1989

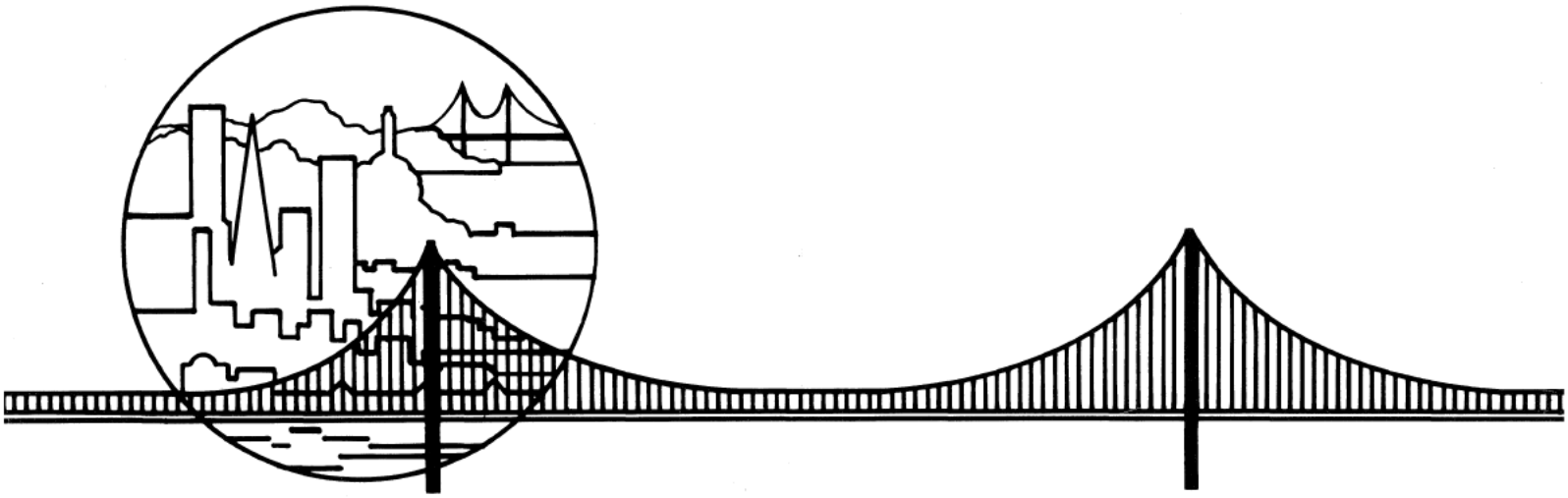
NEW RESEARCH PROGRAM AND ABSTRACTS

AMERICAN
PSYCHIATRIC
ASSOCIATION

142nd Annual Meeting

MAY 6–11, 1989

San Francisco, California



OVERCOMING STIGMA

PROGRAM
AND
PAPERS ON NEW RESEARCH

IN SUMMARY FORM

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

SAN FRANCISCO, CALIFORNIA
May 6-11, 1989

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, Hospital & Community Psychiatry, or another publication of their choice.

American Psychiatric Association

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

AMERICAN PSYCHIATRIC ASSOCIATION
142nd Annual Meeting
MAY 6–11, 1989
San Francisco, California

OVERCOMING STIGMA

May 6, 1989

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 1989 New Research Program.

This year's program reflects the increasing importance of basic and clinical neuroscience to psychiatry. Again this year all New Research Sessions are centralized in the Hilton. Another improvement is posters will remain displayed on the day of their presentation until 5:00 p.m. Thus, meeting goers who have a schedule conflict at the time of a poster presentation, in which they are interested, may view the poster later at their convenience. They are organized by topic and have been expanded to accommodate a bumper crop of excellent submissions including a new additional poster session featuring submissions submitted by young investigators.

The program begins Monday, May 8 at 9:00 a.m. with the Young Investigators' Poster Session. It continues at 10:45 a.m. with Research Advances in Psychiatry: An Update for the Clinician with special emphasis on clinical relevance, genetics, schizophrenia, obsessive compulsive disorder, eating disorders, and anxiety disorders. New Research Session 4, Tuesday, May 9, 10:30 a.m.–12 noon will be the Science Policy Session: Diversification of Psychiatric Research Funds: The Private Sector.

The New Research Oral/Slide Sessions will be held Tuesday, May 9, through Thursday, May 11, from 9:00 a.m.–10:30 a.m. Sessions will focus on schizophrenic and anxiety disorders (Tuesday); mood, personality, substance abuse, and eating disorders (Wednesday); and organic mental disorders, AIDS, and childhood disorders (Thursday). Poster Sessions, also held Monday, May 8, 9:00 a.m.–10:30 a.m., Tuesday May 9, through Thursday May 11, from 12 noon to 2:00 p.m., will be devoted to Young Investigators (Monday); schizophrenic and organic mental disorders, biologic and forensic psychiatry, brain imaging, and genetics (Tuesday); mood disorders, psychopharmacology, consultation/liaison and AIDS (Wednesday); and anxiety, personality, substance abuse and eating disorders, child psychiatry, psychotherapy and diagnostic issues (Thursday).

The 36 Oral/Slide and almost 400 Poster presentations are as 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.

And last but by no means least, we must acknowledge the many men and women who have acted as reviewers of the new research submissions to whom it is our pleasure to express here our gratitude for their vital contribution. Their names are listed alphabetically on the next page.

Sincerely,

Charles A. Kaufmann

Charles A. Kaufmann, M.D.
Chairperson
New Research Subcommittee of the
Scientific Program Committee

Outside Reviewers for New Research Program

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James J. Strain, M.D.
Trey Sunderland, M.D.
Kenneth J. Tardiff, M.D.
Gary J. Tucker, M.D.
Joe P. Tupin, M.D.
Thomas W. Uhde, M.D.
Fred Vokmar, M.D.
B. Timothy Walsh, M.D.
Daniel R. Weinberger, M.D.
George E. Woody, M.D.
Stuart C. Yudofsky, M.D.

NEW RESEARCH

Monday, May 8, 1989, 9:00 a.m.-10:30 a.m.

New Research 1—Poster Session—Yosemite Room, Ballroom Level, Hilton

YOUNG INVESTIGATORS' POSTER SESSION

Moderator: Harold Alan Pincus, M.D.

NR1 Abuse and Self-Injury in Adolescent Inpatients
Timothy G. Lesaca, M.D.

NR2 Ventricle-Brain Ratio in Schizophrenia: Clinical Correlations
John R. Dequardo, M.D., Raymond Kloss, M.D., Rajiv Tandon, M.D.

NR3 Trait Anxiety and Psychomotor Activity
Duncan Clark, M.D., Roy King, M.D., Jurgen Margraf, Ph.D., Walton T. Roth, M.D., Stewart Agras, M.D., C. Barr Taylor, M.D.

NR4 Anticholinergics and Cardiac Function During ECT
Shashidhar M. Shettar, M.D., Leon Grunhaus, M.D., Atul C. Pande, M.D., Rajiv Tandon, M.D., Ziad Kronfol, M.D.

NR5 Relationship Between Sleep EEG Measures and ECT Seizure Length
Shashidhar M. Shettar, M.D., James E. Shipley, M.D., Leon Grunhaus, M.D., Roger F. Haskett, M.D., Alan S. Eiser, Ph.D.

NR6 Spread of Cocaine Among Adults and Adolescents
John E. Hickey, L.C.S.W., Anne F. Kolar, M.D., Barry S. Michaelson, M.A., Anneke Chung, B.A., Carolyn Haynie, M.D., Barry S. Brown, Ph.D.

NR7 Cocaine: Perceived Risk and Sources of Information
John E. Hickey, L.C.S.W., Barry S. Brown, Ph.D., Anne S. Chung, B.A., Anne F. Kilar, M.D., Barry S. Michaelson, M.A.

NR8 Age and the Prevalence of Dissociation
Robert W. Hermanowski, B.S., Moshe S. Torem, M.D., Kathryn J. Curdue, M.D.

NR9 Profile of Dropouts and Attenders in a Family Support Group
Mary L. De Florio, M.D., Stephen A. Cole, M.D., Samuel Simmens, Ph.D., Robert Shapiro, Ph.D., Stuart Barr, M.D., Danny Wu, M.D.

NR10 Negative Symptom Assessment in Schizophrenia
Raman Sood, M.D., Rodney J. Pelchat, M.D., Larry D. Alphs, M.D., Jerome Levine, M.D., Harini Balu, M.D., Allen Raskin, Ph.D.

NR11 Comparison of Negative Symptom Scale
Jose de Leon, M.D., George M. Simpson, M.D., William H. Wilson, M.D.

NR12 CCRT: A Method for Comparing Neurotics and Borderline
Ellen K. Schlefer, M.D., Michael A. Selzer, M.D., John Clarkin, Ph.D., Frank Yeomans, M.D., Lester Luborsky, M.D.

NR13 Serotonin Probes in Obsessive Compulsive Disorder
Teresa A. Pigott, M.D., Dennis L. Murphy, M.D., Michele T. Pato, M.D., James L. Hill, Ph.D., Gay Grover, M.S.N., Chawki Benkelfat, M.D.

NR14 Clomipramine Versus Buspirone in OCD: A Controlled Trial
Michele T. Pato, M.D., Teresa A. Pigott, M.D., James L. Hill, Ph.D., Gay Grover, M.S.N., Suzanne E. Bernstein, B.S., Dennis L. Murhpy, M.D.

NR15 Somatostatin in Alzheimer's Disease
Susan E. Molchan, M.D., David R. Rubinow, M.D., Brian A. Lawlor, M.D., Rick A. Martinez, M.D., James L. Hill, Ph.D., Alan M. Mellow, M.D., Trey Sunderland, M.D.

NR16 The Impact of Locked Units on Seclusion Practices
Michael J. Sedlacek, M.D., William J. Burke, M.D., Steven Wengel, M.D.

NR17 The DST: Refinement of Predictive Value
Scott B. Patten, M.D.

NR18 Effect of Vasopressin and Naloxone on Cortisol
E. Jane Garland, M.D., A. P. Zis, M.D.

NR19 Metabolic Rates in OCD and Comprisons with Panic Disorders
Thomas E. Nordahl, M.D., Chawki Benkelfat, M.D., William E. Semple, Ph.D., Murray B. Stein, M.D., Thomas A. Mellman, M.D., Michael Gross, M.D., Thomas W. Uhde, M.D., Robert M. Cohen, M.D.

NR20 5-HT Function in the Biochemical Response to MCPP
John P. Selbyl, M.D., Dennis S. Charney, M.D., John H. Krystal, M.D., Lawrence H. Price, M.D., George R. Heninger, M.D.

NR21 Do Mast and Cage Scores Help Detect Alcoholism?
Connie M. Marsh, M.D., Donna A. Vaughan, M.D.

NR22 Long-Staying Inpatients: A Descriptive Study
Terry M. Brown, D.O., Robert N. Golden, M.D., David Ekstrom, M.Ph., Helen L. Miller, M.D., Dwight L. Evans, M.D.

NR23 Cognitive Impairment in Tardive Dyskinesia
Michael F. Egan, M.D., James Gold, Ph.D., Terry Goldberg, Ph.D., Darrell G. Kirch, M.D., David G. Daniel, M.D., Richard Jed Wyatt, M.D., Daniel R. Weinberger, M.D.

NR24 DSPECT in Obsessive Compulsive Disorder
John R. Debus, M.D., Michael D. Devous, Ph.D., John W. Cain, M.D., John Battaglia, M.D., S. Nadeem Ahmed, M.D., A. John Rush, M.D.

NR25 Effect of Weight Loss on Brain Neuropeptide mRNAs
Mark A. Smith, M.D., Linda S. Brady, Ph.D., Philip W. Gold, M.D.

NR26 Psychiatry Resident Identification in a Strike
Robert Kohn, M.D., Ronald M. Wintrob, M.D.

NR27 Anti-HLA Antibodies and Chlorpromazine
Robert C. Alexander, M.D., Mark A. Coggiano, M.S., Richard Jed Wyatt, M.D.

NR28 Brain Structure and Function in Schizophrenia
Ana Maria Andia, M.D., Julie Kuck, M.A.

NR29 Ventricular Brain Ratios in Dementia: Depression and Controls
Rick A. Martinez, M.D., Susan E. Molchan, M.D.,James L. Hill, Ph.D., Brian A. Lawlor, M.D., David Rubinow, M.D., Trey Sunderland, M.D.

NR30 Stimulant/Haldol Study of SPEM CPT and P50 in Normals
Dolores Malaspina, M.D., Edward Maclin, Ph.D., Barbara Cornblatt, Ph.D., Eliza A. Coleman, B.A, Harold Sackeim, Ph.D., Charles A. Kaufmann, M.D.

NR31 Substance Abuse in Borderline Personality Disorder
Rebecca A. Dulit, M.D., Minna Fyer, M.D., Timothy Sullivan, M.D., Allen J. Frances, M.D.

NR32 AIDS Knowledge and Attitudes in Psychiatric Staff
Carol L. Alter, M.D., Gregory Miller, M.D., Ellen Dickinson, M.D.

NR33 Effects of Different Light Wavelengths in SAD
Dan A. Oren, M.D., George C. Brainard, Ph.D., Jean R. Joseph-Vanderpool, M.D., Elizabeth Sorek, R.N., Scott Johnston, B.A., Norman E. Rosenthal, M.D.

NR34 Deep White Matter Hyperintensity on MRI
Raymond F. Deicken, M.D., Victor I. Reus, M.D., Luisa Manfredi, B.A., Owen M. Wolkowitz, M.D.

NR35 Changes in Cerebral Laterality with the Menstrual Cycle
Margaret Altemus, M.D., Bruce Wexler, M.D., Glenna King, B.A.

NR36 Comparison of Symptoms in OCD and Tourette's
Kathy J. Tobias-Smith, M.D., David L. Pauls, Ph.D.

NR37 Structural Changes in Astrocytes in an Experimental Model of Temporal Lobe Epilepsy
Aldo Joseph Castiglioni Jr., M.D., Steve Peterson, Ph.D., Evelyn Tiffany-Castiglioni, Ph.D.

NR38 Alcoholism and CSF IgG Synthesis in HIV Seropositive Men
Karen P.G. Drexler, M.D., James Rundell, M.D., George Brown, M.D., Susan Paolucci, M.D., Joseph Pace, M.D., Susan McManis, M.D.

NR39 Irritability and Apathy in Huntington's Disease
Carol E. Peyser, M.D., Marshal F. Folstein, M.D., Sergio E. Starkstein, M.D., Susan E. Folstein, M.D.

NR40 Fluoxetine Induced Mania
David E. Hon, M.D., Sheldon H. Preskorn, M.D.

NR41 Abuse, Dissociation and PTSD in LLPDD Patients
Margaret F. Jensvold, M.D., Frank Putnam, M.D., Kari Muller, B.A., Peter J. Schmidt, M.D., David R. Rubinow, M.D.

NR42 Effects of Typical and Atypical Neuroleptics on Plasma and Urinary Monoamine Metabolites
Husseini K. Manji, M.D., John Hsiao, M.D., Jerry Oliver, B.S., David Pickar, M.D., William Z. Potter, M.D.

NR43 Effects on Chronic Lithium Treatment on Signal Transduction Mechanisms in HL60 Cells
Jose A. Bitran, M.D., Fabian Gusovsky, Ph.D., Husseini Manji, M.D., William Z. Potter, M.D.,

NR44 Effect of Age on Plasma Levels of Nortriptyline
Steven J. Bupp, M.D., Sheldon H. Preskorn, M.D.

NR45 Weight Change and EEG Sleep in MDD
Timothy Hsu, M.D., James E. Shipley, M.D., John F. Greden, M.D., Roger F. Haskett, M.D., Leon Grunhaus, M.D., Alan Eiser, Ph.D.

NR46 Age-Related Changes in Major Depressive Disorder
Timothy Hsu, M.D., James E. Shipley, M.D., John F. Greden, M.D., Roger F. Haskett, M.D., Leon Grunhaus, M.D., Atul Pande, M.D.

NR47 Transient Hyperthyroxinemia in Affective Disorders
Rima Styra, M.D., Russell Joffe, M.D.

NR48 Drug Abuse in Schizophrenia: Clinical Correlates
Lisa Dixon, M.D., Gretchen Haas, Ph.D., Peter Weiden, M.D., John Sweeney, Ph.D., Denise Hien, M.A.

NR49 Carbamazepine: Effective for Aggressive Youths?
Richard R. Pleak, M.D., Daniel T. Williams, M.D., Boris Birmaher, M.D.

NR50 Depression in Patients with Diabetes Mellitus
Liane J. Leedom, M.D., Woerner P. Meehan, Ph.D., Warren Procci, M.D., Adina Zeidler, M.D.

NR51 Psychiatric Comorbidity in a Private Drug and Alcohol Treatment Center
Mark A. Hurst, M.D., Kathy E. Shy, M.D., Barry I. Liskow, M.D., Stephen L. Stern, M.D.

NR52 Idazoxan: A Novel ALPHA-2 Antagonist and Antidepressant
Ossama T. Osman, M.D., Matthew V. Rudorfer, M.D., Husseini Manji, M.D., William Z. Potter, M.D.

NR53 Abnormal Respiratory Physiology in Panic Disorder
Cameron S. Carter, M.D., Richard Maddock, M.D.

NR54 Beta-Blockers For Performance Anxiety in Musicians
Elissa M. Sanders, M.D.

NR55 Use of the SCL-90-R With Adolescents
James J. McGough, M.D., John F. Curry, Ph.D.

NR56 Development of Agoraphobia in Panic Disorder
Franklin R. Schneier, M.D., Lynn Martin, M.S., Salvatore Mannuzza, Ph.D., Donald Ross, Ph.D., Michael R. Liebowitz, M.D., Abby J. Fyer, M.D.

NR57 Brain Density in Schizophrenia
David G. Daniel, M.D., Debra Kostianovsky, M.D., Emily Kim, M.D., Terry E. Goldberg, Ph.D., Manuel F. Casanova, M.D., Joel E. Kleinman, M.D., Daniel R. Weinberger, M.D.

NR58 Pocket Computer Aids Weight Loss: Does Not!
Martha S. Losch, W. S. Agras, M.D., C. Barr Taylor, M.D.

NR59 Seclusion, Restraint and Medication Refusal
Peter J. Davidson, M.D., Dennis McBride, Ph.D.

NR60 Quantitative SPECT: Normal and Pathologic States
Renee M. Dupont, M.D., Guy Lamoureux, M.D., J. Christian Gillin, M.D., William Ashburn, M.D., Samuel Halpern, M.D.

NR61 Cross Situational Manifestations of ADHD: Now You See it Now You Don't
Joseph A. Whitfield, M.D., Peter S. Jensen, M.D.

NR62 A Study of MDMA Use Among Psychiatrists
Mitchell B. Liester, M.D., Charles S. Grob, M.D., Gary L. Bravo, M.D., Roger N. Walsh, M.D.

NR63 Lithium Improves Post-Meal Plasma Glucose Insulin Action in Diabetic Rats
Leslie R. Vogel, M.D., Andrea Giaccari, M.D., Luciano Rossetti, M.D.

NR64 WITHDRAWN

NR65 Psychiatric Presentations of Wilson's Disease
Mayada Akil, M.D., Denise Dutchak, M.D., Velha Yuzbasiyan-Gurkan, M.D., George J. Brewer, M.D., Joseph A. Schwartz, M.D.

NR66 Baseline Thyroid Function in Psychotic Depression
Martin T. Wilner, M.D., Richard P. Brown, M.D., Jaw-Sy Chen, Ph.D., Katherine S. Johnson, R.N., Peter E. Stokes, M.D., J. John Mann, M.D.

NR67 Event-Related Potentials in Elderly Patients
Ma-Li Wong, M.D., Mary Schroeder, Ph.D., Richard B. Lipton, M.D., Walter Ritter, Ph.D., Herbert G. Vaughan Jr., M.D.

NR68 The Geriatric Depression Scale in Dementia
Michael Houston, Susan J. Boust, M.D., William J. Burke, M.D., William H. Roccaforte, M.D.

NR69 Incest Survivors: Obstetric/Gynecologic Problems
Trudy K. Shahady, B.A., Gregory M. Gillette, M.D., Kevin R. Robertson, M.A.

NR70 TRH-Test: Depressives with Agitation, Suicidality
Mark H.N. Corrigan, M.D., James C. Garbutt, M.D., Gregory M. Gillette, M.D., Dana E. Quade, Ph.D.

NR71 Insulin Kinetics and Glucose in Eating Disorders
Julio Licinio, M.D., Katherine Halmi, M.D., Peter E. Stokes, M.D.

NR72 Subtyping Aggression in Humans
Benedetto Vitiello, M.D., David Behar, M.D., David Stoff, Ph.D., Alexander Ricciuti, Ph.D.

NR73 VBR in Schizophrenia: A Factor Analytic Study
Steven B. Schwarzkopf, M.D., Stephen C. Olson, M.D., Jeffrey A. Coffman, M.D., Judy A. McLaughlin, M.S., Henry A. Nasrallah, M.D.

NR74 CRF, Sympathetic Activity and Immune Function
Lee D. Jones, M.D., Michael R. Irwin, M.D., Michaelyn Provencio, B.S.

NR75 A Reappraisal of a Limit-Cycle Model of Sleep
Kevin O'Connor, M.D., J. Christian Gillin, M.D., Arnold Mandell, M.D.

NR76 Bulimia and Depression Assessed by PET
Jennifer O. Hagman, M.D., Monte S. Buchsbaum, M.D., Joseph C. Wu, M.D., Chandra A. Reynolds, B.A., Barton J. Blinder, M.D.

NR77 Fenfluramine Stimulation of Prolactin Release in OCD
William A. Hewlett, Ph.D., Sophia Vinogradov, M.D., Sarah Berman, John Czernansky, M.D., William S. Agras, M.D.

NR78 Preliminary Findings of a New Teen Suicide Program
Daniel Grosz, M.D., Gregory M. Asnis, M.D., Jill M. Harkavy Friedman, Ph.D., Jim Zimmerman, Ph.D., Herman M. van Praag, M.D., Laura Lemle, Ph.D.

NR79 Varying Response to Desipramine in Panic Disorder
Oren Kalus, M.D., Gregory M. Asnis, M.D., Wiepke Cahn, M.A., Eileen Rubinson, M.S.W., Jill M. Harkavy Friedman, Ph.D., Daniel Grosz, M.D.

NR80 A Survey of Suicidal Behaviors in an Adult OPD
Gregory M. Asnis, M.D., Jill M. Harkavy Friedman, Ph.D., Brunhild Kring, M.D., Naveed Iqbal, M.D.

NR81 Co-Morbid Profile: Depression and Alcoholism
Ihsan M. Salloum, M.D., Juan E. Mezzich, M.D., Chul Ahn, Ph.D.

NR82 Menstrual Cycle Symptom Changes Correlate with Changes in Gonadal Steroids and Platelet Uptake Kinetics
Margaret G. Spinelli, M.D., J. John Mann, M.D., John A. Sweeney, Ph.D.

Tuesday, May 9, 1989, 9:00 a.m.-10:30 a.m.

New Research 2—Oral/Slide Session—Anza Room, Ballroom Level, Hilton

SCHIZOPRENIC DISORDERS

Chp.: John C. Markowitz, M.D.

NR83 Cognitive Correlates of Hippocampal Volumes — 9:00 a.m.
Robert M. Bilder, Ph.D., Bernard Bogerts, M.D., Jeffrey A. Lieberman, M.D., Manzar Ashtari, Ph.D., Jose M.A. Alvir, D.P.H., Joseph Zito, M.D.

NR84 Monoclonal Antibodies to Investigate Schizophrenia — 9:15 a.m.
William G. Honer, M.D., Charles A. Kaufmann, M.D., Joel E. Kleinman, M.D., Manuel F. Casanova, M.D., Peter Davies, Ph.D.

NR85 Prepyriform Cortex Abnormalities in Schizophrenia — 9:30 a.m.
Manuel F. Casanova, M.D., Richard Saunders, Ph.D., Nicholas Carosella, M.D., Daniel R. Weinberger, M.D., Joel E. Kleinman, M.D.

NR86 D2 PET Scans in Twenty-Five Drug Naive Schizophrenics — 9:45 a.m.
Larry E. Tune, M.D., Dean F. Wong, M.D., Godfrey D. Pearlson, M.D., L. Trevor Young, M.D., Victor Villemagne, M.D., Robert F. Dannals, Ph.D.

NR87 Schizophrenia and High Levels of Soluble IL-2 Receptors — 10:00 a.m.
Mark H. Rapaport, M.D., Cathy G. Mc Allister, Ph.D., David Pickar, M.D., Darryl Kirch, M.D., David L. Nelson, M.D., Steven M. Paul, M.D.

NR88 Twin Concordance in Schizophrenic Disorders — 10:15 a.m.
Sidsel Onstad, M.D., Ingunn Skre, Ph.D., Svenn Torgersen, Ph.D., Einar Kringlen, M.D.

Tuesday, May 9, 1989, 9:00 a.m.-10:30 a.m.

New Research 3—Oral/Slide Session—Balboa Room, Ballroom Level, Hilton

ANXIETY DISORDERS

Chp.: Arnold Werner, M.D.

NR89 Aging, Alcoholism and Panic Disorder Prevalence — 9:00 a.m.
John H. Krystal, M.D., Philip Leaf, Ph.D., Martha Bruce, Ph.D., Dennis S. Charney, M.D.

NR90 Circadian Cosine Model Predicts Anxiety in Panic — 9:15 a.m.
Justin A. Kenardy, B.Sc., C. Barr Taylor, M.D., Leslie Fried, M.Sc.

NR91 Cortisol, Prolactin and Lactate Induced Panic — 9:30 a.m.
Eric Hollander, M.D., Michael R. Liebowitz, M.D., Franklin Schneier, M.D., Laszlo Papp, M.D., Gregory Dalack, M.D., Donald F. Klein, M.D.

NR92 Anxiety Disorders in Families of Inhibited Children — 9:45 a.m.
Jerrold F. Rosenbaum, M.D., Joseph Biederman, M.D., Dina R. Hirschfeld, B.A., Jerome Kagan, Ph.D.

NR93 Developmental Antecedents of OCD — 10:00 a.m.
Margaret Klitzke, D.O., Steven A. Rasmussen, M.D., Charles Zeanah, M.D., Daniel Stern, M.D.

NR94 Phenelzine and Atenolol in Social Phobia — 10:15 a.m.
Franklin R. Schneier, M.D., Jack M. Gorman, M.D., Abby J. Fyer, M.D., Eric Hollander, M.D., Raphael Campeas, M.D., Michael R. Liebowitz, M.D.

NEW RESEARCH

Tuesday, May 9, 1989, 12:00 noon-2:00 p.m.

New Research 5—Poster Session—Yosemite Room, Ballroom Level, Hilton

SCHIZOPHRENIA AND ORGANIC MENTAL DISORDERS, BIOLOGIC AND FORENSIC PSYCHIATRY, BRAIN IMAGING AND GENETICS

Moderator: Charles A. Kaufmann, M.D.

NR95 Frontal Hypoperfusion in Drug Naive Schizophrenics
Jorg J. Pahl, M.D., Nancy C. Andreasen, M.D., Greg A. Cohen, M.S., K. Rezai, M.D., P.K. Kirchner, M.D.

NR96 Lack of Ventriculomegaly by MRI in Schizophrenia
Stephen C. Olson, M.D., Jeffrey A. Coffman, M.D., Steven B. Schwarzkopf, M.D., Judy A. McLauglin, M.S., Henry A. Nasrallah, M.D.

NR97 Frontal Lobe Size in Schizophrenics by MRI
Anand K. Pandurangi, M.D., Anthony L. Pelonero, M.D., Jay M. Otero, B.S., Lyn Nadel, M.D., Jae Y. Lee, B.A.

NR98 Suicidal Behavior in Schizophrenia
Gretchen L. Haas, Ph.D., John Lauriello, M.D., Lisa Dixon, M.D., Margaret Rea, Ph.D., John Sweeney, Ph.D., Peter Weiden, M.D.

NR99 Neuroendocrine Effects of Clozapine in Schizophrenia
Carmen Z. Lemus, M.D., Jeffrey A. Lieberman, M.D., Celeste A. Johns, M.D., Simcha Pollack, Ph.D., Bruce L. Saltz, M.D.

NR100 Cholinergic Excess and Negative Schizophrenia
Rajiv Tandon, M.D., Kenneth R. Silk, M.D., James E. Shipley, M.D., John F. Greden, M.D.

NR101 Negative Symptoms: Relationship to Family History
Frederic J. Sautter, Ph.D., Barbara E. McDermott, Ph.D., David L. Garver, M.D.

NR102 Predicting Outcome of Schizophrenia: New Findings
Stanley R. Kay, Ph.D., Lisa M. Murrill, M.A.

NR103 Differentiating Negative and Deficit Symptoms
Barbara E. McDermott, Ph.D., Frederic J. Sautter, Ph.D.

NR104 Schizophrenia and Correlates of Family Attitudes
Eugenia T. Randolph, Ph.D., Shirley M. Glynn, Ph.D., Spencer Eth, M.D., Andrew L. Shaner, M.D., Walter B. Van Vort, M.D., Denise H. Paz, Ph.D.

NR105 Hypoplasia of Vermal Lobules VI and VII in Schizophrenia
Henry A. Nasrallah, M.D., Stephen B. Schwarzkopf, M.D., Jeffrey A. Coffman, M.D., Stephen C. Olson, M.D.

NR106 Remoxipride in Schizophrenia: A Haloperidol Controlled Multicentre Double-Blind Dose-Finding Clinical Trial
Yvon D. Lapierre, M.D.

NR107 Autoantibodies and Schizophrenia
Anthony L. Pelonero, M.D., Anand K. Pandurangi, M.D., Vincent P. Calabrese, M.D.

NR108 New Views on Amine Metabolites in Schizophrenia
P. Eric Konicki, M.D., Alan Breier, M.D., Allen R. Doran, M.D., Owen M. Wolkowitz, M.D., Carlos N. Pato, M.D., David Pickar, M.D.

NR109 Negative Symptoms in Early Phase of Schizophrenia
Joseph Ventura, M.A., Keith H. Nuechterlein, Ph.D., Michael Green, Ph.D., Jim Mintz, Ph.D.

NR110 Gating and Habituation in Schizophrenia
David L. Braff, M.D., Mark A. Geyer, Ph.D., Robert W. Butler, Ph.D., Robert S. Mansbach, Ph.D., Neal Swerdlow, M.D., Christian Grillon, Ph.D.

NR111 Hypofrontality, Neuropsychology and Schizophrenia
David L. Braff, M.D., Sidney Zisook, M.D., Munro Cullum, Ph.D., Robert Heaton, Ph.D., Lewis L. Judd, M.D., Igor Grant, M.D.

