosomoff, R.N., M. Jorge, M.A., E. Abdel-Moty, Ph.D.

Summary:

Aim: Patients suffering from hypomagnesemia develop muscle weakness, restlessness, leg cramps, paresthesias and decreased concentration. These are symptoms frequently described by chronic pain patients. In addition, chronic pain patients often abuse alcohol, which can cause hypomagnesemia. These observations led us to a pilot investigation of magnesium levels in chronic pain patients.

Methods: Serum magnesium levels (normal value 1.6 - 2.6 MG/DL) were measured in 201 consecutive chronic pain patients. Any magnesium level below normal was repeated, and, if indicated, the patient was treated.

Results: The magnesium values for the patient group were found to be normally distributed with the mean (1.777), mode (1.7) and median (1.8) values being nearly equal. The range for all patients was between .8 and 2.4 MG/DL, and 95% of the magnesium levels were between 1.2 and 2.2 MG/DL; 14.9% of the patients had abnormal values below 1.6 MG/DL.

Conclusions: (1) A significant proportion of chronic pain patients appear to have clinically defined hypomagnesemia; (2) A comparison of the ranges between normals and chronic pain patients indicates that the magnesium distribution of chronic pain patients is skewed to the lower end of normal values; (3) Further studies of serum magnesium levels in chronic pain patients are indicated.

NR540 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Screening for Psychiatric Disorders in the General Hospital: A Validation and Calibration Study

David M. Clarke, M.D., Psychol. Med., Monash University, Prince Henry's H. St. Kilda RD, Melbourne, VI 03004, Australia; Graeme Smith, M.D., Dean McKenzie, B.A.

Summary:

Screening patients for psychiatric morbidity has been useful in C-L psychiatry research as well as clinical work. However, the most widely used screening instruments have not been adequately validated in general hospital patients or against DSM-III-R diagnoses. We undertook a comprehensive examination of GHQ, the Hospital Anxiety & Depression Scale, the STAI, and the BDI. A total of

179 randomly selected medical and surgical patients completed the questionnaires and were interviewed using the Structured Clinical Interview SCID-R. Thirty-eight percent of patients obtained a DSM-III-R diagnosis; 25% depression, 12% anxiety, 11% drug abuse or dependence and 2% a diagnosis with predominant somatic symptoms. Eleven percent of patients had more than one diagnosis. Rating scales were examined for their ability to identify "cases" of depression, anxiety, or any psychiatric diagnosis, using the QROC described by Kraemer (1988). In addition a range of validity coefficients was calculated for each possible cut point. The scales that performed best were the 60-, 36-, and the 28-item GHQ scored in the manner described by Goodchild & Duncan-Jones (1985) to identify chronic illness. All scales identified drug abuse and dependence, and anxiety disorders, poorly. The Implications for DSM-III-R are discussed. It is recommended that the GHQ, scored for chronicity, be used to identify affective disorders, and that other questions be used to screen for drug abuse and dependence. A dimensional scale should be used for research of anxiety disorders. Sensitivities and specificities of the various scales will be given.

NR541 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Psychophysiologic Correlates in Asthmatics

David A. Baron, D.O., OCD, NIMH Bldg 10 3N238, 9000 Rockville Pike, Bethesda, MD 20892; William Samuel, M.D.

Summary:

A questionnaire assessing biographical information, medical history, and "panic-fear" was administered to 22 asthma patients; laboratory and pulmonary function data were also gathered. Pulmonary function was negatively correlated with age, age of asthma onset, smoking history, number of children in the household, self-rated asthma severity, asthma interference with work/school or physical activity, and with feelings of panic occurring during an attack. Frequency of medical treatment was positively correlated with number of children, number of family members with asthma, self-rated asthma severity, asthma interference with activities, generalized feelings of anxiety, and a tendency to hyperventilate during an attack. Hyperventilation was positively correlated with number of family members having asthma-related disorders but negatively with confidence in and satisfaction with one's physician. Generalized anxiety was negatively correlated with measures of immune system function. The results indicate that, among asthmatics, pulmonary function is impaired and need for medical treatment increased by social stressors (e.g., number of children), psychological stressors (panic-fear), and (somewhat surprisingly) reduced immune responsiveness. The data suggested that a learned familial tendency toward hyperventilation may contribute to a high frequency of doctor's visits as well as to dissatisfaction with medical treatment.

NR542 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Religiosity and Psychosocial Adjustment in Cancer

Basawaraj M. Karajgi, M.D., Psychiatry, Queens Hospital Center, 82-68 164 Street 5A-9 T Bldg, Jamaica, NY 11432; Arthur Rifkin, M.D., Seshagiri Doddi, M.D., Luz Alvarez, M.D., Zully M. Mateus, M.D., Pedro Polanco, M.D.

Summary:

Previous research has shown that religious belief is associated with better life satisfaction in patients with advanced cancer. Those patients reported lower levels of pain. In this present study, 50 ambulator patients randomly selected from the medical oncology clinic, were interviewed to measure religiosity, pain, depressive and anxious symptoms, and psychosocial adjustment. Religiosity was measured by: 1) a six-item scale of religious imagery; 2) the importance of religion, on a visual analogue scale (VAS); and 3) attribution of illness to God's will, on a VAS. Pain was measured also on a VAS. Psychosocial adjustment was measured by the PAIS (Psychosocial Adjustment to Illness Scale).

Results: None of the religious variables showed a correlation to psychosocial adjustment (all correlations are less than 0.1). Pain was highly correlated with poor adjustment ($p = .000$), as were anxiety (Hamilton Rating Scale for Anxiety, $p = .000$), and depression (Hamilton Rating Scale for Depression, $p = .000$). The strengths and weaknesses of these findings, and their implications for treatment of these patients, will be discussed.

NR543 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Death-Mindedness in General Surgery Patients

Caryl E. Boehnert, Ph.D., Psychiatry, Univ of Minnesota UMHC, 420 Delaware St. SE. Box 393, Minneapolis, MN 55455; Lynn Trochel, B.A., Allan Callies, B.A.

Summary:

This retrospective study of 852 surgical patients at the University of Minnesota Medical School assesses death-mindedness. Of the 852 cases, all of whom were inpatients on surgery services, including oncology, during 1983, 350 died and 500 lived. Medical charts were reviewed for comments by the patients regarding conviction or desire for death, hopelessness, and behavioral indications of death-mindedness (such as making a will). There was no significant difference between those who lived and those who died on type or frequency of these comments. Seventy-seven percent of all patients had no verbalizations of death-mindedness, whereas 17 percent were assessed as death-minded. Of the 40% of patients who died, 28% correctly predicted their own death. There was only a 10% false positive rate. A log linear analysis indicated that individuals who were death-minded or considered highly fearful without an Axis I disorder were more likely to die than similar individuals with an Axis I disorder. There was also a small number of patients who routinely predicted their own death during each admission for surgery, but recovered uneventfully thereafter. Implications for future research are discussed.

NR544 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Fear of Recurrence and Breast Conserving Surgery

Richard G. Margolese, M.D., Dept. of Oncology, Jewish Gen. Hosp., 3755 Cote Ste Catherine, Montreal PQ, Canada H3T 1E2; Jean-Claude Lasry, Ph.D., Robert A. Stern, M.D., Julie Beckwith, M.S.N., Claire E. Morey, B.S., George Mason, Ph.D., Arthur J. Prange, Jr., M.D.

Summary:

Fear of recurrence has been at the heart of the controversy between surgeons favoring mastectomy and those advocating lumpectomy, a breast-conserving operation. The debate has continued despite demonstration that survival rates were equivalent for both surgeries (Fisher et al., 1985). We have already reported a lack of difference between mastectomy and lumpectomy patients on fear of cancer recurrence (Lasry et al., 1987). These preliminary data were collected on the first 123 patients of a study that accrued a total 227 breast cancer patients, randomly assigned to three treatment arms (NSABP protocol B-06), as well as a control group of 63 benign biopsy patients.

Reclassification of patients according to a multiple surgical intervention group modifies the results reported in the previous paper. There are no differences according to the type of surgery, but there are according to the number of surgical interventions. Patients who underwent several operations report a greater fear of cancer recurrence and a worse body image (as is consistently found for mastectomy patients). And, contrary to our original hypothe-

sis, patients who undergo radical surgery do not manifest a lesser fear of cancer recurrence. The expected trade-off between breast-conserving procedure and fear of recurrence did not materialize.

NR545 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Psychiatric Effects of Subclinical Hypothyroidism

John J. Haggerty, Jr., M.D., Psychiatry, Univ of NC, CB#7 160 Medical School Wing B, Chapel Hill, NC 27599

Summary:

Subclinical hypothyroidism (SCH), in which thyroid hormone concentrations are normal, but basal and/or TRH stimulated TSH concentrations are elevated, affects at least 5% of the population. Studies in psychiatric patients have linked SCH with depression and cognitive dysfunction. The aim of this study was to determine whether neuropsychiatric dysfunction also occurs in individuals with SCH who are not seeking psychiatric treatment. We obtained structured psychiatric history (SADS-L) in 27 female volunteers who identified themselves to have risk factors for SCH, but were not currently being treated for psychiatric or endocrine disorders. They then underwent definitive thyroid evaluation by TRH infusion testing. All subjects had a normal FT_4I. Fifteen subjects were found to have SCH as defined by TSH (ultrasensitive) delta max >20, while 12 were completely euthyroid (ET). These groups were similar in terms of age, education and current mood ratings. SCH subjects had a higher lifetime prevalence of major depression (53%) than did ET subjects (17%)($p = .06$). Eleven of these subjects also received blinded neuropsychological testing. Subjects with SCH tended to perform more poorly than ET subjects on measures of verbal recall (WMS Immediate Logical Memory, $p = .08$), visuospatial recall (Rey-Ostereith Complex Figure Immediate Recall, $p = .09$), and attention (2&7 Test Error Rate, $p = .02$). These findings parallel data from clinical populations indicating that SCH may have important neuropsychiatric consequences.

NR546 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Quantitative MRI Findings in HIV-1 Infected Males

Elizabeth H. Aylward, Ph.D., Psychiatry, Johns Hopkins Hospital, 600 N. Wolfe St. Meyer 3-166, Baltimore, MD 21205; Julie McArthur, B.S.N., Justin McArthur, M.D., Brian Shi, Gerald Dalpan, M.D., Patrick E. Barta, M.D., Godfrey D. Pearlson, M.B.

Summary:

Results from three MRI studies with HIV-1-infected males will be presented: (A) Serial MRI scans were performed on 48 HIV-1 seropositive (SP) and 10 HIV-1 seronegative (SN) men with a mean inter-scan interval of 496 days. Planimetric brain measurements, including ventricle-to-brain ratio (VBR), bifrontal ratio (BFR) and bicaudate ratio (BCR) were obtained. Analysis revealed that SP and SN subjects did not differ on the MRI measures, but that longitudinal decreases in degree of immunosuppression (CD4 count) were significantly correlated with increases in BFR and BCR. (B) in order to determine whether the changes in BCR and BFR reflected caudate atrophy, volumetric measurement of the caudate, putamen, and globus pallidus was carried out on a subset of the SP subjects from Study A. Analysis revealed no significant correlation between these volumes and degree of immunosuppression. This suggests that the BCR and BFR may reflect changes elsewhere than basal ganglia (e.g., surrounding white matter). (C) Data exploring relationships between neuroanatomical and cognitive measures in demented SP's will be presented.

NR547 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Quantitative SPECT and MRI in Mild Huntington's Disease

Gordon J. Harris, Ph.D., Psychiatry, Johns Hopkins University, 600 N. Wolfe St. Meyer 3-166, Baltimore, MD 21205; Godfrey D. Pearlson, M.B., Elizabeth Aylward, Ph.D., Joy Roberts, B.S., Patrick E. Barta, M.D., Edwaldo E. Camargo, M.D., Susan E. Folstein, M.D.

Summary:

We examined 10 patients with mild Huntington's disease (HD), aged 43.9 ± 15.8 years (range 29-72) and nine controls, group-matched for sex and age. All subjects had MRI and [I-123] IMP SPECT scans. From MRI, caudate and putamen volumes, bicaudate ratios (BCR), and whole brain and CSF volumes were calculated. SPECT regional cerebral blood flow values of caudate, putamen and thalamus were calculated using matched MRI images as a guide to region placement.

On MRI, the region showing greatest atrophy was putamen, which had a 54.3% reduction in HD patients compared with controls ($p < 0.000001$). There have been no previous studies of putamen volumes in HD. By contrast, caudate volume was reduced only 28.1% ($p = 0.06$) and BCR was reduced 29.8% ($p = 0.001$). BCR difference and degree of overlap was consistent with prior CT studies. Caudate MRI measures had a significant degree of overlap, while putamen volume completely discriminated the groups.

SPECT findings differed from MRI; caudate showed the greatest reduction in perfusion ($p < 0.005$) compared with putamen ($p < 0.05$) and thalamus ($p > 0.30$).

Therefore, in mild HD, the putamen undergoes most severe atrophy, while the caudate suffers the largest decrease in regional blood flow.

NR548 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Trends of a Unique VA Consultation/Liaison Service

Samuel O. Okpaku, M.D., Psychiatry, Vanderbilt Univ, A2215 Medical Center North, Nashville, TN 37232; Peter Loosen, M.D., Norman Stephenson, Ph.D.

Summary:

The Veterans Administration (VA) Health Care Services represent a major component of the nation's health care services. The psychiatric departments of the VA medical centers provide a variety of services, including consultation-liaison services within general hospital settings.

Surprisingly, however, few studies have been carried out to explore the characteristics of the patients served and the types of services provided by these consultation-liaison services. In addition, there is a current controversy over the appropriateness for psychologists to prescribe for selected patients within the Department of Defense.

This paper will describe the characteristics of the patients referred to a unique consultation-liaison service consisting of two distinct units — a psychology consultation service and a psychiatric consultation service. Mental health consultations can be requested directly from either of these units. This paper will compare and contrast patients referred to these units. In addition, attention will be drawn to (a) the severity of the physical illness in these patients, (b) the presence of comorbidity in this population, (c) pertinent issues related to psychotropic management, and (d) education functions of the consultation-liaison service.

NR549 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Longitudinal Validity of DSM-III-R Alcohol Dependence

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Summary:

To our knowledge, no prospective studies have charted the longitudinal validity of the DSM-III-R diagnosis of alcohol dependence (AD) for a single subject group. Our purpose was to assess the predictive validity of this diagnosis. We re-interviewed subjects (N = 404) chosen at random from general hospital admission lists at baseline and again three years later, with a modified version of the original structured interview. Subjects were 51% male, 91% white, with an age range of 18 to 58 years at baseline. We assessed AD status using the DSM-III-R criteria as written and by using a more conservative construction of the criteria requiring positive evidence in three symptom domains: impaired control, social/physical problems and physiologic dependence.

AD prevalences were as follows (baseline, follow-up): DSM-III-R as written, 39.5% and 28.4%, DSM-III-R domains, 30.7% and 21.8%. Follow-up prevalence rates were 72% and 71% of baseline, respectively. However, there was considerable shift in AD diagnosed subjects: 21 (5% of N) non-AD subjects at baseline were AD at follow-up, while 57 (14% of N) AD subjects at baseline were non-AD at follow-up. Of baseline AD subjects failing to meet criteria at follow-up, only 2% (eight subjects) reported no alcohol problems in any of the three domains; the remaining 49 (12% of N) reported ongoing alcohol problems in at least one symptom domain. We conclude that prevalence figures vary over a three-year period, and that longer prospective assessment must be done before a clear pattern of predictive validity can be established for this diagnosis.

NR550 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Pain Disorders: A Proposed Classification for DSM-IV

Steven A. King, M.D., Psychiatry, Maine Medical Center, 22 Bramhall Street, Portland, ME 04102; James J. Strain, M.D.

Summary:

Pain is one of the problems most frequently encountered by health professionals. However, the DSM-III-R diagnosis that addresses this issue — Somatoform Pain Disorder — is rarely employed and its basic construct is problematic. It excludes the majority of cases of chronic pain where both psychological and organic factors are present; it fosters the questionable concept that "somatoform" or "psychogenic" pain is different from "organic" pain; and it fails to address the difficulties encountered in attempting to correlate the level of pain with physical findings.

The authors, who are coordinating the review of Somatoform Pain Disorder for DSM-IV, propose that this diagnosis be replaced by a new category — Pain Disorders — with the following five subgroups: (1) Pain Related to a Known Organic Factor; (2) Pain Related to Psychological Factors; (3) Pain Related to Another Mental Disorder; (4) Pain Related to both Organic and Psychological Factors; and (5) Pain Not Otherwise Specified.

This system is a rational move forward that is consistent with current conceptualizations of pain. It will enable psychiatrists to take a more active role in the evaluation and management of this problem. Case studies demonstrating the advantages of the proposed system will be presented.

NR551 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Subsyndromal Somatization and Hypochondriacal Worry

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Summary:

Existing research has approached the concept of somatization in two ways: as a history of medically unexplained symptoms, the extreme form of which is somatization disorder, and as hypochondriacal worry or belief that one has or is vulnerable to illness despite reassurances to the contrary. In this paper we show how family medicine patients identified by these two definitions differ from nonsomatizers in beliefs about their bodies, symptoms, and illness, and in their health care utilization over 12 months. Of 685 patients, 114 met Diagnostic Interview Schedule criteria for subsyndromal somatization disorder (SSI 4,6) and 95 displayed elevated levels of hypochondriacal worry. Twenty-four patients met criteria for both forms of somatization. Hypochondriasis was associated ($p < .001$) with increased bodily awareness, self-consciousness, emotional vulnerability, symptom preoccupation, pathological symptom attributions and a pessimistic cognitive style. In contrast, subsyndromal somatization disorder was not associated with elevated illness cognitions. Subjects with either high levels of medically unexplained symptoms or hypochondriacal worry reported more somatic symptoms on one-year follow-up. Hypochondriasis increased physician visits by two per year, while subsyndromal somatization disorder increased visits by four per year. In logistic regression models, medically unexplained symptoms increased the likelihood of talking to a doctor about emotional problems and using specialty mental health care over the following year. Hypochondriacal worry only increased the likelihood of talking to a doctor about emotional problems. No synergistic effects of combined subsyndromal somatization and hypochondriasis on symptomatology or utilization were observed.

NR552 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Quality of Life and Breast Cancer Surgery

Jean-Claude M. Lasry, Ph.D., Dept. of Psychiatry, Jewish Gen. Hosp., 4333 Cote St. Catherine, Montreal PQ, Canada H3T 1E2; Richard G. Margolese, M.D.

Summary:

Protocol B-06 of the National Surgical Adjuvant Breast Project (NSABP) compared three treatment procedures: total mastectomy (TM), lumpectomy (LP) and lumpectomy followed by breast radiation therapy (LPR). The five- and 10-year follow-up results revealed that disease-free survival and overall survival are the same for the three types of treatment (Fisher et al., 1985).

The objective of the present research is to compare the quality of life of patients who had undergone breast-conserving surgery (LP or LPR) with that of patients who had received a radical modified mastectomy (TM). The study accrued 227 breast cancer patients, randomly assigned to three treatment arms, and a benign biopsy control group of 63 patients. Results showed that breast-conserving surgery is related to a better body image but not to changes in self-esteem, depression or quality of life (Spitzer scale). An expected trade-off between breast conservation and greater fear of recurrence did not materialize. Surgery disrupts sexual functioning of breast cancer patients whatever the type of surgical intervention.

NR553 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Premorbid Psychopathology in Somatoform Pain Syndrome

Peter B. Polatin, M.D., Psychiatry, UTSW Med. Sch. Dallas, 6207 Lakehurst, Dallas, TX 75230; Regina K. Kinney, B.A., Robert J. Gatchel, Ph.D.

Summary:

Patients with chronic pain are clinically found to demonstrate high incidences of affective, anxiety, and substance abuse disorders. This has raised the question of causality: do certain psychopathologies predispose to chronic pain or vice versa? In this study we administered the SCID-I to 98 patients (65 males, 33 females) with chronic low back pain who met DSM-III-R criteria for somatoform pain disorder, to delineate pre-existing psychopathologies. Thirty-nine percent admitted to pre-existing substance abuse disorder (41% of the males, 33% of the females). Twenty-nine percent had had at least one episode of major depression prior to the onset of chronic pain (36% of the females, 25% of the males). Twenty-one percent had had pre-existing symptoms consistent with an anxiety disorder, primarily in the category of phobias (15%) and markedly more so in the female (36%) than the male (14%) group. These results suggest that substance abuse disorders are found in patients who later develop a somatoform pain disorder significantly above the base rate in the general population. Pre-existing major depression and anxiety disorders, while common in this group, do not significantly exceed the base rate.

NR554 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Type A Hypothesis: Identification of Toxic Complex

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Summary:

The determination of TABP's (Type A Behavior Pattern) prevalence, the definition of psychological risk profile and the analysis of "toxic" components of TABP in two samples (coronary versus control) were the principal goals of this study. The population ($n = 360$) was drawn from coronary care unit at the Hospital Clinico de Barcelona (coronary sample) and from Sandoz Laboratories (control sample). The psychological evaluation included Jenkins Activity Survey (JAS), Eysenck Personality Questionnaire (EPQ), Buss-Durkee Inventory (BDI) and Bortner Questionnaire (BQ).

There were significant differences among groups with regard to TABP's prevalence: 31.84% (coronary) versus 17.85% (control). Significant differences also were found among groups in relation to personality variables: high neuroticism and low extraversion (coronary), while control group was high in extraversion and low in neuroticism.

Comparison of mean scores between patients and controls suggested the existence of psychological risk profile described by hostility, (hostility, resentment), aggressiveness (attack, negativism), emotion (neuroticism, guilt), age, global type A, job involvement. Multivariant analysis indicated in the coronary group the existence of three principal components: the most important one was Hostility complex.

NR555 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Triazolam: Intermittent Administration

Anthony Kales, M.D., Psychiatry, Penn State University, 500 University Drive, Hershey, PA 17033; Rocco L. Manfredi, M.D., Alexandros Vgontzas, M.D., E. O. Bixler, Ph.D., Antonio Vela-Bueno, M.D., Kathy Tyson, B.S.