NR112 Neural Implants in Parkinson's Disease: Implications for Schizophrenia
Barry D. Jones, M.D., Alain Labelle, M.D., David Grimes, M.D.

NR113 Ventral Tegmental Pathology in Schizophrenia
Manuel F. Casanova, M.D., Thomas M. Hyde, M.D., Terry E. Goldberg, Ph.D., Daniel R. Weinberger, M.D., Joel E. Kleinman, M.D.

NR114 Correlates of Prefrontal Atrophy in Schizophrenia
Jeffrey L. Peters, M.D., Jeffrey K. Yao, Ph.D., David Shaw, Ph.D., Thomas C. Neylan, M.D., Doris McAdam, R.N., Daniel P. van Kammen, M.D.

NR115 Neuroleptic Noncompliance in Schizophrenia
Peter Weiden, M.D., Alan Manevitz, M.D., Lisa Dixon, M.D., Neal DeChillo, M.S.W., Bruce Rapkin, Ph.D., Allen J. Frances, M.D.

NR116 Work Adjustment and Symptoms of Schizophrenia
Shirley M. Glynn, Ph.D., Eugenia T. Randolph, Ph.D., Spencer Eth, M.D., Gregory B. Leong, M.D., George G. Paz, M.D., Denise H. Paz, Ph.D.

NR117 Effects of the D1 Agonist SKF38393, Combined with Haloperidol, in Schizophrenic Patients: A Preliminary Report
Michael Davidson, M.D., Phil Harvey, Ph.D., Peter Powchik, M.D., Rami Kaminski, M.D., Linsey Bergman, B.S., Kenneth L. Davis, M.D.

NR118 CSF NPY in Schizophrenia
Daniel P. van Kammen, M.D., Jeffrey L. Peters, M.D., Joel Gelernter, M.D., David Shaw, Ph.D., Thomas C. Neylan, M.D.

NR119 Management of Risk of Relapse in Schizophrenia
William C. Wirshing, M.D., Kathleen Johnston-Cronk, B.S., Stephen R. Marder, M.D., Robert P. Liberman, M.D., Thad Ekman, Ph.D.

NR120 Sex Differences in Olfactory Function in Schizophrenia
Lili C. Kopala, M.D., Campbell Clark, Ph.D., Trevor Hurwitz, M.D.

NR121 Oculomotor Impairments in Schizophrenia
John A. Sweeney, Ph.D., Gretchen Haas, Ph.D., Brett Clementz, M.A., Peter Weiden, M.D., James Hill, M.A., Allen J. Frances, M.D.

NR122 Temporal Lobe Changes in Schizophrenia
Patrick E. Barta, M.D., Godfrey D. Pearlson, M.D., Richard E. Powers, M.D., Larry E. Tune, M.D.

NR123 Unconscious Processing of Emotional Stimuli
Bruce E. Wexler, M.D., Gary E. Schwartz, Ph.D., George Bonano, B.A., Stephen Warrenburg, Ph.D., Larry Jamner, Ph.D., Jon Michaelis, Ph.D.

NR124 Effects of a Program for Schizophrenic Relatives
Hughes J. Cormier, M.D., Gaston Guimond, M.D., Real Morin, M.D., Sylvie Vaillancourt, M.A., Christian Gingras, B.Sc., Suzanne Ricard, M.Ps.

NR125 Schizophrenia: P300 Topography and Positive Symptoms
Martha E. Shenton, Ph.D., Steven F. Faux, Ph.D., Robert W. McCarley, M.D., Michael Coleman, M.A., Virginia Penhune, A.B., Amy Ludwig, B.A.

NR126 MEG Auditory Evoked Fields in Schizophrenic Women
Martin L. Reite, M.D., Dana Scheuneman, B.A., Peter Teale, M.S.E.E., Steven Linnville, Ph.D., Leigh Goldstein, M.S.

NR127 Transdermal Nicotine and Smoking Behavior in Psychiatric Patients
Neil Hartman, M.D., Gregory B. Leong, M.D., Shirley Glynn, Jeffrey N. Wilkins, M.D., Murray E. Jarvik, M.D.

NR128 Shortened T2 of Caudate in MRI Study of Tardive Dyskinesia
George Bartzokis, M.D., H. Jordan Garber, M.D., Virginia J. Griswold, M.D., Stephen R. Marder, M.D., William H. Oldendorf, M.D.

NR129 Vulnerability and Presentation of NMS
Pavlos Sakkas, M.D., John M. Davis, M.D., Hva Jin, M.D.

NR130 Cross-Cultural Survey of Tardive Dyskinesia Prevalence Among Three Ethnic Groups of Chronic Psychiatric Patients
John Sramek, Ph.D., Swati Roy, Ph.D., Tom Ahrens, Ph.D., Edmond H. Edmond Pi, M.D.

NR131 Brain Cholinergic Reduction in NMS or Fatal Catatonia
Stephen J. Kish, Ph.D., J. Gilbert, M.D., R. Kleinert, M.D., G.F. Walter, M.D., M. Minauf, M.D., O. Hornykiewcz, M.D.

NR132 Incidence of Akathisia in Patients on Clozapine
Paul E. Keck Jr., M.D., Bruce M. Cohen, M.D., Andrew Satlin, M.D., Jonathan O. Cole, M.D.

NR133 The Acute Effects of Smoking on Tardive Dyskinesia
William C. Wirshing, M.D., Jeremy Engel, B.A., Edward Levin, Ph.D., Jeffrey L. Cummings, M.D., Jed Rose, Ph.D.

NR134 Circadian Activity Rhythm in Alzheimer's Disease
Andrew Satlin, M.D., Martin H. Teicher, M.D., Harris Lieberman, Ph.D., Ross Baldessarini, M.D., Ladislav Volicer, M.D., Yvette Rheaume, R.N.

NR135 Dyskinesia in the Demented Elderly
Andrew Satlin, M.D., Gudarz Davar, M.D., Jonathan O. Cole, M.D., Ross J. Baldessarini, M.D., David W. Marby, B.A.

NR136 Validity of Global Functional Rating in DAT
Gary L. Gottlieb, M.D., Raquel E. Gur, M.D., Barbara L. Malamut, M.A., Andrew J. Saykin, Psy.D., Barbara A. Kamholz, M.D., Ruben C. Gur, Ph.D.

NR137 The Screening Cerebral Assessment of Neppe: A Bedside Screening Tool
Vernon M. Neppe, M.D.

NR138 Changes in Selective Free CSF Amino Acids in Alzheimer's Disease
Nunzio Pomara, M.D., Dennis Deptula, Ph.D., Rajkumar Singh, M.D., Peter A. LeWitt, M.D., Miriam Banay-Schwartz, Ph.D.

NR139 Parkinson's Disease, Dopamine and Personality
Matthew A. Menza, M.D., Nancy Forman, M.D., Harris Goldstein, M.D., Lawrence Golbe, M.D.

NR140 Limitations of the Mini-Mental State Examination
William O. Faustman, Ph.D., James A. Moses Jr., Ph.D., John G. Csernansky, M.D.

NR141 Characterizing Organic Delusional Syndrome
Jack R. Cornelius, M.D., Juan E. Mezzich, M.D., Horacio Fabrega, M.D., Marie D. Cornelius, Ph.D., Richard F. Ulrich, M.S.

NR142 Aura Predicts Psychopathology in Seizure Patients
Edward K. Silberman, M.D., Neil Sussman, M.D., Gerald Skillings, Ph.D., Mimi Callanan, M.S.N.

NR143 Depression in Alzheimer's Disease: Diagnosis by Psychiatry and Other Medical Specialties
Barbara C. Black, M.H.S., David A. Loewenstein, Ph.D., Carl Eisdorfer, M.D.

NR144 Psychiatric Illness in Wolfram Syndrome Patients
Ronnie Gorman Swift, M.D., Debra B. Sadler, B.A., Diana O. Perkins, M.D., Michael Swift, M.D.

NR145 Depression and Cognition in Parkinson's Disease
Sergio E. Starkstein, M.D., John Paul Fedoroff, M.D., Thomas Preziosi, M.D., Robert G. Robinson, M.D., Helen S. Mayberg, M.D.

NR146 Effect of Depression on Longitudinal Symptom Change in Alzheimer's Disease
Elisse Kramer-Ginsberg, Ph.D., Blaine S. Greenwald, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

NR147 Reaction Time Evaluation as a Neuropsychiatric Tool
Angelo Bosio, M.D., Rosangela Rosola

NR148 Longitudinal Studies in Elderly Depressed Patients
Anastasios Georgotas, M.D., Robert E. McCue, M.D., Thomas B. Cooper, M.A.

NR149 Combined ECT and Tricyclics in Elderly Patients
John P. Nelson, M.D., Lloyd Benjamin, M.D.

NR150 Late Life Depressive Pseudodementia
Blaine S. Greenwald, M.D., Elisse Kramer, Ph.D., Eileen Wachter, M.D., Miklos F. Losonczy, M.D., Paul Aisen, M.D.

NR151 Drug Treatment of Depression in the Frail Aged
Ira R. Katz, M.D., George M. Simpson, M.D., Vijay Jethanandani, M.D., Thomas Cooper, Cathy Muhly, R.N., Patricia Parmelee, Ph.D.

NR152 B Vitamins Improve Memory in Geriatric Depression
Iris R. Bell, M.D., Frank Morrow, Ph.D., Stephanie Mirages, M.A., Gayle Perrone, B.S., Joel Edman, M.S., David Marby, B.A., Michele Greenwald, R.N.

NR153 Predictors of Depression in the Urban Elderly
Gary J. Kennedy, M.D., Howard Kelman, Ph.D., Cynthia Thomas, Ph.D.

NR154 Vitamin B12 and Cognition in Geriatric Depression
Joel S. Edman, M.S., Iris R. Bell, M.D., Richard Linn, Ph.D., Nancy Hebben, Ph.D., Diane Ray, Ph.D.

NR155 Gender Differences in Caregiver Coping
William Borden, Ph.D., Rhoda R. Frankel, M.A., Ben Gierl, M.D., Sharon Berlin, Ph.D.

NR156 Late Life Psychosis and Structural Brain Injury
Ira M. Lesser, M.D., Bruce L. Miller, M.D., Kyle B. Boone, Ph.D., Elizabeth Hill, R.N., C. Mark Mehringer, M.D.

NR157 Delayed Antidepressant Effect in the Elderly
Robert E. McCue, M.D., Anastasios Georgotas, M.D., Thomas B. Cooper, M.A., Narmada Nagachandran, M.D.

NR158 Brain CT and Outcome of Geriatric Depression
George S. Alexopoulos, M.D., Robert C. Young, M.D., Charles A. Shamoian, M.D.

NR159 L-Deprenyl Treatment of Older Depressives
Trey Sunderland, M.D., Robert M. Cohen, M.D., Karen E. Thompson, B.S., Brian A. Lawlor, M.D., Alan M. Mellow, M.D., Paul A. Newhouse, M.D., Pierre N. Tariot, M.D., Edward A. Mueller, M.D., Dennis L. Murphy, M.D.

NR160 Adjunctive Lithium Carbonate in Nortriptyline Resistant Elderly Depressive
Ben Zimmer, M.D., Charles F. Reynolds III, M.D., Joe E. Thornton, M.D., Carolyn C. Hoch, Ph.D., James M. Perel, Ph.D., Mary A. Schlernitzauer, R.N.

NR161 ZK 112 119: A Novel B-Carboline Anxiolytic
David N. Stephens, Ph.D., Ralph Schmiechen, Ph.D.

NR162 Endocrine Responses to Apomorphine in Schizophrenia
Fabrice Duval, M.D., Luc-Andre Granier, M.D., M-Claude Mokrani, Ph.D., Juarez Oliveira Castro, M.D., Jean-Paul Macher, M.D.

NR163 An Augmented Test of Response to TRH
Fabrice Duval, M.D., M-Claude Mokrani, Ph.D., Luc-Andre Granier, M.D., Marc-Antoine Crocq, M.D., Jean-Paul Macher, M.D.

NR164 Dysregulated CSF POMC Peptides in Depression
Samuel Craig Risch, M.D., Ned H. Kalin, M.D.

NR165 Melatonin and Hour of Suicide
Paul A. Kettl, M.D., Tracey Collins, M.S., Edward O. Bixler, Ph.D.

NR166 Alzheimer's Disease Alpha2 Adrenergic Receptors
Grant N. Ko, M.D., Murray A. Raskind, M.D., Daniel M. Dorsa, Ph.D., J. Smood, B.S., K.L. Davis, M.D.

NR167 Dopamine Function in Cocaine Withdrawal
Joseph M. Palumbo, M.D., Lawrence H. Price, M.D., John H. Krystal, M.D., Scott W. Woods, M.D., Dennis S. Charney, M.D., Thomas Kosten, M.D., Herbert Kleber, M.D.

NR168 Asymmetrical Hemispheric Control of Heart Rate
Richard D. Lane, M.D., Robert Novelly, Ph.D., Carol Cornell, M.A., Sharon B. Zeitlin, M.S., Gary E. Schwartz, Ph.D.

NR169 Contribution of MDD and BPD to 5-HT Responsivity
Michael D. De Meo, M.D., P. Anne McBride, M.D., Jaw-Sy Chen, Ph.D., Katherine Johnson, R.N., J. John Mann, M.D.

NR170 Differences Between 3H Cocaine and 3H GBR-12935 Binding
Paul Berger, M.D., David Tanen, Frank Vocci, Ph.D., John Elsworth, Ph.D., Robert Roth, Ph.D., Martin Reith, Ph.D.

NR171 The Influence of h-CRH upon DST-Outcome
Klaus B. Wiedemann, M.D., Flortan J. Holsboer, M.D.

NR172 Brain Neuropeptides: Modification by Indocin and ECT
Aleksander A. Mathe, M.D., Elvar Theodorsson, M.D., Carina Stenfors, M.Sc., Orsolya Hoffman, M.D.

NR173 Amino Acid Markers in Psychiatric Disorders: A Preliminary Study
Vance Norum, M.D., James B. Roufs, M.S.R.D.

NR174 Do Serum Dexamethasone Levels Improve the DST?
Douglas Mossman, M.D., Eugene Somoza, M.D.

NR175 MAOIs, Hypothermia, Hyperactivity and the 24 Hour Clock
Wallace C. Duncan, Ph.D., Bo Gao, M.Ms., Thomas A. Wehr, M.D.

NR176 Mesolimbic Dopamine Neurons in Cell Culture
Stephen Rayport, M.D., David Sulzer, Ph.D.

NR177 Rhythms of Platelet Protein and 3H-IMI Binding
Edward DeMet, Ph.D., Aleksandra Chicz-DeMet, Ph.D.

NR178 Severity of Offense and Disorder Rates
Emil R. Pinta, M.D., Gerald Bean Jr., Ph.D.

NR179 Diagnoses in Adolescent Sex Offenders
William Huckaby, Ph.D., Hans Steiner, M.D.

NR180 Morning Increase in the Risk of Inpatient Battery
John J. Mooney, M.D., Doris Pearsall, Ph.D., John Orav, Ph.D.

NR181 Nadolol to Treat Aggression in Autistic Adults
John J. Ratey, M.D., Gillian O'Driscoll, Miriam Blumenkrantz, Karen J. Lindem, James R. Fletcher

NR182 Nadolol to Treat Aggression in Psychiatric Patients
John J. Ratey, M.D., Paul Sorgi, M.D., Karen Lindem, Gillian O'Driscoll, James R. Fletcher, Maria Daehler, et. al

NR183 5-HT Post-Synaptic Function in Aggression
Emil F. Coccaro, M.D., Larry J. Siever, M.D., Richard Kavoussi, M.D., Paul Rinaldi, M.A., Debbie Morrison, M.A., Luana Howard, R.N.

NR184 Effects of a School Shooting on Mental Health: Medical and Public Safety
Ira H. Sloan, M.D., Ronald H. Rozensky, Ph.D., Robert McSay, M.D., Leslie Kaplan, A.C.S.W., Stephen Saunders, M.S.

NR185 The Efficacy in SPECT in Geriatric Dementia Evaluation
Gary R. Horowitz, D.O., Alice Scheff, M.D., Gretta Leopold, M.D., Terri Morris, Ph.D., Jacqueline Nemec, M.D.

NR186 SPECT Pattern of Sleep Apnea and Alzheimer Disease
Bruce L. Miller, M.D., Ismael Mena, M.D., Robert Giombetti, M.D., James Daly, M.D., Steve L. Read, M.D., Karen Garrett, C.P.T.

NR187 MRI in Obsessive Compulsive Disorder
Charles H. Kellner, M.D., Richard Holgate, M.D., Bob R. Jolley, M.D., Linda Austin, M.D., Bruce Lydiard, M.D., James C. Ballenger, M.D.

NR188 Increased PET DA D2 Receptors Across Psychoses
Godfrey D. Pearlson, M.D., Christopher Ross, M.D., Dean F. Wong, M.D., Jonathan Links, Ph.D., Robert Dannals, Ph.D., Larry E. Tune, M.D.

NR189 Effects of Memory on Cerebral Metabolism in Normal Subjects
Robert P. Rose, M.D., John T. Metz, Ph.D., Lester I. Debbold, M.D., Daniel J. Luchins, M.D., Malcolm D. Cooper, M.D.

NR190 Memory Influences on Human Cerebral Metabolism
Robert P. Rose, M.D., Lester I. Debbold, M.D., John T. Metz, Ph.D., Daniel J. Luchins, M.D, Malcolm D. Cooper, M.D.

NR191 Linkage Analysis of the 11pter Region in MDI
Charles D. Mellon, M.D., William F. Byerley, M.D., John J. Holik, B.A., Angela M. Lubbers, B.A., Mark Leppert, Ph.D., Ray White, Ph.D.

NR192 Psychiatric Features in Fifty Huntington's Disease At-Risk Subjects
Jorg J. Pahl, M.D., Lewis R. Baxter Jr., M.D., John C. Mazziotta, M.D., Michael E. Phelps, Ph.D.

NR193 Genetic Database in Mood Disorders
Ronald Allan Remick, M.D., Patricia A. Baird, M.D., Adele D. Sadovnick, Ph.D., Marlene J. Huggins, M.Sc., A.P. Zis, M.D.

NR194 Family Study of Lithium Response
Martin Alda, M.D., Paul Grof, M.D., Petr Zvolsky, M.D., Eva Grof, M.D., Mary Walsh, M.S.W.

NR195 Molecular Genetic Studies Using D2 Dopamine Receptor
William F. Byerley, M.D., Charles Mellon, M.D., John J. Holik, B.A., Angela M. Lubbers, B.A., Ray White, Ph.D., Mark Leppert, Ph.D.

NR196 Molecular Genetics of Schizoprenia
James L. Kennedy, M.D., Luis A. Giuffra, M.D., Lennart Wetterberg, M.D., L.L. Cavalli-Sforza, M.D., Hans W. Moises, M.D., Kenneth K. Kidd, Ph.D.

NEW RESEARCH

Wednesday, May 10, 1989, 9:00 a.m.-10:30 a.m.

New Research 6—Oral/Slide Session—Anza Room, Ballroom Level, Hilton

MOOD DISORDERS

Chp.: John M. Kane, M.D.

NR197 Bipolar Disorder in the Elderly — 9:00 a.m.
Andrew Satlin, M.D., David W. Marby, B.A., Iris R. Bell, M.D., Benjamin Liptzin, M.D.

NR198 Effect of Rearing on CSF Norepinephrine in Monkeys — 9:15 a.m.
Michael H. Ebert, M.D., Gary W. Kraemer, Ph.D., Dennis E. Schmidt, Ph.D., William T. McKinney, M.D.

NR199 Biological Abnormalities in Premenstrual Dysphoria — 9:30 a.m.
Uriel Halbreich, M.D., Nathan Rojansky, M.D., Amiram Barkai, Ph.D., John Piletz, Ph.D., James Perel, Ph.D., Frank Barbarossa, Ph.D.

NR200 Mapping and Cloning in Region of X-Linked BPD Gene — 9:45 a.m.
Sue Klapholz, M.D., Chris N. Traver, M.S., Richard Hyman, Ph.D., Ronald W. Davis, Ph.D.

NR201 Normalization of Lymphocyte Beta-Receptors by ECT — 10:00 a.m.
John C. Mahler, M.D., Phillip J. Wilner, M.D., Kathryn S. Johnson, R.N., James P. Halper, M.D., Richard P. Brown, M.D., J. John Mann, M.D.

NR202 Cognitive Therapy of Endogenous Depression — 10:15 a.m.
Michael E. Thase, M.D., Anne D. Simons, Ph.D.

NEW RESEARCH

Wednesday, May 10, 1989, 9:00 a.m.-10:30 a.m.

New Research 7—Oral/Slide Session—Balboa Room, Ballroom Level, Hilton

PERSONALITY, SUBSTANCE ABUSE AND EATING DISORDERS

Chp.: Susan J. Fiester, M.D.

NR203 Therapist Interventions With Borderline Patients — 9:00 a.m.
Harold W. Koenigsberg, M.D., Otto F. Kernberg, M.D., Ann Appelbaum, M.D.

NR204 Plasma HVA in Schizotypal Personality Disorder — 9:15 a.m.
Richard J. Kavoussi, M.D., Larry J. Siever, M.D., David Bernstein, Ph.D., Emil F. Coccaro, M.D., Michael Davidson, M.D., Ken L. Davis, M.D.

NR205 Smoking Cessation, Depression, and Antidepressants — 9:30 a.m.
Alexander H. Glassman, M.D., Lirio S. Covey, Ph.D., Fay Stetner, M.S.

NR206 Reduced Plasma GABA Activity in Men at Risk for Alcoholism — 9:45 a.m.
Howard B. Moss, M.D., Jeffrey Yao, Ph.D., Mark Burns, Ralph E. Tarter, Ph.D.

NR207 A Family Study of Psychiatric Disorders Associated With Bulimia Nervosa — 10:00 a.m.
Joy Kassett, M.S.W., E. M. Maxwell, M.S.W., Elliot S. Gershon, M.D., Harry A. Brandt, M.D., David C. Jimerson, M.D.

NR208 Effect of Weight Loss on Brain Neuropeptide mRNAs — 10:15 a.m.
Mark A. Smith, M.D., Linda S. Brady, Ph.D., Philip W. Gold, M.D.

NEW RESEARCH

Wednesday, May 10, 1989, 12:00 noon-2:00 p.m.

New Research 8—Poster Session—Yosemite Room, Ballroom Level, Hilton

MOOD DISORDERS, PSYCHOPHARMACOLOGY, CONSULTATION/LIAISON AND AIDS

Moderator: Federick M. Quitkin, M.D.

NR209 Thin and Thick Boundaries: A New Personality Dimension
Ernest L. Hartmann, M.D., Robert Harrison, Ph.D., Judith Bevis, Ph.D., Deirdre Barrett, Ph.D., Stephanie Beal, M.A., Robert Kunzendorf, Ph.D.

NR210 Rhythms in Depression: Temperature and Cortisol
Charles P. Pollak, M.D., George S. Alexopoulos, M.D., Margaret L. Moline, Ph.D., Daniel R. Wagner, M.D.

NR211 Migraine and Depression: The Zurich Cohort Study
Kathleen R. Merikangas, M.D., Jules Angst, M.D., Hansreudi Isler, M.D.

NR212 Cognition in Endogenous and Organic Depression
Bruce Cohen, M.D., Sergio E. Starkstein, M.D., Robert G. Robinson, M.D., John R. Linsey, M.D., Peter V. Rabins, M.D., Marshall Folstein, M.D.

NR213 Abnormal Visual Evoked Potential in Melancholia
Russell G. Vasile, M.D., Frank Duffy, M.D., Gloria McAnulty, Ph.D., John J. Mooney, M.D., Kerry Bloomingdale, M.D., Joseph J. Schildkraut, M.D.

NR214 TRH Test in Treatment of Depression
Paul J. Goodnick, M.D., Irl L. Extein, M.D., Mark S. Gold, M.D.

NR215 Wellbutrin and Prozac in Depressive Subtypes
Paul J. Goodnick, M.D., Irl L. Extein, M.D.

NR216 Sodium Valproate Treatment of Bipolar Patients
Jeffrey Clothier, M.D., Thomas Freeman, M.D., Peggy Pazzaglia, M.D., Michael D. Lesem, M.D., Alan Swann, M.D.

NR217 Serotonin-2 Receptor Binding Sites in Depression
Ghanshyam Pandey, Ph.D., Subhash Pandey, Ph.D., Philip Janicak, M.D., Robert C. Marks, M.D., John M. Davis, M.D.

NR218 PRO-GAMMA-MSH Levels in Depression
Murray A. Morphy, M.D., Giovannia A. Fava, M.D., Robert C. Pedersen, M.D., Maria Zielezny, Ph.D., Nicoletta Sonino, M.D., Alexander C. Brownie, Ph.D.

NR219 Premenstrual Dysphoric Changes in Depressed Patients
Joseph E. Malikian, Ph.D., Stephen Hurt, Ph.D., Jean Endicott, Ph.D., Jeanne R. Delaney, R.N.

NR220 Insulin Receptor Binding in Depressed Patients
Keith Caruso, M.D., Robert Rees-Jones, M.D., Peter E. Stokes, M.D., James H. Kocsis, M.D.

NR221 Medical Adrenal Suppression in Major Depression
Beverley E. Pearson Murphy, M.D., Veena Dhar, M.D., A. Missagh Ghadirian, Guy Chouinard, M.D., Robert Keller, M.D.

NR222 Affective Disturbances in Preclinical Hyperthyroidism
Siegfried Kaumeier, M.D., Dr. Martina Rockel, Prof. Klaus H. Usadel, Dr. Josef Teuber, Dr. Schmidt Reinhold, Prof. Hafner Heinz

NR223 Cognitive Impairment and Brain Structure in Bipolars
Jeffrey A. Coffman, M.D., Henry A. Nasrallah, M.D., Robert A. Bornstein, Ph.D., Stephen C. Olson, M.D., Steven B. Schwarzkopf, M.D.

NR224 Altered Sympathomedullary Responsivity in MDD
Philip J. Wilner, M.D., Katherine Johnson, R.N., Jaw-Sy Chen, Ph.D., John A. Sweeney, Ph.D., J. John Mann, M.D.

NR225 SPEM Abnormality in Major Depression, ECT Effects
Dolores Malaspina, M.D., Xavier F. Amador, Ph.D., Harold Sackeim, Ph.D., Eliza A. Coleman, B.A., Sukdeb Mukherjee, M.D.

NR226 Disruption of Noradrenergic Rhythm in Depression
Larry J. Siever, M.D., Martin Teicher, M.D., Emil Coccaro, M.D., Kim Owen, M.D., Ren Kuy Yang, M.D., Steven Gabriel, Ph.D.

NR227 B-Endorphin Related Symptoms in Late Luteal Disorder
A. James Giannini, M.D., David M. Martin, M.S.

NR228 Transdermal and Oral Clonidine in Late Luteal Phase Disorders
A. James Giannini, M.D., David M. Martin, M.S.

NR229 Psychobiologic Effects of Beta-Adrenergic Blockade
Robert N. Golden, M.D., Terry Brown, D.O., Manuel Tancer, M.D., George Mason, Ph.D., Lillie Burnett, M.S.N., Dwight L. Evans, M.D.

NR230 Cholecystokinin Secretion in Depressive Subtypes
Thomas D. Geracioti, M.D., Jean R. Joseph-Vanderpool, M.D., Norman E. Rosenthal, M.D., Mitchell A. Kling, M.D., Themis Kamilaris, M.D., Roger A. Liddle, M.D., Phillip W. Gold

NR231 The Cornell Dysthymia Rating Scale
Barbara J. Mason, Ph.D., James H. Kocsis, M.D., Allen J. Frances, M.D.

NR232 Progesterone and Provera in the Treatment of MRMD
Peter J. Schmidt, M.D., Christine Hoban, M.S.W., Gay N. Grover, M.S.N., George M. Merriam, M.D., David R. Rubinow, M.D.

NR233 Longitudinal Sleep Endocrine Study in Depression
Axel Steiger, M.D., Isabella Heuser, M.D., Florian Holsboer, M.D.

NR234 Reliability of Recall of Past Depressive Symptoms
Delbert G. Robinson, M.D., Jose Alvir, Ph.D.

NR235 Atypical Forms of Recurrent Major Depression
Michael E. Thase, M.D., Linda Carpenter, B.A., David J. Kupfer, M.D.

NR236 CSF Neuropeptide Changes in Depression and Suicide
Mihaly Arato, M.D., Csaba Banki, M.D., Laszlo Tothfalusi, Ph.D., Garth Bissette, Ph.D., Charles B. Nemeroff, M.D., Huda Akil, Ph.D.

NR237 Bright Light Benefit Unrelated to REM Latency
Daniel F. Kripke, M.D., J. Christian Gillin, M.D., Daniel J. Mullaney, M.S.

NR238 The Clinical Use of Anticholinergic Drugs to Control Extra- Pyramidal Side Effects
Angelo Bosio, M.D., Rosangela Rosola

NR239 Ultra Brief Pulse ECT Clinical Trial
Vaclav Hyrman, M.D., Lancelot L. Patrick, M.D., Laurence K. Weldon, Ph.D.

NR240 LLPDD: Interaction of Circadian Rhythms
Sally K. Severino, M.D., Daniel R. Wagner, M.D., Margaret L. Moline, Ph.D., Stephen W. Hurt, Ph.D.

NR241 Can Neurophysiologic Measures Predict Antidepressant Response?
Jonathan W. Stewart, M.D., Gerard Bruder, Ph.D., Frederic Quitkin, M.D.

NR242 Depression, Personality Disorder and CSF 5-HIAA
Barbara Stanley, Ph.D., Lil Traskman-Benz, Ph.D., J. John Mann, M.D., Allen J. Frances, M.D., Michael Stanley, Ph.D.

NR243 CSF Findings in Elderly Suicide Attempters
J. Sidney Jones, M.D., Barbara Stanley, Ph.D., J. John Mann, M.D., Allen J. Frances, M.D., Ronald Winchel, M.D., Michael Stanley, Ph.D.

NR244 Longitudinal IMI Binding in Adolescent Suicide Attempts
Lee S. Cohen, M.D., Michael Stanley, Ph.D., Paul D. Trautman, M.D., Alyssa Morishima, M.S., Erica Wilheim, B.A., David Shaffer, M.D.

NR245 Neuropeptides and Suicide
Csaba M. Banki, M.D., Garth Bissete, Ph.D., Mihaly Arato, M.D., Charles B. Nemeroff, M.D.

NR246 Prediction of Suicide by Multiple Indicators
William A. Scheftner, M.D., Michael Young, Ph.D., Louis Fogg, Ph.D., Jan Fawcett, M.D

NR247 Empirical Estimation of Near-Term Suicide Risk
Jerome A. Motto, M.D., Alan G. Bostrom, Ph.D.

NR248 Pituitary POMC Gene Expression Following Suicide
Juan F. Lopez, M.D., Stanley J. Watson, M.D., Alfred Mansour, Ph.D., Miklos Palkovits, Ph.D., Mihaly Arato, M.D., Huda Akil, Ph.D.

NR249 Suicide in Late-Life: Psychological Autopsy Findings
Yeates Conwell, M.D., Kurt H. Olsen, M.A., Eric D. Caine, M.D., Catherine Flannery, M.D.

NR250 Stress and the Biology of Affective Episodes
Alan C. Swann, M.D., Jack Croughan, M.D., Steven K. Secunda, M.D., Stephen H. Koslow, Ph.D., James W. Maas, M.D., Peter E. Stokes, M.D.

NR251 Social Dominance, Depression and Immunity
Donna J. Holmes, Ph.D., Elizabeth Pinner, B.A., Steven J. Schleifer, M.D., Jacqueline A. Bartlett, M.D., Steven E. Keller, Ph.D.

NR252 Does Stress Related Amenorrhea Really Exist?
Stephanie D. Jofe, M.D., Dara K. Lee, B.A., Joanne F. Waldstreicher, M.D., David A. Schoenfeld, Ph.D., Gloria S. Mok, M.A., Janet E. Hall, M.D., William F. Crowley Jr,, M.D.

NR253 Stress Prevention for Medical Students
M. Bruce Sarlin, M.D., James T. Halper, M.D., Harlow T. Fischman, Ph.D., Keith W. Sedlacek, M.D., Donald C. Ross, Ph.D., Eric Marcus, M.D., Henrietta Wolland, M.P.H., Samuel Perry III, M.D.

NR254 Familial Traumatic Injury and Immunity
Steven J. Schleifer, M.D., Steven E. Keller, Ph.D., Barbara J. Scott, Cheryl H. Cottrol, M.D., Thomas J. Valente

NR255 ECT and Memory: The Role of Treatment Schedule
Baruch Shapira, M.D., Avraham Calev, Ph.D., Bernard Lerer, M.D., Doron Niual, B.A., Nurith Tubi, B.A., Heinz Drexler, M.D.

NR256 Gradual Sunrise Illumination for Treatment of SAD
David Schlager, M.D., Michael Terman, Ph.D.

NR257 Brain Thyroid Hormone Economy is Selectively Altered by Treatment With Desmethylimipramine
Mary B. Dratman, M.D., Floy L. Crutchfield, Ph.D., Monika B. Schoenhoff, M.S.E., Marc A. Vengrove, D.O., Janice T. Gordon, Ph.D., Peter C. Whybrow, M.D.

NR258 Fluoxetine-TCA Combined for Resistant Depression
Jeffrey B. Weilburg, M.D., Jerrold F. Rosenbaum, M.D., Gary S. Sachs, M.D., Mark H. Pollack, M.D., Maurizio Fava, M.D., Jonathan Worth, M.D.

NR259 Low Dose Trazodone Reduces MAOI Sleep Disturbances
Frederick Jacobsen, M.D.

NR260 Propranolol in Neuroleptic-Induced Akathisia: A Double-Blind Placebo Controlled Study
Mark S. Kramer, M.D., Robert A. Gorkin, M.D., Celeste DiJohnson, B.S., Patricia Sheves, B.S.N.

NR261 Antidepressant Effect of Oral S-adenosyl-methionine
Bruce L. Kagan, M.D., David Sultzer, M.D., Nicholas Rosenlicht, M.D., Robert H. Gerner, M.D.

NR262 Four Cases of Chloroquin Induced Psychoses
Gayle Bigelow, M.D., Nahum Spinner, M.D.

NR263 Discontinuation of Lithium in Remitted Bipolar Illness
Ehud Klein, M.D., Rami Meiraz, Peretz Lavie, M.D., Albert Hefez, M.D., Robert H. Lenox, M.D.

NR264 Hypnotic-Neuroleptics in the Control of Agitation
Enrique S. Garza-Trevino, M.D., Leo E. Hollister, M.D., John E. Overall, Ph.D.

NR265 Milacemide in the Treatment of Major Depression
Ann K. Morrison, M.D., Kenneth A. Kobak, M.S.W., John H. Greist, M.D.

NR266 Effects of HCTZ Versus Furosemide on Serum Lithium
Brian L. Crabtree, Ph.D., James E. Mack, Ph.D., Cynthia D. Johnson, M.S.N., Barry A. Amyx, M.D.

NR267 Fluoxetine Treatment of Bipolar II Depression
Sylvia Simpson, M.D., J. Raymond DePaulo, M.D.

NR268 Evaluation of a New Steady-State Lithium Prediction Method
Mary A. Gutierrez, Pharm.D., Neal R. Walker, Pharm.D., Barry A. Kramer, M.D.

NR269 Mood Variability in Normal Subjects on Lithium
Denise Dufer, M.D., Rachel Monderer, M.D., Mitchell Cohen, M.D., Dennis Barton, A.B., Harold Fuller, M.D., Michael Clark, M.D., J. Raymond DePaulo, M.D.

NR270 Optimal Esmolol Dose for Heart Rate and Blood Pressure Control in ECT
Anthony L. Kovac, M.D., Manuel P. Pardo, M.D., Jane S. Lauchland, M.D.

NR271 Desipramine Effects on Resting Metabolic Rate
R. Bruce Lydiard, M.D., Michele Laraia, M.S.N., Gail W. Stuart, Ph.D., Joseph J. Zealberg, M.D., W. Alex Morton, Pharm.D.

NR272 Effects of Fluvoxamine on Catecholamine Function
R. Bruce Lydiard, M.D., Lyle K. Laird, Pharm.D., W. Alex Morton, Pharm.D., Thomas E. Steele, M.D., Charles H. Kellner, M.D.

NR273 Comparison of Clonazepam and Lorazepam in Mania
Jacques Bradwejn, M.D., Greg B. Meterissian, M.D., Christian Shriqui, M.D., Diana Koszycki, M.A.

NR274 Limited Access to ECT for Public Patients (Calif)
Barry A. Kramer, M.D.

NR275 Predictors of Tricyclic Failure in Depression
J. Craig Nelson, M.D., Carolyn Mazure, Ph.D., Peter I. Jatlow, M.D.

NR276 Nicotine Potentiates Haloperidol in Tourette Cases
Brian J. McConville, M.D., Andrew B. Norman, Ph.D., Harold M. Fogelson, M.D., Karen W. Parker, R.N., William M. Klykylo, M.D., Paul S. Sanberg, Ph.D.

NR277 Lorazepam Treatment of Catatonia: A Study of Seven Cases
Patricia I. Rosebush, M.D., Ann Hildebrand, M.D., Brian Furlong, M.D., Michael Mazurek, M.D.

NR278 Cigarette Smoking and Neuroleptics
Rakesh K. Bansil, M.D., Norman Hymowitz, Ph.D., Steven Keller, Ph.D., Anwar Y. Ghali, M.D.

NR279 Effects of Different Light Wavelengths in SAD
Dan A. Oren, M.D., George C. Brainard, Ph.D., Jean R. Joseph-Vanderpool, M.D., Elizabeth Sorek, R.N., Scott Johnston, B.A., Norman E. Rosenthal, M.D.

NR280 Sudden Death: A Complication of TCA Therapy
Sheldon H. Preskorn, M.D., Pamela K. Widener, B.S.

NR281 Using Plasma Levels to Adjust Imipramine Dosing
Steven J. Bupp, M.D., Sheldon H. Preskorn, M.D.

NR282 Clinical Use of Loading Dose Haloperidol Decanoate
Tram K. Tran-Johnson, Pharm.D., Larry Ereshefsky, Pharm.D., Stephen R. Saklad, Pharm.D., Jerome Tilles, M.D., Robert C. Lyman, M.D., Davis M. Chester, Ph.D.

NR283 Continuation and Maintenance ECT-Efficacy and Safety
Richard Jaffe, M.D., William R. Dubin, M.D., Richard Roemer, Ph.D., Louis Lipschutz, M.D., Beth Shoyer, M.G.A.

NR284 Depression and Tinnitus: Nortriptyline Treatment
Mark Sullivan, M.D., Wayne Katon, M.D., Robert Dobie, M.D., Connie Sakai, M.S.P.A.

NR285 Chest Pain Dysphia and Psychiatric Disorder
Robert G. Harper, Ph.D., John R. Stroehlein, M.D., Francis Kane, Jr., M.D.

NR286 Drug Free Schizophrenics Show Left-Sided P3 Deficit
Steven F. Faux, Ph.D., Paul G. Nestor, Ph.D., Robert W. McCarley, M.D., M.E. Shenton, Ph.D., T. Horvath, M.D., K. Davis, M.D.

NR287 Psychiatric Morbidity in Irritable Bowel Syndrome
Mark D. Fossey, M.D., R. Bruce Lydiard, M.D., William H. Marsh, M.D., James C. Ballenger, M.D.

NR288 Psychopathology and Atypical Chest Pain in the Emergency Room
Lawson Wulsin, M.D., Lesley Mussio, M.D., James R. Hillard, M.D., Peter Geier, M.D.

NR289 Neuroendocrine Aspects of Chronic Fatigue Syndrome
Mark A. Demitrack, M.D., George P. Chrousos, M.D., Stephen E. Straus, M.D., Janet K. Dale, R.N., Markus J.P. Kruesi, M.D., Philip W. Gold, M.D.

NR290 Quality of Life with a Cardiac Defibrillator-Aicd
Milton H. Miller, M.D., David Cannom, M.D., Annette Brodsky, Ph.D.

NR291 Medical Compliance in Heart Transplant Recipients
Michael E. Swain, M.D., Michael Levick, C.S.W., Marge Gier, C.S.W., Kathy Grady, R.N., Bonnie Grusk, R.N., Deborah Couch, M.D.

NR292 Sleep in Cushing's Disease
Henry W. Lahmeyer, M.D.

NR293 Birth Order in DSM-III-R Somatization Disorder
Frank W. Brown, M.D., G. Richard Smith, M.D., Samuel W. Perry, M.D., Allen J. Frances, M.D., Baruch Fishman, Ph.D., Pamela Weiler, B.M., Karen Fogel, R.N., Joanne Ryan, R.N.

NR294 Psychiatric Diagnoses in Volunteers for HIV Testing
Lawrence B. Jacobsberg, M.D., Samuel W. Perry, M.D., Allen J. Frances, M.D., Baruch Fishman, Ph.D., Pamela Weiler, B.M., Karen Fogel, R.N., Joanne Ryan, R.N.

NR295 Risk Behavior and HIV Testing
John W. Bobo, Ph.D., Baruch Fishman, Ph.D., Samuel W. Perry, M.D., Lawrence B. Jacobsberg, M.D., Joanne M. Ryan, R.N.

NR296 Findings on Screening Checking in HIV Dementia
James W. Dilley, M.D., Alicia Boccellari, Ph.D., Ann Davis, Andrew Moss, Ph.D., Peter Bacchetti, Ph.D., Bridget Wagner, M.D.

NR297 Psychological Responses to HIV Serological Testing
Samuel Perry, M.D., Lawrence B. Jacobsberg, M.D., Baruch Fishman, Ph.D., Allen J. Frances, M.D., Allan B. Novick, M.A., Ronald R. Rein, M.A.

NR298 Stress Prevention Training After Antibody Testing
Baruch Fishman, Ph.D., Samuel Perry, M.D., Lawrence B. Jacobsberg, M.D., Allen J. Frances, M.D., Pamela Weiler, M.A., Allan B. Novik, M.A.

NR299 Antisocial Personality: Higher AIDS Risk in Intravenous Drug Users
Robert K. Brooner, Ph.D., George E. Bigelow, Ph.D., Frederick Schaerf, M.D.

NR300 Neuropsychological Function in HIV Asymptomatic Males
Deborah Belsky-Barr, M.A., Samuel W. Perry, M.D., Rex Swanda, Ph.D., Lawrence B. Jacobsberg, M.D., Richard Shindledecker, M.A., Steven Mattis, Ph.D., William B. Barr, Ph.D.

NR301 HIV Infection: Psychiatric and Neurological Findings
Robert Kertzner, M.D., Jack Gorman, M.D., Janet Williams, D.S.W., Yaakov Stern, Ph.D., Richard Mayeux, M.D., Anke Ehrhardt, Ph.D.

NR302 Medical Student Attitudes About the AIDS Epidemic
Carol A. Bernstein, M.D., Judith Rabkin, Ph.D., Robert Kertzner, M.D., Ray Goetz, Ph.D.

NR303 Mandatory HIV Testing of Intravenous Drug Users
Mark H. Pollack, M.D., Lawrence D. Rosen, B.A., Eileen Coppola, R.N.P.

NR304 HIV Dementia in Drug Users: Neuropsychological Data
Leonard Handelsman, M.D., Marvin J. Aronson, Ph.D., Gail Maurer, Ph.D., Sanford Herman, M.D., Robert Ness, M.A., Jeffrey Jacobson, M.D.

NR305 HIV Dementia in Drug Users: Neurological Evaluation
Jill A. Wiener, M.D., A. James Rowan, M.D., Leonard Handelsman, M.D., Marvin J. Aronson, Ph.D., Gail Maurer, Ph.D., Gladys Velazquez, M.D.

NR306 Can MRI Abnormalities Predict AIDS Dementia
Miklos Losonczy, M.D., Leonard Handelsman, M.D., In Sook Song, M.D., Sun Park, M.D., Sanford Herman, M.D., Marvin J. Aronson, Ph.D.

NR307 Detection of SPEM Abnormalities in HIV Infected Patients
Robert E. Litman, M.D., Christine Ollo, Ph.D., Thomas Clem, B.S.E.E., Daniel W. Hommer, M.D., David Rubinow, M.D., David Pickar, M.D.

NR308 Dissociation in Relation to Childhood Abuse
James A. Chu, M.D., Diana L. Dill, Ed.D.

NR309 Hypnotizability, Dissociation, and Absorption
David A. Baron, D.O., Peter J. Schmidt, M.D., Bernard Frankel, M.D., David R. Rubinow, M.D.

NR310 Results of Outreach to Homeless Mentally Ill Veterans
Robert A. Rosenheck, M.D., Peggy Gallup, M.P.H., Catherine Leda, M.P.H., Dennis Thompson, Paul Errera, M.D.

NR311 Engagement of Homeless Psychiatrically Ill Veterans in VA Domiciliary Treatment
Robert A. Rosenheck, M.D., Catherine Leda, M.P.H., Sharon Medak, Dennis Thompson, Richard Olson, M.H.A.

NR312 Admitting a Relative During Hospitalization
Aris D. Liakos, M.D.

NR313 Race and Ethnicity in Biological Research
William B. Lawson, M.D., Mi Talluri, M.D., Charles F. Morgan, B.S.

NR314 Psychiatric Morbidity in Urban and Rural New Zealand Women
Sarah E. Romans-Clarkson, M.B., Valerie A. Walton, M.A., G. Peter Herbison, M.Sc., Paul E. Mullen, M.B.

NEW RESEARCH

Thursday, May 11, 1989, 9:00 a.m.-10:30 a.m.

New Research 9—Oral/Slide Session—Anza Room, Ballroom Level, Hilton

ORGANIC MENTAL DISORDERS AND AIDS

Chp.: Charles A. Kaufmann, M.D.

NR315 Relationship Between Neuropsychological and Immune Variables in HIV Positive Asymptomatic Men — 9:00 a.m.
James W. Dilley, M.D., Alicia Boccellari, Ph.D., Ann Davis, Andrew Moss, Ph.D., Peter Bacchetti, Ph.D., Myla Young, M.D.

NR316 Early Detection of HIV Effects on Brain Function — 9:15 a.m.
Andrew Leuchter, M.D., Thomas F. Newton, M.D., Wilfred Vangorp, Ph.D., Eric Miller, Ph.D.

NR317 123IodoQNB SPECT in Alzheimer's and Pick's Disease — 9:30 a.m.
Daniel R. Weinberger, M.D., Raymond E. Gibson, Ph.D., Richard Coppola, D.Sc., Douglas W. Jones, Ph.D., Karen F. Berman, M.D., Allen R. Braun, M.D., Barry R. Zeeberg, Ph.D., Trey Sunderland, Ph.D., Richard C. Reba, M.D.

NR318 Dementia and Tangle Formation in Alzheimer's Disease — 9:45 a.m.
Linda M. Bierer, M.D., Daniel P. Perl, M.D., Vahram Haroutunian, Ph.D., Philip Kanof, M.D., Daniel Lobel, M.A., Kenneth L. Davis, M.D.

NR319 An Inhibitor of the Cholinergic Receptor in Alzheimer's — 10:00 a.m.
Gary D. Tollefson, M.D., Marlyse Wiebanga, B.S., William H. Frey, II, Ph.D.

NR320 Tourette's Syndrome is not Linked to D2 Receptor — 10:15 a.m.
Joel Gelernter, M.D., Andrew J. Pakstis, Ph.D., Phillip Chappell, M.D., R. Kurlan, M.D., D.K. Grandy, Ph.D., J. Bunzow, Ph.D., A.E. Retief, Ph.D., M. Litt, Ph.D., O. Civelli, Ph.D., K.K. Kidd, Ph.D.

NEW RESEARCH

Thursday, May 11, 1989, 9:00 a.m.-10:30 a.m.

New Research 10—Oral/Slide Session—Balboa Room, Ballroom Level, Hilton

CHILDHOOD DISORDERS

Chp.: Peter S. Jensen, M.D.

NR321	Follow-Up of Extreme Temperament from Age 7 to 16 Michel Maziade, M.D., Jacques Thivierge, M.D., Robert Cote, Ph.D., Bruno LaPlante, M.D.	9:00 a.m.
NR322	Young Adult Mental Status of Hyperactive Boys Salvatore Mannuzza, Ph.D., Rachel G. Klein, Ph.D., Noreen Bonagura, M.S.W., Patricia Malloy, B.S.W., Tina L. Giampino, B.A.	9:15 a.m.
NR323	Homeless Adolescents: Life Style and Sexual Behavior Milton Greenblatt, M.D., Marjorie J. Robertson, Ph.D.	9:30 a.m.
NR324	Coping of Japanese Children in the USA: One-Year Later Hisako M. Koizumi, M.D., Jennifer Farkas, Ph.D., Tetsunori Koizumi, Ph.D.	9:45 a.m.
NR325	Serotonin Mediated Responses in Autistic Disorder P. Anne McBride, M.D., George M. Anderson, Ph.D., Margaret E. Hertzig, M.D., John A. Sweeney, Ph.D., Donald J. Cohen, M.D., J. John Mann, M.D.	10:00 a.m.
NR326	Imipramine and Childhood MDD: Levels and Response Sheldon H. Preskorn, M.D., Elizabeth Weller, M.D., Carroll W. Hughes, Ph.D., Ronald Weller, M.D., Mary A. Fristad, M.A.	10:15 a.m.

NEW RESEARCH

Thursday, May 11, 1989, 12:00 noon-2:00 p.m.

New Research 11—Poster Session—Yosemite Room, Ballroom Level, Hilton

ANXIETY, PERSONALITY, SUBSTANCE ABUSE AND EATING DISORDERS; CHILD PSYCHIATRY; PSYCHOTHERAPY AND DIAGNOSTIC ISSUES

Moderator: Susan J. Fiester, M.D.

NR327 Psychological Predictors of Response to CO2
Ronald M. Rapee, Ph.D., Michelle Q. Craske, Ph.D., David H. Barlow, Ph.D.

NR328 Anxiety Disorders and ADHD, RS
Walid O. Shekim, M.D., Sacha Bystrisky, M.D., Esther B. Hess, M.A.

NR329 Long-Term Efficacy of Imipramine in Panic Disorder
Linda M. Nagy, M.D., John H. Krystal, M.D., Dennis S. Charney, M.D., Kathleen R. Merikangas, M.D., Scott W. Woods, M.D.

NR330 Clinical Characteristics of Housebound Agorphobics
Alan L. Gordon, M.D., Cynthia A. Berry, M.D., John W. Norton, M.D., Steven A. Rasmussen, M.D.

NR331 Lactate Induced Panic in Alcoholics
Deborah S. Cowley, M.D., Carl F. Jensen, M.D., Donald J. Johanessen, M.D., Lorne Parker, M.D., Stephen R. Dager, M.D., R. Dale Walker, M.D.

NR332 CO2 Symptom Profile: Panic Disorder and Agoraphobia
Diana Koszycki, M.A., Jacques Bradwejn, M.D., James F. Campbell, Ph.D.

NR333 Increased Inspiratory Resistance in CO2 Induced Panic
Laszlo A. Papp, M.D., Jack M. Gorman, M.D., Eric Hollander, M.D., Robert Gully, B.A., Julie Hatterer, M.D., Donald F. Klein, M.D.

NR334 Relationship of CSF-PGE to MHPG, HVA, 5HIAA in Panic
Raymond F. Anton, M.D., William Z. Potter, M.D., James L. Ballenger, M.D., Bruce Lydiard, M.D.

NR335 Cholecystokinin Panic: Patient Control Differences
Jacques Bradwejn, M.D., Diana Koszycki, M.A., Greg B. Meterissian, M.D., Christian Shriqui, M.D.

NR336 Subtypes of Panic Disorder and Drug Response
Wolfgang Maier, Nicolas Argyle, M.B., Raben Rosneberg, M.D., David Shera, M.A., Philip W. Lavori, Ph.D., Otto Benkert, M.D.

NR337 Long-Term Outcome of Panic Disorder
Mark H. Pollack, M.D., Jerrold F. Rosenbaum, M.D., George E. Tesar, M.D., Gary S. Sachs, M.D., Lee S. Cohen, M.D., Lawrence D. Rosen, B.A.

NR338 Periodicity in Panic Disorder
Michael Kahan, M.D., Charlotte Zitrin, M.D., Richard Swinson, M.D., Lawrence McDonald, M.D.

NR339 Public Speaking in Social Phobic Subtypes
Andrew P. Levin, M.D., Diana Sandberg, M.D., John Stein, M.A., Michael R. Liebowitz, M.D.

NR340 Panic Disorder Prevalence in Cardiology Patients
Richard J. Goldberg, M.D., Philip Morris, M.D., Frederic Christian, M.D., James Badger, R.N., Stephen Chabot, M.D., Matthew Edlund, M.D.

NR341 Course of Panic Disorder in Pregnancy
Lee S. Cohen, M.D., Jerrold F. Rosenbaum, M.D., Vicki L. Heller, M.D.

NR342 Trazodone for Clomipramine and Lithium Resistant Obssessive Compulsive Disorder
Haggai Hermesh, M.D., Dov Aizenberg, M.D., Hanan Munitz, M.B.

NR343 Fluvoxamine Versus Desipramine in OCD
Wayne K. Goodman, M.D., Pedro L. Delgado, M.D., Lawrence H. Price, M.D., Joseph Palumbo, M.D., Steven A. Rasmussen, M.D., Dennis S. Charney, M.D.

NR344 Neuroendocrine Sensitivity in Obsessive Compulsive Disorder
Eric Hollander, M.D., Concetta Decaria, M.S., Franklin Schneier, M.D., Julie Hatterer, M.D., Laszlo Papp, M.D., Michael R. Liebowitz, M.D.

NR345 Tritiated Imipramine Binding in OCD
Donald Black, M.D., Michael Kelly, Pharm.D., Carol Myers, Pharm.D., Russell Noyes, Jr., M.D.

NR346 Obsessional Paranoia: Response to 5HT Antidepressants
Jane L. Eisen, M.D., Steven A. Rasmussen, M.D.

NR347 Religion and Guilt in OCD Patients
Kerrin L. White, M.D., Sara E. Quay, B.A., Gail Steketee, Ph.D.

NR348 Clomipramine in Obsessive-Compulsive Disorder
Matig R. Mavissakalian, M.D., Bruce Jones, M.D., Steve Olson, M.D.

NR349 Repeat M-CPP Challenge During Fluoxetine Treatment in Obsessive Compulsive Disorder
Eric Hollander, M.D., Concetta Decaria, M.S., Raphael Campeas, M.D., Gregory Dalack, M.D., Laszlo Papp, M.D., Michael R. Liebowitz, M.D.

NR350 Neuroleptic Addiction in Fluvoxamine-Refractory OCD
Christopher J. McDougle, M.D., Wayne K. Goodman, M.D., Lawrence H. Price, M.D., Pedro L. Delgado, M.D., John H. Krystal, M.D., Dennis S. Charney, M.D., George R. Heninger, M.D.

NR351 Tryptophan Depletion Alters Mood in OCD Patients
Pedro L. Delgado, M.D., Wayne K. Goodman, M.D., Lawrence H. Price, M.D., Dennis S. Charney, M.D., George K. Aghajanian, M.D., George R. Heninger, M.D.

NR352 Post Traumatic Stress in NYC Emergency Services
Michael Blumenfield, M.D., Todd Hertzberg, Michael Riley, John Keating, Ph.D.

NR353 Relapse Imagery With PTSD Alcoholics
Francis R. Abueg, Ph.D., Julie Kriegler, Ph.D., Hsiao-Ti Falcone, M.A., Harvey Dondershine, M.D., Fred Gusman, M.S.W.

NR354 Heart Rate Correlates of PTSD
Graham M. Reid, M.D., Stephen R. Paige, Ph.D., Joseph E.O. Newton, M.D.

NR355 24h Urinary Cortisol and Catecholamines in PTSD
Roger K. Pitman, M.D., Scott Orr, Ph.D.

NR356 Predicting Emotional Responses to Disasters
Bruno Lima, M.D., Shaila Pai, Ph.D., Hernan Chavez, M.D., Nelson Samaniego, M.D., Julio Lozano, M.D.

NR357 Psychiatric Sequelae of Abuse in Nonpsychiatric Patients
Nicholas G. Ward, M.D., Garth G. Gulick, B.S., Albert S. Carlin, Ph.D., Joanne Beaubien, B.S.

NR358 Fluoxetine Trial in Borderline Personality
Jack R. Cornelius, M.D., Paul H. Soloff, M.D., James M. Perel, Ph.D., Richard F. Ulrich, M.S.

NR359 Neuropsychological Testing in Borderline Disorder
Kathleen M. O'Leary, M.S.W., Pim Brouwers, Ph.D., David L. Gardner, M.D., Rex W. Cowdry, M.D.

NR360 Estimating the Community Prevalence of BPD
Marvin Swartz, M.D., Dan G. Blazer, M.D., Linda K. George, Ph.D., Idee Winfield, Ph.D., Dana Hughes, Ph.D.

NR361 Assessing Change in Psychodynamic Psychotherapy
Marcia Goin, M.D., Gordon Strauss, M.D., Robert Martin, M.D.

NR362 Indications for Ambulatory Alcohol Detoxication
Motoi Hayashida, M.D., Arthur Alterman, M.D., Charles O'Brien, M.D., A. Thomas McLellan, Ph.D., Marian Droba, M.D., Karen Sweeney, P.A.

NR363 Substance Use By Psychiatry Residents
Patrick H. Hughes, M.D., Scott E. Conrad, M.D., Dewitt C. Baldwin, Jr., M.D., David V. Sheehan, M.D., Carla L. Storr, M.P.H.

NR364 Transdermal Clonidine Versus Chlordiazepoxide in Acute ETOH Withdrawal
Gregory R. Baumgartner, M.D., Randall C. Rowen, Pharm.D.

NR365 Intensive Case Management for the Chronic Public Inebriate I: Implementation
Mark L. Willenbring, M.D., Joseph P. Whelan, Michael E. O'Neil, M.A., James O. Dahlquist, J.D.

NR366 The Effect of Alcoholism on Depression in Mental Illnesses
John Louks, Ph.D., James Talone, Ph.D., James Smith, Ph.D., Carole Hayne, Ph.D.

NR367 An Innovative Treatment for Cocaine Addiction
James A. Halikas, M.D., Kenneth D. Kemp, M.D., Kenneth L. Kuhn, M.D., Gregory A. Carlson, Fred S. Crea

NR368 Serotonergic Function in Subgroups of Alcoholics
Laure B. Buydens-Branchey, M.D., Marc Branchey, M.D.

NR369 Buprenorphine Treatment of Cocaine Abuse
Thomas R. Kosten, M.D., Charles J. Morgan, M.D., Herbert D. Kleber, M.D.

NR370 Nicotine Withdrawal Cessation by Fluoxetine
William E. Hapworth, M.D., Mada Hapworth, Ph.D., David M. Martin

NR371 Cognitive Deficits Associated With Cocaine Abuse
Stephanie O'Malley, Ph.D., Herbert D. Kleber, M.D., Frank H. Gawin, M.D., Robert Heaton, Ph.D.

NR372 Opiate Withdrawal Effects on Regional Cerebral Blood Flow
John H. Krystal, M.D., Thomas R. Kosten, M.D., Scott W. Woods, M.D., John Seibyl, M.D., Lawrence H. Price, M.D., George Zubal, Paul Hoffer, M.D., Herbert D. Kleber, M.D., Dennis S. Charney, M.D.

NR373 Psychopathological Profiles in Early Substance Use
Welmoet B. van Kammen, Ph.D., Rolf Loeber, Ph.D., Magda Stouthamer, Ph.D.

NR374 Quantitative Drug Tapers Using Lower Drug Dosages
Steven I. Altchuler, M.D., Michael A. Palmer, M.D., S.C. Lin, M.D.

NR375 Prolactin, Cocaine Dependence and Treatment
Henry R. Kranzler, M.D., Dale J. Wallington, B.S.

NR376 Acute Cocaine Reduces Brain Glucose Metabolism in Drug Users
Nicola G. Cascella, M.D., Edythe D. London, Ph.D., Motoki Sano, M.D., Dean F. Wong, M.D., Ronald I. Herning, Ph.D., Jonathan M. Links, Ph.D.

NR377 Buprenorphine Responders: A Diagnostic Subgroup?
Richard B. Resnick, M.D., Elaine Resnick, M.S.W., Marc Galanter, M.D.

NR378 The Alcoholic's Sensitivity to Intravenous Diazepam
Bryon H. Adinoff, M.D., Daniel W. Hommer, M.D., Thomas Clem, Ph.D., Jeff Moran, Ph.D., Steven M. Paul, M.D., Markku Linnoila, M.D.

NR379 Alcohol Abuse in a Schizophrenic Population
Cynthia Pristach, M.D., Cedric M. Smith, M.D.

NR380 Treatment Given to Dual Diagnosed Men Alcoholics
Elizabeth J. Nickel, M.A., Elizabeth Penick, Ph.D., Barbara J. Powell, Ph.D., Jan Campbell, M.D., Barry I. Liskow, M.D., Marsha R. Read, Ph.D.

NR381 Apomorphine Challenge in Cocaine Abusers
Eric Hollander, M.D., Edward Nunes, M.D., Concetta DeCaria, M.S., Steven Wager, M.D., Donald F. Klein, M.D., Frederic Quitken, M.D.