Summary:

The intermittent administration and withdrawal of triazolam 0.5 mg, temazepam 30 mg and placebo were assessed in a 12-night sleep laboratory study of 18 insomniac subjects. Six subjects were randomly assigned to each of three parallel groups. Each drug group was administered the respective drug on two occasions for periods ranging from one to four nights with each period followed by one to two withdrawal nights. Even though the drug administration periods were quite brief, withdrawal of triazolam consistently produced rebound insomnia, while with temazepam this effect was more variable. These results are consistent with previously reported findings of rebound insomnia in normal sleepers after only a single night's use of triazolam in the same dose. Thus, even under conditions of brief, intermittent use and withdrawal, triazolam consistently produces rebound insomnia following abrupt withdrawal, thereby reinforcing drug-taking behavior and increasing the potential for drug dependence. This finding, combined with the lack of significant efficacy for the currently recommended dose of triazolam (0.25 mg) and the now well-established profile (from controlled studies) for adverse reactions to triazolam (hyperexcitability states and amnesia/organic mental disorders), indicates that triazolam, at any dose, has a very narrow benefit-to-risk ratio. This information is of critical importance in physician education in the United States as regulatory action here has lagged, while worldwide there have been multiple drug regulatory agency actions against, and warnings about, triazolam's frequent and severe adverse reactions.

NR556 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Low Energy Emission Therapy Treatment for Insomnia

Milton K. Erman, M.D., Sleep Disorders, Scripps Clinic, 10666 N. Torrey Pines Road, La Jolla, CA 92037; Roza Hajdukovic, M.D., Boris Pasche, M.D., Alexandre Barbault, Merrill M. Mitler, Ph.D.

Summary:

We have reported on the efficacy of Low Energy Emission Therapy (LEET), a nonpharmacologic treatment utilizing intrabuccally emitted electromagnetic fields, in the treatment of persistent insomnia. In the present study, 60 subjects between the ages of 21 and 50 were studied using a repeated measures design. Subjective estimates of total sleep time and sleep latency were used for study entry criteria and to measure outcome. Subjects were assigned to active or placebo groups using a randomized double-blind design. Treatment with LEET was given three times per week for a four-week period.

In the active treatment group, reduction of subjective sleep latency was 51.9 minutes, versus a 0.2 minutes reduction for the control group ($t = 2.3; df = 58; p < 0.03$). Increase in subjective total sleep time was 122.7 minutes in the active group versus 28.4 minutes for the control group ($t = 2.9; df = 58; p < 0.005$). These data, along with previously reported findings demonstrating changes in EEG activity and psychological test measures in patients receiving active treatment with LEET, provide further support for the hypothesis that LEET has physiologic activity in man and is an effective treatment for psychophysiologic insomnia.

NR557 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Sleep Disturbances and Episodic Mental Symptoms

M. Eileen McNamara, M.D., Psychiatry, R.I. Hospital, 593 Eddy St. APC-608B, Providence, RI 02903; Richard P. Millman, M.D., Barry S. Fogel, M.D.

Summary:

Although temporal lobe epilepsy is quite often considered to

underlie nonspecific, episodic complaints such as mood swings, dizziness, agitation or atypical sensory symptoms, such "funny spells" may have a wide differential diagnosis. We reviewed the sleep architecture findings of 50 patients referred for 24-hour ambulatory cassette EEG for whom "funny spells" had led to a clinical suspicion of temporal lobe epilepsy. No patient was referred for a sleep disorder, and only one complained of a sleep-related symptom. Overall, 36% of the patients had a possible sleep abnormality suggested by A/EEG. These included sleep fragmentation in 22%, alpha intrusion sleep in 4%, hyposomnia of less than five hours in 4%, hypersomnia of greater than 10 hours in 6%. The 11 patients with sleep fragmentation were referred for polysomnography; five of these were studied. All five (10%), had a primary sleep disorder, including three with obstructive sleep apnea, one with nocturnal myoclonus, and one with sleep/wake cycle disturbance. These findings suggest that: (1) the evaluation of a patient who complains of nonspecific episodic symptoms should include a detailed sleep history, (2) sleep disorders should be considered in the differential diagnosis of "funny spells," and (3) A/EEG may be a useful diagnostic procedure for such patients.

NR558 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Sleep Abnormalities in Chronic Fatigue Syndrome

M. Eileen McNamara, M.D., Psychiatry, R.I. Hospital, 593 Eddy St. APC-608B, Providence, RI 02903; Steven Sepe, M.D., Richard P. Millman, M.D., John J. Campbell, M.D., Barry S. Fogel, M.D.

Summary:

Although fatigue and sleep alterations are cardinal symptoms of Chronic Fatigue Syndrome (CFS), the sleep architecture findings of CFS have not been systematically studied. The 24-hour sleep-wake patterns, as determined by ambulatory monitoring, of the first six patients serially referred for Holmes-criteria-defined CFS are described. None of these patients were referred for a sleep problem. Three of the six had evidence for a primary sleep disorder, later confirmed by polysomnography as obstructive sleep apnea, alpha intrusion sleep, and nocturnal myoclonus. The other three patients had abbreviated REM latency consistent with major depression. Two of these three were successfully treated with antidepressants, leading to resolution of their symptoms. This preliminary series suggests that heterogeneous patterns of primary and secondary sleep disturbance are associated with CFS.

NR559 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Sleep Apnea: Hypoxia and Neuropsychologic Deficits

Alexandros N. Vgontzas, M.D., Psychiatry, Penn State University, 500 University Drive, Hershey, PA 17033; Ralph A.W. Lehman, M.D., Edward O. Bixler, Ph.D., Lynne D. Curran, B.A., Raymond P. Zarlengo, M.D.

Summary:

There is some controversy as to whether the neuropsychological deficits demonstrated to occur with sleep apnea result from sleep disturbance, hypoxia or both. Twenty-five patients who had obstructive sleep apnea of sufficient severity to warrant recommendation for tracheostomy were assessed for severity of apnea and neuropsychological function immediately before and approximately six months after tracheostomy. At baseline, the total number of apnea-hypopnea events, minimum oxygen saturation, and maximum oxygen desaturation were significantly correlated with deficits of the Verbal IQ (VIQ), but not Performance IQ (PIQ), of the WAIS-R ($p<0.05$). In contrast, there was no correlation between sleep disturbance indices (total wake time, sleep stage 1) and VIQ, PIQ and Full Scale IQ (FSIQ). Further, there was a significant correlation between reduction in sleep disturbance (sleep stage 1) and the pre- to post-treatment change in PIQ ($p<0.05$), whereas there was no correlation between reduction of apnea or sleep disturbance and the pre- to post-treatment change in VIQ. These findings support that: 1) hypoxia, not sleep disturbance, is the primary causative factor of verbal/cognitive deficits associated with severe sleep apnea, 2) post-treatment improvement of apnea or sleep disturbance does not significantly affect impaired verbal/cognitive skills, and 3) sleep disturbance reduction correlates significantly with post-treatment improvement in performance skills, though the contribution of a practice effect could not be assessed.

NR560 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Therapeutic Alliance and Psychiatric Emergency Room

Ronald C. Rosenberg, M.D., Psychiatry, Kings County Hospital, 606 Winthrop Street, Brooklyn, NY 11203; Martin Kesselman, M.D.

Summary:

The authors discuss a method for assessing the therapeutic alliance at the time of evaluation in the psychiatric emergency room. Routine initial assessment of patient expectations improves the rapport between the clinician and the patient, facilitates data gathering, and directs treating clinicians towards important issues in patient management. Analysis of 159 consecutive cases reveals an important relationship between patient's expectations of benefit from hospitalization and past experiences of benefit from medication and verbal therapy and prior acknowledgement that one is ill. In addition, specific symptom experiences such as hallucinations, suicidal and homicidal ideation relate significantly to specific patterns of expectations, while no significant direct relation was found to more traditional measures, such as demographics, diagnostic groups, global assessment of functioning, and surprisingly, the circumstances of arrival.

NR561 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Measurements of Day Treatment Center Effectiveness

Mary Lou Edgington, RN.C., Psychiatry, VA Medical Center, 3200 Vine Street, Cincinnati, OH 45220; Eugene C. Somoza, M.D.

Summary:

The goal of this study was to determine the effectiveness of a day treatment center (DTC) on the evolution of the mental health of psychiatric patients. All patients for whom the DTC intake was between October 1, 1986 and December 1, 1988 were included in this study. This represented 25% of all the patients ever treated at this DTC. Effectiveness was measured by the number of emergency room visits and the number of hospitalizations. Of the 99 patients studied, 45 had more emergency room visits pre-DTC than post-DTC, whereas for 18 this was reversed. This was statistically significant to the $p<0.005$ level. There was no significant difference in the number of hospitalizations pre- and post-DTC. For the 50 geriatric patients (age >59) the DTC experience decreased the number of emergency room visits in a statistically significant manner ($p<0.01$). This was not the case for the younger group, which showed the same tendency, but did not reach statistical significance. Other independent variables that will be discussed are the psychiatric diagnosis and the number of people living with the patient.

NR562 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Effect of Crisis Intervention in Acute Psychiatry

Nageswara Rao Punukollu, M.B., Psychiatry, St. Lukes Hospital, Blackmoorfoot Rd Crosland Moor, Huddersfield, England.

Summary:

Huddersfield Crisis Intervention Team has been set up in one sector of a health district, covering one fourth of the population of the district. The work of the team has been and is being evaluated, comparing it with three other similar sectors where there are no crisis teams operating. Evaluation techniques used are GHQ-30, SCL-90-R, SBAS, and sociodemographic information forms. Analysis of the four sectors from February 1st, 1989 to January 31st, 1990, using chi square test for goodness of fit demonstrates significant reduction in the occupied bed days and average length of stay of patients in the sector covered by the crisis team, compared with the remaining three sectors. All four sectors are of similar population, with comparable socioeconomic situations. Further observations relating to this research will be discussed.

NR563 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Mental Health Service Use Among Homeless Veterans

Peggy Gallup, Ph.D., NEPEC, VA Medical Center, 950 Campbell Avenue, West Haven, CT 06516; Robert Rosenheck, M.D., Catherine Leda, M.S.N.

Summary:

Introduction/Methods: Previous studies have suggested that the homeless mentally ill have insufficient access to mental health services. In 1987 the VA established a 43-site outreach program for homeless chronically mentally ill veterans. This study used structured clinical assessment and psychiatric service utilization data on 2,981 homeless veterans to identify determinants of mental health service use. *Results:* Altogether, 34% had at least one psychiatric outpatient visit during the six months prior to assessment (mean = 9.2 visits) and 31.8% had a psychiatric hospitalization. Multivariate analysis showed mental health service utilization was positively associated with severity of psychiatric symptomatology, educational level, and VA financial support. Mental health service use was negatively associated with having spent more time living in the street or in shelters, being black, and age. No association was noted with substance abuse or past involvement in the criminal justice system. *Conclusions:* Although based on a clinical sample, these results are consistent with those from a community study of the homeless (Padget, et al., 1990). Veterans with more severe psychiatric symptomatology are more likely to obtain mental health services. The most destitute of these veterans appear to be either less motivated to seek help or to face greater barriers in accessing services. Regardless of the explanation, these data support the importance of aggressive community outreach in providing mental health services to the homeless mentally ill.

NR564 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Gender and Homeless Mentally Ill

Paula N. Goering, Ph.D., Psychiatry, Clarke Institute of Psych, 250 College Street, Ste 737, Toronto Ontario, Canada M5T1R8; Donald Wasylenki, M.D., Myreille St. Onge, M.Sc., Darianna Paduchak, B.A., William Lancee, M.Sc.

Summary:

Empirical evidence is scant about possible gender differences in the service needs of the homeless mentally ill. The Hostel Outreach Program has case managers linked to male and female shelters in Toronto. This report will draw on information from a longitudinal evaluation to compare the characteristics and course of male and female clients.

A comprehensive baseline assessment utilizing standardized instruments, interviews with clients and case managers and record reviews had been repeated nine months after program entry for 35 men and 24 women. Both sexes are socially disadvantaged with similar histories of chronic homelessness, psychotic illness and psychiatric treatment. At baseline, total and subscale BPRS scores did not differ. Interpersonal skills measured with the S.L.O.F. were lower for the men, who had even smaller social networks (X = 2.5) than the women (X = 3.9), with fewer supportive, close relationships and worse housing conditions. At the nine-month follow-up, residential stability, symptoms, social functioning and social networks had improved for both sexes and gender differences were attenuated.

In this sample of severely ill clients there are more similarities than differences in service needs of men and women. The women's slight advantage with regard to social skills and resources may be related to better conditions in their shelter system with smaller, more supportive hostels. Both groups have responded positively to assertive case management.

NR565 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Use of Nationwide Registers in Predicting Admission After Childbirth

Marianne C. Kastrup, M.D., Psychiatric, Hvidovre Hospital, Brondbyosterve 160, Hvidovre 02650, Denmark.

Summary:

A nationwide study links the Danish National Psychiatric Case Register and the Danish National Birth Register using the identification number of the mother as linkage. The study includes all women who gave birth to a child during the period January 1, 1973 to December 31, 1983 and who were admitted to a psychiatric institution two years before to two years after the childbirth. The data are on 6,671 women with 10,291 childbirths and 26,235 psychiatric admissions. All information about the study population available in the registers is included in the study.

To identify factors of predictive value for later admission, a multiple contingency analysis is undertaken with the event "psychiatric admission during the first 30 days after childbirth" as outcome variable. Independent variables are available in both registers at the time of the childbirth. An analysis of these variables independently shows several significantly related to the outcome variable, and an analysis of two and three factor associations shows a number of variables conditioned by one or two other variables, leaving "age of mother" and "previous childbirth" as the significant variables. Similar analyses are now being undertaken using other time intervals.

NR566 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Homeless Suburban State Hospital Admissions

Miklos F. Losonczy, M.D., Pilgrim Psych. Center, Box A, Brentwood, NY 11717; Martin Darcy, M.S.W., Douglas Carbonara, Ph.D.

Summary:

Homelessness among the chronic mentally ill population is known to be a problem in urban areas, but its magnitude in affluent suburban settings has received little study. Sixty-nine consecutive admissions to a 2,000-bed chronic-care, state facility serving Nassau County, N.Y., were examined. Nineteen (27%) of these individuals were homeless (H) at the time of admission. Comparison of the homeless with the nonhomeless (NH) admissions showed no significant group differences in age, sex, education level, marital

status, ethnic origin, number of previous admissions, legal status or primary psychiatric diagnosis. Eighty-four percent of the H had a primary DSM-III-R diagnosis of schizophrenia, while 68% of the NH met criteria; 32% of the H versus 18% of the NH also had a secondary substance abuse diagnosis. The only significant group differences reflected the higher rate of the homeless population leaving the facility prematurely. Six of the 19 H have left AMA within two months of the present admission, and none by regular discharge; while four of the 50 nonhomeless left AMA, and 26 by regular discharge (chi square 18.2, $p < .01$). Eleven of the 16 homeless subjects with previous admissions to our facility left against medical advice (AMA) on the previous admission, compared with eight of the 31 nonhomeless on their previous admissions (chi square 8.1, p.005). In summary, the homeless population is predominantly schizophrenic, with a high rate of secondary substance abuse and a clearly increased likelihood of leaving prematurely. Current clinical practice may need to be reexamined to have an impact on homelessness of chronic psychiatric patients.

NR567 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Deinstitutionalization by Law: Psychiatric Patients in Italy Before and After the Psychiatric Reform Act

Carlo A. Altamura, M.D., Psychiatry, University of Milan, Via F. SFORZA 35, Milano 20122, Italy; Gianluigi Tacchini, M.D., Santina Maggi, M.D., Anna M. Moroni, Ph.D., Antonio Musazzi, M.D.

Summary:

In 1978 Law 180 forced the deinstitutionalization process that already was taking place: new admissions to mental hospitals were blocked, residential facilities, outpatient units, and psychiatric wards inside general hospitals were to be built where they did not exist. Change was quite sudden and unprepared, and literature indicates great dishomogeneity in implementation of community services both at national and regional levels. Our work tracks the route of the patients through the various services, with particular regard to psychiatric ward admissions and contacts with outpatient and first aid units at the University of Milan, which comprises the whole set of services and a law-defined catchment area of about 420,000 population.

Two full consecutive years before the law ('76-'77) and two after it ('82-'83) were analyzed for a total 4,806 cases. Data showed that diagnoses shifted towards the more chronic and severe conditions, new chronicity developed inside the community against the theoretical issues of the Reform Act, lengths of instay increased by four times on average, short-term readmissions are frequent (12% of all admissions), neurotic conditions are seldom seen in outpatients services (4% of all patients), and a new form of community segregation developed inside the services.

NR568 Wednesday May 15, 3:00 p.m.-5:00 p.m.

DSM-III-R Disorders in Vietnamese Refugees

Joseph Chen, M.D., Psychiatry, UC San Francisco, 521 Parnassus Ave Ste C-126, San Francisco, CA 94143; Walter Hinton, M.D., Nang Du, M.D., Carolee G. Tran, B.A., Francis Lu, M.D., Jeanne Miranda, Ph.D.

Summary:

Though surveys show high levels of depression and anxiety in Vietnamese refugees, there are no community surveys of the prevalence of psychiatric disorders. *Objectives:* To determine the prevalence and predictors of DSM-III-R psychiatric disorders in newly arrived Vietnamese refugees. *Method:* Vietnamese refugees aged 18 to 65 undergoing mandatory health screening at a large public hospital were consecutively interviewed by a native Vietnamese-speaking psychiatrist using a written Vietnamese translation of the SCID (Structured Clinical Interview for DSM-III-R). *Results:* We interviewed 211 of 233 eligible subjects (90% recruitment rate). Overall, 20% had one or more DSM-III-R disorders. Prevalence of specific disorders was: adjustment disorder (11.8%), major depression (5.7%), dysthymic disorder (3.8%), post-traumatic stress disorder (3.3%), generalized anxiety disorder (3.3%), and psychosis (1%). After adjusting for age, gender, marital status, and ethnicity, refugees who recalled specific traumatic events, refugees who were veterans and/or "reeducation camp" survivors, and refugees who migrated alone to the U.S. were significantly (p.05) more likely to have a psychiatric disorder. *Conclusions:* DSM-III-R disorders are common in newly arrived Vietnamese refugees. These results highlight the importance of traumatic events as independent predictors of psychiatric disorder in this population.

NR569 Wednesday May 15, 3:00 p.m.-5:00 p.m.

Medical Student's Attitudes on Public Psychiatry

Anthony L. Pelonero, M.D., Psychiatry, Medical College of VA, Box 710 MCV Station, Richmond, VA 23298; William T. Ferriss, M.S.W.

Summary:

Few studies have examined factors involved in choosing public psychiatry as a career. To expose medical students to public psychiatry and destigmatize their attitudes towards state hospitals, third-year medical students on psychiatry clerkships were assigned a day at a nearby state mental hospital. From January 1988 to January 1990, attitudes were measured before and after visiting. Topics surveyed included: career interest in psychiatry, public hospital practice, level of state hospital care, patients' response to treatment, state hospital employees' attitudes, state hospital professionals' level of training, and rating of physical facilities.

Results and Discussion: 188 students yielded 179 usable survey pairs. The study group was 65% male, 35% female, 88% white, 3% black, 9% other. Mean age was 26 years, (range 21-40). Using multivariate analysis of variance, there was a strong and significant effect on responses as measured by pre- and post-visit surveys ($F = 48.54$, $p > .0001$). Students reported more favorable views after the visit. A state hospital experience for trainees in psychiatry may be a critical factor in choosing public psychiatry as a career. Since attitudes towards psychiatry continue to develop during clerkships, students should be afforded broad exposure to career options in psychiatry, including the state mental hospital.

NR570 Thursday May 16, 9:00 a.m.-10:30 a.m.

Non-REM Sleep in Depression Studied With PET

Monte S. Buchsbaum, M.D., Psychiatry, Univ of Calif. Irvine, Dept. of Psych UC Irvine, Irvine, CA 92717; Andrew P. Ho, B.S., Christian J. Gillin, M.D., Joseph Wu, M.D., Stephen Lottenberg, M.D., William E. Bunney, M.D.

Educational Objectives:

To present information on methods and clinical applications of positron emission tomography in depression.

Summary:

Using 18-F-2-deoxyglucose (FDG) positron emission tomography (PET), we studied 10 male, unmedicated, unipolar depressed subjects (age 34.4 ± 9.6, mean Hamilton 25 ± 9.33) and 12 normal subjects (age 25.9 ± 7.8) during the first nighttime non-rapid eye movement sleep (NREM) period. Patients received 5 mCi FDG five minutes after onset of NREM sleep and were awakened and moved to the scanner 35 minutes after injection of FDG.

Patients with depression had higher whole brain metabolic rates (16.7 ± 6.8) than normals (11.6 ± 3.0). Relative metabolic rate was significantly lower in the left middle frontal gyrus (1.09 ± 0.05)

of the patients than in controls (1.14 ± 0.02), a finding we previously observed in a separate group of waking patients and controls. Glucose metabolic rate during NREM sleep was found to be negatively correlated with the percentage of stages 3 and 4 sleep during the uptake period ($r = 0.52$, $p = 0.014$), but patients and controls did not differ in the percentage of stages 3 and 4 during uptake period. These data are consistent with the hypothesis that depressed patients are hyperaroused (higher absolute metabolic rate), but also suggest that the hypofrontality found in waking patients is also present in an apparently inattentive state.

References:

1. Buchsbaum MS, Gillin JC, Wu J, et al: Regional cerebral glucose metabolic rate in human sleep assessed by positron emission tomography. *Life Sciences* 45:1349-1356, 1989.
2. Buchsbaum MS, Wu J, DeLisi LE, et al: Frontal cortex and basal ganglia metabolic rates assessed by positron emission tomography with 18-F-2-deoxyglucose in affective illness. *J of Aff Dis* 10:137-152,1986.

NR571 Thursday May 16, 9:00 a.m.-10:30 a.m.

Opiate Receptors in Depression Measured with PET

Helen S. Mayberg, Radiology, Johns Hopkins Hospital, 600 N. Wolfe St. Nelson B1-130, Baltimore, MD 21205; Robert F. Dannals, M.D., Chris A. Ross, M.D., Alan A. Wilson, Ph.D., Hayden T. Havert, Ph.D., J. James Frost, M.D.

Educational Objectives:

To present our recent PET scan data implicating disturbances of brain opioid systems in patients with depression.