NR382 Family Function in Girls with Eating Disorders
Regina C. Casper, M.D., Maryann V. Troiani, Psy.D.

NR383 Stealing in Eating Disordered Patients
Dean D. Krahn, M.D., Pamela Flegel, B.S., Karen K. Canum, R.N., Kenneth R. Castagna, M.S.W.

NR384 Axis-II Personality Disorders in Weight Control
William H. Berman, Ph.D., Ellen Raynes, Ph.D., Steven Heymsfield, M.D., Margaret Fauci, R.N., Sigurd Ackerman, M.D.

NR385 Sex Abuse: Role in Eating Disorder
Vivian L. Folsom, M.S.S., Dean D. Krahn, M.D., Karen K Canum, R.N., Laura Gold, Ph.D., Ken R. Silk, M.D.

NR386 Fluoxetine in Bulimia Nervosa: Double Blind Study
Gregory G. Enas, Ph.D., Harrison G. Pope, M.D., Louise R. Levine, M.D.

NR387 Zinc Deficiency and Eating Disorders
Laurie L. Humphries, M.D., Beverly S. Vivian, R.D., Mary A. Stuart, Ph.D., Craig J. McClain, M.D.

NR388 Treatment Compliance of Older Problem Drinkers
Roland M. Atkinson, M.D.

NR389 Eating Behaviors During the Menstral Cycle
Martha Fankhauser, M.S., Rebecca Potter, M.D., Catherine Shisslak, Ph.D.

NR390 Eating Disorders in the Psychiatric Emergency Room
Aimee S. Johnson, M.D., James R. Hillard, M.D.

NR391 Serotonin: A Trait Disturbance in Anorexia Nervosa?
Walter H. Kaye, M.D., Harry E. Gwirtsman, M.D., Michael H. Ebert, M.D.

NR392 Dieting and Bulimia: A Continuum of Behaviors
Adam Drewnowski, Ph.D., Doris K. Yee, M.A., Dean D. Krahn, M.D.

NR393 Endocrine Effects of Cortisol Blockade in Anorexia
Harry A. Brandt, M.D., Mitchel A. Kling, M.D., Mark A. Demitrack, M.D., Harvey J. Whitfield, M.D., Margaret Altemus, M.D., Philip W. Gold, M.D.

NR394 Linkage Studies of Panic Disorder
Raymond R. Crowe, M.D., Russell Noyes, M.D., Robert Wesner, M.D., Stephen Samuelson, M.D., Rickey Wilson, M.D.

NR395 Bone Density in Anorexia and Bulimia Nervosa
Michael Newman, M.D., Katherine Halmi, M.D.

NR396 Opioids Affect Taste Preferences for Sugar and Fat
Adam Drewnowski, Ph.D., Blake Gosnell, Ph.D., Dean D. Krahn, M.D., Karen Canum, R.N.

NR397 Family Interactions in Bulimia Nervosa
D. Blake Woodside, M.D., Lorie F. Shekter-Wolfson, M.S.W., Marion P. Olmsted, M.A.

NR398 Concomitant Disorders in Childhood Depression
Carroll W. Hughes, Ph.D., Sheldon Preskorn, M.D., Elizabeth Weller, M.D., Ronald A. Weller, M.D., Ruth Hassanein, Ph.D.

NR399 Separation Anxiety Disorder in Pediatric Primary Care
Jose L. Ayuso-Gutierrez, M.D., Maria T. Alonso, M.D., Nuria Perez de Lucas, M.D., Olvido Latorre, M.D.

NR400 Designing a Children's Psychiatric Facility
Mardelle M. Shepley, D. Arch, John Boerger, B.Arch.

NR401 Children's Interview for Psychiatric Syndromes: A Validity Study
Marijo Teare, M.A., Mary A. Fristad, Ph.D., Elizabeth Weller, M.D., Ronald A. Weller, M.D., Paul Salom, Ph.D.

NR402 A Family Study of Social Phobia: Preliminary Report
Abby J. Fyer, M.D., Salvatore Mannuzza, Ph.D., Lynn Y. Martin, M.S., Mark Gallops, M.Phil., Donald F. Klein, M.D.

NR403 Clonazepam in Panic Disorder
Linda Beauclair, M.D., Rejean Fontaine, M.D., Naomi Holobow, Ph.D., Lawrence Annable, B.Sc., Guy Chouinard, M.D.

NR404 Cross Cultural Differences in Panic Disorder
Heinz Katschnig, M.D., Gerald L. Klerman, M.D., Raimund Buller, M.D., Joseph A. Deltito, M.D., Philip W. Lavori, Ph.D., Michaela Amering, M.D.

NR405 Childhood Abuse and Limbic System Dysfunction
Martin H. Teicher, M.D., Carol Glod, M.S., Chester Swett, Jr., M.D., Janet Surrey, Ph.D., Catherine Brasher, B.S.

NR406 Therapeutic Parameters: Strategic Versus Exploratory
John O. Beahrs, M.D., John L. Butler, M.D., David J. Drummond, Ph.D., Stanley G. Sturges, M.D., Claudette H. Beahrs, M.S.S.W.

NR407 Urinary Markers and Drug Cognitive Therapy Comparison
Gary D. Tollefson, M.D., Michael J. Garvey, M.D., Mark D. Evans, Ph.D., Christopher S. Vye, Ph.D., Steven D. Hollon, Ph.D., Vincente B. Tuason, M.D.

NR408 Suicidal Behaviors in AIDS and HIV Positive Patients
F. Patrick McKegney, M.D., Mary A. Odowd, M.D., Carmen Natali, M.D., Jill M. Harkavy, Ph.D., Gregory M. Asnis, M.D.

NR409 Comparing Methods to Assess Patients for Therapy
K. Roy Mackenzie, M.D.

NR410 Reliability of Therapists' Process Estimates
John O. Beahrs, M.D., John L. Butler, M.D., David J. Drummond, Ph.D., Claudette H. Beahrs, M.S.S.W.

NR411 Inpatient Group Processes Parallel Unit Dynamics
E. Michael Kahn, M.D., I. Terry Sturke, M.S.

NR412 A State Hospital Family Psychoeducational Program
Shirley M. Glynn, Ph.D., Robert Pugh, M.A., Gordon Rose, Ph.D.

NR413 Tracking the Pathogenesis of Marital Distress
Frederick S. Wamboldt, M.D., David Reiss, M.D.

NR414 Psychiatric Comorbidity in Somatization Disorder
Frank W. Brown, M.D., G. Richard Smith, M.D.

NR415 On the Abnormality of Normal Control Groups
Robert W. Butler, Ph.D., Melissa Jenkins, B.A., David L. Braff, M.D.

NR416 Utility of Computer-Assisted DSM-III-R Diagnosis
Michael B. First, M.D., Lewis A. Opler, M.D., Robin M. Hamilton, M.D., Jill Linder, M.D., Louis S. Lindfield, M.D., Jonathan M. Silver, M.D., Nina L. Toshav, M.D., David Kahn, M.D., Janet B.W. Kahn, D.S.W., Robert L. Spitzer, M.D.

NR417 A Brief DSM-III Based Patient Classification System
John W. Goethe, M.D., Hal Mark, Ph.D.

NR418 The Meaning and Measurement of Apathy
Robert S. Marin, M.D., Ruth C. Biedrzycki, M.Ed., Sekip Firinciogullari, M.S.

NR419 Importance of Axis II Diagnoses in Axis I Research
Kenneth R. Silk, Drew Westen, Ph.D., Naomi E. Lohr, Ph.D., Laura Gold, Ph.D., Edna Pressler, M.A.

NR420 Optimizing REM Studies With the INFO-ROC Technique
Eugene Somoza, M.D., Douglas Mossman, M.D.

NR421 Sexual Harassment of Medical Students
Andrea Jacobson, M.D., Gwenyth K. McConnell, B.A.

NR422 Resident's Attitudes Towards Pregnancy
Devra Braun, M.D., Virginia L. Susman, M.D.

NR423 The Continuing Stigma (1938-1988) of Viennese Psychiatry
Norbert Loimer, M.D., Rainer Schmid, Ph.D.

NR424 Graphic Display of Psychiatric History and Treatment
Mark D. Rego, M.D., Seth M. Powsner, M.D., Robert S. Byck, M.D.

NR425 Sexual Trauma: The Cause of Multiple Pathology?
Ingunn Skre, Ph.D., Sidsel Onstad, M.D., Svenn Torgersen, Ph.D., Einar Kringlen, M.D.

NR1 **Monday, May 8 9:00 a.m.–10:30 a.m.**

ABUSE AND SELF-INJURY IN ADOLESCENT INPATIENTS

Timothy G. Lesaca, M.D., Chestnut Ridge Hospital, 930 Chestnut Ridge Road, Morgantown, WV 26505

Summary:

To test the hypothesis that prior experience of sexual or physical abuse increases the likelihood of self-injurious behaviors by adolescents during psychiatric hospitalization, a retrospective examination of the inpatient psychiatric records of 66 consecutive admissions to a psychiatric adolescent unit was conducted. Information extracted included any documented history of sexual or physical abuse, the perpetrator of abuse, any event of self-injury during hospitalization, and the method and bodily area of injury. Of the 66 patients, 21.2% were sexually abused and 13.6% were physically abused. The biologic fathers were overwhelmingly the main perpetrators of all abuses. Hand injury was the most frequent method of self-injury, and 38.9% of all self-injuries occurred while the patient was in the seclusion room. It was found that the sexually abused females were significantly more likely than nonabused females to exhibit self-injurious behaviors. Also, the sexually or physically abused male group was over three times more likely to self-injure than the nonabused male group. This study should help clinicians identify patients at risk for inpatient self-injury and thus decrease their risk for harm.

NR2 **Monday, May 8 9:00 a.m.–10:30 a.m.**

VENTRICLE-BRAIN RATIO IN SCHIZOPHRENIA: CLINICAL CORRELATIONS

John R. Dequardo, M.D., Psychiatry, Univ of Michigan, 1500 East Med Ctr Dr., UH 9C9150, Ann Arbor, MI 48109; Raymond Kloss, M.D., Rajiv Tandon, M.D.

Summary:

Cerebral atrophy and enlarged ventricular size in schizophrenic patients have been associated with negative symptoms, cognitive dysfunction, and poor outcome. To confirm these findings and evaluate the relationship between ventricular size and DST, head CT scans in 30 schizophrenic (DSM-III-R and RDC) inpatients were performed. Measures of ventricle-brain ratio (VBR), maximum width of the third ventricle, and cortical atrophy were obtained by digital planimetry. Positive/negative/depressive symptoms were assessed with the BPRS, SANS, and HAM-D, respectively, and a 1 mg valid DST performed at drug-free baseline and four weeks after neuroleptic treatment. VBR was correlated ($p<0.05$) with global severity and negative symptoms, particularly ($p<0.01$) the "cognitive" SANS items (alogia and attentional impairment). Enlarged ventricles were associated with poor clinical improvement (as measured by BPRS change score) and showed a trend towards association ($p<0.10$) with positive family history for schizophrenia. Third ventricular width was associated with negative symptoms, particularly ($p<0.01$) the "affective" SANS items (affective blunting, anhedonia-asociality, and avolitionapathy). Third ventricular width, but not VBR, was correlated with baseline post-dex cortisol ($p<0.05$) and platelet MAO levels ($p<0.05$). These findings suggest that VBR and third ventricular width may be related to different aspects of schizophrenic pathophysiology.

NR3 **Monday, May 8 9:00 a.m.–10:30 a.m.**

TRAIT ANXIETY AND PSYCHOMOTOR ACTIVITY

Duncan Clark, M.D., Psychiatry, Stanford University, 830 University Drive, Menlo Park CA 94025; Roy King, M.D., C. Barr Taylor, Jurgen Margraf, Ph.D., Walton T. Roth, M.D., Barr C. Taylor, M.D.

Summary:

While anxious children have been shown to have relatively low levels of activity (Buss, et al., 1980; Korner, et al., 1985), the relationship between trait anxiety and activity has not been studied in adults. In this study, 47 panic disorder patients and 27 control subjects were assessed for trait anxiety using the Spielberger STAI and mean daily activity using the Vitalog monitor. In panic disorder patients, there was a negative correlation between trait anxiety and activity ($r=-.24$; $p=.05$, one-tailed), while in control subjects there was a positive correlation ($r=.37$; [$<.05$, one-tailed). Combining these samples, an "inverted U" relationship between trait anxiety and activity was observed, with this relationship best expressed by the following quadratic equation: Activity$=-.14$ Trait Anxiety^2 + 13 Trait Anxiety -33. This formula accounted for a statistically significant proportion of the variance in activity ($F=3.75$; d.f.$=2, 71$; $p<.05$). Thus, a systematic but nonlinear relationship between trait anxiety and mean daily activity was demonstrated.

NR4 **Monday, May 8 9:00 a.m.–10:30 a.m.**

ANTICHOLINERGICS AND CARDIAC FUNCTION DURING ECT

Shashidhar M. Shettar, M.D., Psychiatry, Univ of Mich Hospital, 1500 E. Med Ctr Dr Box, 0118, Ann Arbor, MI 48109; Leon Grunhaus, M.D., Atul C. Pande, M.D., Rajiv Tandon, M.D., Ziad Kronfol, M.D.

Summary:

Parasympathetic stimulation produced by ECT may cause cardiac asystole and other arrhythmias for which anticholinergic premedication has been used in routine ECT practice. We compared the magnitude of cardiac asystole following brief pulse bidirectional ECT in a sample of 19 inpatients who received ECT sequentially with and without premedication with intramuscular glycopyrrolate. Lead II EKG was recorded prior to, during and after ECT. Cardiac measures of each subject were averaged for the ECTs with and without glycopyrrolate premedication, and comparisons were made so that each patient served as their own control. Cardiac asystole following ECT was defined as the time interval between the end of electrical stimulation to the appearance of the first complete QRS complex on the EKG recording. This interval was significantly longer in the nonglycopyrrolate ECTs (1.93±1.13s) versus the glycopyrrolate ECTs (0.73±0.38s) (paired t=, $p<0.0002$). No significant arrhythmias or changes in vital signs were observed regardless of whether glycopyrrolate premedication was used. In conclusion, it appears that brief pulse bidirectional ECT has significant immediate effects on atrioventricular conduction, with some patients demonstrating asystole of up to six seconds. Glycopyrrolate significantly decreases this asystole during ECT. The clinical implications of this will be discussed.

NR5 **Monday, May 8 9:00 a.m.–10:30 a.m.**

RELATIONSHIP BETWEEN SLEEP EEG MEASURES AND ECT SEIZURE LENGTH

Shashidhar M. Shettar, M.D., Psychiatry, Univ of Mich Hospital, 1500 E. Med Ctr Dr, Box 0118, Ann Arbor, MI 48109; James E. Shipley, M.D., Leon Grunhaus, M.D., Roger F. Haskett, M.D., Alan S. Eiser, Ph.D.

Summary:

It has been reported that cumulative seizure length (SzL) over the course of ECT treatment (Tx) is important for clinical response, but there are no reports of the relationship between this parameter and EEG sleep variables. Fifteen inpatients on the Clinical Studies Unit at the University of Michigan who underwent ECT and EEG sleep recordings were selected for the study. Thirteen patients had MDD and two were schizoaffective by SADS/RDC, three patients were psychotic, and the entire sample had a HRSD (17-item scale) mean±SD of 26±7.5. All the patients were drug free a minimum of 10 days (mean±SD of 13.6±1.7 days) prior to two consecutive nights of sleep EEG recordings, which were averaged for data analysis.

Pearson correlations showed that there were no correlations between SzL and REM latency or sleep efficiency, or any other sleep measures except those related to REM density (RD), which was associated with first Tx SzL ($r=.65$, $p<.01$), as well as cumulative SzL ($r=.72$, $p<.01$) and mean SzL ($r=.77$, $p<.001$) through six Tx. We divided the group into those with RD above (n=7) or below (n=8) a RD of 2.5. There was no difference in age, episode length, length of stay, discharge HRSD, or number of Tx, but the high RD group did have a higher admission HRSD (30.9±6.4 vs 21.8±5.7, $p<.05$) and had longer first SzL (66.7±13.1 sec vs 46.6±7.2 sec), as well as longer cumulative SzL (352.8±100.0 sec vs 227.7±49.2) and mean SzL (54.8±7.6 vs 38.2±8.2, all $p<.01$) through six Tx. In sum, patients with high RD had a more severe illness at admission but were equally responsive to ECT. This may be related to their having greater SzL during ECT.

NR6 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

SPREAD OF COCAINE AMONG ADULTS AND ADOLESCENTS

John E. Hickey, L.C.S.W., Addiction Research Center, P.O. Box 5180, Baltimore, MD 21224; Anne F. Kolar, M.D., Barry S. Michaelson, M.A., Anneke Chung, B.A., Carolyn Haynie, M.D., Barry S. Brown, Ph.D.

Summary:

The purpose of this study was to explore the spread of cocaine among youth and adult populations and to understand the differences between the age groups. Structured interview schedules were used to obtain data regarding drug history, initiation and maintenance of cocaine use. Subjects were 20 adolescents aged 14 to 21, and 90 adults, aged 26 to 53, all in treatment for cocaine abuse. In both groups friends were the main providers of cocaine for the initial experience (youth: 55.0%, adult: 62.2%). Both groups reported few friends who did not use cocaine at the time of their initiation and almost no drug abstinent friends. Among the adult population, 37.8% reported using heroin prior to cocaine initiation, compared with 15% of the youths interviewed. The adolescents, however, were more involved with marijuana (youth: 95.0%, adult: 73.3%) and PCP (youth: 45%, adult: 6.7%) prior to cocaine initiation. More of the adult population injected cocaine at initiation (youth: 10.0%, adult: 35.5%). No subjects initiated cocaine use with by smoking "crack," though two adolescents freebased the drug.

NR7 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

COCAINE: PERCEIVED RISK AND SOURCES OF INFORMATION

John E. Hickey, L.C.S.W., Addiction Research Center, P.O. Box 5180, Baltimore, MD 21224; Barry S. Brown, Ph.D., Anneke S. Chung, B.A., Anne F. Kilar, M.D., Barry S. Michaelson, M.A.

Summary:

We interviewed 20 adolescents aged 14 to 21, and 90 adults, aged 26 to 53, cocaine abusers in seven Baltimore-area treatment programs. Using a structured interview it was found that 87.8% of the adults and 80.0% of the youths had experienced at least one negative consequence of their cocaine use, other than addiction, prior to entry into treatment. The most common negative experience reported by both groups was the loss of reality testing. While juveniles sampled had entered treatment within a year of first cocaine use, adults entered treatment 7.9 years after first use and reported an average of 6.6 years of cocaine use before experiencing the first negative consequence. The difficulty of mounting a credible argument about risk as a counter-argument to pressures to use cocaine is made apparent by the long "honeymoon period" (6.6 years) between first cocaine use and first adverse consequence reported by adults.

Both adolescents and adults rated books and magazines as most accurate about cocaine, with television a close second. In terms of amount of information about cocaine use, adolescents ranked television first and friends second, while adults reversed the order ranking friends first and television second.

NR8 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

AGE AND THE PREVALENCE OF DISSOCIATION

Robert W. Hermanowski, B.S., Psychiatry, NE OH Univ Col of Med, 431 Elgin Avenue NW, Canton, OH 44708; Moshe S. Torem, M.D., Kathryn J. Curdue, M.D.

Summary:

In recent years there has been a resurgence of interest in multiple personality disorder and other dissociative phenomena. This is evidenced by the large amount of recent literature about dissociation, both as a psychopathological entity and as a common experience in healthy people. Several authors have alluded to a relationship between dissociative phenomena and age. However, to our knowledge there have been no studies that have directly compared the prevalence of dissociation in older and younger adults.

We have conducted such a study through the use of two self-report measures: Sander's Perceptual Alteration Scale (PAS), and Bernstein and Putnum's Dissociative Experiences Scale (DES). In our paper, we examine the results, showing a significant difference in the prevalence of dissociative experiences in older and younger people. This is followed by a discussion focused on the implications of this research for advancing our knowledge of the natural progression of dissociation with age, and the natural history of dissociative disorders, including multiple personality.

NR9 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

PROFILE OF DROPOUTS AND ATTENDERS IN A FAMILY SUPPORT GROUP

Mary De Florio, M.D., Psychiatry, St. Vincent's Hospital, 144 W. 12th Street, Day Hosp., New York, NY 10011; Stephen A. Cole, M.D., Samuel Simmens, Ph.D., Robert Shapiro, Ph.D., Stuart Barr, M.D.

Summary:

This study attempted to isolate factors contributing to family attendance in a multiple family psychoeducational treatment group following inpatient admission for schizophrenia or schizoaffective disorder. Epidemiological, demographic, and attitudinal data were gathered from 22 patients and their families who attended a family support group at the New York Veterans Administration Medical Center over a three-year period, 1981–1984. Statistical evaluation revealed a family and patient profile of those most likely to attend. This pilot study attempted to discover factors that would reduce dropout rates and improve family-patient relationships.

Attendance rates are compared for five sets of variables: 1. demographics 2. severity of illness and adverse reactions to medication 3. access/barriers to obtaining health care 4. family's rejection of the patient 5. family's attitude toward the group.

Attendance rates were enhanced by intact marriage of the parents, greater severity of the patient's illness (younger age of onset) and adverse reactions to medication (side effects and limitations of activity), fewer barriers to obtaining health care, the family's belief that they could help the patient get better, having a positive attitude towards the family support group, and feeling accepted by the group as an equal.

NR10 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

NEGATIVE SYMPTOM ASSESSMENT IN SCHIZOPHRENIA

Raman Sood, M.D., Psychiatry, University of Maryland, 22 South Greene Street, Baltimore, MD 21201; Rodney J. Pelchat, M.D., Larry D. Alphs, M.D., Jerome Levine, M.D., Harini Balu, M.D., Allen Raskin, Ph.D.

Summary:

The negative symptom assessment scale (NSA) was developed by Alphs et al. to overcome a number of deficiencies in existing scales including the lack of sufficient items to assess the full range of negative symptoms. It was initially standardized on young inpatient and outpatient schizophrenics. An expanded version was used in this study to extend the generalizability to older, more chronic inpatient schizophrenics. The sample consisted of 100 inpatients at Perry Point VAMC. Average age was 50, mean length of stay 6.5 years, and mean total hospitalization 17 years. All received DSM-III-R disgnoses of schizophrenia or schizoaffective disorder. A factor analysis of the NSA (normal varimax rotation) yielded seven factors. Most of the variance (45%) was accounted for by factor 1: Affect/Emotion. It was comparable to a similarly labeled factor in the original sample. Key items included reduced emotional range and experience, blank expressionless face and reduced gestures. Age and total length of stay were significantly correlated with Factor 1. Two new factors emerged. These were labelled Emotion Perception and Speech Retardation. These factors appear to reflect the effect of age and chronicity of illness and the addition of new items.

NR11 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

COMPARISON OF NEGATIVE SYMPTOM SCALES

Jose de Leon, M.D., Psychiatry, MCP EPPI, 3200 Henry Avenue, Philadelphia, PA 19129; George M. Simpson, M.D., William H. Wilson, M.D.

Summary:

Over the past decade, the positive/negative symptom dichotomy has become a central paradigm for biological research regarding schizophrenia. The concept of negative symptoms is a critical element in hypotheses of etiology, studies of psychopharmacology, and treatment approaches. We have reviewed three general types: 1) nonspecific scales (BPRS, Modified Krawiecka), 2) specific scales (SANS, Pogue-Geille, Pearlson, SNRS, PANSS), and 3) statistically designed scales (Lewine). There is considerable variability among the scales regarding the types of items and specific symptoms that are included. Some of the items reflect clinical symptoms and signs; other items rate psychosocial performances or neuropsychological deficits. There is only one item that every negative symptom scale includes, i.e., flattening of affect. Poverty of speech is included in all scales except those derived from the BPRS. Some items considered to be negative symptoms on one scale are considered positive on another, or are not included as either positive or negative. Results from one negative symptom scale cannot be properly compared to those obtained from other scales. The research carried out on negative symptoms is undermined by this lack of agreement.

NR12 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

CCRT: A METHOD FOR COMPARING NEUROTICS AND BORDERLINES

Ellen K. Schlefer, M.D., Psychiatry, New York Hospital, 21 Bloomingdale Road, White Plains, NY 10605; Michael A. Selzer, M.D., John Clarkin, Ph.D., Frank Yeomans, M.D.

Summary:

The Core Conflictual Relationship Theme (CCRT), a guided, clinical method developed by Luborsky for determining a patient's dynamic theme, is used to distinguish Borderline Personality Disorder (BPD) from "neurotic" patients, i.e., patients who carry certain DSM-III-R disorders to be outlined below. CCRTs from 10 BPD patients, diagnosed according to DSM-III-R, are compared with CCRTs from 10 neurotic patients. First, a quantitative method is used to compare the number and completeness of "relationship episodes" (REs), narratives used to determine the CCRT. Second, a method to show identity diffusion and primitive defenses consistent with a borderline character structure is outlined, and the two groups of patients are compared. Finally, the CCRTs of BPD patients are shown to contain themes alleged to be present in BPD patients. The promise of the CCRT method is that it can be used to evaluate change in BPD patients during psychotherapy.

NR13 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

SEROTONIN PROBES IN OBSESSIVE COMPULSIVE DISORDER

Teresa A. Pigott, M.D., SCN LCS, NIMH Bldg 10/3D41, 9000 Rockville Pike, Bethesda, MD 20892; Dennis L. Murphy, M.D., Michele T. Pato, M.D., James L. Hill, Ph.D., Gay Grover, M.S.N., Chawki Benkelfat, M.D.

Summary:

To further investigate the role of serotonin (5-HT) in the pathophysiology of obsessive-compulsive disorder (OCD), we administered the selective serotonergic agonist, m-chlorophenylpiperazine (m-CPP) to 12 subjects after pretreatment with the 5-HT_1/5-HT_2 antagonist metergoline. All 12 subjects (six patients with OCD and six healthy controls) received a 4-mg oral dose of metergoline (MTG) followed one hour later by an intravenous (iv) dose of m-CPP (0.1 mg/kg) of placebo, administered under double-blind, placebo-controlled, random-assignment conditions. Despite MTG pretreatment (which blocked m-CPP-induced prolactin and temperature increases), both patients and controls manifested substantial behavioral effects, including anxiety, dysphoria, and functional impairment similar to that reported by Charney et al and by our group with iv m-CPP. Unlike our previous report with oral m-CPP, the OCD patients did not experience an exacerbation of OC symptoms. A subgroup of OCD patients who received m-CPP without MTG pretreatment also manifested significant behavioral effects, but again did not exhibit an exacerbation of their OCD symptoms. The lack of m-CPP-induced exacerbation of OC symptoms, coupled with the failure of MTG to block m-CPP-induced behavioral effects despite evidence of neuroendocrine and temperature blockade suggests that: 1) anxiety and other behavioral effects elicited by iv m-CPP appear to be mediated by mechanisms other than those regulating physiological responses, and 2) iv m-CPP may result in such profound behavioral effects that OCD symptoms cannot be elicited or cannot be delineated from anxiogenic or other mood effects.

NR14 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

CLOMIPRAMINE VERSUS BUSPIRONE IN OCD: A CONTROLLED TRIAL

Michele T. Pato, M.D., SCN LCS, NIMH Bldg 10/3D41, 9000 Rockville Pike, Bethesda, MD 20892; Teresa A. Pigott, M.D., James L. Hill, Ph.D., Gay Grover, M.S.N., Suzanne E. Bernstein, B.S., Dennis L. Murphy, M.D.

Twenty patients with obsessive-compulsive disorder (OCD) (DSM-III-R criteria) were compared in a random assignment, parallel design, double-blind treatment trial using the novel anxiolytic buspirone (30–60 mg) and the tricyclic antidepressant clomipramine (150-300 mg). Patients received medication for a total of six weeks, following two weeks of placebo. All patients were rated at two-week intervals by blind raters using the Yale-Brown Obsessive-Compulsive Scale, NIMH Obsessive-Compulsive Scale, NIMH Global Rating Scores, and Hamilton Depression Scale. Repeated measures analysis of variance showed significant and similar improvement ($p<.001$ for most measures) across the rating scales for both medication groups, suggesting similar efficacy for buspirone and clomipramine in the treatment of OCD. This finding of similar efficacy is important for two reasons. First, prior to this study clomipramine has generally been found to be superior to other drugs and placebo in the treatment of OCD. Second, these two drugs are both thought to have primary actions on the brain serotonergic system (clomipramine as a serotonin (5HT) selective reuptake inhibitor and buspirone as a $5HT_{1A}$ receptor agonist). Thus, this study further supports the hypothesis that drugs that are therapeutically effective in this disorder or that can activate OCD symptomalogy may do so through effects on brain serotonin mechanisms.

NR15 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

SOMATOSTATIN IN ALZHEIMER'S DISEASE

Susan E. Molchan, M.D., SCN LCS, NIMH Bldg 10/3D41, 9000 Rockville Pike, Bethesda, MD 20892; David R. Rubinow, M.D., Brian A. Lawlor, M.D., James L. Hill, Ph.D., Rick A. Martinez, M.D., Alan M. Mellow, M.D., Trey Sunderland, M.D.

Summary:

Somatostatin-like immunoreactivity (SLI) has been consistently shown to be decreased in the cortex and cerebrospinal fluid (CSF) of patients with Alzheimer's disease (AD). SLI has also been found to be decreased in the CSF of patients with major depression. Furthermore, behavioral symptoms and biological markers of depression are common in AD. Because somatostatin has been associated with disturbances in sleep, appetite, locomotion, and memory in animals, we examined whether CSF SLI was related to depressive symptoms in AD patients.

CSF SLI was significantly decreased ($p<0.05$) in 62 AD patients (37.1 ± 15.5 pg/ml) compared to 17 elderly depressives (49.3 ± 13.9 pg/ml). In both of these patient groups, SLI was significantly decreased ($p<0.05$) compared to 12 age-matched controls (62.8 ± 15.9 pg/ml) as previously reported for smaller samples. Within the AD group, SLI showed a strong correlation with the Dementia Mood Assessment Scale, a measure of depression in AD patients ($r=0.51$, $p<0.002$, $N=34$), and a modest correlation with measures of dementia severity such as the Global Dementia Scale ($r=-0.28$, $p<0.04$, $N=55$). This study is the first to show such a relationship between CSF SLI and depression in AD. Because AD and major depression can have overlapping clinical symptoms, further understanding of the decreased SLI in these conditions may help elucidate the biological mechanisms in each disease.