Summary:

The opioid peptides have long been implicated in the regulation of mood. Pharmacological studies and CSF measurements of endogenous opioids in depression have been reported, including a recent autoradiographic demonstration of increased mu opiate receptors in depressed patients committing suicide (1). Accordingly, mu opiate receptor binding was measured in eight patients with major depression (DSM-III criteria) refractory to pharmacological therapy, and eight age-comparable nondepressed volunteers using C-11 carfentanil (CFN) and positron emission tomography (PET).

Regional mu opiate receptor binding was measured using a single dose of CFN (20 mCi, specific activity >2500 Ci/mmole) following x-ray CT localization of an imaging plane parallel to the glabellar-inion line passing through the caudate, thalamus, cingulate, prefrontal and occipital cortex. Temporal cortex, motor-sensory and parietal cortex were sampled on adjacent planes. The relative binding potential (Bmax/Kd) was estimated for each region using the (region-occipital)/occipital ratio (2).

Mu opiate receptor binding was significantly increased in all limbic-associated regions in the depressed patients compared with the nondepressed controls ($F(1,14) = 7.94$, $p = 0.015$): prefrontal cortex (35%), temporal cortex (33%), cingulate (20%) and caudate (25%). Binding did not differ between patients and controls in thalamus, pre-motor, motor-sensory or parietal cortex. These increases are consistent with a primary increase in opiate receptor number or affinity, or a response to low endogenous opioid levels in patients with severe depression. Future correlations of regional opiate receptor binding with quantitative psychiatric disease parameters may help to further elucidate the role of the opiate system in depression.

References:

1. Biegon A, Gross-Isserof R: Quantitative autoradiography of opiate receptors in brains of suicide victims. *Soc Neurosci Abstr* 16(1):801, 1990.
2. Frost JJ, Douglass KH, Mayberg HS et al: Multicompartmental analysis of 11C-carfentanil binding to opiate receptors in humans measured by PET. *J Cereb Blood FLow Metab,* 9:398-409, 1989.

NR572 Thursday May 16, 9:00 a.m.-10:30 a.m.

G Proteins in Postmortem Brain in Bipolar Disorder

L. Trevor Young, M.D., Biochem. Psychiatry, Clarke Int. of Psych, 250 College Street, Toronto Ont., Canada, M5T 1R8; Peter P. Li, Ph.D., Stephen J. Kish, P.D., Jerry J. Warsh, M.D.

Educational Objectives:

To help the learner become more knowledgeable regarding membrane protein and receptor functions in brain in bipolar affective disorder. In addition, the learner will be introduced to new ideas about the potential mechanism of action of antimanic agents.

Summary:

Evidence implicating postreceptor disturbances in affective disorders, including bipolar affective disorder (BAD), together with the recent observations that lithium acts on the coupling of neuroreceptors to effector responses at the guanine nucleotide binding (G)-binding level, suggest that abnormalities in G-protein function may occur in BAD. The concentrations of G-protein subunits were estimated in membranes prepared from postmortem pre-frontal cortex (Brodman's area 10) using SDS-PAGE and immunoblotting with specific polyclonal antisera against specific G-protein subunits: G_{sa}, G_{ia}, G_{oa} and G_{β}. Mean frontal cortical G_{sa} subunit (52 kDa species) levels were significantly elevated (34%) in seven subjects who had been diagnosed with BAD (confirmed by chart review) as compared with seven age- and sex-matched controls. In contrast, no significant differences were found in the other G-protein subunits measured. Significantly increased mean G_sa immunoreactivity was also found in occipital cortex (more than 80%) but not in cerebellum (22%) obtained from the same subjects. As increased G-protein a subunit concentrations may enhance functional responses to receptor activation, these findings implicate disturbances in stimulatory G-protein mediated signal transduction in the pathophysiology of BAD.

References:

1. Avissar S, Schreiber G, Danon A, Belmaker RH: Lithium inhibits adrenergic and cholinergic increases in GTP binding in rat cortex. *Nature* 331:440-442, 1988.
2. Birnbaumer I, Abramowitz J, Brown AM: Receptor-effector coupling by G proteins. *Biochem. Biophys. Acta* 1031:163-224, 1990.

NR573 Thursday May 16, 9:00 a.m.-10:30 a.m.

Treatment of Hypertriglyceridemia and Depression

Robert L. Kunkel, M.D., Psychiatry, Jewish Hospital, 3200 Burnet Avenue, Cincinnati, OH 45229; Murray Tieger, Ph.D., Charles J. Glueck, M.D., Trent Tracy, P.A., James Speirs, B.A., Patricia Stricker, R.D.

Educational Objectives:

To evaluate the nature of a reversible causal relationship between very high plasma triglycerides and depression.

Summary:

In 15 men and 10 women with severe primary/familial hypertriglyceridemia (HTG), our specific aim in a 54-week single-blind treatment (Rx) period was to determine whether triglyceride (TG) lowering with Type V diet and gemfibrozil (Lopid) (1.2 g) would be accompanied by amelioration of depression and improved cognition, as tested by Beck, (BDI), Hassles (HAS) and HAS intensity indices, locus of control index, and the Folstein Mini-Mental status (FMM) test. After baseline, Rx was given for 54 weeks; no psychoactive drugs or counseling were given. At nine visits every six weeks, lipids were measured, plasminogen activator inhibitor (PAI), serum viscosity, PO_2, and serum fibrinogen were measured at alternate visits. At all nine visits, compared with baseline, median TG fell (230-302 mg/dl, $p \leq .001$), and median HDLC rose (4-7 mg/dl,

$p \leq .03$); medial cholesterol fell (34-55 mg/dl, $p \leq .05$) at seven of nine visits. BDI fell at eight of nine visits ($p = .06$ to $p = .0003$), from a median score of 7 at baseline to 2 at 54 weeks Rx ($p \leq .01$), a major reduction in depression. The median HAS score fell from 15 at baseline to 10 at 54 weeks Rx, $p \leq .05$. Mean FMM rose on Rx, but not significantly, $p < 0.1$. In the 12 points with baseline TG > 500, TG correlated with both BDI and HAS. By stepwise regression, from 45% to 86% of the percent of fall in HAS could be accounted for independently by the percent of fall in TG, $p = .017$ to $p = .0001$. In the 12 points with TG > 500, serum viscosity fell on Rx (9% to 15%, $p \leq .05$ to $p \leq .10$). We speculate that there may be reversible causal relationship between high TG and depression, possibly by correction of metabolic defects such as high serum viscosity which reduce cerebral oxygenation.

References:

1. Fallat RW, Glueck CJ: Familial and acquired Type V Hyperlipoproteinemia. *Atherosclerosis* 23:41-62, 1976.
2. Robertson HT, et al: Red cell oxygen affinity in severe hypertriglyceridemia. *Proc Soc Exp Biol Med* 159:437-440, 1978.

NR574 Thursday May 16, 9:00 a.m.-10:30 a.m.

Disorientation and Bilateral Suprathreshold-Dose ECT Treatment

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Educational Objectives:

To describe how factors that contribute to disorientation after ECT may be ameliorated under lower doses of energy, that it is probably the stimulus variables rather than the drugs given in association with ECT that cause disorientation, and that age, IQ, and psychotic symptoms affect disorientation and should be taken into account in treatment of depression.

Summary:

Thirty-seven major depressive inpatients were assessed for disorientation after eight out of 12 moderately-suprathreshold-dose ECT treatments they received. Twenty of these patients were also assessed after simulated ECT (including anaesthesia, muscle relaxant and atropine only) on four out of eight assessments. Post-ictal disorientation was assessed immediately after each treatment. Inter-ictal disorientation was assessed two to three days after treatment. Real, but not simulated, ECT produced post-ictal disorientation. Post-ictal disorientation decreased from the first to the second treatment, but did not change from the third to the last assessment. Post-ictal disorientation time was shortest for *person*, longer for *place* and longest for *time*, and showed a temporal time gradient. Inter-ictal disorientation increased linearly over treatments and two stimulus variables, seizure length and electrical stimulus strength, correlated with post-ictal disorientation. Partial correlations were calculated showing that these two influences were independent of each other. Seizure duration and stimulus strength were independent of the background variables of age, IQ, and psychotic symptomology, which affected the length of post-ictal disorientation.

References:

1. Daniel WF, Crovitz HF, Weiner, RD. Neuropsychological aspects of disorientation. *Cortex*, 23: 169-187, 1987.
2. Sackheim HA, Portnoy S, Neeley P, Steif BL, Decina P, Malitz S. Cognitive consequences of low dosage ECT. *Annual NY Academy of Sciences*, 462: 326-340, 1986.

NR575 Thursday May 16, 9:00 a.m.-10:30 a.m.

A New Flexible Method to Target Tricyclic Doses

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Educational Objectives:

To help participants 1) describe how a Bayesian pharmacokinetic model can be used to predict maintenance dose requirements; 2) discuss its role in tricyclic therapy; and 3) appreciate the limitations of this and other prospective dosing techniques.

Summary:

Existing methods to predict tricyclic antidepressant (TCA) maintenance doses are limited by requiring standard test doses and timed serum sampling. We prospectively tested a new pharmacokinetic model that allows flexible dosing and sampling to determine maintenance requirements in patients receiving TCAs.

Thirty-two patients entered the study. Drug levels were measured three days after starting TCA therapy. These were analyzed using a Bayesian pharmacokinetic model to determine drug clearance and volume of distribution. This information was then used to predict the serum concentration expected from a maintenance dose chosen by the psychiatrist. In phase I ($n = 17$), patients received imipramine without specific test doses. In phase II ($n = 15$), patients received either amitriptyline, imipramine, desipramine, doxepin or nortriptyline (50-75mg on day 1, 75-100mg on day 2). Accuracy of the predictions was then compared between the two phases.

The mean prediction errors (model bias) in phases I and II were -15.5 ± 27.3 and -12.3 ± 21.8 ng/mL and were not different ($p > 0.05$). The absolute prediction errors (model precision) were 18.5 ± 25.1 and 18.8 ± 16.0 ng/mL and were not different ($p > 0.05$). Predicted and observed serum concentrations were significantly correlated ($r = 0.932$, $p < 0.001$). Two slow metabolizers were identified (clearance < 0.1L/kg/hr).

This new method allows determination of maintenance dose requirements early in therapy without standard test doses or timed sampling. An additional benefit is early identification of slow metabolizers, preventing potential drug toxicity.

References:

1. Fernandez M, et al: Prediction of imipramine serum levels in enuretic children by a Bayesian method: comparison with two other conventional dosing methods. *Ther Drug Monitor* 11:637-41, 1989.
2. Preskorn SH: Tricyclic antidepressants: the hows and whys of therapeutic drug monitoring. *J Clin Psychiatry* 50 (7 suppl):34-42, 1989.

NR576 Thursday May 16, 9:00 a.m.-10:30 a.m.

No Association Between DRD2 Allele and Alcoholism

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Educational Objectives:

To present data showing no association between an allele at DRD2 D2 dopamine receptor and alcoholism, and to discuss some of the pitfalls of genetic analysis.

Summary:

We attempted to replicate a previously claimed positive allelic association between the A1 allele of DRD2 $D_2SSB_32_2ESB_3$ dopamine receptor and alcoholism (Blum et al., 1990). Our subjects were 43 unrelated individuals, diagnosed by the SCID interview, with alcohol dependence by DSM-III-R. There were no opiate abusers; none met current criteria for cocaine dependence. Controls were not screen psychiatrically and, therefore, presumably included

alcoholics at about the population prevalence. We studied the TaqI system at DRD2 previously described by Grandy et al. (1989) (Am J Hum Genet 45:779-785), as recognized by a 1.7 kb subclone of ^{9}hD2G1 (A1 allele, 6.6 kb band; A2 allele, 3.7 kb).

We found no differences in allele frequencies at locus DRD2 between alcoholics and controls. The allele frequencies in both groups agreed closely with those observed in previously described control populations.

The results are as follows:

		Number			Frequency	
	N	A1A1	A1A2	A2A2	A1	A2
Controls:	65	2	20	43	0.18	0.82
Alcoholics:	43	1	17	25	0.22	0.78
					(Chi square 0.10, not significant)	

Thus, we were not able to replicate the results of Blum et al. (1990); our results agree with those of Bolos et al. (1990). We conclude that our data do not support an allelic association between the A1 allele at DRD2 and alcoholism.

References:

1. Blum K, Noble EP, Sheridan PJ, et al: Allelic association of human dopamine D_2 receptor gene in alcoholism. *JAMA* 263:2055-2060, 1990.
2. Bolos AM, Dean M, Lucas-Derse S, et al: Population and pedigree studies reveal a lack of association between the dopamine D_2 receptor gene and alcoholism. *JAMA* 264:3156-3160, 1990.

NR577 Thursday May 16, 9:00 a.m.-10:30 a.m.

Phenotypic Markers In Familial Alcoholism

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Educational Objectives:

To describe the segregation, in families with multigenerational alcoholism, of four phenotypic markers suggested by others to discriminate sons of alcoholics from the age-matched control males, and to outline the utility of these markers as an adjunct to linkage analysis.

Summary:

In families with multigenerational alcoholism, phenotypic abnormalities that hypothetically predict risk for subsequent alcohol abuse are shared by active alcoholics, abstinent alcoholics and nonalcoholic offspring of alcoholic fathers. We have examined the segregation of four of these indices in 15 nuclear families derived from multigenerational kindreds. Exaggerated response of lymphocyte adenylate cyclase to adenosine or other agonist challenge is present in 70% of multigenerational alcoholics (n = 40) and in fewer than 10% of controls (n = 56). Segregation is consistent with an autosomal dominant gene. The presence or absence of a specific Msp I cleavage site in the X-linked monoamine oxidase A gene is highly correlated with platelet MAO activity, but does not discriminate persons with presumed susceptibility alleles from the general population. Low basal plasma endorphin characterizes about 50% of multigenerational alcoholics and 25%-30% of high-risk persons (n = 48). Cardiovascular hyperreactivity to an ethanol challenge is typical of 40%-50% of abstinent multigenerational alcoholics and 50%-60% of the offspring (n = 72) of these hyperreactive persons. Family studies suggest that phenotypic markers may be more highly penetrant than the disease phenotype and thus may be valuable for future study of segregation and linkage of specific susceptibility genes.

References:

Crabb DW. Biological markers for increased risk of alcoholism and for quantitation of alcohol consumption. *J. Clin. Invest.* 85:311-315, 1990.

NR578 Thursday May 16, 9:00 a.m.-10:30 a.m.

Imipramine Treatment of Depressed Alcoholics

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Educational Objectives:

The objectives are: to show that primary depression can be diagnosed in active alcoholics; to show that imipramine treatment can relieve this depression and aid in control of drinking.

Summary:

A variety of studies have shown that the comorbidity of depressive and anxiety disorders with alcoholism is quite high and may predict a poorer outcome with standard treatment. Identifying the minority (10-15%) of alcoholic patients with clear primary mood or anxiety disorders by using lifetime psychiatric history and then targeting these for specific pharmacologic intervention is a strategy that has not yet been tested in systematic trials.

We report on the first 45 patients of a planned sample of 80 who completed a 12-week double-blind trial of imipramine and placebo while receiving standard psychosocial treatment. Of these, 64% treated with imipramine had remission of their depressive disorder and significant reductions in alcohol consumption, while only 20% had this outcome with placebo ($X^2 = 8.7$, $p < .003$). This provides strong evidence that primary depression can be identified in the context of active alcoholism and that treating this with antidepressant medication substantially improves outcome, at least in the short term.

References:

1. Ciraulo DA, Jaffe JH: Tricyclic antidepressants in the treatment of depression associated with alcoholism. J. *Clin. Psychopharm.* 1:145-150, 1981.
2. Liskow BI, Goodwin DW: Pharmacologic treatment of alcohol intoxication withdrawal and dependence: a critical review. *J. Stud. Alcohol.* 48:356-370, 1987.

NR579 Thursday May 16, 9:00 a.m.-10:30 a.m.

Buprenorphine in Heroin Dependence Treatment

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Educational Objectives:

To present status of buprenorphine in opioid dependence treatment and the outcome of a controlled clinical trial in heroin addicts who are unwilling to accept methadone maintenance or enter a residential therapeutic community and, consequently, are outside the healthcare system.

Summary:

A controlled trial of buprenorphine, a partial mu-receptor agonist with low dependence liability and toxicity, indicates 1.5-8.0 mg/day is acceptable and highly efficacious in reducing heroin craving and use for many heroin addicts who remain outside the current healthcare system. Heroin dependent subjects (SS) unwilling to enter methadone maintenance or a therapeutic community, were main-

tained for 12 weeks, after being assessed, single-blind, for the lowest daily sublingual dose (8.0 mg max) that blocked heroin craving. Urine drug screens were done every two weeks to confirm abstinence. Abstinent SS were randomly assigned, double-blind, to receive: 1) dose reductions for five weeks to zero dose, then placebo for two weeks; or 2) the same dose for seven weeks. Baseline and weekly ratings were made of heroin craving and abstinence symptoms. SS were terminated for increased craving/symptoms or if heroin was used. Those who completed the trial had no increase in craving or symptoms and did not use heroin. Twenty-eight of 35 SS were abstinent and entered the discontinuation trial [mostly male, married and employed. Means (ranges): age 36 years (28-48); years addicted = 10.6 (3-31); heroin/day = $71.5 ($20-150)]. Outcome shows a highly significant difference between 13 SS who received dose reductions; [12 terminated; one completed] and 15 SS who received no dose reductions; [two terminated; 13 completed] (Chi Square = 8.98; $p < .005$). The findings have important public health implications in reducing the spread of AIDS by intravenous heroin users.

References:

1. Mello NI, Mendelson JH: Buprenorphine supresses heroin use by heroin addicts. *Science* 207:657-659, 1980.
2. Bickel WK, Stitzer ML, Bigelow GE, et al: A clinical trial of buprenorphine: comparison with methadone in the detoxification of heroin addicts. *Clinical Pharmacology and Therapeutics* 43(1):72-78, 1988.

NR580 Thursday May 16, 9:00 a.m.-10:30 a.m.

Phenelzine Versus Haloperidol in Borderline Personality

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Educational Objectives:

1. To describe the pharmacologic response of BPD patients to phenelzine, haloperidol, and placebo; 2. To review the pharmacologic response of BPD patients to other medications.

Summary:

We report the first double-blind, placebo-controlled comparison of a neuroleptic (haloperidol up to 4 mg) with an MAOI antidepressant (phenelzine up to 60 mg) in 108 randomly assigned borderline inpatients defined by DIB and DSM-III-R criteria. Medication trials lasted five weeks with weekly self and observer ratings and plasma drug level determinations. Significant improvement (paired t tests) occurred within all three groups over time on measures of depression, hysteroid dysphoria, borderline psychopathology, global symptom severity, anxiety, impulsivity, and schizotypal symptoms, thus demonstrating a prominent placebo effect. Significant within-group improvement occurred with phenelzine and haloperidol but not placebo in treating hostility, and with phenelzine and placebo but not haloperidol in treating atypical depression. Three way comparisons (ANCOVA) indicated superior efficacy for phenelzine, followed by placebo and then haloperidol on measures of depression, and for phenelzine followed by haloperidol and then placebo in treating hostility. Pairwise comparisons revealed significant efficacy for phenelzine vs. placebo against hostility, but not against atypical depression or hysteroid dysphoria. Surprisingly, pairwise comparisons demonstrated no therapeutic superiority for haloperidol on any measure when compared with either placebo or phenelzine, and haloperidol was significantly worse than placebo in treating depression.

References:

1. Soloff PH, George AW, Nathan RS, et al.: Progress in pharmacotherapy of borderline patients. *Arch Gen Psychiatry* 43:691-697, 1986.
2. Parsons B, Quitkin EM, McGrath PJ, et al.: Phenelzine, imipramine, and placebo in borderline patients meeting criteria for atypical depression *Psychopharmacol Bull* 25:524-534, 1989.

NR581 Thursday May 16, 9:00 a.m.-10:30 a.m.

Tryptophan Depletion Alters Feeding in Bulimia

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Educational Objectives:

To present data on the effects of acute tryptophan depletion in patients with bulimia nervosa compared to controls; this will include effects on feeding, mood and serum ratios of tryptophan to other large neutral amino acids. To discuss the significance of these results relative to our knowledge of serotonin activity.

Summary:

Several lines of evidence suggest that binge behavior and mood disturbances in bulimia nervosa patients may be related to altered serotonin activity. For example, a reduction in serotonin activity would reduce satiety and increase bingeing behavior. To test this hypothesis, we employed a new paradigm of acute tryptophan (TRP) depletion (Delgado et al., 1990). On one day, the plasma ratio of TRP, the precursor of serotonin, to other large neutral amino acids (LNAA) was reduced by having subjects ingest a mixture of LNAA *without* TRP (active day). This was contrasted with a day in which subjects ingest all LNAA *including* TRP (placebo day). Mood and feeding behavior was assessed by a double-blind design in six bulimia nervosa subjects and three matched control women.

The effect of TRP depletion on calorie consumption was determined by calculating the ratio of calories consumed on the TRP depletion day (active day) to the placebo day. On the TRP depletion day, bulimic women consumed 40% *more*, whereas control women consumed 28% *less* than their caloric intake on the placebo day. This effect of TRP depletion on caloric consumption was significantly different between bulimics and controls (Mann-Whitney $U \leq 15.0$, $p \leq .03$). Interestingly, the increase of caloric intake in bulimic women was divided equally across all macronutrients. We also found that bulimic women had a significant increase in depression and anxiety on the TRP depletion day compared with the placebo day, whereas control women showed no significant change in mood. Preliminary data show that the plasma TRP/LNAA ratio decreased by >90% on the TRP deficient day but also by 60%-65% on the TRP supplemented day in both groups.

These data show that acute TRP depletion increases dysphoric mood states and stimulates feeding in bulimics compared with controls. In addition, these data support previous studies suggesting that this experimental paradigm may be an important aid in studies of serotonin metabolism.

References:

1. Charney DS, Price LH, et al: Serotonin function and the mechanism of antidepressant action: reversal of antidepressant-induced remission by rapid depletion of plasma tryptophan. *Arch Gen Psych* May 1990.
2. Kaye WH, Gwirtsman HE, Brewerton TD, George DT, Wurtman RJ: Bingeing behavior and plasma amino acids: a possible involvement of brain serotonin in bulimia nervosa. *Psych Research* 23:31-43, 1988.

NR582 Thursday May 16, 12 noon-2:00 p.m.

Phenelzine Treatment of Melancholia

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M.D., Frederic M. Quitkin, M.D., Karyl G. Cole, M.D., Jonathan W. Stewart, M.D., Delbert G. Robinson, M.D., Alfreda H. Howard, M.A., Sabina Meyer, B.S., Carmen Z. Lemus, M.D.

Summary:

A collaborative study was undertaken in which patients with unipolar, major depression, melancholic subtype, were treated with phenelzine, imipramine, or placebo. After a one- to two-week period of single-blind placebo, patients (age range 18-70) were treated in double-blind fashion for six weeks with phenelzine 45-90 mg/day, imipramine 150-300 mg/day, or placebo. Change was measured with the Hamilton scale for depression (HAM-D) and Clinical Global Impression (CGI). The criterion for response was a final CGI of 2 (much improved) or 1 (very much improved). Forty-six patients completed the double-blind phase. Response rates at week 6 were as follows: phenelzine 12/19 (63 percent), imipramine 8/13 (61 percent), and placebo 6/14 (42 percent). Data analysis and more detailed data on completers and dropouts will be presented. Phenelzine appears to be a useful medication for melancholic major depression.

NR583 Thursday May 16, 12 noon-2:00 p.m.

A Linkage Study of Bipolar Disorder and Distal 5Q

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Summary:

Objective: The distal region of 5q currently is an area of great interest in genetic linkage studies of bipolar disorder. A number of candidate genes for the disorder are found there, including those for the $\alpha 1$ and $\beta 2$ adrenergic receptors, the GABA-A receptor $\alpha 1$ subunit, the dopamine D1 receptor, and the glucocorticoid receptor (GRL) at 5q31-32. The purpose of this study was to determine whether linkage exists between vulnerability to bipolar disorder and DNA markers at the GRL locus and other loci in the distal 5q region. *Method:* The subjects comprised 106 of the 120 members of the extended Amish Pedigree 110. A previously reported two allele RFLP was detected by the BclI at the GRL locus using the cDNA hGR1.2 insert as the probe. Two point linkage analysis was performed using LIPED. *Results:* The maximum lod score obtained was 0.73 at $\theta = 0.20$. No negative lods were obtained. *Conclusions:* The mildly positive maximum lod score neither supported nor definitively excluded linkage between bipolar disorder and the marker at the GRL locus. Studies using additional markers in this region in the Amish, three Icelandic, and several other North American pedigrees are currently being carried out.

NR584 Thursday May 16, 12 noon-2:00 p.m.

Cerebral Volume is Reduced in Bipolar Disorder

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Summary:

We have previously reported a reduction in brain volume in schizophrenia. Here we report finding a similar reduction of brain size in bipolar disorder.

Bipolar patients (N = 32, mean age 32.6 years) and healthy controls (N = 39, mean age 28.8 years) consented to participate in the study. MRI scans were obtained on a GE 1.5 Tesla scanner, using T1-weighted pulse sequence (T1 = 800 ms, TR = 1500 ms). A coronal brain series (24-30 slices), .5 cm thick with .5 cm intervals, was obtained. The MRI data were transferred to a SUN/PIXAR image processing work station for measurement. Each coronal slice was traced for areas of the cerebrum, lateral, and third ventricles. Volumes were calculated by summing the volumes of slices and intervals. Intraclass correlation coefficients were greater than .95 for measurements. Differences between groups were calculated using a two-way ANOVA and sex and diagnosis as independent variables.

Mean cerebral volume in bipolar patients (1130.48 $\pm$ 128.31 cc) was significantly smaller ($P = .0287$) than in controls (1194.58 $\pm$ 120.83 cc). Each of the right and left hemispheres were smaller in the bipolar group. The mean lateral ventricular volume in bipolars was not different from controls (13.69 $\pm$ 9.05 vs 12.43 $\pm$ 8.52 cc). But third ventricular volume was significantly larger ($p = .0001$) in bipolars (.44 $\pm$ .19 vs. .29 $\pm$ .14 cc). As with schizophrenia, neurodevelopmental impairment should be considered as a possible etiology for these findings in bipolar disorder.

NR585 Thursday May 16, 12 noon-2:00 p.m.

DST, TRH and Clonidine Tests in Psychiatry

Fabrice Duval, M.D., Psychiatry, C.H. Specialise, Service Du Dr Macher, Rouffach 68250, France; M-Claude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Juarez Oviveira Castro, M.D., Sergio Valdivieso, M.D., Jean-Paul Macher, M.D.

Summary:

The hormonal responses to a series of neuroendocrine challenges were studied in 71 drug-free inpatients - 26 with *DSM-III-R* major depressive episode (MDE) (13 M, 13 F; aged 36.5 $\pm$ 7.3 SD yrs), 14 with *DSM-III-R* schizophrenia (SCZ) (9 M, 5 F; 31.2 $\pm$ 7.9 SD yrs), 12 with *DSM-III-R* schizoaffective disorder (SAD) (8 M, 4 F; 34.4 $\pm$ 11.2 SD yrs) - and 19 hospitalized controls (12 M, 7 F; 33.3 $\pm$ 8.1 SD yrs).

The hormonal differences between the four groups were studied by canonical analysis. Canonical variables based on the results of the clonidine test (GH stimulation, cortisol, and prolactin changes), the DST (log postdexamethasone plasma cortisol levels), and the difference between the 8 AM and 11 PM TRH-TSH tests ($\Delta\Delta$TSH), clearly discriminated the depressed group from controls and other psychopathological states. The SAD group could not be isolated as a separate profile because of its great biological heterogeneity. Endocrine differences across groups did not seem to be an artifact of factors known to influence plasma hormones.

These findings suggest that endocrine results vary according to diagnosis, and that multihormonal responses to batteries of neuroendocrine tests could be useful in the classification of subjects.

NR586 Thursday May 16, 12 noon-2:00 p.m.

TRH-TSH Tests and Antidepressant Treatment Outcome

Fabrice Duval, M.D., Psychiatry, C.H. Specialise, Service Du Dr Macher, Rouffach 68250, France; M-Claude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Gabrielle Wagner, Sergio Valdivieso, M.D., Jean-Paul Macher, M.D.

Summary:

TRH-induced TSH stimulation (ΔTSH) was studied at 8 AM and 11 PM in 18 inpatients with *DSM-III-R* major depressive episode (MDE), after washout and again after four weeks of antidepressant treatment. After washout, MDEs demonstrated blunted 11 PM-ΔTSH ($p < 0.0005$), and $\Delta\Delta$TSH (difference between 11 PM-ΔTSH and 8 AM-ΔTSH) ($p < 0.00005$) compared with 17 hospitalized controls. Seven (39 percent) of MDEs had a blunted 11 PM-ΔTSH (i.e. less than 6 uU/ml), and 13 (72 percent) had a blunted $\Delta\Delta$TSH (i.e. less than 2.5 uU/ml), where as only three (17 percent) had a blunted 8 AM-ΔTSH (i.e. less than 3.5 uU/ml).

Patients were restudied after treatment. TSH responses at 8 AM

and 11 PM were not significantly changed by antidepressant drugs. However, antidepressants increased $\Delta\Delta$TSH values ($p<0.03$). Ten (55 percent) patients responded to treatment. Pretreatment TRH-TSH results were not predictive of greater treatment response. $\Delta\Delta$TSH normalization was associated with clinical improvement, and failure to normalize was associated with poor response ($p<0.02$). Our results suggest that $\Delta\Delta$TSH might be a state-related marker of clinical progress and could be applied to the monitoring of antidepressant drug action.

NR587 WITHDRAWN

NR588 Thursday May 16, 12 noon-2:00 p.m.

Verapamil Compared to Lithium in Acute Mania

Enrique S. Garza-Trevino, M.D., Psychiatry, UT Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284; John E. Overall, Ph.D., Leo E. Hollister, M.D., William F. Alexander, M.D.

Summary:

A double-blind randomized trial compared varapamil HCL (V) with lithium carbonate (L) for treatment of patients meeting *DSM-III-R* criteria for mania. Baseline and four weekly evaluations used the Petterson Mania Scale (PMS), the Brief Psychiatric Rating Scale (BPRS), and the Clinical Global Impression (CGI) to evaluate therapy. Twenty patients completed the protocol (12 V, 8 L). Observed reduction in PMS total score averaged 44 percent for V patients and 39 percent for L patients across four weeks. Repeated measures of the analysis of covariance (ANCOVA), with baseline covaried, revealed nonsignificant overall differences between the treatments in all the three evaluating instruments (BPRS, PMS and CGI), and nonsignificant differences as well in the linear trends across the four weeks of treatment. Estimates of within-patient reliabilities were for PMS 0.74, BPRS 0.61, CGI severity 0.72, CGI improvement 0.55. Between-patient reliabilities for PMS 0.62, BPRS 0.70, CGI severity 0.77, CGI improvement 0.20. Side effects were few in both groups; however, more patients in the V group got more concomitant treatments (Haloperidol HCL and Lorazepam I.M.) than the patients on the L group. Since only three of the 12 V patients got most of the concomitant medication we believe that concomitant treatments were not responsible for the nonsignificant results.

NR589 Thursday May 16, 12 noon-2:00 p.m.

Seasons and Platelet 5HT Uptake: A Cohort Study

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Summary:

Platelet serotonin uptake has been proposed as a model of neuronal serotonin uptake. Investigators have reported seasonal variation in platelet 5HT uptake, but with considerable interindividual variability. We sought to reduce this variability by conducting a longitudinal study of normal subjects over a one-year period. *Methods:* Subjects were without medical or psychiatric illness, medication-free; and were studied between 8:00 and 9:00 AM on ten occasions at approximately monthly intervals. Platelet 5HT uptake was performed by the method of Tuomisto and Tukainien. Platelet aliquots 10^7/ml were incubated in 8 concentrations of 3H-5HT for three minutes, separated by filtration, and radioactivity counted. Diffusion at different concentrations was calculated and substracted from total uptake to produce a saturation curve. LineweaverBurk plots were constructed and Vmax was computed using the method of least squares. *Results:* Data were grouped into the usual four seasons and each season compared to every other. There was a highly significant ($p>0.0001$) increase in platelet 5HT uptake in summer with the nadir in winter and early spring. Although greatest interindividual variability also occurred during the summer months, all subjects demonstrated increased uptake in summer and decreased uptake in winter. Data suggest a physiologic pattern of seasonal platelet 5HT uptake in normals, which is consistent with reports of seasonal variation in CNS 5HT and its metabolites.

NR590 Thursday May 16, 12 noon-2:00 p.m.

The Cerebral Neurobiology of Hope and Hopelessness

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Summary:

Using positron emission tomography, intercorrelations between Gottschalk speech content measures of positive hope, negative hope, and total hope scores with localized cerebral glucose metabolic rates in a group of ten normal young male subjects were obtained. Positive and negative hope scores tended to have significant correlations with glucose metabolism in opposite cerebral hemispheres, and when similar cerebral locations were involved, the significant correlations were in the opposite directions. These findings point to yes-no cerebral mechanisms.

In whole brain, positive hope scores were found to have significant positive correlations with glucose metabolic rates in the parietal lobe, left temporal cortex, occipital cortex, and right occipital cortex. In medial cortical and subcortical gray areas, these significant positive correlations of positive hope scores were found in the right precuneus and right superior frontal gyri. In the lateral cortical areas, positive correlations between positive hope scores and glucose metabolic rates occurred in the left posterior superior parietal and right lateral occipital gyri. Significant negative correlations between positive hope scores occurred in the left temporal lobe, left and right medial temporal gyri, left superior frontal gyrus, right putamen, and left anterior thalamus.

The implications of these and associated findings are discussed.

NR591 Thursday May 16, 12 noon-2:00 p.m.

Phenylacetic Acid in Panic Disorder and Depression

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Summary:

Catecholamine metabolites have been shown to vary considerably among a variety of psychiatric disorders. Phenylacetic Acid (PAA), a metabolite of 2-Phenylethylamine (PEA), has been reported to have an abnormal excretion profile in certain depressive and psychotic disorders, and may be increased in schizoaffective disorders. In addition, PAA may be diminished in panic disorder with secondary depression, but not with uncomplicated panic disorder.

This study examined total daily PAA excretion among subjects with major depression ($N=44$), panic disorder ($N=80$), and normal controls ($N=53$). No significant differences were found among groups at baseline. Correlation analyses between total PAA and Hamilton Depression, CGI Severity and Montgomery-Asberg scale scores, showed no significance in the depression group. Hamilton Anxiety, panic attack frequency, and SCL-90 scores (for depression, anxiety, and phobic anxiety), failed to show significant correlations for patients in the panic disorder group. The only significant correlation noted was total PAA and Global Phobia Scores in the group with primary panic disorder (Pearson Correlation Coefficient $= -0.236$, $p=0.05$).

The lack of significant differences between the depressed, panic, and normal control groups will be discussed in light of the current information known regarding PEA and its urinary metabolite, PAA.

NR592 Thursday May 16, 12 noon-2:00 p.m.

Interhemispheric Serotonergic Asymmetry in the Human Brain

Mihaly Arato, M.D., Hamilton Psych Hospital, P.O. Box 585, Hamilton Ontario, Canada L8N-3K7; Kornelia Tekes, Ph.D., Laszlo Tothfalusi, Ph.D., Ede Frecska, M.D., Rick Guscott, M.D., J. Duncan Maccrimmon, M.D.

Summary:

Although hemispheric lateralization of various functions in the human brain is quite well known, the neurochemical nature of hemispheric differences has been recently investigated. Serotonin (5HT) dysfunction has been implicated in the pathophysiology of several psychiatric disorders (depression, suicide, OCD, eating disorders, etc.). Our findings show a clear-cut asymmetry of some 5HT mechanisms in the human brain.

We have measured various 5HT indices - ^{3}H-imipramine binding (IB), 5HT, and 5HIAA (5HT metabolite) contents - in both medio-frontal cortices in 42 subjects. Increased IB (higher Bmax values), 5HT, and 5HIAA contents were found in the right frontal cortex compared with the left in 90 percent of the cases. The same asymmetry was seen in premature neonates (n = 10) suggesting that a "normal" (right-sided dominance) of some serotonergic mechanisms is an inborn characteristic of the human brain.

In contrast to the medio-frontal cortex data, sampling the orbital frontal cortex revealed a gender related difference, namely higher IB on the right side in women compared to men. This higher "serotonin potential" may provide a physiologic basis for the better impulse, aggression, and sexual behavior control in women.

Our in vivo results, using quantified EEG mapping of auditory evoked potentials, tend to support the post-mortem chemical findings. After giving relatively specific 5HT-ergic drugs, IV chlorimipramine or oral fluoxetine, we have seen higher activity on the right side/more inhibition on the left in normal controls.

NR593 Thursday May 16, 12 noon-2:00 p.m.

Therapeutic Efficacy of L-Thyroxine in PMS

Peter J. Schmidt, M.D., BPB, NIMH Bldg 10 3N238, 9000 Rockville Pike, Bethesda, MD 20892; Gay N. Grover, M.S.N., Margaret F. Jensvold, M.D., David R. Rubinow, M.D.

Summary:

Previous studies have reported evidence of a high prevalence of thyroid axis dysfunction in women with premenstrual syndrome (PMS). We have identified in large samples of women with PMS an increased prevalence of hypothyroidism or hyperthyroidism (10 percent), elevated thyroid auto-antibody titers (13 percent), and abnormal response to TRH stimulation (35 percent). One study suggested the efficacy of thyroid hormone supplementation in PMS. In this study, we evaluated the efficacy of L-thyroxine in PMS in relation to TSH response to TRH. Thirty women with prospectively confirmed PMS entered a seven-month, double-blind, placebo controlled trial of L-thyroxine (0.1 mg/day). All women had normal basal thyroid function tests and received a TRH stimulation test prior to study entry. All women completed daily symptom self-ratings throughout the duration of the trial. Twenty-four have completed the trial. ANOVA with repeated measures showed no significant differences in efficacy between L-thyroxine and placebo. TSH response to TRH did not predict response to L-thyroxine. Thus, although abnormalities of thyroid function appear with greater than expected frequency in women with PMS, PMS is not simply masked hypothyroidism and the uniform prescription of thyroid hormone replacement in this condition is unwarranted.

NR594 WITHDRAWN

NR595 Thursday May 16, 12 noon-2:00 p.m.

Alprazolam Treatment of Premenstrual Dysphoria

Rebecca Potter, M.D., Psychiatry, University of Arizona, AHSC 1501 North Campbell Ave, Tucson, AZ 85724; Martha P. Fankhauser, M.S., Lynda Bologna, R.N., Judith Steward, R.N., Stephen Scheiber, M.D., Betty Jo Tricou, M.D.

Summary:

Low-dose alprazolam was studied in a double-blind, placebo-controlled fashion in 40 women with the diagnosis of late luteal phase dysphoric disorder. The study design included a two-menstrual cycle for the diagnostic phase, and a two-month placebo washout phase. The study groups were assigned to either six-menstrual cycle treatment with alprazolam (N = 20), or a three-cycle treatment of alprazolam and three cycles of placebo treatment (N = 20). Results from the study indicated that intermittent alprazolam treatment in total doses of 1 mg/day significantly relieved the majority of mood and behavioral symptoms associated with premenstrual symptoms. Anxiety and depression rating scores were also significantly reduced on alprazolam treatment. The placebo cross-over group continued to have a reduction in premenstrual symptoms during placebo treatment, which may indicate a carry over effect.

NR596 Thursday May 16, 12 noon-2:00 p.m.

Depression in Women After an Adverse Birth Outcome

Martha A. Teitelbaum, Ph.D., DVS/FSB, Natl Ctr. Hlth. Stat., 6525 Belcrest Rd. Room 840, Hyattsville, MD 20782; Karen Bouden, M.A., Ben Z. Locke, M.S.P.

Summary:

This research uses data from the 1988 National Maternal and Infant Health Survey (NMIHS) to examine the relationship between birth outcome and women's depressive symptomatology. Previous research on this topic has been limited to small samples of volunteers. The NMIHS, however, sampled 20,000 women who had a live birth, fetal, or infant death in 1988. The respondents were selected using a stratified random sample of 1988 birth certificates, fetal death certificates, and infant death certificates. Women who were black or who had low birth weight infants were oversampled. This analysis is based on the first 3,566 respondents to the NMIHS.

Symptoms of depression were measured using the Center for Epidemiologic Studies Depression Scale (CES-D). Respondents' scores on the CES-D, obtained six to 18 months after the event, varied by type of birth outcome. Women who experienced a fetal or infant loss had significantly higher scores on the CES-D than did women who had normal weight live births. In addition, depressive symptomatology was associated with other factors, including respondent's race, age, education, income, time since event, and other pregnancy outcomes. However, when these variables and birth outcome were entered into a multivariate analysis, fetal and infant deaths were clearly the strongest predictors of respondents' scores on the CES-D.

NR597 Thursday May 16, 12 noon-2:00 p.m.

Cross-Cultural Meaning of Somatic Symptoms in Depression

Albert Diefenbacher, M.D., Psychiatrie, Ereie Universitat, Eschenallee 3, D-1000 Berlin 19, Germany; Gerhard Heim, Ph.D., Martina Heiche

Summary:

Cross-cultural studies on mental health problems can clarify the pathoplastic influence of different cultural backgrounds on course

and outcome of psychiatric disorders. One problem in this context relates to the role of somatic symptoms of depressive patients belonging to non-Western cultures. We investigated 6,000 psychiatric inpatients of the psychiatric department of the Free University of Berlin and documented their psychopathology ratings on computerized AMDP-files (Arbeitsgemeinschaft für Methodik und Dokumentation in der Psychiatrie 1979). A total of 160 of these were of Islamic confession (mostly of Turkish origin and members of the immigrated community). According to their ICD-9-diagnosis, all Islamic patients with depressive syndromes (n = 42) (i.e. ICD 296.1, 300.4, 309.0, 309.1) were selected and compared retrospectively with a randomly selected age-matched German patient group of equal sex-ratio and diagnostic composition regarding psychological and somatic symptomatology and socio-cultural features. Islamic patients different in comparison to German patients as to their greater score on the "vegetative-somatic" scale, but not as to the extent of the 'depressive syndrome' of the AMDP-system (Gebhardt et.al. 1983). Despite an overall decrease of these syndromes at discharge, Islamic patients still had more somatic complaints than their German controls. We conclude that this difference results from culturally determined different illness concepts. It is suggested that the psychiatric treatment of Islamic inpatients must pay special attention to physiotherapeutic measures as a means in the self-interpretation of well-being.

NR598 Thursday May 16, 12 noon-2:00 p.m.

Depression, Compulsive Personality and Serotonin

Marc M. Ansseau, M.D., Dept. of Psychiatry, Univ of Liege, C.H.U. Du Sart Tilman, Liege, Belgium B-4000; Benoit J. Troisfontaines, M.D., Patrick G. Papart, M.D., Remy Von Frenckell, Ph.D.

Summary:

Based on the evidence that serotonergic antidepressants are effective in obsessive-compulsive disorder, we hypothesized that major depressive patients with an underlying compulsive personality could preferentially respond to a serotonergic antidepressant. A total of 46 major depressive outpatients were treated with fluvoxamine (100-200 mg/d) over an eight-week period with clinical assessments at baseline and after two, four, and eight weeks of treatment. Twenty-two patients exhibited a compulsive personality, according to *DSM-III* criteria; in contrast, the other 24 patients did not exhibit more than one compulsive feature. The comparison of changes over time in Hamilton depression scores showed significantly better improvement in the compulsive subgroup after eight weeks of treatment ($p = 0.001$), a difference that was already present after four weeks using the endogenomorphy subscale. No significant differences were present between the two subgroups with regard to the number of reported side effects, mainly of digestive type. Therefore, these results suggest that in major depressive patients, an underlying personality represents an argument toward the selection of a serotonergic antidepressant.

NR599 Thursday May 16, 12 noon-2:00 p.m.

Flexinoxan, a 5-HT1A Agonist in Major Depression

Marc M. Ansseau, M.D., Dept. of Psychiatry, Univ of Liege, C.H.U. Du Sart Tilman, Liege, Belgium B-4000; William R. Pitchot, M.D., Antonio M. Gonzalez Moreno, M.D., H. Hansennemichel, B.Sc., Patrick G. Papart, M.D., R. Van Der Hoop Gerritsen, M.D., L. Dianne Bradford, M.D.