NR16 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

THE IMPACT OF LOCKED UNITS ON SECLUSION PRACTICES

Michael J. Sedlacek, M.D., Psychiatry, University of NE Med Ctr, 42nd and Dewey Avenue, Omaha, NE 68105; William J. Burke, M.D., Steven Wengel, M.D.

Summary:

The use of seclusion and restraint in psychiatry continues to be an area of debate. Attitudes and practices have varied from wholesale warehousing of psychiatric patients to the belief that the only proper treatment milieu is an open unit. Factors said to correlate with the use of seclusion in psychiatric units include patient, milieu, and staff factors; whether a unit was locked or unlocked has not been addressed. We have been able to explore this issue by a retrospective review of seclusion incidents on an adult inpatient university psychiatry service, before and after the units were converted from locked to open units. We hypothesized that unlocked units would correlate with an increased use of seclusion compared to locked units. Data were collected on 227 seclusion episodes of 86 patients occurring in the years preceding and following the switch. We found no evidence of an increase in the frequency of seclusion or any difference in patient factors such as age, diagnosis, and behaviors leading to seclusion; milieu factors such as on which shift seclusion occurred; and staff factors such as duration of seclusion and use of medication. A change from a locked to an open facility did not increase the use of seclusion.

NR17 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

THE DST: REFINEMENT OF PREDICTIVE VALUE

Scott B. Patten, M.D., Psychiatry, University of Calgary, 1403 29 Street N.W., Calgary Alberta, Canada T2N 2T9

Summary:

The dexamethasone suppression test (DST) is the most extensively studied biological test in psychiatry. Despite this, its role in the diagnostic assessment of psychiatric patients remains undefined. In situations where the usefulness of a diagnostic test is not clearly defined it is often helpful to examine the diagnostic implications of the test using a statistical approach. One statistical parameter, the predictive value (PV), is particularly helpful in qualifying the contribution to clinical judgment made by diagnostic tests. Predictive value is a function of pretest probability, sensitivity and specificity and can be estimated using Bayes' theorem of conditional probability. In this study, the records of 243 consecutively admitted psychiatric inpatients are examined, and Bayes' theorem was used to quantify the usefulness of the DST in various clinical situations. The study demonstrates how the application of Bayes' theorem can augment clinical judgments about the use and interpretation of the DST.

NR18 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

EFFECT OF VASOPRESSIN AND NALOXONE ON CORTISOL

E. Jane Garland, M.D., Psychiatry, University of BC, 2255 Wesbrook Mall, Vancouver BC, Canada V6T 2A1; A. P. Zis, M.D.

Summary:

The mechanism of hypercortisolemia and dexamethasone (DEX) nonsupression in depression is unclear, but hypothalamic-pituitary-adrenal (HPA) dysregulation is presumed. It has been reported that neither corticotropin-releasing hormone (CRH) nor vasopressin (VP) alone can overcome DEX suppression in normal subjects. Endogeneous opioids exert a tonic inhibitory effect on the HPA axis, and the opioid antagonist naloxone (NAL) potentiates the hypercortisolemic effects of CRH, while opioid agonists inhibit the pituitary response to VP. This study examines whether NAL and VP, alone or in combination, can overcome DEX suppression in healthy subjects. In nine male subjects pretreated with 1 mg of DEX, plasma cortisol was measured at baseline and at 15-minute intervals after the single-blind intravenous bolus administration of VP (3 U), NAL (0.2 mg/kg) and VP-NAL combination in a Latin Square design. NAL alone did not produce an escape from DEX suppression. Vasopressin alone produced an escape (cortisol $>$ 140 nmoles/L) in four subjects with no evidence of additional effect from naloxone. In two subjects, cortisol levels did not change significantly in any of the three experimental conditions. These results do not demonstrate a role for opioidergic blockade in DEX nonsuppression. The data do suggest a heterogeneity of pituitary corticotroph response to VP in DEX-treated normals similar to that which has been reported in depressed patients. These findings will be discussed in light of current theories of hypercortisolemia and DEX nonsuppression in depression.

NR19 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

METABOLIC RATES IN OCD AND COMPARISONS WITH PANIC DISORDER

Thomas E. Nordahl, M.D., Psychiatry, Univ of Calif. Davis, 4403 V. Street, Sacramento, CA 95817; Chawki Benkelfat, M.D., William E. Semple, Ph.D., Murray B. Stein, M.D., Thomas A. Mellman, M.D., Michael Gross, M.D., Thomas W. Uhde, M.D., Robert M. Cohen, M.D.

Summary:

In a recent preliminary study, (Nordahl, et al in press) comparing eight medication-free patients with obsessive-compulsive disorder (OCD) with 30 normal controls, we found increased glucose metabolic rates in the oribital-frontal cortex of OCD patients. In this study five more medication-free patients with OCD were studied. The orbital frontal metabolic differences persist in this extension on the right side (two-tailed, t-tests $p \leq .05$). In addition, we have studied with positron emission tomography and F-18 Fluorodeoxyglucose (FDG), 12 medication-free patients with panic disorder (presented Midwinter Conf. Tahoe, Jan. 1989). We compared the regional metabolic rates of patients with OCD versus those of panic disorder patients in regions including: orbital frontal cortex, basal ganglia, anterior cigulate, C-occipital cortex, right-hippocampus ($p = .06$); regions in which at least one of the patient groups differed from normal controls. In those regions mentioned, the two patient groups did not statistically differ in regional glucose metabolic rates, though some (nonsignificant) differences existed in the mean values of the mentioned regions. Clinical comparisons with regional metabolic values will be presented.

NR20 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

5-HT FUNCTION IN THE BIOCHEMICAL RESPONSE TO MCPP

John P. Selbyl, M.D., Medicine, Yale Univ Sch of Med, 47 Bradley Avenue, Branford, CT 06405; Dennis S. Charney, M.D., John H. Krystal, M.D., Lawrence H. Price, M.D., George R. Heninger, M.D.

Summary:

The absence of a selective serotonin-2 (5-HT_2) receptor agonist for human use has made it difficult to evaluate the contributions of brain 5-HT systems to psychiatric disorders. M-chlorophenylpiperazine (MCPP), a drug that has been instrumental in studying the role of 5-HT systems in panic disorder, obsessive-compulsive disorder, and depression, appears to act at 5-HT_1 and 5-HT_2 receptors in animals. This study evaluated the contribution of 5-HT_2 receptors to the effects of MCPP in humans by assessing the ability of ritanserin, a selective 5-HT_2 antagonist, to block MCPP-induced behavioral and neuroendocrine responses. *Methods:* Healthy subjects participated on four test days in a randomized order where they received: 1) Placebo-MCPP (0.1 mg/kg, i.v.), 2) ritanserin (5 mg., p.o.)-MCPP, 3) placebo-placebo, 4) ritanersin-placebo. Ritanserin/placebo was administered 50 minutes prior to MCPP/placebo. Behavioral and neuroendocrine ratings began 30 minutes prior to ritanserin and continued for 180 minutes after MCPP administration. *Results:* Data are currently available on our first three subjects. The MCPP-induced prolactin rise was diminished by ritanserin in two subjects. MCPP-induced anxiety was diminished in one of two subjects with anxiety. *Comment:* While preliminary, these data suggest that MCPP-induced prolactin secretion and behavioral effects may be mediated, in part, by 5-HT_2 receptors, consistent with preclinical data. If our larger sample supports these data, it would indicate the utility of MCPP as a 5-HT_2 probe in humans.

NR21 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

DO MAST AND CAGE SCORES HELP DETECT ALCOHOLISM?

Connie M. Marsh, M.D., Psychiatry, UKSM-Wichita, 1010 N. Kansas, Wichita, KS 67214; Donna A. Vaughan, M.D.

Summary:

To assess the prevalence of alcoholism in psychiatric inpatients, and to determine if promptly providing screening scores to patients' physicians would increase their diagnostic sensitivity, 197 psychiatric inpatients were screened using the Michigan Alcoholism Screening Test (MAST) and the CAGE. Of 197 patients, 41% scored positive on one or both tests, but physicians diagnosed only 28% of the 41% as alcoholic. These findings support previous studies showing a high prevalence of alcoholism among psychiatric inpatients, but serious underdiagnosis. Physicians informed of screening results diagnosed 34% of those screening positive on either or both MAST and CAGE, compared to 25% diagnosed by noninformed physicians; this was not statistically significant. However,if the screening was positive on *both* the MAST and CAGE, or if the MAST scores were severely elevated, informed physicians were more likely than noninformed physicians to diagnose alcoholism, a statistically significant finding.

The results are promising and indicate the importance of routinely screening psychiatric patients for alcoholism, increasing physician awareness of the relevance of screening tests, and the need for further research on validity, sensitivity, and specificity of screening tests.

NR22 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

LONG-STAYING INPATIENTS: A DESCRIPTIVE STUDY

Terry M. Brown, D. O., NIMH RM 3S239 Bldg 10, 9000 Rockville Pike, Bethesda, MD 20892; Robert N. Golden, M.D., David Ekstrom, M.Ph., Helen L. Miller, M.D., Dwight L. Evans, M.D.

Summary:

We performed a retrospective case control study in order to learn more about the clinical and demographic characteristics of psychiatric inpatients who were admitted to our university hospital adult inpatient service over a two-year period, we identified 29 patients whose length of stay was in the 97.5 percentile or greater. We then randomly selected 29 control subjects from the subgroup of patients who had a length of stay that was exactly at the median (21 days).

The average length of hospitalization of the long-stay patients (LSP) was 111 days (range: 86–183). The LSP group contained a significantly greater percentage of patients who were scheduled elective admissions, as opposed to unscheduled admissions from the emergency room. They received significantly more medical/surgical consultations. Diagnostic differences between the LSP and control groups were not impressive, although patients in the former group were less likely to carry a principal diagnosis of adjustment disorder or a history of substance abuse. The most striking finding was a dramatically high prevalence of a history of physical and/or sexual abuse in the LSP group (46% vs. 17% for the control group). The clinical implications of these findings will be discussed.

NR23 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

COGNITIVE IMPAIRMENT IN TARDIVE DYSKINESIA

Michael F. Egan, M.D., NPB, NIMH Neuroscience Center, 2700 Martin Lurther K. Ave SE, Washington, DC 20032; James Gold, Ph.D., Terry Goldberg, Ph.D., Darrell G. Kirch, M.D., David G. Daniel, M.D., Richard Jed Wyatt, M.D., Daniel R. Weinberger, M.D.

Summary:

Several reports have suggested that schizophrenics with tardive dyskinesia (TD) have marked cognitive impairment, more negative symptoms, and increased VBR, as compared with TD-free patients. Neuropsychological testing instruments used to demonstrate this have been relatively crude. We sought to define more clearly the nature of the cognitive deficit by using the Halstead-Reitan and the WAIS-R in patients with TD compared with age- and education-matched controls. *Method:* Of 250 charts reviewed, 31 schizophrenics with TD were identified who had received a WAIS-R and the Halstead-Reitan. Most had BPRS data and CT scans as well. *Results:* The mean age of all patients was 29. There were no significant differences between the groups on any WAIS-R or Halstead-Reitan measure. On the BPRS there were some minor differences, but no evidence of increased negative symptoms. Furthermore, there were no differences between groups in the VBR as measured by CT scan.

Discussion: The results suggest that TD in this age group is not associated with clinically significant differences in neuropsychological functioning, psychopathology, or evidence of structural brain changes. This is different from what has been reported in older patients with TD. It suggests that organic cognitive impairment evolves over time, and is not present early on.

NR24 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

DSPECT IN OBSESSIVE COMPULSIVE DISORDER

John R. Debus, M.D., Psychiatry, UT Southwestern, 5323 Harry Hines Blvd, Dallas TX 75235; Michael D. Devous, Ph.D., John W. Cain, M.D., John Battaglia, M.D., S. Nadeem Ahmed, M.D., A. John Rush, M.D.

Summary:

Positron Emission Tomography (PET) studies have revealed elevated metabolic rates in the caudate nuclei, orbital gyri and cerebral hemispheres in obsessive-compulsive disorder (OCD) patients compared with normal controls (Baxter et al., 1987, 1988). This report will focus on an ongoing series of symptomatic OCD patients studied at rest with ^{133}Xenon using Dynamic Single Photon Emission Computerized Tomography (DSPECT). At this writing, the series includes 12 medication-free patients, all of whom were diagnosed with the SCID interview and met DSM-III-R criteria for OCD. The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) was used to quantify obsessive and compulsive symptoms. Regional blood flow values for preselected regions will be presented and compared to age- and sex-matched normal controls. We expect that a larger series of symptomatic patients, as well as recently remitted, formerly ill, patients will be included in this report.

NR25 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

EFFECT OF WEIGHT LOSS ON BRAIN NEUROPEPTIDE RNA

Mark A. Smith, M.D., Clin. Neuroendocrinology, NIMH/NIH, Bldg 36 Room 2D-15, Bethesda, MD 20892; Linda S. Brady, Ph.D., Philip W. Gold, M.D.

Summary:

Clinical studies have implicated neuropeptides in eating disorders as evidenced by decreased concentrations of proopiomelanocortin (POMC) products such as B-endorphin and increased levels of corticotropin-releasing hormone (CRH), arginine vasopressin (AVP) and neuropeptide Y (NPY) in the CSF of patients with anorexia nervosa. The question remains, however, whether this endocrine profile is specific to eating disorders or simply represents the normal compensatory response to weight loss. We addressed this question by using in situ hybridization to quantify brain neuropeptide mRNA levels (reflecting neuropeptide secretion) in male and female rats placed on a 10 gram/day diet for 14 days during which time they lost 35% of their body weight relative to the control groups which fed ad libitum. Frozen brain sections were thaw-mounted onto slides and ^{35}S-oligonucleotide probes used for hybridization to the neuropeptide mRNAs. Results indicated that POMC mRNA decreased by 50%, whereas NPY mRNA levels increased by over 100% in the arcuate nucleus of both male and female rats placed on the diet. These changes were specific to the arcuate nucleus as POMC mRNA in the pituitary and NPY mRNA in the locus ceruleus were unchanged. No changes in hypothalamic CRH, dynorphin or vasopressin mRNA levels occurred in the underweight rats of either sex. These results indicate that increased NPY and decreased B-endorphin CSF concentrations in anorexia nervosa may represent normal physiological consequences of weight loss. However, increased secretion of CRH and vasopressin in anorexia nervosa may represent a pathological response to weight loss. In particular, CRH, which is an appetite suppressant, may be important in the pathophysiology of anorexia nervosa.

NR26 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

PSYCHIATRY RESIDENT IDENTIFICATION IN A STRIKE

Robert Kohn, M.D., Psychiatry, Brown University, 152 Irving Avenue, Providence, RI 02906; Ronald M. Wintrob, M.D.

Summary:

A study of the attitudes of psychiatry residents and staff psychiatrists toward a strike by nursing and mental health workers in a psychiatric teaching hospital was undertaken. All residents (20) and 47 staff was significantly different from that of attendings; 21% of the residents volunteered service during the strike compared to 66% of the attendings ($p<0.004$). Staff psychiatrists were asked what action they would have taken if they were residents; there was a somewhat less inclination to volunteer. Asked what they would have done if they were attendings, 58% ($p = 0.000$) of the residents indicated they would have volunteered service. The significance of the findings demonstrates that residents are still in the process of developing their identification as psychiatrists. The significance of these and other findings from this study will be discussed.

NR27 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

ANTI-HLA ANTIBODIES AND CHLORPROMAZINE

Robert C. Alexander, M.D., NIMH ST. Elizabeths, Neurosciences Research Inst., Washington, DC 20032; Mark A. Coggiano, M.S., Richard Jed Wyatt, M.D.

Summary:

Chlorpromazine (CPZ) and several other ligands related to the dopaminergic system have been reported to interfere with the action of alloantibodies directed against HLA-A1. This finding is the basis of the hypothesis that the HLA-A1 antigen has structural similarities to dopamine receptors and may play an important role in the course and outcome of schizophrenia. Other investigators have measured the difference in cytotoxic titres of antisera absorbed by untreated peripheral blood leukocytes preincubated in solutions containing 5×10^{-7} to 0.6×10^{-3}M CPZ and found that CPZ inhibited the absorption of antisera directed against HLA-A1. We attempted to replicate this finding using peripheral blood lymphocytes from three healthy HLA-A1/B8 donors in a complement-mediated lymphocytotoxicity assay. We found that CPZ was cytotoxic to peripheral blood lymphocytes at concentrations greater than 1.5×10^{-5}M, and that CPZ did not inhibit the action of antisera directed against HLA-A1 and -B8. A number of association studies have shown inconstant association between various HLA antigens and schizophrenia, although recent genetic linkage studies have failed to show that HLA plays a role in susceptibility to schizophrenia. Our failure to replicate interference between anti-HLA antibodies and chlorpromazine is further evidence against a role for the HLA system in schizophrenia or its treatment.

NR28 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

BRAIN STRUCTURE AND FUNCTION IN SCHIZOPHRENIA

Ana Maria Andia, M.D., Psychiatry, Univ of Cal San Diego, 3427 4th Avenue, San Diego, CA 92103; Julie Kuck, M.A.

Summary:

Computed tomographic abnormalities in schizophrenics, corroborated by magnetic resonance imaging, have been related to cognitive impairment, poor outcome and a preponderance of negative symptoms. We present the results of a study of 38 chronic schizophrenics diagnosed by DSM-III-R criteria and followed at the UCSD Outpatient Research Center.The patients underwent MRI scans, extensive neuropsychological testing, and assessment of negative and positive symptoms by the Andreasen scales (SANS and SAPS, respectively). Nine patients (24%) had cortical and central volume loss, seven patients (18%) had single or multiple punctate high intensity white matter foci, and 22 patients (58%) had completely normal MRI scans. Patients with volume loss exhibited more severe cognitive impairment than schizophrenics with normal MRI's with statistically significant differences in verbal IQ, full scale IQ, two impairment index ratings, and category trails testing. The patients with high intensity foci performed better in all aspects of the neuropsychological tests than did the patients with volume loss. In fact, although their scores were lower than those of patients with normal scans, these differences, except for the full scale IQ results, were not statistically significant. All three groups of patients performed similarly on the Wisconsin Card Sorting Test, an index of frontal lobe function. Positive and negative symptom severity were not significantly different among the three groups of schizophrenics.

NR29 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

VENTRICULAR BRAIN RATIOS IN DEMENTIA: DEPRESSION AND CONTROLS

Rick A. Martinez, M.D., SCN LCS, NIMH Bldg 10/3D41, 9000 Rockville Pike, Bethesda, MD 20892; Susan E. Molchan, M.D., James L. Hill, Ph.D., Brian A. Lawlor, M.D., David Rubinow, M.D., Trey Sunderland, M.D.

Summary:

Cortical atrophy and ventriculomegaly are often routine radiographic findings in dementia patients. To explore the relationship between structural changes demonstrated by CT scan, diagnosis, clinical and biological measures of disease severity in AD, we studied 32 dementia subjects (mean age 63.0 years $\pm$ 1.60 SE), 13 elderly depressives (66.9 $\pm$ 2.0 years), and 12 healthy controls (60.2 $\pm$ 3.0 years). All subjects had cranial CT scans without contrast. Ventricular brain ratios (VBR's) were determined by measuring user-defined regions of interest of the lateral ventricles and the intracranial areas. The VBR differed significantly between the diagnostic groups [$F(2,54) = 5.87$, $p < 0.01$) with the demented subjects (0.15 ± 0.01) having a significantly larger ratio than the normals (0.10 ± 0.01); the ratio of the depressed subjects was intermediate (0.12 ± 0.01) and did not differ significantly. Within the AD group, there were no correlations between clinical measures of dementia severity or duration and the VBR. Interestingly, there was a significant correlation between CSF somatostatin and the VBR ($n = 24$, $r = -0.45$, $p < 0.03$); however, there was no significant correlation with the CSF monoamine metabolites. Furthermore, there was no correlation between VBR and the post-DST cortisol levels ($n = 24$). We conclude that the VBR may be used to differentiate groups of demented patients from healthy controls. While it does not correlate with clinical measures of dementia severity or with adrenocorticoid function, further longitudinal studies will be required to test whether VBR scores are meaningful biological measures to follow over time in individual patients.

NR30 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

STIMULANT/HALDOL STUDY OF SPEM CPT AND P50 IN NORMALS

Dolores Malaspina, M.D., Psychiatry, Columbia University, 722 W 168th Street Box 58, New York, NY 10032; Edward Maclin, Ph.D., Barbara Cornblatt, Ph.D., Eliza A. Coleman, B.A., Harold Sackeim, Ph.D., Charles A. Kaufmann, M.D.

Summary:

Given the robust, but indirect, evidence for hyperdopaminergic function in schizophrenia, this study was undertaken to examine directly the effect of catecholamine manipulation in normal subjects on several well-described neurophysiological and attentional measures that have been associated with vulnerability to schizophrenia. The aim of the study was to examine the degree, direction and correlation among changes in these measures that could be induced by challenge doses of dextroamphetamine and haloperidol.

Eight normal male subjects, aged 21–36 years, were interviewed with the SCID by a psychiatrist and found to be without personal or first-degree relative family history of major affective or schizophrenic disorders. All subjects had normal physical examinations and EKGs, and they were not using medications or other substances. Each subject reported for two test days, receiving 0.3 mg/kg PO dextroamphetamine on each test day and a later dose of either 2 mg haloperidol or placebo im on alternate test days in a randomized counterbalanced order. On each test day subjects received the test battery at baseline, 1 1/2 hours after the amphetamine dose, and then again one hour after the placebo or haloperidol.

The test battery included: 1) Profile of Mood Scale; 2) a blood sample for HVA, amphetamine, and haloperidol; 3) EOG recorded smooth pursuit eye movements; 4) blink rate; 5) measure of suppression of the p50 wave of the auditory evoked potential in a conditioning-test paradigm; and 6) the continuous performance test, a multidimensional version tapping effortful processing and shown not to ceiling in normal adults.

The effects on these measures and correlations among them will be presented.

NR31 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

SUBSTANCE ABUSE IN BORDERLINE PERSONALITY DISORDER

Rebecca A. Dulit, M.D., Psychiatry, Payne Whitney Clinic, 525 East 68th Street, New York, NY 10021; Minna Fyer, M.D., Timothy Sullivan, M.D., Allen J. Frances, M.D.

Summary:

Purpose: Substance abuse is clinically recognized as common in borderline personality disorder (BPD) and is often a major obstacle to effective psychotherapy. Little is known, however, about the nature and frequency of substance abuse in BPD or the effect of substance abuse on BPD psychopathology. This study reports data on subsance abuse in a large sample of inpatient DSM-III BPDs.

Methods: Diagnostic, demographic and hospital course data were gathered retrospectively on 137 DSM-III BPD inpatients. Interrater reliability was good.

Results: Of 137 BPDs, 92 (67%) received current DSM-III substance abuse or dependence diagnoses. Of these 92, 73% used alcohol and 70% used sedative-hypnotics; only 6% did not use either. 35% of drug user BPDs no longer met BPD criteria when their drug use was not counted towards meeting criteria (an impulsive behavior). These 35% were older at index admission ($p<.05$) and at ages of first OPD treatment ($p<.05$) and first hospitilization ($<.05$), and had fewer hospitalizations ($p<.05$) than nonuser BPDs or users who still met BPD criteria when their drug use was discounted. These 35% were also less impulsive ($p<.001$) and less likely than other BPDs to have an identity disturbance ($p<.001$) or a history of minipsychotic episodes ($p<.001$).

Significance: This study confirms clinical impressions that substance use is extremely common in BPD. Alcohol and sedative-hypnotics appear to be the drugs of choice in this BPD sample. Most significantly, we have identified a possible subgroup of BPDs in whom substance abuse is necessary to meet BPD criteria and who differ substantially from other BPDs. This subgroup may represent a distinct population with a different natural course and specific treatment needs. These results also raise important questions about the role of substance abuse in the diagnosis of BPD.

NR32 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

AIDS KNOWLEDGE AND ATTITUDES IN PSYCHIATRIC STAFF

Carol L. Alter, M.D., Psychiatry, New York Hospital W. Chest, 21 Bloomingdale Road, White Plains, NY 10605; Gregory Miller, M.D., Ellen Dickinson, M.D.

Summary:

Psychiatrists have a central role in treating patients with AIDS. While some studies have explored physician and lay knowledge and attitudes about AIDS none has addressed these issues for psychiatrists. To document what psychiatrists know about AIDS and what relationships may exist between knowledge and attitudes about treating patients with AIDS, we developed a 30-item, self-administered questionnaire. The attitudes section was composed of a series of questions assessing willingness to treat (WTT) AIDS patients, and several ethical questions dealing primarily with issues of confidentiality. Knowledge and attitudes were assessed independently. We sampled all attendings and residents ($n = 27$) in the acute inpatient service of a university-affiliated, psychiatric hospital. Respondents answered $78.1 \pm 0.8\%$ of the knowledge questions correctly. There was no relationship between knowledge and WTT ($R = 0.13$, $p < 0.9$), knowledge and ethics ($R = 0.13$, $p < 0.5$) or WTT and ethics ($R = 0.14$, $p < 0.5$). Fifty-two percent noted that they were significantly more uncomfortable treating AIDS patients compared with treating other patient groups (chi square 12.54, d.f. = 1, $p < 0.001$). When educating clinicians about AIDS, consideration should be given to combining cognitive approaches as well as the examination of emotional and attitudinal reactions toward patients with AIDS.

NR33 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

EFFECTS OF DIFFERENT LIGHT WAVELENGTHS IN SAD

Dan A. Oren, M.D., Clinical Psychobiology, NIMH Bldg 10 RM 4S239, 9000 Rockville Pike, Bethesda, MD 20892; George C. Brainard, Ph.D., Jean R. Joseph-Vanderpool, M.D., Elizabeth Sorek, R.N., Scott Johnston, B.A., Norman E. Rosenthal, M.D.

Summary:

Although the eye has been implicated in the antidepressant effects of phototherapy in seasonal affective disorder (SAD), the form of light needed and its mechanism of action is unclear. We randomly assign SAD patients to red or green light treatments for one week in a crossover design. During treatment, patients are exposed to light for two hours each morning. Patients are off light for one week between treatments. Therapies consist of equal quanta exposures (2.3×10^{15} photons/sec/cm^2) of colored light comparable to that achieved by standard, bright, full-spectrum phototherapy. Light sources are Philips F40R (half-peak bandwidth, 615-685 nm) and F40G (half-peak bandwidth, 505-55 nm) lamps, filtered through a clear pyramidal diffuser, an ultraviolet filter, and a yellow gelatin filter to remove light emitted below 450 nm. Eleven patients have been treated to date with a total of 17 conditions. Mean decreases ($\pm$S.D.) in Hamilton Depression Rating scores for red and green lights are 5 ± 7 and 10 ± 5 respectively, despite patients' similar expectations. It appears that green light has efficacy similar to full-spectrum lights, whereas red resembles placebo. The study is ongoing and the final results and their implications will be discussed.

NR34 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

DEEP WHITE MATTER HYPERINTENSITY ON MRI

Raymond F. Deicken, M.D., Psychiatry, Univ of Calif. SF, 786 43rd Avenue, San Francisco, CA 94121; Victor I. Reus, M.D., Luisa Manfredi, B.A., Owen M. Wolkowitz, M.D.

Summary:

Magnetic resonance imaging (MRI) studies have documented deep white matter hyperintensity (DWMH) in many different clinical populations including those with psychiatric disorders. The authors evaluated MRI of DWMH in 90 adult psychiatric inpatients (mean $\pm$SD age = 45 ± 21.7 years). MRI scans were performed on a 0.5 Tesla Diasonics MT/S system using spin-echo technique. Patients were divided into two groups according to the presence or absence of DWMH. Selected clinical characteristics such as age, psychiatric diagnosis, BPRS and GAS scores, cerebrovascular risk factors, neurological exam, EKG, EEG, and family history were compared between the two groups. DWMH on MRI was present in 42% of patients, with a higher incidence of DWMH in patients older than 50 years (87.9%) compared to patients younger than 50 years (15.8%). Patients with DWMH demonstrated significantly more hypertension, abnormal neurological exams, and abnormal EKG's by chi-square analysis ($p < .005$) than patients without DWMH. DWMH occurred in 89% of patients with dementia, 51.6% of patients with major depression, and 30.7% of patients with bipolar disorder. These results suggest that DWMH may have pathophysiological significance for psychiatric disorders.

NR35 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

CHANGES IN CEREBRAL LATERALITY WITH THE MENSTRAL CYCLE

Margaret Altemus, M.D., Clin. Neuroendocrinology, NIMH BPB Bldg 10 RM 3S231, 9000 Rockville Pike, Bethesda, MD 20892; Bruce Wexler, M.D., Glenna King, B.A.

Summary:

Accumulating evidence shows that information processed initially by the right cerebral hemisphere carries a more negative affective charge than information processed initially by the left hemisphere. To explore this as a possible mechanism in premenstrual dysphoria, we report here a study of 29 healthy cycling women who completed three months of daily mood ratings and who are also tested weekly for one menstrual cycle to detect possible increases in right hemisphere activation premenstrually. We used fused auditory dichotic tests, in which two similar words are presented simultaneously through left and right earphones. Each word crosses to the opposite hemisphere, but only one of the words is perceived. There is a right ear (left hemisphere) advantage for language stimuli since language centers are in the left hemisphere. The degree of this advantage can be modulated by changes in activation of other hemispheric processes. We found a significant decrease in right ear advantages for language stimuli during the premenstrual week compared with each of the other three weeks of the cycle. We also found that women who experienced more premenstrual dysphoria had significantly lower right ear advantages throughout the cycle. We speculate that such shifts in laterality, possibly mediated by changes in hypothalamic-pituitary-gonadal function, could contribute to the experience of mood changes with the cycle.

NR36 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

COMPARISON OF SYMPTOMS IN OCD AND TOURETTE'S

Kathy J. Tobias-Smith, M.D., Child Study Center, Yale University, 230 S. Frontage Road, New Haven, CT 06510; David L. Pauls, Ph.D.

Summary:

Previous studies have demonstrated that obsessive-compulsive disorder (OCD) occurs in patients who carry a diagnosis of Tourette's syndrome (TS). We hypothesized that O-C symptoms would present differently in Tourett's syndrome when compared to OCD. We studied 33 adults with TS and 33 adults with OCD. The patients were randomly selected from two outpatient clinics and from the Connecticut Tourette's Syndrome Association. A semistructured interview was used to confirm the diagnosis of TS and OCD. This interview elicited information about obsessions, compulsions, and features of an obsessive-compulsive personality. The analyses focus on the symptom variability in the content of the rituals and obsessions in OCD and TS, i.e., contamination rituals versus touching and arranging rituals. The perliminary data suggest that there is a difference in the symptom presentation of obsessions and compulsions in OCD when compared with TS patients with O-C symptoms. This study will help further elucidate the heterogeneous symptomatology and phenomenology of OCD.

NR37 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

STRUCTURAL CHANGES IN ASTROCYTES IN AN EXPERIMENTAL MODEL OF TEMPORAL LOBE EPILEPSY

Aldo Joseph Castiglioni Jr., M.D., Antomy, Texas A&M University, College Station, TX 77843; Steve Peterson, Ph.D., Evelyn Tiffany-Castiglioni, Ph.D.

Summary:

Ferrous or ferric chloride injected into mammalian cortex induces paroxysmal spiking or bursting neuronal electrical activity. In the present studies we injected either $FeCl_2$, $FeCl_3$ or NaCl (5 ul volume,100 mM, sterile) unilaterally into the hippocampi of Sprague-Dawley rats as a model of temporal lobe epilepsy. Electroencephalograms were recorded serially from skull-mounted electrodes in the awake, freely behaving rats for three weeks postsurgery. Rats receiving injections of iron compounds developed epileptiform discharges characterized by afterdischarge and burst of spikes. A control group given NaCl injections showed only transient EEG abnormalities that disappeared within a few days. Three weeks after injection, rats were perfused intracardially with saline and formalin and brains removed. The brains were stained by a modification of the Golgi method which stains glia and neurons. Sizes of astrocytes in the dentate gyrus and neocortex contralateral to injections were measured with a Zeiss Videoplan. Astrocytes were larger in the cortex of Fe-injected rats ($m = 71.1u$ for $FeCl_3$ and $m = 66.7u$ for $FeCl_2$) compared to NaCl-injected rats ($m = 8.0u$) with $p < 0.001$. However, there was no difference either in size or shape of astrocytes in the dentate gyrus between experimental and control rats, indicating that the changes seen in cortex did not result from mechanical damage by the injection procedure. We previously showed that activity of the astroglial enzyme glutamine synthetase increases in neocortex contralateral to cortical Fe injections. The present findings show that epileptiform discharges may rapidly induce structural changes as well as metabolic changes in astrocytes far removed from the discharge focus. These changes in astrocytes may initially serve a protective function to minimize neuronal damage.

NR38 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

ALCOHOLISM AND CSF IgG SYNTHESIS IN HIV SEROPOSITIVE MEN

Karen P.G. Drexler, M.D., Psychiatry, Wiford Hall USAF Med Ctr, 8815 Shady Leaf, San Antonio, TX 78250; James Rundell, M.D., George Brown, M.D., Susan Paolucci, M.D., Joseph Pace, M.D., Susan McManis, M.D.

Summary:

Alcholism's detrimental effects on immune defense are well documented in the medical literature. In this study, we examine the effects of alcoholism on central nervous system (CNS) involvement in HIV seropositive individuals. We divided individuals into alcoholic and nonalcoholic groups based on their Michigan Alcoholism Screening Test (MAST) scorer. Individuals with a MAST score greater than four are considered alcoholic. We used cerebrospinal fluid (CSF) IgG synthesis rates as a possible marker for CNS involvement by HIV. Twenty-eight individuals had two CSF IgG synthesis evaluations. Four were alcoholic. We found no significant difference in CSF IgG synthesis at first evaluation. At second evaluation, the mean CSF IgG synthesis was significantly higher in the alcoholic group (23.93 mg/day) versus the nonalcoholic group (4.15 mg/day, $p<0.05$). Thus, alcoholism may contribute to earlier CNS involvement in HIV seropositive individuals.

NR39 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

IRRITABILITY AND APATHY IN HUNTINGTON'S DISEASE

Carol E. Peyser, M.D., Psychiatry, Johns Hopkins Hospital, Osler 320 Johns Hopkins Hosp., Baltimore, MD 21205;

Summary:

Irritability and apathy are psychopathological features of many disorders including schizophrenia, depression, Huntington's disease (HD) and other neurological diseases, but few standardized measures are available. We developed two new scales measuring irritability and apathy and demonstrated their reliability and concurrent validity in HD patients.

Fifty-two HD patients were examined with these new scales (each involving caregivers rating patients on 14 items), the Mini-mental state exam, a Quantitative Neurological Exam and HD activities of daily living scale (ADL).

To assess reliability, irritability and apathy scales were administered to a subsample of 24 patients both at home and in clinic. Correlation by a Pearson Coefficient (PCC) was .89 P = .000 for apathy scale and .9 P = .000 for irritability scale.

Apathy correlated with disease severity measured by ADL impairment (P.C.C. = .6577 P = .000) and with severity of cognitive decline (P.C.C. = .3903 P = .003) but not directly with deficits on motor exam. Irritability related inversely to neurological exam deficits indicating the irritability can occur early in HD.

These data demonstrate the reliability and validity of the new scales and suggest that apathy in HD relates to frontal-striatal functions that modulate cognition rather than motor function. These reliable scales can now be applied to other psychiatric and neuropsychiatric disorders.

NR40 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

FLUOXETINE INDUCED MANIA

David E. Hon, M.D., Psychiatry, UKSM-Wichita, 1010 North Kansas, Witchita, KS 67214; Sheldon H. Preskorn, M.D.

Summary:

Fluoxetine is a selective serotonin reuptake blocker recently released for the treatment of depression. In previous case reports, it has been associated with manic induction in five young patients exceeding the manufacturer's starting dose of 20 mg per day (Table 1). Given the age of these patients, it is conceivable they may actually have been bipolar patients experiencing their first manic episodes. In contrast, the cases presented here (cases A, B, and C in the Table) describe three elderly men with recurrent depression who experienced their first manic episodes on the recommended starting dose of fluoxetine. Interestingly , these three men had undergone decades of conventional treatment, yet did not experience manic induction until exposed to fluoxetine. These patients required traditional antimanic pharmacotherapy in addition to drug discontinuation. The duration of their manic episode following fluoxetine discontinuation was compatible with its pharmacokinetics. These observations suggest that fluoxetine is inducing mania in these unipolar patients rather than simply uncovering an underlying bipolar disorder.

NR41–Monday, May 8, 9:00 a.m. **10:30 a.m.**
ABUSE, DISSOCIATION AND PTSD IN LLPDD PATIENTS

Margaret F. Jensvold, M.D., BPB, NIMH Bldg 10 3N238, 9000 Rockville Pike, Bethesda, MD 20891; Frank Putnam, M.D., Kari Muller, B.A., Peter J. Schmidt, M.D., David R. Rubinow, M.D.

Summary:

An increased prevalence of history of severe abuse has been described in patients with dissociative disorders as well as patients with premenstrual syndrome (LLPDD) in one study. We examined the relationship between LLPDD, lifetime history of severe abuse, history of PTSD, and tendency to dissociate. Relative to controls (n = 8), carefully diagnosed patients with LLPDD (n = 20) reported a greater lifetime history of severe abuse (40% vs. 0%; Fisher's Exact, p = 0.06). PMS patients also showed significantly greater dissociative index (DES) scores than controls, with a greater tendency to dissociate in the luteal phase in patients but not controls (36 patients, 34 controls; DES scores: LLPDD, luteal, 14.04 and follicular, 10.45; controls, luteal, 4.24 and follicular, 4.19; ANOVA, diagnosis effect, $p < .001$; time effect, $p < .01$; time by diagnosis effect, $p < .01$). Patients who had been severely abused tended to have higher DES scores compared to patients not severely abused (mean luteal DES score = 14.68 and 9.83, respectively). Finally, current PTSD was diagnosed in 30% of patients (6/20) and no controls (0/8), with PTSD symptoms confined to (n = 2) or exacerbated during (n = 4) the premenstruum. Possible ways in which abuse may be a relevant factor in the development or expression of LLPDD will be discussed.

NR42 **Monday, May 8, 9:00 a.m.–10:30 a.m.**
EFFECTS OF TYPICAL AND ATYPICAL NEUROLEPTICS ON PLASMA AND URINARY MONOAMINE METABOLITES

Husseini K. Manji, M.D., Clinical Pharm., Natl. Inst. Mental Hlth., 9000 Rockville Pike, Bethesda, MD 20892; John Hsiao, M.D., Jerry Oliver, B.S., David Pickar, M.D., William Z. Potter, M.D.

Summary:

Recent studies have demonstrated alterations in plasma homovanillic acid (HVA) levels following chronic neuroleptic treatment, leading to the speculation that these changes reflect changes in central dopaminergic output. We have recently shown that under certain conditions, changes in renal clearance can affect plasma HVA. Eight schizophrenic patients were administered fluphenazine, placebo, and clozapine in a double-blind, crossover protocol. Chronic fluphenazine and clozapine treatment resulted in significant variations of plasma HVA levels and renal HVA clearance, in the absence of consistent changes in urinary HVA. Thus, neuroleptic-induced changes may not represent changes solely in dopaminergic tone and HVA production; renal clearances also need to be considered. Interestingly, unlike fluphenazine, clozapine caused a marked elevation of urinary normetanephrine (NMN) (from 2.1 + 0.9 to 4.9 + 1.6 micromoles/24 hrs); no changes were seen in urinary MHPG or HVA levels. These findings are consistent with clozapine's relatively potent alpha$_2$ antagonistic properties, and may reflect increases in norepinephrine release.

NR43 **Monday, May 8, 9:00 a.m.–10:30 a.m.**
EFFECTS ON CHRONIC LITHIUM TREATMENT ON SIGNAL TRANSDUCTION MECHANISMS IN HL60 CELLS

Jose A. Bitran, M.D., Clinical Pharm., Natl. Inst. Mental Hlth., 9000 Rockville Pike, Bethesda, MD 20892; Fabian Gusovsky, Ph.D., Husseini Manji, M.D., William Z. Potter, M.D.

Summary:

Lithium's effects on signal transduction are currently the focus of extensive research. We studied the effects of LiCl on dibutyryl cAMP-differentiated HL60 cells. These neutrophil-like HL60 cells express a chemotactic peptide (fMLP) receptor, which is coupled via a guanine nucleotide binding protein to phospholipase C (PLC). Activation of PLC generates two distinct second messengers, IP3 and diacylglycerol (DAG). IP3 releases CA^{+2} which activates Ca^{+}-dependent processes. DAG activates protein kinase C (PKC), which in HL60 cells is postulated to be coupled to the Na^{+}/H^{+} antiporter, and thereby regulates intracellular pH. fMLP thus induces a dose-dependent biphasic change in the intracellular pH of HL60 cells. Pretreatment of HL60 cells with 1 or 10 mM LiCl for five days resulted in a marked attenuation of fMLP's effects on pH. In contrast, fMLP-induced increases in intracellular CA^{+2} or phosphiositide breakdown were unchanged. These results indicate that chronic lithium treatment alters intracellular signaling at a site distal to the fMLP receptor. This may represent a novel pharmacological effect of LiCl, namely, an impairment of the PKC-activated Na^{+}/H^{+} antiporter.

NR44 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

EFFECT OF AGE ON PLASMA LEVELS OF NORTRIPTYLINE

Steven J. Bupp, M.D., Research, Psychiatric Inst., 929 North St. Francis, Wichita, KS 67214; Sheldon H. Preskorn, M.D.

Summary:

In 109 hospitalized patients taking nortriptyline (NOR), we examined the effects of age and sex upon interindividual variability in plasma NOR levels.

Patients were 69 females and 40 males with ages ranging from 11–85. Standardizing plasma levels for dosage revealed an average of 1.44 (+/−.77)ng/ml/mg, with a range from .43 to 4.4 (10-fold variation). Linear regression of plasma levels per milligram and age revealed a positive correlation ($r = .20$, $F = 4.7$; $df = 1, 107$; $p = .03$). This relationship was almost exclusively determined by patients over 40 years of age ($y = .02x + .27$; $r = .30$; $F = 6.4$; $df = 1, 62$; $p < .005$).

In summary, age but not sex was found to correlate with higher plasma NOR levels per milligram dose, supporting lower dosing strategies in the elderly. Linearity offers a rational method for dosage adjustment within individuals.

NR45 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

WEIGHT CHANGE AND EEG SLEEP IN MDD

Timothy Hsu, M.D., Psychiatry, Univ Michigan, 1500 E. Medical Center Drive, Ann Arbor, MI 48109; James E. Shipley, M.D., John F. Greden, M.D., Roger F. Haskett, M.D., Leon Grunhaus, M.D., Alan Eiser, Ph.D.

Summary:

A retrospective analysis was done to assess the effect of weight change during a depressive episode on EEG sleep measures. All patients had an RDC diagnosis of Major Depressing Disorder (MDD) and were divided into two groups according to whether they reported a loss ($n = 43$) or gain ($n = 17$) of 4–20 kg weight. Thus, subjects who reported less than ± 4 kg or more than ± 20 kg were excluded. The two groups did not differ with respect to age, sex, inpatient vs outpatient status or Hamilton ratings. Differences in RDC subtypes were not significant. After two weeks drug-free, all patients had two nights of EEG sleep recorded. No significant differences (p .05) were noted in sleep latency, time awake, time asleep, sleep efficiency, total REM or REM latency minus awake, although REM latency values for both gainers and losers were below normal (49.3 ± 30.1 min and 38.7 ± 25.8 min, respectively).

Weight gainers did have more delta sleep (28.0 ± 27.8 min vs 11.1 ± 16.4 min, $p < .05$), and less time awake during the last two hours of sleep (14.1 ± 24.7 min vs 2.2 ± 0.8, $p < .01$), and lower REM density (1.6 ± 0.4 vs 2.2 ± 0.8, $p < .05$).

These results suggest that several sleep measures may be associated with relative change in weight during the course of a depressive episode. The extent to which the weight gainers in our sample would meet the Quitkin criteria for atypical depression is of interest, as such patients have been reported to have similar sleep patterns.

NR46 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

AGE-RELATED CHANGES IN MAJOR DEPRESSIVE DISORDER

Timothy Hsu, M.D., Psychiatry, Univ Michigan, 1500 E. Medical Center Drive, Ann Arbor, MI 48109; James E. Shipley, M.D., John F. Greden, M.D., Roger F. Haskett, M.D., Leon Grunhaus, M.D., Atul Pande, M.D.

Summary:

A retrospective analysis was performed to compare changes in clincial and physiological markers of depressive illness in relation to increasing age. All 116 patients met Research Diagnostic Criteria for Major Depressive Disorder (MDD) and were divided into three groups by age: 16–35 (n = 48), 36–55 (n = 46), and 56–75 (n = 22). Patients with major medical or neurological illnesses were excluded. Clinical evaluation included structured interviews using the SADS. After at least two weeks drug free, all patients underwent two consecutive nights of polysomnographic recording. Data were analyzed using one-way analysis of variance (ANOVA) across all three groups with follow-up comparisons.

On clinical interviews, patients aged 16–35 reported more sleep (2.4 ± 1.9 vs 1.1 ± 0.3 by SADS, $p < .004$), more suicidality (4.0 ± 0.9 vs 3.3 ± 1.2 by SADS, $p < .026$), more panic (1.83 ± 0.8 vs 1.25 ± 0.4 by SADS, $p < .011$) and more depersonalization (2.0 ± 1.3 vs 1.2 ± 0.5 by SADS, $p < .009$). By contrast, the patients aged 56–75 had higher Hamilton scores (22.7 ± 4.6 vs 19.9 ± 4.0, $p < .013$), higher 4 PM serum cortisol values on the dexamethasone suppression test (DST; 8.2 ± 6.9 vs 3.0 ± 2.6, $p < .0004$), less slow-wave sleep on overnight EEG sleep recording, (4.7 ± 7.2 min vs 30.1 ± 26.8 min, $p < .0001$), and a shorter REM latency (28.3 ± 26.7 min vs 54.7 ± 25.1 min, $p < .0001$).

Together, these findings suggest that depressive symptoms experienced by young adults are not only qualitatively different from that of the elderly, but that fundamental differences in pathophysiology may be involved. However, further normative studies are needed with regard to putative biological markers of depressive illness, especially in elderly populations.

NR47 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

TRANSIENT HYPERTHYROXINEMIA IN AFFECTIVE DISORDERS

Rima Styra, M.D., Psychiatry, St. Michaels Hospital, 30 Bond Street, Toronto Ontario, Canada M5B 1W8; Russell Joffe, M.D.

Summary:

Several studies have shown that between 5% and 33% of patients newly admitted to general psychiatric wards show a transient elevation of serum thyroxine levels. Conclusions from this previous research are limited, in that the patient population studied included a heterogeneous group of patients with a variety of poorly defined psychiatric diagnoses and uncontrolled drug use.

To date we have examined thyroid function tests in a group of 56 patients, who were recently admitted to an inpatient unit at St. Michael's Hospital with a diagnosis of primary major effective disorder according to Research Diagnostic Criteria (bipolar n = 22, unipolar = 34). We anticipate a sample of 120 at the date of presentation. Preliminary analysis showed a 20% prevalence (11 patients) of transient hyperthyroxinemia (TH) in this homogeneous group of affectively ill patients. The occurrence of TH was found not to be associated with patient variables such as sex, age and subtype of affective disorder; however, there was a trend towards a greater proportion of females in the TH group (2M:9F). We also examined the relationship of baseline thyroid function tests and global clinical criteria of response to the first antidepressant drug used in depressed bipolar and unipolar major affective disorder. Our TH group had an 11% response rate and our normal serum thyroxine (T_4) group had a 62.5% response rate to antidepressants. Patients with transient hyperthyroxinemia were less likely to respond to the first antidepressant used than patients who had normal T_4 values ($X^2 = 5.5$, $df = 1$, $p = .0189$). Clinical and theoretical implications of these findings will be discussed.

NR48 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

DRUG ABUSE IN SCHIZOPHRENIA: CLINICAL CORRELATES

Lisa Dixon, M.D., Psychiatry, Payne Whitney Clinic, 525 East 68th Street, New York, NY 10021; Gretchen Haas, Ph.D., Peter Weiden, M.D., John Sweeney, Ph.D., Denise Hien, M.A.

Summary:

Introduction: The comorbidity of schizophrenia and substance abuse has become an important clinical and scientific problem. Substance abuse has been viewed as an attempt by schizophrenics to self-medicate and as a possible etiologic factor in schizophrenia. *Methods:* Eighty-three consecutively admitted SCID-diagnosed DSM-III-R schizophrenic (n = 68), schizoaffective (n = 12) and schizophreniform (n = 3) inpatients were assessed for substance abuse and given DSM-III-R diagnoses. An independent research team conducted clinical evaluations at admission and discharge (BPRS, SANS, GAS, Premorbid Adjustment Scale). *Results:* Forty patients (48%) received drug abuse or dependence diagnoses (cannabis = 26, alcohol = 21, cocaine = 14, hallucinogens = 5, stimulants = 5, sedatives = 5, other = 2). There were no significant differences between drug-using (DU) and non-drug-using (NDU) groups on the BPRS, SANS and GAS at admission. However, DU patients showed fewer symptoms at discharge on BPRS dimensions of paranoia and suspiciousness ($p<.001$), thought disorder ($p<.02$), and anergia ($p<.01$). During early adolescence, DU's did significantly better than NDU's on sexual adjustment ($p<.02$), and non-alcohol-drug-users (NADU) did significantly better than NDU's on social adjustment ($p<.05$). During late adolescence, NADU's did better than NDU's on sociability ($p<.05$), peer relations ($p<.05$), and sexual adjustment ($p<.05$). *Discussion:* This study confirms the high rate of substance abuse among schizophrenics and corroborates previous reports of schizophrenics' selective use of potentially psychotomimetic substances. Based on these findings, we hypothesize that schizophrenics who abuse drugs may represent a subgroup of schizophrenics with certain better clinical and prognostic characteristics, but whose substance abuse may adversely affect outcome.

NR49 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

CARBAMAZEPINE: EFFECTIVE FOR AGGRESSIVE YOUTHS.

Richard R. Pleak, M.D., Child Psychiatry, NYS Psychiatric Inst., 722 W. 168th St. Box 60, New York, NY 10032; Daniel T. Williams, M.D., Boris Birmaher, M.D.

Summary:

Carbamazepine's (CBZ's) use for impulse disorders in adults has lead to it being increasingly prescribed for children and adolescents with impulsive and aggressive behavior, despite the lack of controlled studies of CBZ in such youths. This report is on CBZ's effectiveness and side effects in 13 aggressive 7–15 year-old inpatients unresponsive to traditional treatments. CBZ was titrated until a blood level of 8–12 ug/ml or a maximum dose was reached, held at that level for 4 weeks, then tapered off. Restarting CBZ was optional. Ratings included the Overt Aggression Scale (OAS) and the Clinical Global Impressions scale (CGI). Of 13 youths given trials, 6 had mild to marked improvement, with significant decreases on CBZ in mean total OAS scores ($t = 2.94$, $p<.032$, two-tailed) and CGI severity indices ($t = 4.96$, $p<.004$). Two subjects showed no change, 3 had increased aggression and impulsivity, 1 became hypomanic, and 1 manic. Of the 13 who responded, 1 developed an abnormal EEG and 1 had the first recurrance in years of absence seizures; however, both were able to continue on CBZ. While CBZ may be of benefit in some aggressive youths, neuropsychiatric excitation may also occur. Double-blind studies of CBZ in aggressive youths are clearly warranted.

NR50 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

DEPRESSION IN PATIENTS WITH DIABETES MELLITUS

Liane J. Leedom, M.D., Psychiatry, Harbor UCLA, 1000 West Carson, Torrance, CA 90509; Woerner P. Meehan, Ph.D., Warren Procci, M.D., Adina Zeidler, M.D.

Summary:

The purpose of this study was to investigate the prevalence of symptoms of depression in patients with type II diabetes mellitus. Seventy-one consecutive outpatients with type II diabetes mellitus participated in this study; 46 nonmedically-ill visitors to the same clinic served as age-, sex-, race-, and economically-matched controls. Medical histories were obtained from patients and controls. Patients underwent complete physical and neurologic examinations. Patients and controls completed the Beck and Zung depression inventories, and questionnaires regarding subjective symptoms of neuropathy. Diabetic patients with complications scored significantly higher than either controls or patients without complications on the Beck (Mean = 19,6 and 7) and Zung (Mean = 48, 36 and 32). A significant proportion of the patients with diabetic complications scored in the range of clinical depression on the Beck (23/31) compared to controls (10/46) and patients without complications (12/40). For diabetic patients with complications, the cognitive subscale of the Beck was highly correlated with the total score ($r = 0.96$). Symptoms of depression were also associated with the use of antihypertensive medications in diabetic patients with complications. Furthermore, patients of both sexes with complications had significantly more symptoms of sexual dysfunction. In summary, patients with type II diabetes were more likely to suffer from symptoms of depression and sexual dysfunction if complications were also present. Depression inventory scores of patients with complications revealed a high level of cognitive depression. Somatic symptoms alone did not account for elevated Beck and Zung scores in diabetic patients.

NR51 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

PSYCHIATRIC COMORBIDITY IN A PRIVATE DRUG AND ALCOHOL TREATMENT CENTER

Mark A. Hurst, M.D., Psychiatry, Ohio State Univ, 473 West 12th Avenue, Columbus, OH 43210; Kathy E. Shy, M.D., Barry I. Liskow, M.D., Stephen L. Stern, M.D.

Summary:

A high rate of coexisting psychopathology has been reported in patients with substance use diagnoses. In this study, we administered the Structured Clinical Interview for DSM-III-R (SCID) to 51 consecutive admissions to a private chemical dependency treatment hospital, 37% of whom were health care professionals (physicians, dentists, nurses). The mean education (14.8 years) and percent of married subjects (55%) in the total population was higher than in previously studied populations. Overall, 51% of the patients had lifetime psychiatric diagnoses other than substance use disorders, with mood disorders (29%), anxiety disorders (16%) and substance-induced psychoses (18%) most common. Significantly less psychopathology was found in health care professionals (28%) compared with other patients (65%), in subjects with more than the mean years of education (30%) compared with less than the mean (69%), and in those who abused either alcohol (29%) or drugs (36%) alone compared with those who abused both alcohol and other drugs (71%) ($p < 0.05$ in all cases). This study found a high rate of psychiatric comorbidity at a private substance dependency treatment center, although less than previously found in VA and public hospitals. Such findings suggest that patients in private treatment programs may benefit from routine psychiatric evaluation.

NR52 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

IDAZOXAN: A NOVEL ALPHA-2 ANTAGONIST AND ANTIDEPRESSANT

Ossama T. Osman, M.D., Psychiatry, NIMH Bldg 10 RM 2D46, 9000 Rockville Pike, Bethesda, MD 20892; Matthew V. Rudorfer, M.D., Husseini Manji, M.D., William Z. Potter, M.D.

Summary:

Alterations of catecholamine receptor sensitivities have been reported in relationship to the etiology and treatment of depression. For instance, platelet alpha$_2$ adrenergic receptors may be subsensitive during depression. This raises the possibility that alpha$_2$ adrenoceptors involved in regulating norepinephrine (NE) release are subsensitive. Thus, yohimbine (an alpha$_2$ antagonist) has been tried as an antidepressant but with equivocal results, perhaps secondary to the wide range of side effects. We therefore studied idazoxan (IDX), a more potent and selective alpha$_2$ antagonist, without any significant adverse effects, in a double-blind placebo-controlled trial. Multiple biochemical and neuroendocrine parameters were obtained. Bipolar depressed patients resistant to conventional treatment, hospitalized on or research ward and drug free for at least three weeks were treated with IDX up to 120 mg daily for six weeks. Preliminary results indicate that IDX is an effective antidepressant with no significant side effects. This antidepressant effect was accompanied by sustained elevation of plasma NE in the absence of consistent effects on MHPG and HVA. There was no significant change in cardiovascular parameters. Neuroendocrine studies utilizing i.v. alprazolam as a challenge test showed that chronic, but not acute, IDX treatment antagonizes the robust growth hormone response to alprazolam. These results demonstrate that chronic alpha$_2$ receptor antagonism alters a variety of physiologic parameters, effects that may be related to its potential as a novel antidepressant.

NR53 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

ABNORMAL RESPIRATORY PHYSIOLOGY IN PANIC DISORDER

Cameron S. Carter, M.D., Psychiatry, UC Davis, 4430 V Street, Sacramento, CA 95817; Richard Maddock, M.D.

Summary:

The place occupied by hyperventilation in the phenomenology and physiology of anxiety disorders has been the subject of much debate. A number of investigators have presented evidence suggesting abnormal respiratory physiology in anxious patients. However, the role of hyperventilation or hypocapnea in producing the symptoms of panic disorder is not clear and it is generally accepted that hyperventilation is a less powerful stimulus of panic than other methods such as lactate, caffeine or isoproterenol infusions or CO_2 inhalation.

In this study 12 patients meeting DSM-III-R criteria for panic disorder with agoraphobia and 12 age-matched controls underwent a volunatary hyperventilation procedure producing a pco_2 of 20 mm of Hg for seven minutes. The patients demonstrated a significant delay in recovery of pco_2 post hyperventilation when compared with controls. This finding suggests a basic abnormality of respiratory physiology in panic disorder characterized by a disruption of the normal negative feedback of hypocapnea to respiratory drive. This finding may represent a biological marker for panic disorder.

Sixty-four percent of panic patients who hyperventilated experienced a panic attack during the procedure, compared with 9% of controls. This suggests that hyperventilation may be a more powerful stimulus of panic than has been previously reported. Methodological reasons why this effect may not have been demonstrated in previous studies are discussed.

NR54 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

BETA-BLOCKERS FOR PERFORMANCE ANXIETY IN MUSICIANS

Elissa M. Sanders, M.D., Psychiatry, Payne Whitney Clinic, 525 East 68th Street, New York, NY 10021, Minna R. Fyer, M.D.

Summary:

Since the first demonstration of the anxiolytic effects of propanolol by Granville-Grossman and Turner in 1966, interest has grown in applying beta-blocker medication to treatment of anxiety symptoms associated with acutely stressful situations. In several studies focused on musical performance, beta-blocker administration has been shown to significantly reduce anxiety symptoms and improve performance outcome. Although the popularity of beta-blockers as a stage-fright antidote for both student and professional muscians has been suggested by recent scientific and media publications, few data are available on the prevalence and actual usage patterns in this population. The purpose of this study is to quantitatively and qualitatively discribe beta-blocker use in a large sample of musical performers. We distributed a comprehensive, anonymous, selfreport questionnaire to a sample of approximately 300 instrumental musicians, recruited from members of (1) an established full-time orchestra, (2) a part-time touring orchestra comprised of professional free-lance musicians, and (3) a student training orchestra at an east coast conservatory. The collected data are being analyzed for the prevalence and predominant pattern of beta-blocker use, including differences in usage among subgroups and the perceived advantages and adverse reactions associated with use. As detailed naturalistic information regarding betablocker usage for performance anxiety has not been previously available, the results presented in this study may significantly improve physician knowledge of therapeutic indications, benefits, and risks of beta-blocker administration for musical performers, as well as for other patient groups with situational anxiety symptoms.

NR55 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

USE OF THE SCL-90-R WITH ADOLESCENTS

James J. McGough, M.D., Psychiatry, Duke University, Box 3812 DUMC, Durham, NC 27710; John F. Curry, Ph.D.

Summary:

The SCL-90-R, a self-report measure useful in study of adult psychopathology, has been infrequently used in adolescent populations. To assess validity the SCL-90-R was administered to 79 adolescent inpatients and correlated with several well-validated self-report scales, K-SADS scales for suicidality and DSM-III-R diagnoses.

All SCL-90-R scales significantly correlated with measures of depression (CDI), anxiety (RCMAS) and social maladjustment (JESNESS). All scales showed positive correlation with suicidal ideation, elevations in Depression being most predictive ($r = 0.46$, $p = 0.0001$). Suicidal tendency within 30 days related to elevations in Depression, Interpersonal Sensitivity, Anxiety, Hostility and Psychoticism. No scale predicted actual suicide attempt. Elevations on Depression and Interpersonal Sensitivity correlated with a diagnosis of mood disorder ($p = 0.0001$). Elevations on Hostility and Paranoia correlated with conduct disorder ($p = 0.05$). Modest elevations in all scales were associated with increased age. There were no associations with IQ or gender.

The SCL-90-R appears to have potential for use with adolescent populations and may help to delineate dimensions of functioning associated with the major disorders of that age group.

NR56 **Monday, May 8 9:00 a.m.–10:30 a.m.**

DEVELOPMENT OF AGORAPHOBIA IN PANIC DISORDER

Franklin R. Schneier, M.D., Psychiatry, NY State Psych Inst, 722 West 168th St. Box 13, New York, NY 10032; Lynn Martin, M.S., Salvatore Mannuzza, Ph.D., Donald Ross, Ph.D., Michael R. Liebowitz, M.D., Abby J. Fyer, M.D.