Summary:

Flesinoxan is a highly potent and selective 5-HT1A full agonist (pKi = 8.8) with at least 80-times weaker affinity for any other receptor. Flesinoxan is active in several animal models of depression such as the behavioral despair test in rats and down-regulates beta-adrenoreceptor response.

In this pilot open study, flesinoxan (4 mg/d) was administered orally for four weeks in 16 major depressive, mostly treatment-resistant inpatients exhibiting a score of at least 19 on the Hamilton depression scale. Weekly ratings included Hamilton depression scale, MADRS, and Clinical Global Impressions.

Preliminary results from the first eight patients showed considerable improvement in depressive symptomatology, with mean MADRS scores (SD) dropping from 30.9 (7.5) to 12.0 (6.3) after four weeks of treatment. The tolerance of flesinoxan was excellent.

In addition, the effect of flesinoxan on temperature regulation as well as on EEG sleep during a placebo-controlled challenge night (after two baseline placebo nights) and at the end of the treatment will be presented and discussed.

NR600 Thursday May 16, 12 noon-2:00 p.m.

Life-Events and Biological Markers of Depression

Marc M. Ansseau, M.D., Dept. of Psychiatry, Univ of Liege, C.H.U. Du Sart Tilman, Liege, Belgium B-4000; Caroline Lamberty, B.Sc., Remy Von Frenckell, Ph.D., Patrick G. Papart, M.D., Marie-Anne Gerard, M.D., Jacques Wautry, B.Sc., Georges Franck, M.D.

Summary:

Over the last decade, the so-called "biological markers" of depression have attracted increasing interest. However, the influence of external events on such biological parameters has been little assessed. The purpose of the present study was, therefore, to analyze the relationship between the life-events preceding hospitalization and abnormalities in the dexamethasone suppression test (DST) and the growth hormone (GH) response to clonidine and apomorphine neuroendocrine challenges in 41 major depressive inpatients. Neuroendocrine procedures have been previously described (Ansseau et al., 1984); the collection of life-events was performed according to the method of Paykel and Mangen. Results showed significantly more total negative impact of life-events among patients exhibiting DST nonsuppression ($p = 0.03$) or blunted GH response to apomorphine ($p = 0.01$). In contrast, blunted GH response to clonidine was not associated with a higher level of life-events. These findings suggest that DST and apomorphine test may represent state markers of depression whereas clonidine test may represent a trait marker.

NR601 Thursday May 16, 12 noon-2:00 p.m.

Major Depression, Family Functioning and Recovery

Gabor I. Keitner, M.D., Butler Hospital, 345 Blackstone Blvd., Providence, RI 02906; Christine E. Ryan, Ph.D., Ivan W. Miller, Ph.D., Nathan B. Epstein, M.D., Duane S. Bishop, M.D., Robert Kohn, M.D.

Summary:

We followed a sample of 78 inpatients with major depression and their families from hospitalization for the depression through 12 months post discharge in order to assess the relationship between subjective and objective measures of family functioning at the acute phase and recovery. Seventy-five percent of the depressed patients who came from objectively rated good functioning families recovered, compared to only 42 percent who came from poor functioning families ($X^2 = 5.23$, $df = 1$, $p = < .02$). Similarly, in families subjectively rated as having good functioning, 61 percent of the depressed patients recovered in contrast to 39 percent who rated themselves as having poor family functioning ($X^2 = 3.60$, $df = 1$, $p = < .06$). Depressed patients, regardless of recovery status, viewed their family functioning as worse than other family members at the acute stage of the illness. By 12 months, not recovered patients and their families and recovered patients only reported

unhealthy family functioning, while the families of recovered patients reported family functioning that was within the healthy range. Given the equivalent severity of depression in both groups of patients at entry into the study, this strongly suggests that healthy family functioning can improve the probability of recovery from a depressive episode. Functioning improved in the families of all patients over the course of the study but did so more comprehensively and consistently in those depressed patients who had recovered by the 12-month follow-up period.

NR602 Thursday May 16, 12 noon-2:00 p.m.

Major Depression and 12-Month Outcome

Gabor I. Keitner, M.D., Butler Hospital, 345 Blackstone Blvd., Providence, RI 02906; Christine E. Ryan, Ph.D., Ivan W. Miller, Ph.D., William H. Norman, Ph.D.

Summary:

Subjects for the study included 78 inpatients with *DSM-III* diagnosis of major depression consecutively admitted to an acute care university-affiliated psychiatric hospital. Patients were assessed at hospitalization and at monthly intervals on a variety of clinical, psychosocial, and family functioning measures for a period of 12 months. By the 12th month of follow-up, 34 of 70 patients (49 percent) met criteria for recovery, suggesting only a 50-50 chance that a depressive episode will remit within one year after discharge from hospital. The average length of time to recovery was 4.9 months after discharge but the majority of patients who recovered did so in less than six months. We used logistic regression analysis to determine which factors were most closely associated with recovery. Results indicated that the five most important factors, explaining 21 percent of the variance (Model Chi-square = 28.70, $p < .0001$), were: shorter length of hospital stay, older age of depression onset, better family functioning, less than two previous hospitalization, and absence of any concurrent illness. Overall our findings show a low rate of recovery for patients hospitalized with major depression. Some variables associated with nonrecovery (e.g., comorbidity, family functioning) are amenable to clinical intervention, but it is suggested that there are two distinct groups of patients with respect to recovery: one that remits quickly and one with a more prolonged course.

NR603 Thursday May 16, 12 noon-2:00 p.m.

Concurrent Panic Disorder and Major Depression

Leon J. Grunhaus, M.D., Psychiatry, University of Michigan, 1500 E. Med Ctr Dr. Box 0116, Ann Arbor, MI 48109; Atul C. Pande, M.D., Roger F. Haskett, M.D.

Summary:

Recent studies suggest that anxious depressives (comorbidity of anxiety and depressive disorders) may have a more severe form of illness, particularly when recurrent panic attacks are present. To further explore the relationship between panic and depressive symptomatology in patients diagnosed as having MDD, we analyzed the reported clinical and longitudinal features of two groups of patients, one having MDD only and the other having MDD and concurrent panic disorder. *Methods:* All patients were evaluated with a: 1. a 14-day drug-free observation; 2. diagnostic interviews by senior psychiatrists and a SADS interviewer; 3. a complete medical and laboratory work up; and 4. a consensus RDC. Patients (N:119) with primary, definite MDD and no panic attacks during the current episode of illness, and no anxiety disorder diagnosis ever, were identified as the MDD-ONLY group. Patients (N:57) having had six or more definite panic attacks in a six-week period, were identified as the MDD-Panic group. *Results:* Age of first episode of illness ($p < .001$), age of first outpatient treatment ($p < .05$), and age of first admission for MDD ($p < .001$) all occur at a younger age in the MDD-PANIC group. MDD-PANIC patients had had more admissions for MDD than the MDD-ONLY group ($p < .05$). Psychic anxiety ($p < .01$), somatic anxiety ($p < .01$), phobia ($p < .001$), inappropriate guilt ($p < .05$), suicidality ($p < .05$), anhedonia ($p < .01$), retardation ($p < .05$), indecisiveness ($p < .001$), hopelessness ($p < .05$), feelings of inadequacy ($p < .001$), social isolation ($p < .01$), and slow thinking ($p < .01$) were all significantly higher in the MDD-PANIC group. Mood was significantly less reactive to positive environmental stimuli in patients with MDD-PANIC ($p < .05$). *Discussion:* Our findings corroborate and strengthen the evidence suggesting that patients with MDD and concurrent panic disorder complain of more severe clinical symptoms and that their illness begins at a younger age.

NR604 Thursday May 16, 12 noon-2:00 p.m.

The Diagnosis of Major Depression by Self-Report

Scott Wetzler, Ph.D., Psychiatry, Montefiore Med. Center, 111 E. 210th Street, Bronx, NY 10467; Douglas B. Marlowe, MA.

Summary:

This study examined the diagnostic efficiency of self-report tests for depression. The MMPI (N = 185) or the MMPI-2 (N = 42), MCMI (N = 148) or MCMI-II (N = 110), and SCL-90R (N = 256) were administered to psychiatric inpatients upon admission, including approximately 50 percent diagnosed by experienced psychiatrists with major depression, and 50 percent with a variety of other psychiatric conditions. The diagnostic efficiency of individual depression scales was evaluated by comparing test-based diagnoses with clinical diagnoses. To make the test diagnosis of major depression, T scores ≥ 70 were used for the MMPI and SCL-90R Depression scales, and ≥ 65 for the MMPI-2 Depression scale; and Base Rate scores ≥ 85 for the MCMI and MCMI-II Dysthymia and Major Depression scales. Overall classification rates were fairly good for the SCL-90R and MMPI Depression (60 percent hit rate) and MCMI Dysthymia scales (70 percent). The MMPI Depression scale was the most sensitive for identifying patients with major depression. Using the entire multidimensional profiles for each test, the depressed patients had significantly different profiles on the MMPI, MCMI, MCMI-II, and SCL-90R in comparison to psychiatric controls ($p < 0.001$). The depressed patients' profiles were characterized by elevations on: SCL-90R (Depression, Anxiety), MMPI (Depression), MMPI-2 (Depression, Psychasthenia), MCMI (Dysthymia, Borderline, Dependent), MCMI-II (Dysthymia, Dependent, Compulsive). These profiles are indicative of high levels of distress, depressive symptomology, anxiety, as well as personality features characteristic of what has been termed "ambivalent dependence." Finally, multiple discriminant function analyses using these multidimensional test profiles generated impressive classification rates of up to 80 percent. In summary, when used appropriately, self-report psychological tests provide an important source of information during an initial evaluation, and in some contexts, may be used in lieu of a psychiatrist's interview.

NR605 Thursday May 16, 12 noon-2:00 p.m.

A Multicentre, Double-Blind, Randomized Study Comparing Paroxetine and Amitriptyline in Patients With Major Depression

V. Rapisarda, Psichiatrica, Universita degli St., Catania, Italy

Summary:

A randomized, double-blind, double-dummy, multicentre, six-week trial was carried out to compare the efficacy and side effects of flexible dosing with paroxetine (20-30 mg given once daily) and amitriptyline (100-150 mg given three times daily) in 303 patients suffering from *DSM-III* major depression. All patients had a score of at least 18 on the 21-item HAMD scale.

The primary rating of efficacy was the HAMD scale, plus physician ratings of severity of illness and clinical improvement. Tolerability and safety were also assessed. Both groups of patients were comparable on entry to the study. Overall, both drugs produced a significant improvement in the depression (total HAMD score, $p<0.001$). No between group difference was noted.

With respect to tolerability, paroxetine exhibited a considerably better profile than amitriptyline, as evidenced by fewer, more transient, and less severe adverse events and, in particular, a greatly reduced frequency of anticholinergic events (30 anticholinergic events with paroxetine versus 84 with amitriptyline). No clinically relevant changes were seen in laboratory investigations. It is concluded that paroxetine and amitriptyline are of equivalent therapeutic efficacy but that paroxetine exhibits an improved adverse events profile.

NR606 Thursday May 16, 12 noon-2:00 p.m.

Echocardiographic Measures of the Safety of ECT

Anthony Messina, M.D., Psychiatry, Payne Whitney Clinic, 525 East 68th Street Box #03, New York, NY 10021; Mary Paranicas, B.A., Barri L. Katz, M.D., John M. Markowitz, M.D., Richard Devereux, M.D.

Summary:

Importance: ECT, often the treatment of choice for depression, is increasingly used for older, medically sicker patients. For cardiac patients ECT is considered safer than tricyclic antidepressants, lacking their known cardiotoxicity. Some data have suggested cardiovascular morbidity and mortality from ECT. We present pilot data from the first study to examine the cardiac effects of ECT using transthoracic echocardiography.

Methods: Patients of mean age 54.1 $\pm$ 15.2 gave informed written consent. After medical clearance, patients underwent bilateral ECT with standard anesthesia and monitoring. Cardiac function was measured by echocardiography immediately preceding and following first seizure induction.

Results: Of the 15 patients entered, 11 had adequate echocardiograms. Seven had $\geq$ 1 cardiac risk factor. All patients had normal left ventricular function before ECT. Following ECT, four of the high risk patients, three of whom were >68 years old, had mild hypokinesis with corresponding abnormal electrocardiograms.

Significance: Four of 11 patients had mild hypokinesis; none had dyskinesia or akinesia. None had myocardial infarctions during treatment. Hypokinesia was found frequently (>40 percent) in a large study of high risk patients undergoing surgical anesthesia, but unlike dys- and akinesias did not predict perioperative myocardial infarction. Hypokinesia may indicate altered loading conditions or electrical activation rather than myocardial ischemia. These preliminary data suggest patients at cardiovascular risk may tolerate ECT without significant echocardiographic changes.

NR607 Thursday May 16, 12 noon-2:00 p.m.

ECT-Induced Cortisol Release in Melancholia

Conrad Swartz, M.D., Psychiatry, Chicago Med. School, 3333 Green Bay Road, North Chicago, IL 60064;

Summary:

This study aimed to determine if ECT-induced cortisol release or post-ECT serum cortisol concentration correlates with depressive state, analogous to the dexamethasone suppression test. Unlike the preceding 20 studies of ECT-induced cortisol release, we administered 2 mg dexamethasone nine hours before ECT to decrease baseline levels. Baseline and 30-minute post-ECT serum cortisol levels were determined for first and last ECT sessions in a series of 24 male depressives. A total of 22 subjects responded to ECT. Every patient showed a serum cortisol increase after the first ECT ($p<10^{-6}$, $t=7.3$, $df=23$), averaging 668 percent over baseline. This is about ten times greater than previously reported ECT-induced cortisol increases, attributable to their omission of dexamethasone. Greater cortisol elevation and post-ECT cortisol occurred with the first ECT than the last ECT for 83.3 percent of subjects ($p=.00094$, binomial test for >19 occurrences; average drop 4.4, SD 8.4 ug/dL, $p=.009$, $t=2.57$, $df=23$). Post-ECT cortisol levels fell from 15.3 (SD 9.3) ug/dL with the first ECT to 8.7 (SD 8.1) ug/dL ($p=.0012$, $t=3.40$, $df=23$) with the last ECT. This demonstrates consistent cortisol decrease with ECT. Because absence of cortisol decrease with ECT is unusual, it might be aberrant and indicate impending relapse.

NR608 Thursday May 16, 12 noon-2:00 p.m.

Prediction of Lithium and Other Drug Doses

Conrad Swartz, M.D., Psychiatry, Chicago Med. School, 3333 Green Bay Road, North Chicago, IL 60064.

Summary:

This paper presents the first known method to apply pharmacokinetic modeling to prediction of desirable doses for lithium and other drugs from one or more blood drug concentrations, without requiring approximations, mathematical expertise, or a computer. One-compartment pharmacokinetic calculations for dose prediction after sequences of one, two, and three test doses and one or two drug blood levels are exactly represented in graphs that take seconds to use for clinical purposes. These graphs account for dose division, blood sampling time, and drug elimination rate. An unexpected new finding from the graphs is that the factor to multiply the test blood drug level by is independent of drug elimination rate if blood is sampled about 24 hours after the last test dose. Solely by calculations the graphs also provide the exact same value that Cooper, Bergner, and Simpson measured for the ratio between steady-state serum lithium level and serum lithium level after a test dose. Clinical application to lithium and antidepressant blood levels will be illustrated, along with a rational strategy for lithium loading doses derived from these graphs.

NR609 Thursday May 16, 12 noon-2:00 p.m.

Linkage Studies of the D2 Gene in Bipolar Families

John R. Kelsoe, M.D., Psychiatry, USCD, M003, La Jolla, CA 92093; Paul Shilling, B.A., Arvin Mirow, M.D., Sharon Hirsch, M.D., Helgi Kristbjnarson, M.D., Tomas Helgason, M.D., J. Christian Gillin, M.D., Janice Egeland, Ph.D.

Summary:

The dopamine D2 receptor is an excellent candidate gene for bipolar disorder because it is a site of action of neuroleptic medication, and because of other data implicating dopaminergic abnormalities in bipolar disorder. The recent clothing of the D2 receptor (Grandy et al., 1989) and identification of a TaqI RFLP had made it possible to map the gene to 11q22 and to test the D2 receptor locus (D2DR) for linkage to neuropsychiatric disorders. Linkage to bipolar disorder has already been excluded in one set of Utah pedigrees (Byerly et al., 1989). We are currently testing the D2 RFLP for linkage to bipolar disorder in Amish pedigree 110, three Icelandic pedigrees, and several other North American pedigrees. In Amish pedigree 110, linkage to bipolar disorder can be excluded to within 5 cM of D2DR ($LOD(\theta=0)=-4.5$). Linkage can also be excluded to within 5 cM of the nearby flanking markers D11S144 and D11S147. Data will also be presented on linkage studies in the other family collections.

NR610 Thursday May 16, 12 noon-2:00 p.m.

Lithium and Sexual Function in Bipolar Patients

A. Missagh Ghadirian, M.D., Allan Memorial Inst., 1025 Pine Avenue West, Montreal Quebec, Canada H3A 1A1; Lawrence Annable, D.S., Guy Chouinard, M.D., Marie-Claire Belanger, R.N.

Summary:

Bipolar affective disorder affects sexual behavior and libido. Although a large number of these patients are treated with lithium, reports in the literature concerning the effects of lithium on sexual function are conflicting and mostly anecdotal. Sexual function was studied on a self-rating scale in 104 patients (45 men and 59 women) with a *DSM-III* diagnosis of bipolar disorder and under treatment with lithium, either alone (35 percent) or in combination with benzodiazepines (49 percent) tricyclic antidepressants (17 percent), neuroleptics (17 percent), tryptophan (10 percent) or carbamazepine (1 percent). The patients were in a euthyroid state at the time of the assessment. Difficulties in sexual functioning were significantly ($p<0.001$) more common in patients treated with a combination of lithium and benzodiazepines (49 percent) than in those treated with either lithium alone (14 percent) or lithium in combination with other drugs (17 percent). No relationship was seen between serum prolactin levels lithium dosages or serum levels and sexual dysfunction scores. These results suggest that lithium when given alone, does not have a major effect on sexual function in patients with bipolar affective disorder.

NR611 Thursday May 16, 12 noon-2:00 p.m.

Abnormal Speech Articulation in Major Depression

Alastair J. Flint, M.D., Psychiatry, Toronto General Hospital, 200 Elizabeth St. 8 Eaton N., Toronto Ontario, Canada M5G 2C4; Sandra E. Black, M.D., Irene Campbell-Taylor, Ph.D., Gillian F. Gailey, M.HSc., Carey Levington, B.Sc.

Summary:

Speech changes have long been recognized as a feature of depression. Most studies of speech in depression have focused on speech rate, speech pause time, and fundamental frequency parameters. Changes in articulation, however, have received very little attention despite their implications for hypotheses on the neurobiology of depression. The purpose of this study was to determine whether major depression is associated with changes in articulation, as measured by computerized acoustic analysis. Thirty patients with *DSM-III-R* major depression were compared with 30 healthy controls on four acoustic measures of articulation. Depressed patients had statistically significant shortened voice onset time and decreased second formant transition compared to controls. The two groups did not differ on spirantisation or voice intrusion errors, although there was a trend for depressives to have more spirantisation. The results demonstrate that major depression is characterized by disordered articulation of speech. These findings are discussed in relation to the known pathophysiology of dysarthrias complicating other neurological disorders.

NR612 Thursday May 16, 12 noon-2:00 p.m.

Antidepressant Treatment of Double Depression

David J. Hellerstein, M.D., Psychiatry, Beth Israel Med. Center, 1st Avenue & 16th Street, New York, NY 10003; Phillip Yanowitch, M.D., Jesse Rosenthal, M.D., Camille Hemlock, M.D., Karen Kasch, B.A.

Summary:

"Double depression," or coexisting dysthymia and major depression, is increasingly realized to be a common psychiatric disorder, and has been reported to be less responsive to antidepressant treatment than uncomplicated major depression. We report on an open label trial with two serotonin-enhancing agents, fluoxetine and trazodone, in treatment of double depression. In our series of 18 double-depressed patients, 14 completed trials of medication. Response was defined by 50 percent or greater decrease in Hamilton-D score *and* a score of 1 or 2 (very much improved or much improved) on the patient-rated CGI. Dropouts were crossed over to the second medication. Dropout rates were 80 percent for trazodone but only 8.3 percent for fluoxetine. At the end of three-month medication trials, seven of 14 completers (50 percent) had responded to medication; at five months, eight of 14, or 57.1 percent, had responded to treatment. This response rate was comparable to that of a sample of 17 similarly-treated patients with dysthymic disorder *without* coexisting major depression.

NR613 Thursday May 16, 12 noon-2:00 p.m.

Reduced Seizure Potential in Animals and Reduced Incidence of Seizures in Depressed Patients During Treatment With the Selective Serotonin Re-Uptake Inhibitor Paroxetine

J.G.C. Rasmussen, Smith Kline Beecham, Great Burgh Epsom, Surrey KT18 5X0 E, England

Summary:

Studies in animals have shown that much higher doses of paroxetine, as compared with amitriptyline, were required to induce seizures.

In clinical studies paroxetine was associated with a statistically significantly ($p<0.05$) lower incidence of seizures - 0.1 percent compared with 0.5 percent for active controls (amitriptyline, imipramine, clomipramine, maprotiline, mianserin) when considered together, and also when compared with clomipramine alone (0.1 percent and 1.0 percent, respectively).

Paroxetine has also been administered to epileptic patients whose condition was well controlled by carbamazepine, phenytoin, or sodium valproate, with no change in anti-epileptic drug plasma levels. No seizures were seen during paroxetine treatment.

It is therefore concluded that paroxetine has a lower potential for causing seizures than other standard antidepressants. Limited experience has shown that paroxetine may be administered with caution to patients receiving anti-epileptic therapy.

NR614 Thursday May 16, 12 noon-2:00 p.m.