Summary:

How panic disorder patients who developed agoraphobia differ from panic disorder patients who develop lesser or no avoidance was examined in a study of 146 patients diagnosed by DSM-III-R workgroup criteria as having Panic Disorder with Agoraphobia (PDA), n = 81, Panic Disorder with Limited Phobic Avoidance (PDL), n = 43), or Panic Disorder, Uncomplicated (PDU), n = 22. The three subtypes were compared in regard to demographics, panic attack symptoms, near-panic attack symptoms, behavioral response to panic attacks, course of panic disorder, and comorbidity.

Discriminant function analysis of 91 variables correctly classified 54% of patients as PDA, PDL, or PDU ($p = .00002$). Agoraphobics reported significantly more dizziness/unsteadiness and fear of passing out than did patients with PDU. Agoraphobics also reported significantly longer duration of panic disorders, more help-seeking and interruption of function in response to panic attacks, and more anticipatory anxiety than patients with PDL or PDU. Responses of patients with limited avoidance generally fell between those of agoraphobics and those of patients without avoidance.

The results support the concept of a continuum of severity of avoidance among patients with panic disorder. They suggest a relationship between agoraphobia and severity of panic attacks that may be due to differences in physiology and/or cognitive set.

NR57 **Monday, May 8 9:00 a.m.–10:30 a.m.**

BRAIN DENSITY IN SCHIZOPHRENIA

David G. Daniel, M.D., NIMH Neurosciences, Center at St. Elizabeth, 2700 Martin Luther King Ave SE, Washington, DC 20032; Debra Kostianovsky, M.D., Emily Kim, M.D., Terry E. Goldberg, Ph.D., Manuel F. Casanova, M.D., Joel E. Kleinman, M.D., Daniel R. Weinberger, M.D.

Summary:

Previous studies have demonstrated differences in regional brain density as derived from CT scan attenuation values between patients with schizophrenia and controls. Interpretation of these findings has been hindered by methodological shortcomings such as the failure to control for head size, scanner calibration differences and other confounding variables. The present study offered methodological improvements over many of the earlier studies by controlling for head size and normalizing the attenuation values for each scan to an internal standard. CT attenuation values in multiple brain regions in 20 patients with chronic schizophrenia were compared with those of 20 age- and sex-matched controls. No significant differences emerged between the patients with schizophrenia and the normal controls. However, in the control subjects, but not in the schizophrenic patients, the mean density of white matter in the left frontal area was significantly higher ($t = -2.83$, $p = .01$) than that in the right. The results are consistent with multiple lines of evidence suggesting left hemisphere dysfunction in schizophrenia and raise questions about the sensitivity and validity of direct comparisons of regional CT attenuation values in detecting subtle anatomical abnormalities.

NR58 **Monday, May 8 9:00 a.m.–10:30 a.m.**

POCKET COMPUTER AIDS WEIGHT LOSS: DOES NOT!

Martha S. Losch, Psychiatry, Stanford University, Lab of Behavioral Med Psyc Bld, Stanford, CA 94305; W.S. Agras, M.D., C. Barr Taylor, M.D.

Summary:

A variety of low-cost programs are available to help overweight individuals lose weight, but these programs generally produce very small weight losses. To determine if monetary incentives could improve weight loss with a computerized behavior modification program, 58 women were randomized to (a) unconditional refund (b) refund contingent on weight loss or (c) refund contingent on adherence to the program. The small, portable computer provided a means for recording exercise, calorie intake, and body weight, and showed graphic displays of these data on request. After 12 weeks, the weight loss for the three groups was 4.1, 6.0, and 3.2 pounds, respectively, (a nonsignificant difference among the groups.) At six months follow-up the weight losses were 4.1, 3.9 and 2.5 pounds. Thus, the computer program was associated with small but significant weight loss which was maintained at six months. More powerful, inexpensive weight loss techniques need to be developed.

NR59 **Monday, May 8 9:00 a.m.–10:30 a.m.**

SECLUSION, RESTRAINT AND MEDICATION REFUSAL

Peter J.Davidson, M.D., Psychiatry, Univ of Washington, Community Division RP-10, Seattle, WA 98195; Dennis McBride, Ph.D.

Summary:

The recent Harper decision in Washington state mandated adversarial judicial hearings in order to overturn neuroleptic medication refusal by committed patients. Unlike the decisions cited as precedents by the Harper court, this new law did not allow for the emergent, forcible medication of dangerous or suicidal patients without a court hearing. This study examined the effect of the Harper decision on the use of seclusion and physical restraint at the Western State Hospital. Time in seclusion and restraint did not covary with populations of medication refusers during the five-month study. More than half of the 185 medication refusers studied were on admitting units. Patients who refused medication and required court hearings did not spend more time in seclusion and restraint than the reference population on the admitting units. Petitions for involuntary treatment were granted in 90% of the hearings. No increase in staff injuries or incidents of patient violence occurred after the Harper decision. The inability to medicate patients with neuroleptics prior to court hearings could not be shown to produce changes in the use of seclusion or physical restraint.

NR60 **Monday, May 8 9:00 a.m.–10:30 a.m.**

QUANTITATIVE SPECT: NORMAL AND PATHOLOGIC STATES

Renee M. Dupont, M.D., Psychiatry, Univ of Cal San Diego, 1752 Wilstone Avenue, Leucadia, CA 92024; Guy Lamoureux, M.D., J. Christian Gillin, M.D., William Ashburn, M.D., Samuel Halpern, M.D.

Summary:

Initial activity using single photon emission computed tomography (SPECT) following injection of I-123 iodoamphetamine (IMP) reflects cerebral perfusion. Activity measured at later times, however, has been hypothesized to result from local metabolic conditions within the brain. Twenty healthy normal controls (mean age = 41.1 years; SD = 10.3) were studied on up to two occasions using IMP SPECT. Each study consisted of three scans: 20 minutes, two hours and four hours post-injection. Images were evaluated using standardized cortical and subcortical uptake maps which allow for pixel by pixel comparison to a composite uptake map for statistical analysis. This method obviates the need for subjective region of interest determination. The cerebellum was highly variable in activity between normals, other areas (e.g., posterior frontal) demonstrated high correlation of activity between individuals and within individuals between scans. The use of the cerebellum as a "normalizing" structure is called into question. The results of initial and follow-up scans in these controls, 10 subjects with HIV infection, 10 subjects with amphetamine withdrawal depression, as well as primary unmedicated major affective disorder and unmedicated schizophrenics will be discussed. The diagnostic relevance of tracer redistrubution in later scans will be presented.

NR61 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

CROSS SITUATIONAL MANIFESTATIONS OF ADHD: NOW YOU SEE IT NOW YOU DON'T

Joseph A. Whitfield, M.D., Dept. of P&N (DPRT), DD Eisenhower Army Med Ct, Fort Gordon, GA 30905; Peter S. Jensen, M.D.

Summary:

The use of psychostimulants for hyperactive children has recently come under fire from parents, educators, advocacy groups, and the media. Part of the controversy stems from questions of whether the syndrome of hyperactivity really exists, or if some children are medicated to control common childhood behavioral problems. Although DSM-III-R specifies that symptoms of inattention, impulsivity, and hyperactivity must be present to make the diagnosis, few studies have addressed whether these symptoms cluster sufficiently to form a syndrome. Furthermore, review of the normal childhood literature suggests the symptoms of ADHD exist in a continuum in "normal" children, indicating that categorization of children with presumed ADHD may result in frequent misdiagnoses. The authors studied 213 children aged 6–12, using mother, father, and teacher reports (using the child behavior checklist CBCL) of ADHD symptoms. Twelve of 14 items listed in the DSM-III-R were available for analysis in the data set. Using principle component factor analysis of all rating items, results indicated a single behavioral problem factor solution rather than separate dimensions of inattention, impulsivity, and hyperactivity. Further factor solution on each rater's CBCL items provided limited support for the construct of AD with and without hyperactivity. Overall findings raise questions about the validity of the DSM-III-R criteria for ADHL. The subjectivity of adult raters' judgment and the variation of children's symptoms between home and school may account for the wide discrepancies in diagnosing ADHD. Further progress is urgently needed in the development of objective measures, biological markers, and more valid diagnostic criteria in order to better define this currently controversial disorder.

NR62 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

A STUDY OF MDMA USE AMONG PSYCHIATRISTS

Mitchell B. Liester, M.D., Psychiatry, Univ of Calif Irvine, 101 The City Drive, Orange, CA 92668; Charles S. Grob, M.D., Gary L. Bravo, M.D., Roger N. Walsh, M.D.

Summary:

3,4-methylenedioxymethamphetamine (MDMA, "Ecstasy") has been at the center of a debate regarding its potential benefits as an adjunct to psychotherapy versus its potential neurotoxic effects. A current paucity of reports on potential benefits of MDMA has contributed to its classification as a Schedule 1 drug. A semistructured interview was given to 20 psychiatrists who had previously taken MDMA, asking about the phenomenology and the psychological and behavioral sequelae of their experience. During MDMA sessions, subjects reported awareness of the following: increased ability to interact with others (85%), altered time perception (85%), decreased appetite (65%), muscular cramping (50%), increased sensitivity to their own emotions (50%), decreased aggression (45%), speech alterations (45%), bruxism (30%), visual hallucinations (20%) and nausea (15%). None reported panic attacks or auditory hallucinations. Reports of MDMA sequelae include: improved social/interpersonal functioning (50%), improved occupational functioning (45%), improved family relationships (30%) and decreased desire for alcohol (25%). Also evaluated were effects of repeated MDMA use on insight gained, pleasure and intensity of the experience. No consistent changer were reported for any of these parameters. When asked about a craving (i.e., need or compulsion) to take MDMA again, none (0%) reported a craving. Fourteen of 20 (70%) reported a desire to take MDMA again. Other areas investigated include the set and setting at the time the MDMA was taken and the dosage taken. Finally, the authors discuss methodologic problems as well as ethical considerations with a study of this type and encourage further research into both the potential benefits and adverse effects of this drug.

NR63 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

LITHIUM IMPROVES POST-MEAL PLASMA GLUCOSE INSULIN ACTION IN DIABETIC RATS

Leslie R. Vogel, M.D., Psychiatry, UTHSC at San Antonio, 7703 Floyd Curl Drive, San Antonio, CA 78284; Andrea Giaccari, M.D., Luciano Rossetti, M.D.

Summary:

We examined the effect of two weeks of lithium administration on *in vivo* glucose metabolism in four groups of awake chronically catheterized rats: Group I = controls (n = 8); Group II = controls treated with lithium carbonate (0.3 mg/ml in drinking water) (n = 8); Group III = 90% partially pancreatectomized rats (n = 8); Group IV = 90% pancreatectomized rats treated with lithium (0.3 mg/ml) (n = 8). Plasma lithium concentration was 1.03 ± .09 meq/l in group II and 1.20 ± .07 meq/l in group IV. Lithium treatment significantly improved meal tolerance in controls (post-metal plasma glucose = 129 ± 2 vs 151 ± 3 mg/dl) and in diabetic (post-meal plasma glucose = 227 ± 35 vs 383 ± 41 mg/dl) rats. Insulin-stimulated glucose uptake was significantly increased by lithium in both control (41.2 ± .9 vs 33.9 ± .9 mg/kg.min) and diabetic (36.8 ± 1.2 vs 24.9 ± .6 mg/kg.min) rats compared to untreated animals. Muscle glycogenic rate, quantitated both by the increment in cold glycogen concentration and by the incorporation of ^{3}H-glucose into glycogen, was severely impaired in diabetic rats compared to controls (5.1 vs 13.0 mg/kg.min). Following lithium, insulin-stimulated muscle glycogen synthesis increased in control (19.8 mg/kg.min) and in diabetic (17.3 mg/kg.min) rats. The lithium-induced increment inglycogen synthesis during the insulin clamp study completely accounted for the improvement in glucose disposal, suggesting that the insulinomimetic effect of the cation is specific for the glycogenic pathway.

NR64
WITHDRAWN

NR65 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

PSYCHIATRIC PRESENTATIONS OF WILSON'S DISEASE

Mayada Akil, M.D., Psychiatry, Univ of Michigan, 1500 E. Med. Center Drive, Ann Arbor, MI 48104; Denise Dutchak, M.D., Velha Yuzbasiyan-Gurkan, M.D., George J. Brewer, M.D., Joseph A. Schwartz, M.D.

Summary:

Psychiatric manifestations of Wilson's disease, an autosomal recessive disorder of copper metabolism, have been described. There is, however, a paucity of information regarding psychiatric symptoms as the initial presentation of Wilson's disease, while its neurologic and hepatic presentations have received more attention. We reviewed the records of 41 patients with Wilson's disease participating in a zinc acetate treatment protocol, and interviewed 12 of these patients. In 57% of all cases, psychiatric symptoms were reported as an initial manifestation of the disease. These symptoms were severe enough to warrant psychiatric intervention in 29% of all patients before the diagnosis of Wilson's disease was made. Personality changes, particularly irritability and aggression, were most commonly described (41.4% of all patients); depression (22%), cognitive changes, anxiety, psychosis and catatonia also occured. These data confirm the need to include Wilson's disease in the differential diagnosis of psychiatric disorders. The disruption of copper metabolism, perhaps through its effect on copper sensitive enzymes, or through copper toxicity may play a role in the production of psychiatric symptoms in this disorder.

NR66 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

BASELINE THYROID FUNCTION IN PSYCHOTIC DEPRESSION

Martin T. Wilner, M.D., Psychiatry, New York, Hospital, 5252 East 68th Street, New York, NY 10021; Richard P. Brown, M.D., Jaw-Sy Chen, Ph.D., Katherine S. Johnson, R.N., Peter E. Stokes, M.D., J. John Mann, M.D.

Summary:

Goals: Hypothalamic-Pituitary-Adrenal (HPA) axis overactivity occurs with higher frequency in patients with Major Depressive Episodes (MDE) with Psychotic Features compared to those without Psychotic Features. Abnormalities in the Hypothalamic-Pituitary-Thyroid (HPT) axis in patients with MDE have been well-documented. This is the first report of a comparison of baseline thyroid function in MDE with and without Psychotic Features. *Methods:* 108 inpatients who met DSM-III-R criteria for MDE with or without Psychotic Features entered the study. Thyroid indices assayed included T3, T4, FT4I, T3RU, and TSH. Severity of illness was assessed by Global Assessment Scale (GAS). Patients on medications known to affect thyroid function and those suffering from active medical illness were excluded. *Results:* We found: (1) Clinically, the psychotic population showed a lower GAS score, reflecting a greater severity of illness compared to the nonpsychotic group (34.35 vs. 40.50, $p = .004$). (2) No significant difference in thyroid function tests in the two groups. (3) To test the hypothesis that thyroid function would be decreased secondary to a central effect on the HPA axis, in which both T4 and TSH would be low, we compared a "Z" transformation of T4 and TSH and found no difference between the two groups. *Significance:* In contrast to an increase of HPA axis abnormalities in MDE with Psychotic versus Nonpsychotic Features, HPT axis function did not appear to differ. This may indicate different effects on the HPA and HPT axes in MDE. More sophisticated strategies for assessing HPT axis abnormalities may detect differences in the subtypes of MDE and are the subject of ongoing research.

NR67 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

EVENT-RELATED POTENTIALS IN ELDERLY PATIENTS

Ma-Li Wong, M.D., Psychiatry NR-OPD, Albert Einstein Col Med, Pelham Pkwy & E. Chester RD, Bronx, NY 10461; Mary Schroeder, Ph.D., Richard B. Lipton, M.D., Walter Ritter, Ph.D., Herbert G. Vaughan, Jr., M.D.

Summary:

Goals: EEG and event-related potentials (ERP) changes are associated with dementia. The prolongation of the latency of the P3 component has received the most attention as an electrophysiological marker for dementia. ERP's were examined in two groups of elderly patients: a group of 24 subjects at low risk for dementia or normals (blessed scores = 0–4), mean age = 82.57, and a group of 14 subjects at high risk for dementia (blessed sxores = 5–8), mean age = 84.20. The age range of subjects varied from 78 to 93 years.

Methods: The electrophysiologic recordings and averaging were done in a Nicolet Med-80 computer with a 16 channel Grass EEG polygraph. The subjects were submitted to the odd-ball paradigm: stimuli were presented binaurally through headphones and consisted of 1000 and 2000 Hz tones; the frequent tone was presented with 0.8 and the rare tone with 0.2 probability.

Results: The mean P3 latency was 381.30 for the normal group and 409.79 for the high-risk group ($p<0.14$); the mean reaction time (RT) was 393.64 and 380.45 respectively ($p<0.69$). The P3 component was not identifiable to one normal and two high-risk subjects, though these subjects performed the task well.

Significance: We studied an older population than had previously been reported; the lack of prolongation of the P3 or RT latency in our high-risk group points to the conclusion that P3 latency may not be useful in predicting or discriminating subjects at high risk for dementia. The lack of identifiable P3 in three of our subjects might point towards the disappearance of the P3 component with advancing age, more so in high-risk groups than in normals.

NR68 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

THE GERIATRIC DESPRESSION SCALE IN DEMENTIA

Michael Houston, Psychiatry, Univ of NE Med Center, 42nd Dewey Avenue, Omaha, NE 68105; Susan J. Boust, M.D., William J. Burke, M.D., William H. Roccaforte, M.D.

Summary:

This study examined the effectiveness of the Geriatric Depression Scale (GDS) in detecting the presence of depression in geriatric patients with mild dementia of the Alzheimer type (DAT). One hundred forty-two outpatients with Clinical Dementia Ratings of 0 (cognitively intact) or 1 (mild dementia) underwent a comprehensive geriatric assessment which included completion of the GDS. Seventy-two of these individuals were felt to have DAT, while 70 were cognitively intact. Results of the GDS were compared to the clinical psychiatric diagnosis assigned by one of two geropsychiatrists. The data were analyzed using Receiver Operating Characteristic curves (ROC's) to determine the GDS's ability to discriminate between depressed and nondepressed patients in the two groups. ROC curves [which plot sensitivity against the fals positives (1-specificity)] have come into increasing use as a method of examining the clinical performance of tests. Additionally, the area lying below the ROC curve (AUC) can be estimated and used as a quantitative measure of test performance (equivalent to the Wilcoxon rank sum).

In the intact group the AUC was 85% ($z = 6.35$, $p < .0001$), supporting the discriminating ability of the GDS in this group. However, in those patients with mild DAT the AUC was only 66% of the total area and not significantly different from chance. We conclude that the GDS is useful as a screening test for depression in cognitively intact geriatric patients, but not in those with mild DAT.

NR69 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

INCEST SURVIVORS: OBSTETRIC/GYNECOLOGIC PROBLEMS

Trudy K. Shahady, B.A., Psychiatry, Univ of North Carolina, c/o Dr. Gillett NCMH, Manning Dr., Chapel Hill, NC 27599; Gregory M. Gillette, M.D., Kevin R.' Robertson, M.A.

Summary:

Previous psychiatric studies have indicated correlation between childhood sexual abuse and premenstrual syndrome (PMS) and chronic pelvic pain. We have examined a wider range of obstetric and gynecologic problems in 27 women referred to our inpatient research unit for depression. These women reported childhood abuse experiences as follows: 15 with incestuous abuse, 12 with physical abuse, nine with both. Gynecologic problems include dysmenorrhea, endometriosis, menstrual irregularity, PMS, and premenopausal hysterectomy for reasons other than malignancy.

Of the 18 women abused either incestuously or physically, 15 (83%) reported some gynecologic problem(s). Only four of the nine nonabused women (44%) reported a gynecologic problem, a significantly lower rate than abused women (Fisher's exact test, $p < 0.0005$). All three women reporting PMS were incest survivors. Six of the 15 incestuously abused women had undergone elective hysterectomy, compared with none of the 12 nonincestuously abused women ($p < 0.025$). These latter two groups showed no significant difference in rates of any obstetric phenomenon (pregnancy, miscarriage, induced abortion, stillbirth).

Our findings are consistent with previous work on sexual abuse as a possible predisposing factor for PMS and pelvic pain. We additionally found childhood incest to correlate strongly with adulthood elective premenopausal hysterectomy.

NR70 **Monday, May 8, 9:00 a.m.–10:30 a.m.**

TRH-TEST: DEPRESSIVES WITH AGITATION, SUICIDALITY

Mark H.N., Corrigan, M.D., Research Unit, Dorothea Dix Hospital, 820 South Boylan Avenue, Raleigh, NC 27611; James C. Garbutt, M.D., Gregory M. Gillette, M.D., Dana E. Quade, Ph.D.

Summary:

Reduced TSH response to TRH has been repeatedly demonstrated in patients with major depression. Several investigators have suggested that more specific symptoms and signs (agitation, violent suicidality, panic attacks) correlate with this neuroendocrine abnormality. However, none of these studies indicate whether these clinical factors independently influence TSH response, or whether both the clinical phenomena and the neuroendocrine marker represent downstream effects of a common biological underpinning.

We studied 46 euthyroid RDC primary unipolar depressed inpatients with a standard 500 microgram IV TRH test, dividing them by gender (27 women, 19 men) and using the Schedule for Affective Disorders and Schizophrenia to rate agitation, suicidal intent, and suicidal lethality. Women with high scores on each of these variables had significantly reduced TSH responses compared to women with low scores ($p < 0.05$, Satterwhaite's t-test), confirming previous findings. Men showed no significant difference on any variable.

We are currently further analyzing our data to determine whether agitation, suicidality and panic correlate independently with reduced TSH response to TRH. We will discuss possible neurobiological models that may account for these observations.

NR71 **Monday, May 8 9:00 a.m.–10:30 a.m.**

INSULIN KINETICS AND GLUCOSE IN EATING DISORDERS

Julio Licinio, M.D., Psychiatry, Cornell Medical Center, 21 Bloomingdale Road, White Plans, NY 10605; Katherine Halmi, M.D., Peter E. Stokes, M.D.

Summary:

Goals: Insulin effects of the regulation of ingestive behavior and body weight. Our goal is to study glucose levels and insulin kinetics in eating disorders before and after treatment.

Methods: Subjects are being studied in the Cornell C.R.C. under four protocols: 1) C-peptide and insulin decay curves. 2) Using C-peptide as a marker of insulin secretion, we apply the kinetic parameters from protocol 1 and measure 24-hour insulin secretion rates, hepatic degradation, peripheral levels, and posthepatic delivery rates of insulin in response to mixed meals. 3) Measurement of insulin kinetics in response to a standard oral glucose load. 4) Intravenous glucose tolerance test, to assess insulin sensitivity.

Preliminary results: We have studied one underweight anorectic restrictor (AN-R), one severe normal-weight bulimic (NW-B), and one recovered NW-B. Plasma glucose measurements every 15 minutes for 24 hours were assessed by cluster analysis. The severe NW-B had four glucose pulses with a peak width (PW) of 191 $\pm$ 75 mg/dl (mean $\pm$ SD), peak height (PH) of 140 $\pm$ 7.9, and peak area (PA) of 5437 $\pm$ 1962, compared to eight glucose pulses in the recovered NW-B, with a PW of 114 $\pm$ 68, PH of 114 $\pm$ 19, and PA of 1111 $\pm$ 714, and seven glucose pulses with a PW of 94 $\pm$ 64, PH of 109 $\pm$ 7, and PA of 1136 $\pm$ 1059 in the AN-R.

Discussion: These preliminary results show that there are marked differences in the 24-hour glucose profiles of the severely ill and recovered patients. We will present data on additional patients and controls on 24-hour insulin secretion, distribution rates and peripheral insulin sensitivity. The insulin responses to mixed meals and to a pure carbohydrate meal will also be compared.

NR72 **Monday, May 8 9:00 a.m.–10:30 a.m.**

SUBTYPING AGGRESSION IN HUMANS

Benedetto Vitiello, M.D., Psychiatry, Medical College of P.A., 3200 Henry Avenue, Philadelphia, PA 19129; David Behar, M.D., David Stoff, Ph.D., Alexander Ricciuti, Ph.D.

Summary:

Animal aggression is classified in different categories, mediated by different brain mechanisms. Few similar attempts have been made in humans. More homogeneous categories of aggression may lead to more specific treatment modalities. In order to validate the subtyping of human aggression into "predatory" (goal-oriented, planned, hidden, controlled) and "affective" (impulsive, unplanned, overt, uncontrolled), we studied 53 aggressive psychiatric patients (10–18 yrs, 44 = M, 9 = F). DSM-III-R diagnoses were: conduct, attention deficit-hyperactivity, atypical psychosis, and personality disorders. The presence over the past month of eight proposed predatory and eight affective behaviors, randomly listed, was scored by independent raters, blind to the purpose of this study. A cluster analysis, using the 10 items with good inter-rater reliability, confirmed the predicted partition, yielding a "predatory" (five items: hides aggression, can control aggression, protect body when aggressive, plans aggression, steals) and an "affective" cluster (five items: uncontrolled aggression, self plans aggression, steals) and an "affective" cluster (five items: uncontrolled aggression, self exposure to harm, sudden aggression, unprofitable aggression, unprofitable damaging of own property). This scale, with a total score from +5 (fully predatory) to −5 (fully affective), had good internal consistency (alpha = .73). The score distribution in this population was bimodal with peaks at +1 (predatory-mixed) and at −2 (affective), thus validating the subtyping. Correlations with clinical scores and treatment implications will be discussed.

NR73 **Monday, May 8 9:00 a.m.–10:30 a.m.**

VBR IN SCHIZOPHRENIA: A FACTOR ANALYTIC STUDY

Steven B. Schwarzkopf, M.D., Psychiatry, Ohio State University, 071 Upham Hall 473 W 12th Ave, Columbus, OH 43210; Stephen C. Olson, M.D., Jeffrey A. Coffman, M.D., Judy A. McLaughlin, M.S., Henry A. Nasrallah, M.D.

Summary:

Introduction: Many schizophrenic patients exhibit lateral and/or 3rd ventricular enlargement. Most studies examining familial/sporadic subgroups find ventriculomegally predominantly in the sporadic group. Here we present: 1) a factor analytic study of ventricular measures in an attempt to define patterns of enlargement in schizophrenia, 2) evidence supporting ventriculomegally in sporadic schziophrenia. *Methods:* 36 male schizophrenics (DSM-III-R) and 14 male controls consented to the study. Family histories were obtained (parental interview, FH-RDC) and patients classified as FH+ (1st and 2nd degree relative hospitalized with psychosis) or FH−. T1 weighted MRI scans were obtained and measures made of midsagittal VBR, coronal VBR (left and right), and third ventricular area (coronal). *Results/Discussion:* FH− patients had larger midsagittal VBR, left VBR, and 3rd ventricular size ($P < .05$, Wilcoxon) than FH+ patients. Factor analysis (four ventricular measures) identified two factors (accounting for 92% of the variance). Factor 1 was weighted (+) on all measures and was not significantly different between groups. Factor 2 was weighted + on all measures and was not significantly different between groups. Factor 2 was weighted (+) on 3rd ventricular area and left VBR, and was significantly greater in the FH− group. Results support reports of ventriculomegally in sporadic schizophrenia. A pattern of 3rd and left, rather than generalized ventricular enlargement was identified.

NR74 **Monday, May 8 9:00 a.m.–10:30 a.m.**

CRF, SYMPATHETIC ACTIVITY AND IMMUNE FUNCTION

Lee D. Jones, M.D., Psychiatry, USCD, V116A 3350 La Jolla Village Dr, San Diego, CA 92161; Michael R. Irwin, M.D., Michaelyn Provencio, B.S.

Summary:

Altered immune function has been associated with states of depression. To understand the link between the brain and the immune system, we have recently developed an animal model and found that intracerebroventricular (ICV) administration of corticotropin releasing factor (CRF) produces an activation of the autonomic nervous system and reduces splenic natural killer (NK) cytotoxicity in the rat. This study further examines the role of the sympathetic nervous system in mediating suppression of NK activity following CRF.

In male Wistar rats, a series of separate experiments explored whether chemical sympathectomy or pharmacologic blockade antagonized the immunosuppressive action of CRF. In the first experiment, treatment with 6-hydroxydopamine produced a significant depletion of splenic norepinephrine ($t = 5.7$, $p < .001$) and completely antagonized CRF-induced suppression of NK cytotoxicity ($F = 3.6$, $df = 3,33$, $p < .02$). Similar results were demonstrated when the animals were treated with nonselective and selective beta-2 antagonists.

These studies suggest that activation of the sympathetic nervous system is a mechanism by which central CRF acutely reduces NK activity and emphasize the potential role of increased sympathetic activity to reduce immune function in depression.

NR75 **Monday, May 8 9:00 a.m.–10:30 a.m.**

A REAPPRAISAL OF A LIMIT-CYCLE MODEL OF SLEEP

Kevin O-Connor, M.D., Psychiatry, UC San Diego VA, V116a 3350 La Jolla Village Dr., San Diego, CA 92161; J. Christian Gillin, M.D., Arnold Mandell, M.D.

Summary:

The McCarley-Massaquoi limit cycle model of sleep was modified by removal of the circadian factor and by addition of factors representing cholinergic and monoaminergic "throughput." Exploration of the behavior of solutions as the throughput factors were varied showed that the limit cycle occurring for all factors equal to unity disappeared for certain combinations of changes: (1) for cholinergic throughputs both set to 1.4 and monoaminergic throughputs set to 0.5, there is an unstable focus, stable node and saddle point, predicting short REM latency and a single very long (90% of sleep) REM episode; (2) for cholinergic throughputs slightly less than unity and monoaminergic throughputs slightly greater than unity, there is an attractive focus, corresponding to damped oscillations of REM activity, stabilizing in prolonged REM episodes as the sleep progresses.

Implications for affective disorders are discussed.

NR76 **Monday, May 8 9:00 a.m.–10:30 a.m.**

BULIMIA AND DEPRESSION ASSESSED BY PET

Jennifer O. Hagman, M.D., Psychiatrym, Univ of Calif. Irvine, Dept of Psych Medsci 1D404, Irvine, CA 92717; Monte S. Buchsbaum, M.D., Joseph C. Wu, M.D., Chandra A. Reynolds, B.A., Barton J. Blinder, M.D.

Summary:

This is the first report of a comparison of PET scans in patients with bulimia and patients with depression. The possibility of a biological relationship between bulimia nervosa and major affective disorder has been explored through neuroendocrine studies, analysis of family history, and psychopharmacology. Although antidepressants have been successfully used in the treatment of bulimia, there has been controversy as to whether bulimia is a variant of major affective disorder, and about the contribution of depressive symptoms to the development and course of the illness. To address this question, eight women with bulimia nervosa (mean age $= 28.6 \pm 6.5$), eight women with unipolar depression ($x = 29.4 \pm 5.7$) and eight women with no history of psychiatric illness ($x = 29.3 \pm 7.7$) underwent PET scans using 2-fluordeoxyglucose and the continuous performance task. All subjects were age- and sex-matched and none were below 10% of ideal body weight. All subjects had been free of psychotropic medication for a minimum of 30 days. Glucose data were analyzed using ANOVA's. Cortical surface was analyzed for hemispheric and sector assymetries and frontal lobe metabolism. Subcortical structures of special interest included the caudate nucleus and temporal lobes which have been implicated in previous PET studies of major affective disorder and anorexia nervosa.