The Potential Role of Antidepressants in the Precipitation of Mania

J.G.C. Rasmussen, Smith Kline Beecham, Great Burgh Epsom, Surrey KT18 5X0, England

Summary:

There have been frequent reports in the literature regarding the possible association between antidepressant drug treatment and the precipitation of mania in susceptible patients, and it has been suggested that antidepressants that exert their therapeutic effects via the serotonergic system may carry a lower risk in this respect. When the incidence of mania with paroxetine, a selective serotonin re-uptake inhibitor was compared with that seen with standard tricyclic antidepressants in a unipolar depressed population, similar values were obtained (0.9 and 0.5 percent, respectively). However, in patients with a previous history of mania, statistically significantly fewer ($p<0.05$) patients receiving paroxetine experienced a manic reaction compared with those receiving active control (2 percent) (3/134) and 11 percent (10/86), respectively). These results of these studies suggest that paroxetine may have a lower potential for causing a manic reaction than the tricyclic antidepressants in patients with a previous history of mania.

NR615 Thursday May 16, 12 noon-2:00 p.m.

Comparative Effects of Selective Serotonin Uptake Inhibitors Paroxetine and Fluoxetine on Food Intake in Rats and Effect of Paroxetine on Body Weight in Depressed Patients

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Summary:

As it has been suggested that the anorectic activity of several serotonin uptake inhibitors in rats correlates with their potency as inhibitors of serotonin uptake in vivo (Angel et al, 1988, Life Sciences, *43*, 657), the relative effects of fluoxetine and paroxetine on food intake in rats have been investigated. Furthermore, as fluoxetine reduces body weight in depressed (Stark and Hardison, 1985, *J. Clin. Psychiat., 46*, 53) and nondepressed obese patients (Levine et al, 1989, Int. J. Obesity, *13*, 635), the effect of paroxetine on body weight in depressed patients who completed six weeks treatment in clinical studies has been examined.

Paroxetine and fluoxetine significantly ($p<0.05$) inhibited pelleted food intake in rats at 10 mg/kg p.o. by 17 percent and 27 percent respectively and at 30 mg/kg p.o. by 24 percent and 27 percent, respectively. Lower doses of both drugs were not significantly active.

In depressed patients, paroxetine had no effect on body weight compared to baseline in nonobese patients (Body Mass Index, BMI <26 for males and <25 for females) who received 10-30 mg daily after 21 and 42 days administration. Patients who received >30 and up to 50 mg daily showed a small, statistically significant but clinically insignificant effect (–0.30 kg) at 21 days. In more overweight patients (BMI >26 males and >25 females), paroxetine, 10-30 mg daily, caused a small, statistically significant weight loss (–0.90 kg) at 42 days, with higher doses up to 50 mg causing a similar small loss of weight (–1.05 kg).

The animal data indicate that the potency of paroxetine and fluoxetine as anorectic agents is not correlated with their potency as serotonin uptake inhibitors, as paroxetine is more potent in this respect than fluoxetine (Thomas et al, 1987, Psychopharmacology, *93*, 193). The weak anorectic activity of paroxetine in rats is compatible with the slight, clinically insignificant weight loss observed in depressed patients in clinical studies.

NR616 Thursday May 16, 12 noon-2:00 p.m.

Paroxetine in the Treatment of Severe Melancholic Depression

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Summary:

A truly effective antidepressant should have activity in severely depressed or melancholic patients. To assess such efficacy for paroxetine, two meta-analyses were undertaken.

Patients with *DSM-III* diagnoses of melancholia were considered and assessed for a full clinical response. This was measured by (a) endpoint HAMD <10, (b) decreased in baseline-endpoint HAMD >50 percent, (c) endpoint CGI score 1 or 2. Paroxetine ($n=245$) was significantly superior to placebo ($n=70$) on all three measures when patients with a baseline HAMD >18 were considered. This superiority for paroxetine ($n=224$) was also seen when many patients with severe melancholia (baseline HAMD >28) were reviewed.

Severely depressed (HAMD >25) hospitalized patients who received paroxetine ($n=109$) were compared with those who received a standard antidepressant ($n=107$). No significant differences was noted between therapies of any of the three outcome measures described above.

These results indicate that paroxetine is superior to placebo and as effective as standard antidepressant therapy in treating patients with severe or melancholic depression.

NR617 Thursday May 16, 12 noon-2:00 p.m.

Wellbutrin Blood Levels and Clinical Response

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Summary:

Blood levels of antidepressants have been previously found beneficial in maximizing therapeutic response to tricyclic antidepressants (Amsterdam, 1980). Preskorn (1983) reported that maximal response to buproprion (Wellbutrin) occurred at blood levels of 25-100 ng/ml. In this preliminary report, we have attempted to replicate this result. Fifteen patients (seven bipolar NOS depression; eight hypersomnic major depression by *DSM-III-R*) underwent a controlled open trial of buproprion. Dosage was initiated at 75mg tid & increased by 75 mg every three days until a maximal dose of 450 mg was reached. Pts stayed at lower dose if improved earlier. The Beck Depression Inventory (BDI) was completed at baseline, two weeks, four weeks, and eight weeks; a blood level was collected after four weeks. As neither dose nor blood level correlated significantly with improvement (.03, .37, resp.), seven pts with blood levels in range of 11-20 ng/ml(low) were contrasted in response to eight pts with levels in range of 30-100 ng/ml (high). The low group (16.3 ± 7.5) showed significant greater improvement than the high group (-1.0 ± 9.6) in mean BDI change ($t=3.84, p=.002$). A total of 6/7 low group patients showed significant improvement with a drop in BDI below 10; only 1/8 high group patients did (Chi-sq $=8.04; p=.005$). Thus, lower buproprion blood levels need to be investigated in order to attain maximal clinical response. This relationship may be curvilinear, rather than linear, in origin with a lower beginning to its therapeutic "window."

NR618 Thursday May 16, 12 noon-2:00 p.m.

Light for SAD: How it is Used and Who Responds

Dan Oren, M.D., IRP, CPB, NIMH Bldg 10 3N228; 9000 Rockville Pike, Bethesda, MD 20892; Frederick Jacobsen, M.D., Constance Carpenter, M.A., Christine L. Cameron, B.S., Thomas A. Wehr, M.D., Norman E. Rosenthal, M.D.

Summary:

Phototherapy has become the standard treatment for wintertime seasonal affective disorder. Nevertheless, little information is available on how light therapy is routinely administered and little data exist to offer guidelines for identifying patients likely to respond to phototherapy. We surveyed SAD patients to determine patterns of self-selected light use. Data obtained from 127 patients indicate that 87 percent of patients derived sustained benefit from phototherapy; over 90 percent of patients used the lights in January and February. Fifty-seven percent of patients used lights in the morning and evening; 21 percent used lights in the mornings; and 20 percent used lights in the evenings. Nine percent of patients did not use light treatment on weekends. Patients experienced a mean of one side effect, with eyestrain (26 percent), headache (25 percent), or insomnia (24 percent) being the most common. We also examined data from 44 women with SAD to determine whether any demographic or diagnostic characteristics would be predictive of a favorable response to phototherapy. Hypersomnia, carbohydrate craving, and suicidality were all associated with lessening of depression after phototherapy ($p=.002$). Both "typical" ($p=.0001$) and "atypical" ($p=0.007$) depressive symptoms correlated with improvement after phototherapy.

NR619 Thursday May 16, 12 noon-2:00 p.m.

Fluoxetine Associated Sexual Dysfunction: Open and Placebo Controlled Trials of Treatment With Yohimbine

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Summary:

Sexual dysfunction has been reported to occur in two to eight percent of patients treated with fluoxetine. However, these figures represent only erectile or orgasmic difficulties and omit changes in sexual desire. Over a three-year period, 54 of 160 outpatients (34 percent) reported the onset of sexual dysfunction following successful treatment of depression with fluoxetine 20-40 mg. Sixteen patients reported decreased libido; 21 patients reported decreased sexual response; and 17 patients reported declines in both areas.

The alpha2-adrenoceptor blocker yohimbine has been used to treat both organic and psychogenic impotence. A total of 15 patients (six women, nine men) complaining of sexual dysfunction with fluoxetine participated in an open trial of yohimbine 5.4 mg TID. Eleven patients reported complete or partial improvement with yohimbine, four patients reported poor responses or intolerable side effects (nausea, anxiety). A double-blind placebo-controlled trial of yohimbine in fluoxetine-associated sexual dysfunction is in progress.

Preliminary findings suggest that: 1) fluoxetine-induced sexual dysfunction may include libidinal as well as physical toxicity and may occur more frequently than previously appreciated; 2) fluoxetine-associated sexual dysfunction may be treated with yohimbine. Results of the open and placebo-controlled trials will be reported and discussed with respect to the neurophysiological actions of fluoxetine and yohimbine.

NR620 Thursday May 16, 12 noon-2:00 p.m.

Effect of Phototherapy on 5-HT Metabolism in SAD

Attila Nemeth, M.D., c/o Mihaly Arato, M.D., Hamilton Psych Hospital, P.O. Box 585, Hamilton Ontario, Canada L8N3K7; Mihaly Arato, M.D., Erika Szadoczky, M.D., Annamaria Falus, Ph.D., Laszlo Tothfalusi, Ph.D., Rick Guscott, M.D.

Summary:

Thirty-one patients with seasonal affective disorder (SAD), and 14 patients with non-seasonal depression (non-SAD) were treated with one hour morning bright light (2500 lux). After seven days 71 percent of the SAD patients improved - post-treatment HDRS score <50 percent of the baseline rating and <10 - while only one of the non-SAD patients was responder.

Parameters of platelet imipramine binding sites (Bmax and Kd) - which is associated with presynaptic serotonin uptake mechanisms - as well as platelet 5-HT content was assessed before and after seven days phototherapy. Mean Bmax value was significantly lower in patients with both SAD and non-SAD than in healthy controls. After phototherapy the Bmax - simultaneously with the clinical improvement - significantly increased in SAD patients (from 734.3 +/–162.3 to 1084.2 +/–293.4 fmol/mg protein). No significant change was observed in non-SAD patients (668.5 +/–297.3 vs 795.6 +/–315.9), and in the healthy controls (1154.2 +/–139.7 vs 1137.8 +/–114). The initial and subsequent Kd values did not differ among the three groups, and there was no significant change in the Kd values.

There was no significant difference in platelet 5-HT content between SAD and non-SAD patients before (0.58+/–0.3 vs. 0.47+/–0.1 nmol/10^8 platelets,) and after seven days phototherapy (0.65+/–0.3 vs 0.57+/–0.3). In SAD patients the platelet 5-HT content continued to increase during the second week of phototherapy up to 0.75+/–0.3.

Our results show that phototherapy influences 5-HT metabolism suggesting that serotonergic dysregulation may play a role in the pathomechanism of SAD.

NR621 Thursday May 16, 12 noon-2:00 p.m.

Primary Care Depression: Psychotherapy or Drugs?

Christopher P. Freeman, M.B., Psychiatry, Edinburgh University, Royal Edinburgh Hospital, Edinburgh, Scotland EH105HF; Allan I. Scott, M.D.

Summary:

Aims (1) To compare the effectiveness of specialist versus routine general practitioner (GP) treatment for depressive disorders in primary care. (2) To examine the effectiveness of two different forms of psychotherapy compared with antidepressant drug treatment in the same group. *Methods*: 121 consecutive referrals who met *DSM-III-R* criteria for major depressive disorder and who gave informed consent were randomly allocated to one of four different interventions: (1) Cognitive behaviour therapy, (2) dynamically orientated counseling, (3) antidepressant drug treatment from a psychiatrist and (4) routine GP care. Treatment was carried out over 16 weeks with assessment by Hamilton and Montgomery-Asberg rating scales at monthly intervals. Follow-up was at six months and 18 months. *Results*: Outcome was analyzed by intention to treat, by a scientific analysis, using mean end point Hamilton and Montgomery-Asberg scores and by predefined levels of recovery. All groups improved considerably with time. In all analyses, specialist treatment showed advantages over routine GP care. One of the most striking findings was the much higher proportion of patients showing complete recovery at four and eight weeks with specialist treatment. When specialist treatments were compared there were advantages for the two psychotherapeutic treatments at the end of 16 weeks but not at 18-month follow-up. All therapeutic contact was timed. This varied from 37 minutes over 16 weeks in the GP group to 20 hours in the dynamic counseling.

NR622 Thursday May 16, 12 noon-2:00 p.m.

A Study to Investigate the Efficacy, Adverse Events, Safety, and Pharmacokinetic Effects of Co-Administration of Paroxetine and Lithium

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Summary:

An open, five-week study was conducted to investigate the effect of adding paroxetine (30 mg) to patients already stabilized on lithium therapy presenting with an acute episode of depression (*DSM-III*). Efficacy was assessed using the 21-item HAMD and CGI. Adverse events were assessed by asking a non-leading question; safety by monitoring vital signs, haematoligical, and biochemical parameters. Pharmacokinetic variables were derived from weekly plasma sampling of lithium and paroxetine levels. Results showed that lithium plasma levels were unaffected by concurrent treatment with paroxetine. Paroxetine plasma levels were within the range expected for an outpatient study. Eighteen of the 19 patients completed the study. No patients withdrew as a result of adverse events, of which tremor and sweating and were the most frequently reported. No safety parameters were considered clinically abnormal. Efficacy measures were significantly improved. From this small study it can be concluded cautiously that paroxetine and lithium may be co-administered, there being no apparent pharmacokinetic or pharmacodynamic interaction.

NR623 Thursday May 16, 12 noon-2:00 p.m.

A Double-Blind Multicentre Study Comparing Paroxetine with Fluoxetine in Depressed Patients

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Summary:

A randomized, double-blind, parallel group, six-week study was undertaken to compare the efficacy and side effects of once- or twice-daily administration of the selective serotonin re-uptake inhibitors, paroxetine and fluoxetine.

After a one-week placebo washout, patients suffering from *DSM-III* major depression and with a score of 18 or more on the 21-item HAMD scale received either paroxetine or fluoxetine. Patients were assessed for efficacy using the HAMD, MADRS, and the CGI rating of severity of illness and clinical improvement. Adverse events were collected in response to a non-leading question plus a specially designed side effects checklist. Both groups of patients were comparable on entry to the study.

Results from 100 patients suggested that paroxetine and fluoxetine exhibited equivalent therapeutic efficacies on all rating scales at week 6, but some trends were noted in favor of paroxetine at earlier assessment points. In addition, patients on paroxetine reported fewer adverse events and rated any events experienced as less severe than did patients on fluoxetine.

NR624 Thursday May 16, 12 noon-2:00 p.m.

Methylphenidate Test in Depression: A Qualitative Study

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Summary:

Several studies have demonstrated the predictive value of challenge stimulant tests in depression. A positive or euphoric response correlates with a positive treatment response to "noradrenergic" antidepressants and a dysphoric response with a positive response to the "serotonergic" antidepressants. But no studies have attempted to define the pre-test clinical characteristics of positive vs negative responders.

Mood response to methylphenidate was evaluated in a double-blind controlled study. Twenty-five patients (11 males, 14 females, mean age: 41 yrs ± 10.6) were included, meeting the *DSM-III-R* criteria of major depressive disorder. After randomization, each patient received 40 mg of methylphenidate p.o. the first day and a placebo the second day or the reverse. The clinical evaluations took place one hour and three hours after each treatment (Beck autoinventory, Montgomery-Asberg DRS, Jouvent multidimensional mood scale and, only for the first evaluation, Hamilton DRS). Moreover, each patient had to qualify the global effect of each treatment (positive, negative or null).

Eight patients exhibited a positive response, nine an exacerbation of their symptoms, and eight no modification. Interestingly, the global severity of the depression was not different in the three groups. Mean ± sd scores at HDRS: positive group 23.7 ± 3.6, negative group 23.6 ± 4.3, null group 24.5 ± 6.9. But, from a qualitative point of view, the positive group differed clearly from the two others by a pre-test higher sub-score of blunted affect and a lower sub-score of impulsivity/irritability, both sub-scores derived from the Jouvent's mood scale. Therefore, a qualitative study of methylphenidate effects on mood appears of heuristic value.

NR625 Thursday May 16, 12 noon-2:00 p.m.

Dysthymia: Response to Fluoxetine and Trazodone

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Summary:

Seventeen patients diagnosed with *DSM-III-R* dysthymic disorder uncomplicated by major depression or other major Axis I disorders completed open-label trials of either fluoxetine or trazodone. Mean doses were 30.9 mg/d and 241.7 mg/d, respectively. After three months of treatment, 12 patients (70.6 percent) responded, according to both clinician-rated and patient-rated criteria (Hamilton-D scores and patient-rated CGI). At five months, five patients had relapsed, leaving seven (41.2 percent) patients in continued remission. We discuss the probability that this represents a true drug response and suggest reasons for the high rate of relapse, in addition to implications for treatment planning. These results concur with Akiskal's proposal that a subgroup of dysthymics may have an attenuated form of major depressive disorder amenable to treatment with antidepressant medication.

NR626 Thursday May 16, 12 noon-2:00 p.m.

The Prevalence of Post-Stroke Depression

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Summary:

The actual prevalence of post-stroke depression (PSD) varies in the literature between 30 percent - 60 percent. A higher incidence of PSD following left brain damage (LBD) has been reported but this finding is currently being challenged by a growing number of researchers. To further evaluate this issue, 94 unilateral rehabilitation stroke patients [49 LBD; 45 Right Brain Damage (RBD)] were administered a clinical interview to assess their mood and determine a *DSM-III-R* diagnosis. Sixty-eight percent of the sample were clinically depressed (major depression = 53 percent LBD; 51 percent RBD; minor depression = 14 percent LBD; 18 percent RBD). No statistical differences were found between LBD and RBD groups (x^2 = .21, ns) suggesting the prevalence of PSD depression to be independent of laterality and of equal severity in both RBD and LBD patients.

NR627 Thursday May 16, 12 noon-2:00 p.m.

The Effect of Enalapril on Serum Lithium Levels

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Summary:

Several authors have reported the development of lithium toxicity following the addition of angiotensin converting enzyme (ACE) inhibitors to a stable lithium regimen. To learn whether this drug interaction predictably occurs, the effect of enalapril on serum lithium levels was investigated. On Days 1 through 25 of the 26-day study, nine healthy male subjects took lithium carbonate 900 mg per day, and on days 11 through 20 took enalapril 10 mg per day.

For each subject, mean serum lithium levels between days 8 and 9 (point 1), days 20 and 21 (point 2), and days 25 and 26 (point 3) were computed. There were no significant differences in serum lithium levels between points 1 and 2 ($t = 1.43$, $p = 0.19$), points 2 and 3 ($t = -1.92$, $p = 0.091$), and points 1 and 3 ($t = -0.61$, $p = 0.56$). For three subjects, the serum lithium level on enalapril appeared from 11 percent to 31 percent higher than on lithium alone.

These results suggest that adding an ACE inhibitor to a stable lithium regimen does not predictably result in elevated serum lithium levels or lithium toxicity. However, medical illness, advanced age, or other factors may affect individual vulnerability to this drug interaction.

NR628 Thursday May 16, 12 noon-2:00 p.m.

Sleep Deprivation May Alter Dopamine Activity

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Summary:

The effects of sleep deprivation (SD) were studied in eight drug-free patients with major depression, five medicated patients with Parkinson's disease, and eight normal controls. A visual adaptation measure thought to be an indicator of dopaminergic tone[1] (Arden ratio = peak ocular potential in light/minimum potential in dark) was recorded along with mood (Hamilton depression scale) and movement disorder ratings (Simpson Angus, Disability, Functional Scales) before and after SD. Baseline Arden ratios in depression were lower than normals ($p < 0.03$). Parkinson's patients had significantly higher baseline Arden ratios than other groups although this difference may be due to treatment with dopamine precursors. Sleep deprivation improved mood in depressed patients ($p = 0.004$), worsened mood in normals ($p = 0.003$), and had no measurable effect in Parkinson's patients. Following SD Arden ratios increased in depressed patients ($p = 0.002$) and Parkinson's patients ($p = 0.015$) but decreased in normal controls ($p = 0.04$). Increases in Arden ratio following SD in major depression were strongly correlated with improvement in mood ($r = -0.767$, $p < 0.001$). Movement disorder improved in Parkinson's patients in response to SD ($p = 0.033$). The present results implicate dopamine in the mechanism of SD.

[1]Economou SG, Stefanis CN: Changes of electrooculogram (EOG) in Parkinson's disease. *Acta Neurol Scand* 1978, 58:44-52.

NR629 Thursday May 16, 12 noon-2:00 p.m.

Platelet Imipramine Binding and Clinical Symptoms

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Summary:

Previous work by our group and others has demonstrated that the number (Bmax), but not affinity (Kd), of platelet [^{3}H]-imipramine binding sites is reduced in elderly patients with depression when compared to either age-matched normal controls or patients with Alzheimer's disease. In the present study, blood samples from 35 consecutive admissions free of psychotropic medication and over 60 yo ($M = 17$, $F = 18$) who met *DSM-III* criteria for major depression, were obtained to measure the number and affinity of platelet [^{3}H]-imipramine binding sites. The Bmax was significantly lower in the patients (mean $\pm$ SD = 723 ± 279 fmol/mg protein) than age-matched controls ($M = 25$, $F = 19$; mean $\pm$ SD = 1106 ± 249 fmol/mg protein; $p < .001$), whereas the Kd was not significantly different in the two groups. Within the depressed patients, there was a significant negative correlation between the number of [^{3}H]-imipramine binding sites and the patients' total score on the Montgomery Asberg Depression Rating Scale (MADRS, $n = 34$, $p < .05$, $r = -.35$) and the Center for Epidemiological Studies-Depression Scale (CES-D, $n = 35$, $p < .02$, $r = -.43$). Within the melancholic subgroup of depressed patients ($n = 22$) there was an even stronger negative correlation between the Bmax and the MADRS ($p < .01$, $r = -.56$) and the CES-D ($p < .01$, $r = -.56$). These findings further support the reduction of platelet [^{3}H]-imipramine binding site density in depression and provide novel information on the relationship of severity of depression to this marker of serotonergic function. Supported by NIMH MH-40159.

NR630 Thursday May 16, 12 noon-2:00 p.m.

Acceleration of Nortriptyline By Sleep Deprivation

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Summary:

Sleep deprivation combined with clomipramine or lithium has been shown to produce an immediate, sustained effect in about 60 percent of patients with major depressive disorder (MDD). We examined the effect of total sleep deprivation (SD) in combination with nortriptyline in 20 patients with major depressive disorder (MDD). Patients underwent a 36-hour SD procedure followed by nortriptyline on the evening after SD. Eleven (55 percent) patients were responders; they showed a rapid and sustained remission after SD, where as nonresponders demonstrated the delayed results expected with nortriptyline, a significant difference (Hotellings $t^2 = 47.29$, $df = 15$, $p = 0.045$). High initial depression scores and absence of depersonalization were associated with response to SD, while being female and middle insomnia were associated with response to the combined regimen by stepwise multiple regression analysis. Women were also more likely than men to show sustained response with the combination therapy (Hotelling's $t^2 = 1226.07$, $df = 16$, $p = 0.007$). The combination of SD with antidepressants is an effective and safe treatment modality, with specific factors, particularly female sex, being associated with the beneficial effect.

NR631 Thursday May 16, 12 noon-2:00 p.m.

Serotonin Function and Antidepressant Action

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Summary:

Brain serotonin (5-HT) content is dependent on plasma levels of the essential amino acid, tryptophan (TRP). We have previously reported that rapid TRP depletion more frequently reversed antidepressant response to monoamine oxidase inhibitors and 5-HT reuptake inhibitors than to desipramine (DMI). This study further investigates the relationship of relapse during TRP depletion to antidepressant type in nonrefractory depressed patients randomly assigned to treatment with either DMI or fluoxetine (FLU). *METHOD:* In an ongoing study, 25 drug-free depressed (*DSM-III-R*) patients were randomly assigned to receive treatment with either DMI or FLU. All patients were either treatment naive ($N = 15$) or had had previously successful antidepressant treatment ($N = 10$). 16 of the 25 patients had therapeutic responses by predetermined criteria to antidepression treatment (DMI 7/10; FLU 12/15) and 16 (six DMI responders and 10 FLU responders) went on to TRP depletion testing. TRP depletion testing involved two two-day tests: a 15-amino acid drink and a follow-up day, in a double-blind, placebo-controlled (TRP depletion and control testing), crossover fashion. Behavioral ratings (Hamilton Depression Scale (HDRS)), and plasma (for TRP levels) were obtained prior to, during, and after testing. Relapse was defined as 50 percent increase in HDRS with total >20. *RESULTS:* Total and free TRP decreased 60-80 percent 5 hrs. after the TRP-free drink. While 5/6 FLU responders relapsed, none of the DMI responders relapsed (one DMI-treated patient experienced a partial relapse). No patient experienced significant depressive symptoms during control testing. *Implications:* Rapid depletion of plasma TRP transiently reverse antidepressant response to FLU but not DMI. Depressive relapse during TRP

depletion appears to be more related to antidepressant type than to patient variables. These data suggest that antidepressants may mediate their therapeutic effects through different mechanisms.

NR632 Thursday May 16, 12 noon-2:00 p.m.

Comorbidity of OCD and Bipolar Affective Disorder

Linda S. Austin, M.D., Psychiatry, Medical University, 171 Ashley Avenue, Charleston, SC 29425; R. Bruce Lydiard, M.D., James C. Ballenger, M.D., Mark D. Fossey, M.D., Joseph J. Zealberg, M.D., Michele Laraia, M.S.N.

Summary:

Although a close association between obsessive-compulsive disorder (OCD) and major depression is well-known, the co-morbidity of OCD and bipolar affective disorder (BPAD) has not been systematically studied. We administered the Structured Clinical Interview for *DSM-III-R* to 71 patients between age 17-16 who met *DSM-III-R* criteria for OCD. Three patients (4.2 percent) met criteria for lifetime prevalence of both disorders. Additionally, we have followed six other patients who met *DSM-III-R* criteria for OCD and BPAD. Contrary to previous observations, we found that OCD symptoms were more severe during manic episodes. Of the nine patients, six met *DSM-III-R* criteria for personality disorders. As a group these nine patients were relatively treatment-resistant; only three achieved satisfactory resolution of symptoms when treated with mood stabilizers and anti-obsessional drugs. Three patients developed manic episodes when treated with anti-obsessional drugs without mood stabilizers. These results confirm that BPAD occurs more frequently in patients than the 0.6 - 1.1 percent lifetime prevalence of BPAD in the general population reported in the ECA survey. OCD patients should be carefully screened for manic symptoms and treated with a mood stabilizer as well as an anti-obsessional agent if both conditions exit.

NR633 Thursday May 16, 12 noon-2:00 p.m.

Self-Report of Mood in Post-Stroke Depression

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Summary:

Post-stroke depression (PSD) is a common and treatable mood disorder. The incidence of PSD after stroke lateralized to the left-hemisphere (LCVA) may be greater than PSD after right-sided stroke (RCVA), and left-anterior localization may be associated with the highest probability of PSD. However, PSD following RCVA has not been widely described. Using the Geriatric Depression Scale (GDS), we studied the *self-report* of depressive symptoms before treatment for PSD following lateralized CVA in 18 right-handed PSD patients (LCVA: n = 9, mean age = 71, 4 female/5 male; RCVA: n = 9, mean age = 68, 4 female/5 male). Patients were consecutive admissions to a specialized neuropsychiatric facility who met *DSM-III-R* criteria for a major depressive episode (Organic Mood Disorder) following a clearly lateralized stroke (CVA diagnosed by history, neurologic exam *and* MRI, or CT). Patients with neuropsychological testing that showed moderate to severe cognitive impairment were excluded.

PSD patients with LCVA endorsed significantly more symptoms of depression ($t = 4.64$, $df = 16$, $p < .01$) on the GDS (mean +/- s.d. = 20 +/- 4) than PSD patients with RCVA (mean +/- s.d. = 8 +/- 6). These results suggest that PSD after RCVA may occur more frequently than previously reported, since decreased self-report of depressive symptoms can obscure the diagnosis of depression, and may represent a psychiatric manifestation of the denial syndromes which can accompany some right-hemisphere lesions (e.g. anosognosia).

NR634 Thursday May 16, 12 noon-2:00 p.m.

Comorbidity of Substance Abuse and Psychiatric Disorders

Kathleen R. Merikangas, Ph.D., Psychiatry, Yale University, 40 Temple Street Lower Level, New Haven, CT 06510; Bruce Rounsaville, M.D.

Summary:

This paper presents the current state of knowledge regarding the co-occurrence of substance abuse and psychiatric disorders. The associations between alcoholism with affective disorders and with anxiety disorders, and between drug abuse with affective disorders, anxiety disorders, and antisocial personality are systematically reviewed. The major emphasis of the paper is on the investigation of the possible mechanisms for the associations through the use of family study data.

The major findings are that substance abuse and psychiatric disorders, particularly the affective and anxiety disorders, are strongly associated both in clinical and epidemiologic samples. Moreover, the major mechanisms for the association can be attributed to a causal mechanism, whereby the substance abuse is a complication of the psychiatric disorder, or the converse, where the substance abuse causes the manifestation of psychiatric symptoms and disorders. These findings demonstrate that substance abuse and psychiatric disorders do not result from shared underlying etiologic factors. The implications of these findings for classification and treatment are discussed.

NR635 Thursday May 16, 12 noon-2:00 p.m.

Sex Difference in the Course of Depression

Kathleen R. Merikangas, Ph.D., Psychiatry, Yale University, 40 Temple Street Lower Level, New Haven, CT 06510; Jules Angst, M.D.

Summary:

This paper describes the application of prospective longitudinal data from an epidemiologic sample of young adults in Zurich, Switzerland, to define subtypes of major depression. Subjects with major depression were classified according to both duration and episodicity of depressive episodes on a continuum from those with only single episodes of major depression, recurrent episodes of depression of brief duration, to those with recurrent episodes of both major depression plus brief periods of depression.

One of the major findings of the study was the sex difference in the recurrence of major depression. Whereas the sex ratio for the single episode major depressives was approximately equal, the traditional 2:1 female-to-male sex ratio was observed for recurrent major depression and recurrent brief episodes of depression. This suggests that once a depressive disorder occurs, that females are more likely than males to experience recurrent episodes. There was a greater proportion of females with recurrence than males, with twice as many females experiencing recurrent episodes of depression over the follow-up period. These findings suggest the importance of early intervention in women with affective disorders.

NR636 Thursday May 16, 12 noon-2:00 p.m.

Information Processing Deficits in Mania

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Summary:

Some information processing deficits in schizophrenia are stable across different clinical states, suggesting that they constitute vulnerability indicators. Similar deficits in mania have been ob-

served during manic episodes, but their stability across clinical states is uncertain because longitudinal studies have not been conducted.

Seventeen chronic bipolar state hospital patients were tested during and following manic episode. There was an average of 34 days between testing sessions. Manic episode was defined by an expanded version of the Brief Psychiatric Rating Scale. Sixteen normal controls were similarly tested. Subjects received three information processing tests: Continuous Performance Test, Span of Apprehension, and the Backward masking procedure.

All information processing measures showed strong stability across clinical states in terms of both mean value and rank order. Manic patients performed worse than normal controls regardless of clinical state on most measures. Information processing performance was not related to presence of psychotic symptoms in the bipolar group. The stability of information processing deficits across different phases of the illness suggests that these deficits may be vulnerability indicators in this group of chronic bipolar patients.

NR637 Thursday May 16, 12 noon-2:00 p.m.

Clinical Utility of Subtyping Psychotic Depression

Raymond F. Anton, M.D., Psychiatry, Med. Univ of South Carol., 171 Ashley Avenue, Charleston, SC 29425; William Carson, M.D., Earl Burch, M.D.

Summary:

Although major depression with psychotic features (MDPF) is a distinct clinical entity, little information is available regarding the validity and utility of subtyping MDPF into mood congruent (MC) and mood incongruent (MI) feature subtypes. We examined the distinction of these subtypes by evaluating the specific psychotic symptoms of patients with MDPF as well as the differential excretion of urinary free cortisol. Forty inpatients who met *DSM-III* criterior for MDPF, before and after a five-day single-blind placebo period, were rated for severity of all psychotic symptoms listed in the *DSM-III* for MDPF and classified as predominately MC (N = 26) or MI (N = 14). During the placebo period a 24hr. urine was collected for UFC determination (16 MC and 14 MI patients).

The only psychotic symptoms that were more predominant ($p < .05$) in the MC group compared to the MI group were delusions of guilt or sin (72 percent vs. 29 percent) and nihilistic delusions (40 percent vs. 0 percent). Delusions of persecution were more predominant in the MI group compared to the MC group (78 percent vs. 32 percent). There was a great overlap of symptomatology between the two groups in that 71 percent of MI patients had MC symptoms while 50 percent of the MC patients had MI symptoms. Other delusions and visual hallucinations (occurring in 43 percent of the patients) were similar in both groups. UFC (ug/mg. creat.) excretion however was 56 +/– 33 in the MC patients and 34 +/– 16 in the MI patients ($p < .05$).

Although a large overlap of MC and MI symptomatology exists, a few predominant symptoms do appear at a higher rate in each subtype. Additionally, the higher UFC excretion in the MC subtype may suggest a closer linkage to the affective spectrum than for the MI subtype. Future studies should examine other biological and outcome variables to better understand the validity and utility of these classifications.

NR638 Thursday May 16, 12 noon-2:00 p.m.

Circadian Performance and Depressive Disorders

Lawrence J. Whalley, M.D., Psychiatry, Edinburgh University, Royal Edinburgh Hospital, Edinburgh, UK EH105HF; Patricia A. Shering, B.Sc., John Bennie, B.Sc.

Summary:

Abnormalities in circadian physiological rhythms are consistently reported in depressive disorders and may explain many other biological abnormalities. Antidepressant drugs can slow or desynchronize biological rhythms and the efficacy of sleep deprivation and phototherapy were predicted by the circadian rhythm hypothesis of depression. Advances in the study of circadian rhythms permit the long-term collection of performance and endocrine data by noninvasive means acceptable to psychiatric patients. We have tested the hypothesis that depressed patients have desynchronized circadian performance and salivary cortisol rhythms. Six patients were studied in hospital over 28 to 40 days. Three standardized paper and pencil tests that required each patient to search through lines of 30 random letters to detect any one of one, three, or five target letters were set at 1000, 1500, and 2000 hours and salivary cortisol was estimated at 0800, 1200, 1600, and 2000 hours. Results show desynchronization between rhythms during depression and internal resynchronization of psychological rhythms on recovery. Transient recovery was associated with temporary stabilization of phase positions of performance rhythms that desynchronized again on relapse. These findings are related to circadian rhythm hypotheses of depressive disorders, the mode of action of antidepressant drugs and susceptibility to depressive disorders.

NR639 Thursday May 16, 12 noon-2:00 p.m.

The Evolution of Reactive Depression in the USSR

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Summary:

All the records of the subjects admitted for reactive depression to the Department of Psychiatry of Grodno, USSR in the years 1955-1985 (Group I = years 1955-65, Group II = years 1966-75 and Group III = years 1976-1985) were reviewed. Information regarding clinical signs, therapeutic intervention, and evolution of the reaction were collected.

Marked changes of type of trauma were found connected with time. Subjects of Group I were more afflicted by traumatic events related to more vital areas of life; the others, especially those of the most recent group, were afflicted by prolonged subliminal stress related to more differentiated aspects of life, e.g., to the transformation in the family structure and in the working conditions. This has been found to correlate to a decrease in severity of depression and in a prevalence of neurotic signs of shorter duration.

The general improvement and the stability of the cultural and economic life conditions in the USSR is responsible for the increased capacity of the subjects to recognize the stress factors and their long-term consequences, as well as for more adequate coping behaviors. Long-term analysis has also demonstrated that, in any period of time, more severe reactions are related to a less favorable outcome.

NR640 Thursday May 16, 12 noon-2:00 p.m.

Primary Care Depression: Personality and Outcome

Allan I. Scott, M.D., Psychiatry, Edinburgh University, Royal Edinburgh Hospital, Edinburgh, Scotland EH105HF; Christopher Freeman, M.B.

Summary:

Aim: To assess the effects of personality difficulty and disorder on the outcome of treatment of depression treated in primary care. *Methods:* 103 primary care patients suffering from major depressive disorder (*DSM-III-R*) who took part in the Edinburgh Primary Care Depression Study were assessed during 16 weeks of treatment (antidepressant drug treatment, psychotherapy or standard care). Personality was assessed after maximum improvement using the Personality Assessment Schedule (Tyrer et al, 1979) and

in 75 cases a close informant was also interviewed. Clinical progress was assessed monthly using the Hamilton and Montgomery-Asberg depression rating scales. Recovery was defined as a Hamilton score <6. *Results:* 88 patients (85 percent) had one or more abnormal scores indicative of at least 'personality difficulty' on the 24 items. The 38 patients with an abnormal score of 'anxiety' were more depressed throughout and after treatment, and their recovery rate by 16 weeks was half that of the others (34 percent v. 65 percent, $p<0.01$). The 14 patients with 'Dysthymic Personality Disorder' were also more depressed throughout and after treatment, and their recovery rate was half that of those without this personality disorder (36 percent v. 63 percent, $p=0.05$).

NR641 Thursday May 16, 12 noon-2:00 p.m.

New Clinician-Administered Rating Scale for Mania

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Summary:

The authors report the preliminary development of a 15-item clinician-administered rating scale for mania based on the SADS and *DSM-III-R* criteria. This instrument represents an improvement over existing rating scales since it facilitates *DSM-III-R* diagnosis, has more clearly defined anchor points for symptom severity, and a standardized semi-structured clinical interview format. Additionally, it retains the advantages of earlier mania rating scales in that it is designed to assess severity of symptoms as well as change in response to various treatments. Reliability was established by having eight different raters independently view and rate ten videotaped interviews on patients with mixed diagnoses (schizophrenia = 3, major depression = 2, bipolar, manic = 4, bipolar, depressed = 1). All 15 items had acceptable reliability with a mean intra-class correlation coefficient of .75 (range .54 to .98). The agreement among raters for each patient across all items was also acceptable with a mean intra-class coefficient of .78 (range .60 to .98). Preliminary data with 33 patients with mixed diagnoses show significant correlations for 12 of the 15 items with the total score and excellent correlation (r = .92) with the Young Mania Scale, demonstrating good initial validity. Additional subjects are needed to properly address the scale's potential to differentiate among diagnostic groups.

NR642 Thursday May 16, 12 noon-2:00 p.m.

Cognitive Dysfunction in Late-Onset Depression

George S. Alexopoulos, M.D., Psychiatry, NYH-WD Cornell, 21 Bloomingdale Road, White Plains, NY 10605; Steven Mattis, M.D., Barnett S. Meyers, M.D., Robert C. Young, M.D., Janis Chester, M.D.

Summary:

Absence of family history of affective disorders and presence of morphological brain abnormalities have been noted in late-onset depression. These findings raise the question whether one or more neurological brain disorders predispose to late-onset depression. In a previous study, we reported that patients with depression-dementia have later age of onset than elderly patients with depression alone. In this investigation, the hypothesis was tested that non-demented late-onset depressives (LOD) have more cognitive dysfunction than geriatric patients with early-onset depression (EOD).

The subjects were 39 depressed geriatric inpatients and outpatients consecutively admitted to a longitudinal study of depression. Since LOD patients (onset older than 64 years) were somewhat older than EOD subjects, comparisons were made with ANCOVA using age as a covariate. LOD subjects had lower scores than EOD patients in the Memory Subscale of the DRS ($F = 4.2$, $df = 2, 36$, $P<0.05$), and the Visual Naming Scale of the Multilingual Aphasia Examination ($F = 4.0$, $df = 2, 36$, $P<0.05$). Since abnormalities in memory and visual naming may be associated with temporal lobe dysfunction, these findings point to the need for studies of temporal lobe dysfunction in late-onset depression.

NR643 Thursday May 16, 12 noon-2:00 p.m.

Disability and Environment in Late-Onset Depression

George S. Alexopoulos, M.D., Psychiatry, NYH-WD Cornell, 21 Bloomingdale Road, White Plains, NY 10605; Barnett S. Meyers, M.D., Robert C. Young, M.D., Janis Chester, M.D.

Summary:

Clinical, biological, and family history differences have been reported between late- and early-onset depressed patients. Given the relative absence of family history of psychiatric disorders in late-onset depression, it has been speculated that factors other than genetic or familial contribute to this disorder. This study tests the hypothesis that disability and adverse environment are more frequent in late- compared to early-onset geriatric depressives.

The subjects were 39 inpatients and outpatients with major depression who were consecutively admitted to a longitudinal study. All had an extensive systematic clinical assessment; disability and environmental factors were evaluated with the Philadelphia Multiphasic Assessment Instrument. Data were analyzed using ANCOVA with age as a covariate. LOD subjects had lower scores than EOD patients in the Mobility Index ($F = 6.9$, $df = 2, 36$, $P<0.01$). Similarly, LOD subjects had lower scores than EODs on the Environmental Domain Index ($F = 11.8$, $df = 2, 36$, $P<0.001$), as well as on the Neighborhood Domains (Dwelling Unit: $F = 10.5$, $df = 2, 36$, $P<0.002$); Neighborhood: $F = 7.7$, $df = 2, 36$, $P<0.008$). Finally, LOD subjects had lower scores on the Social Support Domain than EOD patients ($F = 20.9$, $df = 2, 36$, $P<0.0001$). These findings are consistent with the hypothesis and raise the question whether disability and adverse environment contribute to the development of late-onset depression.

NR644 Thursday May 16, 12 noon-2:00 p.m.

Neuroleptic-Induced Psychosis in Affective Disorders

John M. Downs, M.D., Psychiatry, UT Memphis, 66 N. Pauline Ste 633, Memphis, TN 38105; Hagop S. Akiskal, M.D., Anna D. Downs, Ph.D.

Summary:

Based on clinical observations, we hypothesized that neuroleptic induced psychosis (NIP) occurs in patients with mood disorders. This neuroleptic (NL) induced schizophrenic-like psychosis superimposed upon the mood disorder may produce a "pseudo" schizoaffective (SA) disorder. The diagnosis may then be changed to a SA disorder. To test our hypothesis, we studied 40 patients that met *DSM-III* criteria for a SA disorder. Six met our criteria for NIP in mood disorders. We compared these subjects' entire treatment course (mean 14.8 yrs) including several variables to a matched group with primary SA disorder. The NIP groups' NL dose was increased ($P=0.01$), as was the incidence of TD ($P=0.0008$). Relapse time ($P=0.04$), and the GAFS values were decreased ($P=0.0001$) compared to the primary SA group. These findings and the case studies, showing the development of first rank symptoms after yrs of NLs and their rapid recurrence when NLs are decreased, are consistent with NIP. We then did a five-year follow-up on both groups. Two NIP subjects greatly improved when their NL was reduced. We believe our findings suggest NIP may occur in subjects with mood disorders and may alter their disease and worsen their prognosis. Our findings also indicate that NIP may be reversible in some patients if diagnosed and the NL treatment changed.

Therefore, NIP in mood disorders may present a new diagnostic and treatment challenge in psychiatry.

NR645 Thursday May 16, 12 noon-2:00 p.m.

Seasonal Variation of Symptoms at 41 Degrees North Latitude

David S. Schlager, M.D., Suny at Stony Brook, HSC T10, Stony Brook, NY 11794; Joseph E. Schwartz, Ph.D., Lisa Brandon, B.S., Evelyn J. Bromet, Ph.D.

Summary:

Mood cycles tied to seasonal change have been identified both among depressed patients and community samples. Such findings have often been limited by selection bias and unreliability of retrospective measures.

We re-analyzed current, self-rated measures from the Hopkins Symptom Checklist (HSCL), collected transversely over a one-year period from 1,870 white collar workers. Five standard symptom dimensions were scored plus a global severity index (GSI, all items) and a modified depression scale (SAD) inclusive of symptoms common among winter depressives.

Inverse correlations were seen, though only among women ($n = 314$), between HSCL symptoms and available daylight at the time of assessment. Among women, shorter days were associated with increased GSI ($R = -.13, p < .05$), anxiety ($R = -.20, p < .0005$), SAD ($R = -.14, p < .02$), and somatization ($R = -.12, p < .05$) scores. The proportion of female "cases," as defined by HSCL severity criteria, was approximately twice as high during December through February as during the rest of the year.

Effects on the data of retrospective distortion or seasonal bias must be considered minimal. Correlation of symptoms with available daylight is consistent with accumulating evidence for the role of light in eliciting or synchronizing mood rhythms. Interactions between season and sex should be considered in clinical and epidemiologic assessment of mood disorders.

NR646 Thursday May 16, 12 noon-2:00 p.m.

Auditory Dysfunction and Late-Onset Depression

Balu Kalayam, M.D., Psychiatry, New York Hospital, 21 Bloomingdale Road, White Plains, NY 10605; Tatsu Kakuma, Ph.D., Robert Young, M.D., Gabriel Tsuboyama, M.D.

Summary:

In elderly patients at a hearing clinic (1,2), we had noted the onset of late life major depression to be associated with increase in pure tone perception thresholds (PTT). We have now examined PTT among patients consecutively admitted to a psychogeriatric service. The sample of geriatric patients ($n = 55$) consisted of: a) late-onset major depressives, with onset of illness after age 60 years (LOD, $n = 23$; mean age = 81.1 yrs ± 6.0 yrs); b) early-onset major depressives, with onset of illness before age 60 years (EOD, $n = 20$; mean age = 72.5 yrs ± 5.9 yrs); and c) patients with other non-dementing late onset psychiatric disorders (OD, $n = 12$; mean age = 72.7 ± 8.6 yrs). PTT was tested at frequencies of 500 to 2000 hertz following adequate treatment for their psychiatric illness and preceding discharge from the hospital. Patients with middle ear pathology were excluded. LODs had higher PTT compared to EODs (LOD mean ± SD = 43.6 dB ± 16.8 dB; EOD mean ± SD = 18.3 dB ± 8.4 dB; $p < .005$ ANCOVA) and ODs (PTT mean ± SD = 22.8 dB ± 7.7 dB; $p < .01$ ANCOVA), after adjusting for differences in age.

In the combined group of depressives ($n = 43$) the ability of PTT to predict age at onset of depression was examined using logistic regression. There was a significant "PTT effect" on age at onset of depression ($x2 = 7.686$, $p < .006$; goodness of fit statistics $g2 = 18.29$, $df = 40$) after adjusting for "age effect" ($x2 = 4.080$, $p < .05$). These findings further support the "specificity" of an association between increased PTT and late-onset depression.

NR647 Thursday May 16, 12 noon-2:00 p.m.

Suicidal Thoughts and Behavior With Paroxetine

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Summary:

Suicidal thoughts and actions are common during depression, occurring in 30-70 percent of patients, depending on the severity of the illness. Recently interest has focused on suicidal ideation being caused by pharmacotherapy.

This possible phenomenon has been explored for the new antidepressant paroxetine, a potent and selective 5-HT uptake inhibitor. Worldwide data were considered, paroxetine ($n = 2963$), placebo ($n = 554$), active control ($n = 1,151$), and the following analyses performed: (a) change in HAMD suicide item over time, (b) disassociation between HAMD suicide and retardation items, (c) worsening of HAMD suicide item.

Both active therapies had a beneficial effect on suicide ideation. Paroxetine did not cause increased disassociation between HAMD items, nor increased emergence of suicidal thoughts. This latter phenomenon seemed to be illness, rather than therapy related.

NR648 Thursday May 16, 12 noon-2:00 p.m.

Neurobiology of Early-Life Trauma in Depression

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Summary:

The relationship between childhood trauma and resultant neurobiological dysfunction in adulthood has been a subject of recent investigation. This study examined the relationships between early-life trauma, alpha-2 adrenergic receptor function, and HPA axis function in patients with major depression. *METHODS:* Initially, 40 drug-free adults with major depression (*DSM-III*) received either the alpha-2 adrenergic receptor antagonist yohimbine 20 mg (p.o.) or placebo (p.o.) on two separate test days. Blood for plasma cortisol (CORT) and plasma-free MHPG was obtained at baseline and throughout the study. Subsequently, a blind retrospective chart review was conducted (N-34) in which the occurrence and severity of specific childhood (birth-age 18) traumatic events were sought. *RESULTS:* Mean baseline CORT levels were significantly higher in those patients without a history of trauma (T(–)) compared with those patients with a history of trauma (T(+)) (13.6 ± 4.4 ug/dl vs 9.8 ± 4.3 ug/dl, $p < 0.02$). No significant difference was found in mean baseline MHPG levels between these two groups (3.9 ± 1.3 ng/ml vs 3.6 ± 1.3 ng/ml, n.s.). A trend toward a more robust placebo-corrected peak change in CORT response to yohimbine was found when comparing patients T(–) and T(+) (2.6 ± 3.4 ug/dl vs –0.1 ± 5.4 ug/dl, $p < 0.1$). Patients T(+) had a significantly earlier age of onset of psychological problems than did patients T(–) (20.9 ± 12.0 years vs 31.2 ± 16.0 years, $p < 0.04$). In T(+) patients, severity of trauma was negatively correlated with baseline CORT ($p < 0.05$) and with age of onset of first psychological problems ($p < 0.02$). *CONCLUSIONS:* These data suggest early-life trauma may be related to HPA function and age of symptom onset in adults with major depression. Patients (T–) appear to demonstrate the hypercortisolism characteristic of endogenous depressives, whereas patients T(+) appear to have normal or reduced HPA activity and to have an earlier age of onset of psychological problems.

NR649 Thursday May 16, 12 noon-2:00 p.m.

Fluoxetine in Major Depressives With or Without History of Suicidality

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Summary:

Research on the effects of fluoxetine (FL) on suicidality are scant and conflicting. Time by time FL has been claimed to induce suicidal ideation (1) and, conversely, to be more effective on suicidal feelings than placebo and mianserin (2). Furthermore, FL and clomipramine are superior to nortriptyline and desipramine in major depressives with a history of suicidal attempts (3). The group of patients treated with FL (mean daily dose: 25mg) has been extended to 59 subjects with a *DSM-III-R* diagnosis of major depression and a baseline minimum score of 22 on HRSD. The percentage of FL-responders (HRSD scores decreased at least by 50 percent after four weeks' treatment) was 66 percent. Responders and nonresponders were matched for FL doses and baseline HRSD scores. Conversely, a history of suicidality in the present or previous depressive episodes affected response to FL: it was effective in 53.1 percent of 32 patients with a negative history of suicidal thinking and acts, compared to 81.5 percent found in 27 patients with suicidal ideation or acts (chi square 4.07; p = .043), and to 91.7 percent of 12 suicide attempters (chi square 4.06; p = .044). Therefore, a history of suicidality seems likely to be an acceptable predictor of a good response to FL.

References: (1) Teicher MH et al., *Am J Psychiatry* 147:207-210, 1990; (2) Muijen M et al., *Acta Psychiatr Scand* 78:384-390, 1988; (3) Sacchetti E et al., in Cassano G.B. and Akiskal H.S. (Eds.): Serotonin-Related Syndromes: Clinical and Therapeutic Links. Royal Society of Medicine Services Limited, London, in press.

NR650 Thursday May 16, 12 noon-2:00 p.m.

A Dose-Response Curve for ECT Outcome Prediction

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Summary:

Despite a half century of experience with electroconvulsive therapy (ECT), we have only limited formulations regarding a dose-response curve for this important somatic treatment. Clinical features of the depressive illness remain the best predictors of response to ECT. Technical parameters thought to contribute to response include stimulus waveform, frequency of treatment sessions, electrode placement, duration of seizures, and cumulative seizure time.

In this pilot study, the rate of resolution of depressive symptoms was compared with cumulative seizure time. Patients had clinical diagnoses of *DSM-III-R* depressive illness known to be remediable by ECT. Ratings with the Hamilton Depression Scale were obtained throughout the treatment course. To date, analysis of the results of the first five patients using simple linear regression methods revealed that treatment courses with correlation coefficients (r) greater than -0.78 are associated with good outcomes, while those with r values below this represent a suboptimal response. Analysis of the slopes of the regression lines yields a similar dichotomization in outcome prediction. This method of study may alert clinicians to the need for making technical changes early in a course of ECT to optimize patient outcome.

NR651 Thursday May 16, 12 noon-2:00 p.m.

Serotonergic Function in Lithium Augmentation

Elinore McCance-Katz, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Lawrence H. Price, M.D., Dennis S. Charney, M.D., George R. Heninger, M.D.

Summary:

Serotonergic mechanisms have been implicated in the pathophysiology of depression and in the neuropharmacology of antidepressant treatment. One measure of central serotonergic function is the prolactin (PRL) response to i.v. L-tryptophan (L-TRP). We used the L-TRP test to assess the role of serotonin in the mechanism of action of lithium augmentation in refractory major depression. We hypothesized that the PRL response would be greater following lithium augmentation than following primary antidepressant treatment alone. *METHOD:* 26 patients with antidepressant-refractory major depression each received 3 L-TRP tests (after two weeks of placebo, after four weeks of active primary antidepressant, and after eight days of lithium augmentation). Each test consisted of L-TRP 7 g i.v. infused over 20 minutes, with serial blood sampling for PRL assayed by RIA. *RESULTS:* The PRL response to L-TRP during lithium augmentation was greater than that following primary antidepressant alone. Primary antidepressant treatment did not increase the PRL response. Lithium augmentation resulted in a statistically significant increase in PRL area under the curve (AUC) ($p \leq 0.035$, t-test of means). *IMPLICATIONS:* This study supports a role for serotonergic mechanisms in the action of lithium augmentation. Additional data on specific antidepressant and clinical correlates will be presented.

NR652 Thursday May 16, 12 noon-2:00 p.m.

Folate and B12 Concentration in Manic Depressive Outpatients Treated With Lithium

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Summary:

Folate and B12 deficiency may occur as a result of poor dietary intake, diminished absorption, increased need for their utilization in the body and other reasons. Recent reports suggest a possible link between the low serum folate levels, lithium treatment, and depressed mood. However, this relationship is still debatable. The authors conducted a study on 187 outpatients of both sexes. Serum levels of lithium and B12 as well as serum red blood cells concentrations were measured in patients with *DSM-III-R* mood and schizoaffective disorders from two McGill University affective disorders clinics: 95 patients from the Allan Memorial Institute (AMI) and 92 from the Montreal General Hospital (MGH). Nonparametric analysis suggested that at both centres, mean and median B12 concentrations were significantly lower in subjects taking lithium as compared to those not taking lithium (Mann-Whitney U, p = 0.30 and 0.040 at AMI and MGH, respectively). Serum and RBC folate levels did not differ significantly between lithium and non-lithium groups. Stepwise multiple regression suggested that at both centres, lithium was a statistically significant predictor of lower serum B12 concentration (p = 0.041 and 0.012 at AMI and MGH, respectively). The results will be further discussed.

NR653 Thursday May 16, 12 noon-2:00 p.m.

Trimipramine Versus Doxepin-Cardiac Safety in Elderly Depressives

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Summary:

The cardiovascular effects of tricyclic antidepressants (TCA's)

are of particular concern when treating geriatric depression. This double-blind, parallel group study compared the cardiac safety and therapeutic efficacy of trimipramine and doxepin in 37 elderly patients with a diagnosis of major depressive episode (*DSM-III* criteria). After a one-week placebo period, patients were randomly assigned to one of two treatment groups receiving either doxepin or trimipramine, up to 200 mg per day, for a period of five weeks.

Both drugs were equally effective in relieving symptoms of depression and anxiety. The trimipramine group did show some lowering of blood pressure but this was not clinically relevant. Although TCA's are reported to be strongly associated with orthostatic hypotension, particularly in the elderly, this was not found in this study. Eight patients in the trimipramine group and ten patients in the doxepin group had pre-existing ECG abnormalities (Eg. T wave and ST segment changes). Three trimipramine patients and five doxepin patients developed occasional premature ventricular or atrial contractions. Of these, two trimipramine patients and one doxepin patient were among those with abnormal ECG's at entry. No other abnormal clinical or EKG findings were noted during the study.

While doxepin has been the treatment of choice for geriatric depression because of its low potential for cardiotoxicity, the results of this study suggest that trimipramine may be an equally safe and effective alternative.

NR654 Thursday May 16, 12 noon-2:00 p.m.

SAD: Circadian Effects of Midday Light Exposure

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Summary:

Hypotheses regarding the mechanism of action of light therapy for fall/winter seasonal depression (SAD) have implicated changes in endogenous circadian phase or amplitude. A validated method for assessing the functioning of the circadian pacemaker uses body core temperature recorded under the minimal masking conditions of a "Constant Routine" (CR) protocol.[2] Avery *et al.*[1] used a modified CR and found a trend toward delayed circadian phase in depressed SAD patients that was advanced following morning light, when depression was alleviated.

We report preliminary results from circadian assessments of SAD outpatients given midday light. In Fall, three depressed women meeting *DSM-III-R* criteria for recurrent major depression, Seasonal Pattern, carried out a 40-h CR before and after five days of light therapy (6000 lux, 10:00-14:00h) during the follicular phase of the menstrual cycle. Three comparable SAD patients received the same protocol in Summer, when euthymic. The table presents body core temperature data [mean ± S.D.], giving the time of the minimum (Tmin) and rhythm amplitude (Ampl; in °F), estimated as per Brown and Czeisler (1985; reference in[2]). Fall depression improved markedly after light (HAMD: Before[5]19 ± 7; After[5]3 ± 1). These preliminary results suggest that in some SAD patients effective midday light therapy in Fall may affect the endogenous circadian timing system.

	Subject	Age	Tmin: Before	After	Ampl: Before	After
SUMMER	S1	40	5:20 ± .31h	3:31 ± .41h	.503 ± .03	.462 ± .01
	S7	28	5:46 ± .31h	4:42 ± .27h	.601 ± .03	.611 ± .05
	S8	52	4:27 ± .58h	2:44 ± .34h	.362 ± .02	.584 ± .03
SUMMER	S1	40	5:16 ± .56h	5:38 ± .43h	.304 ± .03	.380 ± .03
	S5	53	3:25 ± .29h	3:26 ± .62h	.404 ± .01	.492 ± .03
	S6	31	4:46 ± .23h	6:07 ± .37h	.609 ± .06	.412 ± .03

NR655 Thursday May 16, 12 noon-2:00 p.m.

Depression Severity Predicts Medical Disability

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Summary:

Recent studies such as the Medical Outcomes Study (MOS) have demonstrated a cross-sectional correlation between depression severity and functional disability. Chronic tinnitus is a medical illness where differences in disability are poorly accounted for in terms of otological factors (such as differences in loudness, frequency, or quality of the sound heard). In a previous cross-sectional study we have shown that major depression is associated with increased disability due to tinnitus. Here we present longitudinal data demonstrating that decreases in depression severity (Hamilton scores) predict decreases in self-reported tinnitus disability among 52 patients participating in a treatment trial. After accounting through multiple regression for the effects of initial tinnitus disability, initial depression severity, and drug status (nortriptyline or placebo), change in Hamilton Depression Rating Scale scores accounted for 20 percent of the decline in scores on a standard tinnitus disability measure (Iowa) ($r^2 = .20$, $t = -5.08$, $p < .0001$) and 17 percent of the decline in tinnitus disruption of daily activities as measured by visual analog scales ($r^2 = .17$, $t = -3.57$, $p < .0001$). Depression change did not predict change in self-reported loudness ($r^2 = .01$, $t = -.92$, $p > .3$). These associations held for those patients who did and did not meet *DSM-III-R* criteria for major depression. This study thus advances beyond the MOS in its demonstration of a longitudinal association between decreased depression and decreased medical disability.

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Nicotine Use High in Dysthymia or Major Depression

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Summary:

This study explores the association between nicotine use and depressive symptoms in a community sample. Households in Franklin County were identified by a variation of the Wakesburg random dialing technique. One person age 18 or older in each household was randomly identified using Kish tables. A total of 977 subjects completed a five to ten minute telephone questionnaire which included demographic data, questions about depressive symptoms, and history of nicotine use in any form.

Rates of self-reported depressive symptoms were high, with 34 percent of subjects endorsing symptoms suggestive of a history of MDD, and 15 percent endorsing symptoms suggestive of dysthymia. Subjects with dysthymic symptoms were more likely to have ever used nicotine—59 percent versus 50 percent ($p < 0.05$), as were those with symptoms suggestive of MDD—56 percent versus 49 percent ($p < 0.05$). Subjects with dysthymic symptoms were more likely to be currently using nicotine—48 percent versus 39 percent ($p < 0.03$).

Two major studies have reported an association between depression and nicotine use [1,2]. The present study implicates both dysthymia and MDD in the initiation and continuation of nicotine use. More aggressive efforts to identify and treat dysthymia and MDD may enhance public health efforts toward smoking cessation and prevention.

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Light Exposure at Birth and Later Suicide Risk

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Summary:

A variety of evidence links light and suicide. Season rates of suicide correlate with daylight length[1] and suicide occurs primarily during daylight[2]. We sought to explore the link between exposure to sunlight at birth and its effect on later suicide by examining seasonal birth rates of suicide victims at a variety of latitudes where seasonal differences in available daylight vary.

Suicide data for Alaska Natives and Saskatchewan residents over a six-year period and data for Yukon, Montana, Wyoming, and Pennsylvania residents over a five-year period were obtained for the three months surrounding the summer and winter solstice. General population birth rates were also obtained for the same locations. These data were then compared to amount of daylight at the summer and winter solstice at each location. Birth rates for suicide victims were uniformly higher for the time surrounding the summer solstice than for the winter solstice. The proportion of suicide victims born around the summer and winter solstice correlated with the hours of sunlight at the summer ($r = 0.74$, $p = 0.04$) and winter ($r = 0.78$, $p = 0.03$) solstice at each location. Seasonal differences in birth rates of suicide victims correlated with seasonal differences in daylight ($r = 0.96$, $p = 0.001$). General birth rates did not correlate with differences in daylight length at the summer ($r = -0.03$, NS) or winter ($r = -0.25$, NS) solstice.

Thus, exposure to large amounts of daylight in the "critical period" surrounding birth is associated with higher suicide rates later in life.

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Ethnic Differences in Nortriptyline Metabolism

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Summary:

The 10-hydroxymetabolites of nortriptyline (NT) may influence the therapeutic effects and toxicity of NT itself. These effects may be particularly important in non-European ethnic groups. Ghanians, Chinese, and Japanese appear to have considerably different NT kinetics than Caucasians. Responsible mechanisms include genetically determined differences in hepatic hydroxylation of NT to E-10-OHNT, and possible differences in renal clearance of 10-OHNT. We conducted a pilot study comparing six Asians with eight Caucasian young adults [Age,yr(SD):24.5(2.0) vs 28.0(2.9)] in order to assess this. There were no significant differences between the groups in body weight or creatinine clearance. Each subject received a 40 mg oral dose of NT after an overnight fast, and had blood samples for NT and metabolites obtained at 1, 2, 4, 6, 8, 24, and 32 hours afterward. Large effect sizes were observed for the primary pharmacokinetic parameters. The small sample size revealed statistical trends for increased NT and E-10-OHNT availability, and decreased NT clearance in Asians compared to Caucasians. [AUC_{NT}, ng/mlhr(SD): 1509(738) vs 920(529), $p = .07$; $AUC_{E\text{-}10\text{-}OHNT}$: 2671(756) vs 2112(569), $p = .13$; Cl_{NT},1/hr(SD): 32(16) vs 54(24), $p = .08$]. These results strongly suggest a relatively reduced rate of hepatic hydroxylation in Asians, especially since the clearance of formation of E-10-OHNT, was significantly greater in the Caucasian group. However, the relatively larger $AUC_{E\text{-}10\text{-}OHNT}$ in the Asian group, despite decreased rate of hydroxylation and similar creatinine clearance, suggests that E-10-OHNT is handled differently.

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Delusional Thinking and Suicide Attempts in Major Affective Disorders

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Summary:

The relationship between suicidal behavior and delusion in depressed patients is controversial. Time by time the presence or absence of an association between suicidal behavior and delusional thinking has been reported (1, 2, 3). To further investigate this issue we have evaluated whether or not patients classified as delusional in at least two independent depressive episodes have higher chances for suicide attempt during any episode. We have selected 232 patients (146 females; mean age: 56.9 ± 12.3) with a *DSM-III-R* diagnosis of major affective disorders (Bipolar Disorder: $n = 92$; Major Depression, Recurrent: $n = 140$). Delusional patients ($n = 48$) showed a higher risk for suicide attempts (51.1 percent vs 20 percent) than nondelusional ones (Chi square = 17.09; $p < .0001$). This association pertains mainly to major depressives, (Chi square = 13.65; $p < .0005$); only a trend was observed in the case of bipolar patients. Delusion and suicide generally occurred in independent episodes and depression culminated with suicide attempts showed similar HRSD scores in the delusional and nondelusional groups. Therefore, the association between delusion and suicidality plausibly expresses the involvement of inherent personality and/or biological background rather than the greater severity and poorer prognosis coloring delusional depression.

References: (1) Fawcett J. et al., *Am J Psychiatry* 144:35-40, 1987; (2) Roose S.P., *Am J Psychiatry* 140:1159-1162, 1983; (3) Guze S.B. et al., *Arch Gen Psychiatry* 32:1147-1150, 1975.

NR660 Thursday May 16, 12 noon-2:00 p.m.

Urinary Catecholamines and Cortisol in Suicide

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Summary:

A relationship of urinary catecholamines and of urine free cortisol with parasuicide has been reported. We have reexamined this issue in patients admitted to the Liaison Unit, St. Joseph's Hospital, Hamilton, Ontario. Suicide attempters using physical means had significantly higher urinary norepinephrine (NE: 73.5 ± 7.9u/24h; m ± se; $n = 8$) than did control depressed patients (38.2 ± 6.5; $n = 10$). Those taking overdoses of antidepressants (51.9 ± 7.1; $n = 6$), benzodiazepines (65.1 ± 13.3; $n = 5$) or miscellaneous drugs (59.1 ± 11.0; $n = 11$) had intermediate NE values. In those using physical means, suicide intent correlated negatively with NE output ($6 = 0.793$, $p < .01$). In contrast to NE, urine dopamine (402.6 ± 392u/24h), epinephrine (EPI; 14.3 ± 4.0u/24h) the NE/EPI ratio (8.3 ± 0.9) and urine free cortisol (157.9 ± 11.5u/24h) did not differ between groups. There were no differences in age (37.2 ± 2.3 years), Beck Depression score (27.0 ± 2.1), Beck Hopelessness Score (10.00 ± 0.8), Suicide Ideation score (13.4 ± 1.4) or Hamilton Depression Score ($19.7 = 1.5$). In the four parasuicide groups there was no difference in suicide intent (13.2 ± 1.5). These findings indicate that there is increased NE output in those attempting suicide using physical means, but that this increase occurs chiefly in those with the lowest suicide intent.

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