NR77 **Monday, May 8 9:00 a.m.–10:30 a.m.**

FENFLURAMINE STIMULATION OF PROLACTIN RELEASE IN OCD

William S. Hewlett, Ph.D., Psychiatry, Stanford University, Stanford Univ Sch of Medicine, Stanford, CA 94305; Sophia Vinogradov, M.D., Sarah Berman, John Czernansky, M.D., William S. Agras, M.D.

Summary:

Obsessive-compulsive disorder is an anxiety disorder characterized by intrusive thoughts and egodystonic rituals which the patient carries out to reduce anxiety. Current treatments involve pharmacotherapy with medications that block the reuptake of serotonin into the neuronal cells. Serotonin hypotheses relevant to the etiology of OCD have been proposed. Serotonin is also known to be involved in the modulation of endocrine responses. In particular, serotonin in the hypothalamus is thought to trigger the release of a prolactin-releasing factor, which in turn causes the release of prolactin from the anterior pituitary. Fenfluramine is a substituted amphetamine that induces the release of serotonin from neuronal cells and secondarily stimulates the release of prolactin into the bloodstream. Since OCD may involve an abnormality in serotonin transmission, the present study assesses the ability of releasable serotonin to promote prolactin release in the obsessive-compulsive patient as a means of characterizing the central serotonergic state in OCD. Twenty-one medication-free patients with a DSM-III diagnosis of OCD were evaluated using the fenfluramine challenge test. This study compares the maximal prolactin response in these patients compared to those of 20 age- and sex-matched control subjects without a current psychiatric history. Prolactin assays were arranged blind to diagnosis. The results to be reported will characterize the relationship between the ability of fenfluramine to release prolactin and the presence, degree, and nature of obsessions and compulsions.

NR78 **Monday, May 8 9:00 a.m.–10:30 a.m.**

PRELIMINARY FINDINGS OF A NEW TEEN SUICIDE PROGRAM

Daniel Grosz, M.D., Psychiatry, Montefiore Med Center, 111 East 210th Street, Bronx, NY 10467; Gregory M. Asnis, M.D., Jill M. Harkavy Friedman, Ph.D., Jim Zimmerman, Ph.D., Herman M. van Praag, M.D.

Summary:

The recent increase in adolescent suicide has received wide attention. Despite the significance of the problem there are very few programs focused on this high-risk population. We will present our experience in developing a new Adolescent Depression and Suicide Program (ADSP). The ADSP is an outpatient program of Montefiore Medical Center, providing short-term (6–12 weeks) intervention for teenagers who recently made a suicide attempt or are considered to be at a high risk for committing suicide. During its first year, 88 adolescents were evaluated by the ADSP. The mean age of youngsters was 15.7 (range 13–21). Among the recent suicide attempters (n = 62) the majority were females (76%), predominantly hispanic. The most common method used was overdose (80%). We were able to follow up almost 50% of our sample. The follow-up time ranged from a few weeks to almost a year. Most of our sample (n = 61) completed a comprehensive survey of psychosocial and psychopathological variables including measures of life events, depression, impulsivity, aggression and suicidality. The value of these measures as predictors of further attempts and compliance with treatment will be discussed.

NR79 **Monday, May 8 9:00 a.m.–10:30 a.m.**

VARYING RESPONSE TO DESIPRAMINE IN PANIC DISORDER

Oren Kalus, M.D., Psychiatry, Montefiore Med Center, 111 East 210th Street, Bronx, NY 10467; Gregory M. Asnis, M.D., Wiepke Cahn, M.A., Eileen Rubinson, M.S.W., Jill M. Harkavy Friedman, Ph.D., Daniel Grosz, M.D.

Summary:

Apart from imipramine, the efficacy of tricyclic antidepressants in panic disorder (PD) has received surprisingly little attention. We report on a six-week open trial of desipramine in 14 patients (five male, nine female, mean age = 35 years) with PD (RDC/DSM-III). Following a 10-day placebo period, DMI was titrated to a range of 150–300 mg. By week 6, 11 of 14 patients (79%) showed significant improvement on CGI ratings. Both somatic and psychic anxiety (as rated by SADSC) were also significantly improved ($p < .002$, $p < .004$) by week 6, while agoraphobia did not change ($p < .06$). A significant decline in panic attack frequency occurred on placebo ($p < .04$) and at week 8 follow-up, but not at week 6. Interestingly, no other items improved (or worsened) on placebo. Patients who remained moderately ill (by CGI severity scores) (n = 8) at the end of the study had significantly longer duration of illness (213 weeks vs. 30 weeks, $p < .05$) and more residual psychic anxiety ($p < .04$). than those who were normal/borderline ill (n = 6). The two groups did not differ in somatic anxiety, panic attack frequency or degree of agoraphobia. Though DMI appears to be effective in PD, the results suggest that no all patients respond equally well, and that some components of the illness may respond better than others. Diagnostic and treatment implications of these findings will be discussed.

NR80 **Monday, May 8 9:00 a.m.–10:30 a.m.**

A SURVEY OF SUICIDAL BEHAVIORS IN AN ADULT OPD

Gregory M. Asnis, M.D., Psychiatry, Montefiore Med Center, 111 East 210th Street, Bronx, NY 10467; Jill M. Harkavy Friedman, Ph.D., Brunhild Kring, M.D., Naveed Iqbal, M.D.

Summary:

A comprehensive psychiatric evaluation should include an assessment of past and present suicidal behaviors. The Harkavy Asnis Suicide Survey (HASS), a comprehensive self-report instrument, assesses suicidal behavior. Individuals who commit suicide often have a history of prior suicidal ideation and/or attempts, making identification of suicidal behavior critical for designing intervention and prevention strategies. Prior to an OPD evaluation, 190 patients (mean age 32.0 SD 13.9 yrs., 33% males, 67% famales) completed the HASS and the SCL-90.

Twenty-five percent of patients had a least one prior suicide attempt, with over 50% reporting multiple attempts. The first attempt almost always occurred during adolescence. Thirty-three percent had a family member who made an attempt and 20% had a family member who committed suicide.

Fifty-five percent of the sample reported a history of suicidal ideation, with 25% reporting suicidal thoughts in the week prior to evaluation. Recent suidical ideation was more frequent among attempters than among those without a previous attempt (44% vs. 12%, $x^2 = 21.83$, $p < .001$).

Suicidal behaviors are common in psychiatric outpatients and usually start in adolescence. Previous suicide attempts are associated with current suicidal ideation. The associates of suicidal behaviors with DSM-III diagnoses and various clinical dimensions, such as depression and anxiety, will be discussed.

NR81 **Monday, May 8 9:00 a.m.–10:30 a.m.**

CO-MORBID PROFILE: DEPRESSION AND ALCOHOLISM

Ihsan M. Salloum, M.D, Psychiatry, Western Psychiatric Inst., 3811 O'Hara Street, Pittsburgh, PA 15213; Juan E. Mezzich, M.D., Chul Ahn, Ph.D.

Summary:

This study aims at elucidating the clinical picture of patients with the comorbid diagnoses of major depression plus alcohol abuse and/or dependence. A large sample consisting of 3,414 adult patients were selected from 8,130 patients presenting for care at a large metropolitan university hospital during a two-year period. Using a semistructured assessment procedure, patients were diagnosed according to DSM-III criteria and were divided into three subgroups: (1) major depression without alcoholism, (2) alcoholism without major depression, and (3) those with coexisting conditions of major depression plus alcoholism.

These three groups were compared along demographic variables, psychopathological symptoms inventory, social and personal history, and levels of adaptive functioning. Patients in the comorbid group more closely resembled alcoholic patients in terms of premorbid social and personal history, impulsive violent and antisocial symptomatology, frequency of drug abuse reported, and of lower levels of social supports and adaptive functioning. They also resembled those with depressive disorder in terms of severity of depressive symptoms. Another important finding was the strikingly high rate of suicidal behavior among the comorbid group as compared with those of either depressive or alcoholic patients.

These results corroborate previous reports on the similarities between patients with coexisting depression plus alcoholism and alcoholics, and it stresses the high potential of suicidal behavior among them.

NR82 **Monday, May 8 9:00 a.m.–10:30 a.m.**

MENSTRUAL CYCLE SYMPTOM CHANGES CORRELATE WITH CHANGES IN GONADAL STEROIDS AND PLATELET UPTAKE KINETICS

Margaret G. Spinelli, M.D., Psychiatry, Payne Whitney Clinic, 445 East 68th Street, New York, NY 10021; J. John Mann, M.D., John Sweeney, Ph.D.

Summary:

It has been hypothesized that symptoms associated with the premenstrual period may be related to changes in levels of gonadal steroids that modulated brain monoamine function. We therefore studied the relationship between premenstrual symptomatology, levels of estradiol and progesterone, and platelet 5-hydroxytryptamine uptake kinetics in physically healthy women. From the preovulatory week to the premenstrual week, there was a decrease in estradiol and increase in 5-HT uptake Vmax, Km, progesterone and 6/11 behavioral symptoms from baseline preovulatory levels. Significant correlations were found between the degree of increased 5-HT uptake, levels of estradiol and progesterone with several behavioral symptoms. Greater increase in 5-HT uptake and progesterone, and greater decrease in estradiol levels, correlated with a greater decrease in premenstrual symptoms. No significant correlations were seen between absolute levels of all parameters. The complex dynamic relationship among gonadal steroids, neurobiology and behavior may best be described in relative change rather than absolute levels.

NR83 **Tuesday, May 9 9:00 a.m.–10:30 a.m.**

COGNITIVE CORRELATES OF HIPPPOCAMPAL VOLUMES

Robert M. Bilder, Ph.D., Research, Hillside Hospital, 7559 263rd Street, Glen Oaks, NY 11004; Bernard Bogerts,M.D., Jeffrey A. Lieberman, M.D., Manzar Ashtari, Ph.D., Jose M.A. Alvir, D.P.H., Hoseph Zito, M.D.

Educational Objectives:

Generally, to describe the functional significance of abnormal brain morphology in schizophrenia. Specifically, to address the possibility that abnormal patterns of growth in medial temporal regions may limit cognitive development.

Summary:

The neuropsychological (NP) correlates of hippocampal volumes were assessed in 12 patients participating in a study of first-episode schizophrenia. Measurements of right and left posterior hippocampus (PH) and anterior hippocampus/amygdaloid complex (HAC) were made on coronal magnetic resonance (MR) images acquired on a 1.0 Tesla Siemens-Magnetom using 3D gradient echo sequences, with resolution of 1 mm × 1 mm (256 × 256 pixels) and slice thickness of 3.1 mm. The NP measures were taken from a comprehensive battery administered after patients were treated for at least six months.

Larger HAC volumes were generally correlated with better visual and verbal memory test performance. PH volumes, however, tended to show negative correlations with performance. The distinction between HAC and PH was addressed further through construction of anterior/posterior (AP) volume ratios.

		Visual	Verbal			Visual	Verbal
Right	HAC	.62*	.58*	*Left*	HAC	.44	.57*
	PH	−.61*	−.70*		PH	−.11	−.41
	AP Ratio	.69**	.72**		AP Ratio	.27	.54

*: $p < .05$, two-tailed
**: $p < .01$, two-tailed

Significant correlations ($p < .05$, two-tailed) were observed between the right AP ratio and composite indices of Global ($r = .59$); Premorbid ($r = .58$); Memory ($r = .65$); and Motor ($r = .64$) functions. The left AP ratio was correlated only with Visuospatial functions ($r = .57$). Results from an expanded sample will be discussed in the context of a neurodevelopmental hypothesis.

References:

[1]Falkai P, Bogerts B, Rozumek M: *Biological Psychiatry* 24:515–521, 1988.

[2]Bilder RM, Degreef G, Pandurangi AK, Rieder RO, Sackeim HA, Mukherjee S:*Schizophrenia Research* 1:37–45, 1988.

NR84 **Tuesday, May 9 9:00 a.m.–10:30 a.m.**

MONOCLONAL ANTIBODIES IN INVESTIGATE SCHIZOPHRENIA

William G. Honer, M.D., Psychiatry, Columbia University, Box 58 722 West 168th Street, New York, NY 10032; Charles A. Kaufmann, M.D., Joel E. Kleinman, M.D., Manuel F. Casanova, M.D., Peter Davies, Ph.D.

Educational Objectives:

This report describes the application of immunological methods to the investigation of schizophrenia.

Summary:

New approaches may be required to reveal the neuropathological substrate of schizophrenia. We used the approach of Davies (1,2) to generate novel monoclonal antibodies (mabs) to brain antigens in schizophrenia.

Mabs were prepared using post-mortem brain homogenates from four cases of schizophrenia (RDC criteria, Diagnostic Evaluation After Death schedule) comprising five brain regions (nucleus accumbens (NAc), amygdala (Amy), caudate (Cd), temporal (TC), and cingulate (CiC) cortices). 7,600 cell hybrids were screened for mabs which would discriminate between case and control homogenates using an ELISA. A panel of 12 mabs was formed, each of which was selective in at least one of five brain regions tested.

Serial dilution studies using homogenates standardized for protein concentration were performed to study relative abundance of antigens. For seven of the 12 mabs there was complete separation of the results between individual cases and controls; relative differences in antigen levels were two- to four-fold. Patterns of differences varied by region and by mab. In the Amy, mabs EP1 and EP7 were twofold more reactive in controls. In this region mab EP9 reacted twofold more with cases. In contrast to the pattern in Amy, EP9 was threefold more reactive with controls in Cd and CiC. Several of the mabs appeared to exhibit truly qualitative rather than quantitative differences in case-control reactivity.

These preliminary results indicate the success of our strategy to develop probes to investigate the pathophysiology of schizophrenia. Confirmation with a larger series as well as histologic and biochemical characterization of the antigens is in progress.

References:

[1]Wolozin B. et al.. A neuronal antigen in the brains of Alzheimer patients. *Science* 1986;232:648–500.

[2]Wolozin B., Davies P. Alzheimer-related neuronal protein A68: specificity and distribution. *An Neurol* 1987;22:521–526.

NR85 **Tuesday, May 9 9:00 a.m.–10:30 a.m.**

PREPYRIFORM CORTEX ABNORMALITIES IN SCHIZOPHRENIA

Manuel F. Casanova, M.D., NIMH Neurosciences, Center at St. Elizabeth, 2700 Martin Luther King Ave SE, Washington, DC 20032; Richard Saunders, Ph.D., Nicholas Carosella, M.D., Daniel R. Weinberger, M.D., Joel Kleinman, M.D.

Educational Objectives:

Describe a neuropathological correlate of schizophrenia

Summary:

Although there have been many reported morphological abnormalities in the brains of schizophrenic patients, few of them have been corroborated. A case in point are the recent descriptions of temporal lobe pathology in schizophrenic patients. Morphometric studies have indicated reduced temporal lobe volumes in schizophrenic patients, due to a focal or multifocal gray matter lesion. Microscopic studies have further localized the loci of pathology to the entorhinal cortex. Given the fact that both the entorhinal region and prepyriform cortex are closely adjacent anatomical areas, that they both receive prominent dopaminergic projections form the ventral tegmental area, and both bear a similar vulnerability in other degenerative diseases (i.e.; Alzeheimer's disease) we decided to investigate the presence of cytoarchitectural abnormalities in the prepyriform cortex of schizophrenic patients. Serial Nissl-stained microscopic sections were examined from five schizophrenic patients and nine controls, all from the Yakovlev collection. The outer layer of the well pigmented cells of the prepyriform cortex of schizophenic patients was often divided into two laminas. The cytoarchitectural arrangement was similar to the closely adjacent prorhinal region except that the laminas were thicker in number of cells. Heterotopic aggregates similar to those described in the entorhinal region of schizophrenic patients were also identified. The heterotopic-like aggregate of cells were only seen in schizophrenic patients (n = four out of five). The importance of this abnormality will be discussed in terms of similar reports on cytoarchitectural disruption in the entohinal region of schizophrenic patients and their relationship to the dopaminergic hypothesis.

References:

[1]Jacob H, et al: Prenatal developmental disturbances in the limbic allocortex in schizophrenia. *J. Neural Transm* 65:303–326, 1986.

[2]Reyes PF, et al: The prepiriform cortex in dementia of the Alzheimer type. *Arch Neurol* 44:644–645, 1987.

NR86 **Tuesday, May 9 9:00 a.m.–10:30 a.m.**

D2 PET SCANS IN TWENTY-FIVE DRUG NAIVE SCHIZOPHRENICS

Larry E. Tune, M.D., Psychiatry, Johns Hopkins University, 600 North Wolfe St. Meyer3-166, Baltimore, MD 21205; Dean F. Wong, M.D., Godfrey D. Pearison, M.D., L. Trevor Young, M.D., Victor Villemagne, M.D., Robert F. Dannals, Ph.D.

Educational Objectives:

To inform clinicians and researchers of ongoing research using Positron Emission Tomography, into possible involvement of dopamine 2-receptors in the pathophysiology of schizophrenics.

Summary:

In a previous study (Wong, et al, *Science* 234:1558, 1986), we reported elevated D2 dopamine receptor density in ten drug-naive schizophrenics. We now present data from this ongoing project in 25 patients. All patients received two 11-C-N-methylspiperone PET scans, the first in the drug-naive state, the second preceded by 7.5 mg p.o. haloperidol to permit calculation of D2 receptor density (Bmax) using a kinetic model with four compartments. D2 Bmax values in drug-naive schizophrenics (N=25) was 32.1 ± 18.5 (Age=42.5 ± 22.0). This was significantly (p .01) different when compared with 14 normal controls (Bmax=14.4 ± 8.6, Age=33.6 ± 17.5). In addition to age, sex, onset, and duration of illness parameters, nutritional status was evaluated, and all patients were examined with Mini-Mental State Examination, the Present State Examination, and the BPRS. Multiple regression analysis, including backward elimination procedures of receptor density Bmax vs. a number clinical variables demonstrated a trend for sex and psychosis scores (PSE, BPRS) to be important contributors when compared to age, onset, and duration of illness. When the regression analysis required age, there was a similar trend for dependence on the regression model for psychosis scores. There was no significant difference in nutritional status between patients and controls. Lastly, educational level was significantly and inversely correlated with Bmax (r=.05). These findings are compatible with those found in bipolar illness.

References:

[1]Wong, et al, *Science* 234:1558, 1986.

[2]Farde L. Wiesel FA, Hall, H, et al, *Archives of General Psychiatry* 44:671, 1987.

NR87 **Tuesday, May 9 9:00 a.m.–10:30 a.m.**

SCHIZOPHRENIA AND HIGH LEVELS OF SOLUBLE IL-2 RECEPTORS

Mark H. Rapaport, M.D., CNB, NIMH Bldg 10 RM 4N212, 9000 Rockville Pike, Bethesda, MD 20894; Cathy G. Mc Allister, Ph.D., David Pickar, M.D., Darryl Kirch, M.D., David L. Nelson, M.D., Steven M. Paul, M.D.

Educational Objectives:

The educational objective of this presentation is to inform the audience of new evidence of T lymphocyte activation in a cohort of schizophrenic patients and to stimulate further investigation of immunological research in schizophrenia.

Summary:

There are conflicting reports of immunological stigmata associated with schizophrenia; however recent advances in immunology afford new and more precise techniques for assessing the immune system. One advance is the discovery of the cytokine interleukin-2, an important modulator of immune function, and the development of an assay that measures the soluble form of the interleukin-2(IL-2R). Detectable levels of soluble IL-2R are present in all individuals; however, they are increased significantly in active infection and some autoimmune diseases. Increased levels of soluble IL-2R are believed to be an indication of T lymphocyte activation. We have hypothesized that certain forms of psychosis have an autoimmune basis and thus would have activated immune systems which would produce increased numbers of soluble IL-2R. Levels of soluble IL-2R were measured in 126 psychotic individuals and 27 normal controls. The mean soluble interleukin-2 receptor levels ± (SEM) were significantly different for psychotic patients versus controls (439 pg/ml ± 19.8 vs 340 pg/ml ± 31.9, p=0.0001, df 124). A subset of DSM-III diagnosed schizophrenic patients (N=30) had significantly increased levels of IL-2R both while stabilized on neuroleptic and during a medication free period (p=0.0001). Interestingly, paired analysis of these patients on and off antipsychotic agents demonstrates that while medicated patients had even greater mean interleukin-2 receptor levels (614 pg/ml ± 37.2 vs 529 pg/ml ± 30.9, p=0.028, df 29). These findings are preliminary evidence that immunological activation occurs in certain forms of psychosis and may be related to medication state.

Reference:

[1]Delisi LE, Crow TH. Is schizophrenia a viral or immunological disorder? Psychiatric Clinics of North America 9:115–132. 1986. Rubin LA, Kurman CC, Fritz ME, Soluble interleukin-2 receptors are released from activated human lymphoid cells in vitro. *J. Immunol* ;135:3172–7. 1985.

NR88 **Tuesday, May 9 9:00 a.m.–10:30 a.m.**

TWIN CONCORDANCE IN SCHIZOPHRENIC DISORDERS

Sidsel Onstad, M.D., Psychiatry, Uiv of Oslo, P.O. Box 85 Vindern, 0319 Oslo 3, Norway: Ingunn Skre, Ph.D., Svenn Torgersen, Ph.D., Einar Kringlen, M.D.

Summary:

The study included 26 pairs of monozygotic (MZ) and 36 pairs of dizygotic (DZ) twins who were obtained by checking the Norwegian Twin Register with the National Psychosis Register. All twins were personally interviewed with the SCID-I and II and diagnosed according to the DSM-III. Using the probandwise method, combinations of diagnoses were examined for MZ/DZ concordance ratios either by adding a single diagnosis or multiple diagnoses to the group of schizophrenic patients. For schizophrenia alone the MZ/DZ concordance ratio was 14.01. With the single diagnosis approach the maximum MZ/DZ concordance ratio was produced when atypical psychosis was added to schizophrenia (15.42). With the multiple diagnoses approach atypical psychosis, schizoaffective, and schizophreniform disorders combined with schizophrenia represented the highest ratio (17.48). A considerable decrease in the MZ/DZ concordance ratio was observed in either method when spectrum personality disorders were added (1.46). Thus, the genetic impact is clearly demonstrated with regard to schizophrenic syndromes, whereas the genetic loading almost disappears if a broad concept of the schizophrenic spectrum is employed.

NR89 **Tuesday, May 9 9:00 a.m.–10:30 a.m.**

AGING, ALCOHOLISM AND PANIC DISORDER PREVALENCE

John H. Krystal, M.D., Psychiatry, Yale University, CNRU 34 Park Street, New Haven, CT 06508; Philip Leaf, Ph.D., Martha Bruce, Ph.D., Dennis S. Charney, M.D.

Educational Objectives:

1. Providing new information about the natural history of panic disorder. 2. Integration of this new data into a "neurodevelopmental" framework. 3. Educate about potential risks of alcohol abuse.

Summary:

The effects of aging and alcoholism histories (ETOH) on the six-month prevalence rates of panic disorder (PD) were examined using data collected in five communities as part of the Epidemiologic Catchement Area (ECA) study (New Haven, CT; Baltimore, MD; St. Louis, MO; Durham, NC; and Los Angeles, CA). *Methods:* Data were collected from 10,018 complete respondants at the five sites noted above using the Diagnostic Interview Schedule (DIS) for determining diagnoses based on DSM-III criteria. Weighted least squares procedures, Taylor Series Linnearization procedures, Chi-square Tests, and Balanced Repeated Replication Analyses were used to assess group differences and trends within subsamples. *Results:* Men without ETOH exhibited relatively low PD rates (<0.y/100) compared to women without ETOH. Significant declines in PD prevalence were apparent in men older than 64 (X^2=9.3, p<.01) and women older than 54 (X^2=8.5, p<.01). Presence of ETOH was associated with significantly higher PD rates in men (10.8/100 for men 45–54) and women (27.4/100 for women 35–44). ETOH was also associated with an earlier decline in PD prevalence with age in both men and women. In addition, in most patients, the onset of ETOH preceeded the onset of PD, although this difference did not reach statistical significance. *Implications:* The decline in PD prevalence with advanced age could be consistent with age-related decreases in the brain mechanisms underlying panic attacks, such as noradrenergic activation. These data also suggest that alcohol abuse interacts with these processes to produce greater levels of activation in young individuals, but that alcoholism, perhaps through toxic effects, synergizes with normal brain aging to result in an earlier decline in PD rates. Prospective studies will be needed to rigorously evaluate these hypotheses to evaluate individuals longitudinally and to control for factors, such as under-reporting of symptoms in the elderly, but could bias epidemiologic data.

References:

[1]Von Korf MR, et al.: The epidemiology of panic attacks and panic disorder. *Am J. Epidemiol.* 122:970–981,1985.

[2]Krystal JH, et al.: Anxiety Disorders, in *Outpatient Psychiatry: Diagnosis & Treatment, 2nd Ed.,* Edited by A. Lazare, Baltimore: Williams & Wilkins, in press.

[3]Brier A, et al.: Agoraphobia with panic attacks. *Arch. Gen. Psychiatry* 43:1029–1036, 1986.

NR90 **Tuesday, May 9 9:00 a.m.–10:30 a.m.**

CIRCADIAN COSINE MODEL PREDICTS ANXIETY IN PANIC

Justin A. Kenardy, B.Sc., Psychiatry, Stanford University, Behavioral Medicine Program, Stanford CA 94305; C. Barr Taylor, M.D., Leslie Fried, M.Sc.

Educational Objectives:

By the end of the presentation the learner should understand the association between circadian rhythm and anxiety in panic disorder, and implications for the assessment and etiology of panic attacks.

Summary:

Twenty subjects with panic disorder were monitored for 17 hours daily over seven days. Self-report was obtained using portable microcomputers programmed to cue and store the information. Eleven of these patients displayed a predictable circadian cycle for anxiety. For eight of these patients acrophase was in the early afternoon with the remaining three having acrophase in the evening. Patients without a predictable rhythm had more frequent panic attacks over the seven days (mean=7.78) than those with predictable rhythms (mean=4.18). This finding has implications both for the etiology and assessment of panic attacks and panic disorder.

References:

[1]Halaris, A. Chronobiology and Psychiatric Disorders. New York: Elsevier. 1987.

[2]Margraf, J., Taylor, C.B., Ehlers, A., Roth, W.T., and Agras, W.S. Panic Attacks in the Natural Environment. *The Journal of Nervous and Mental Disease,* 175, 558–565. 1987.

NR91 **Tuesday, May 9 9:00 a.m.–10:30 a.m.**

CORTISOL, PROLACTIN AND LACTATE-INDUCED PANIC

Eric Hollander, M.D., Psychiatry, Columbia University, 722 West 168th Street Box 13, New York, NY 10032; Michael R. Liebowitz, M.D., Franklin Schneier, M.D., Laszlo Papp, M.D., Gregory Dalack, M.D., Donald F. Klein, M.D.

Educational Objectives:

To discuss differences in the neuroendocrine response to panic and anticipatory anxiety in panic disorder patients and normal controls. To contrast controls, nonpanickers, and early and late lactate-induced panickers at baseline and during sodium lactate infusion.

Summary:

Sodium lactate infusions reliably induce panic attacks in panic disorder patients but not in normal controls by an unknown mechanism. We measured plasma cortisol and prolactin at baseline and in response to infusion of 0.5 molar sodium lactate in 103 panic disorder patients and 32 normal controls.

Patients who panic after 15 minutes of lactate infusion (late panickers) had significantly higher baseline cortisol levels compared to controls, nonpanickers, and early panickers ($F=9.32$, $p=.003$). In addition, most late panickers manifest a rise in cortisol during the baseline period. In contrast, early panickers have significantly greater somatic distress at baseline, as measured by Acute Panic Inventory. There was no cortisol rise with lactate induced panic. Cortisol elevation occurs with moderate (or anticipatory) anxiety, but not with severe panic anxiety.

Male panickers had significantly elevated baseline prolactin levels, which suppports a role for prolcatin in anticipatory anxiety. Prolactin levels increased in all groups during lactate infusion, which may reflect osmotic effects, but were blunted in late panickers compared to other groups ($F=3.48$, $p=.02$), suggesting a net diminuation of prolactin response in panic anxiety.

Activation of the HPA axis and of neuromodulators with release of cortisol and prolactin do not appear to mediate lactate induced panic. However, activation of these systems may mediate anticipatory anxiety, and suggest differences between early and late panickers.

References:

[1]Hollander E, Liebowitz MR, Cohen B, et al: Cortisol and sodium lactate-induced panic. *Arch Gen Psychiatry* (in press).

[2]Hollander E. Liebowitz MR, Cohen B, et al: Prolactin and sodium lactate-induced panic. *Psych Research* (in press).

NR92 **Tuesday, May 9 9:00 a.m.–10:30 a.m.**

ANXIETY DISORDERS IN FAMILIES OF INHIBITED CHILDREN

Jerrold F. Rosenbaum, M.D., Psychopharmacology, Mass General Hospital, 15 Parkman Street WACC 715, Boston, MA 02114; Joseph Biederman, M.D., Dina R. Hirschfeld, B.A., Jerome Kagan, Ph.D.

Educational Objectives:

Recent research and new data on the link between "behavioral inhibition to the unfamiliar" in children and risk for development of anxiety disorders will be presented. This work offers the possibility of early identification and intervention for children at risk for developing anxiety disorders.

Summary:

To test the hypothesis that behavioral inhibition to the unfamiliar (BI) is an early childhood marker or risk factor for the later development of panic disorder or other anxiety disorders, we have previously reported that children aged two to seven years with panic disorder (PD) and agoraphobia have higher rates of BI than controls and that the rates of psychiatric disorders, particularly anxiety disorders, are higher in the inhibited than in the noninhibited children of parents both with and without psychiatric disorder. We now report on a family study of parents and siblings of BI children ascertained from a nonclinical sample. Psychiatric assessments of parents and siblings of children originally identified at 21 months of age as inhibited (N=22) or uninhibited (N=19) were compared with those of a group of normal comparison children, based on structured interviews (DICA-P and DIS) conducted blindly to the classification of the index child. We have found that family members of an inhibited child had significantly higher rates of social phobia (parents), overanxious disorder (siblings, and parents when children), and a history in the parents of both childhood and adult anxiety disorder. These findings provide further evidence of a link between childhood behavioral inhibition and risk for developing anxiety disorders.

References:

[1]Rosenbaum JF, Biederman J, Gersten M, et al: Behavioral Inhibition in Children of Parents.

[2]Kagan J, Rexnick JS, Snidman N: The Biological Basis of Shyness. Science 240:167–171. 1988.

NR93 **Tuesday, May 9 9:00 a.m.–10:30 a.m.**

DEVELOPMENTAL ANTECEDENTS OF OCD

Margaret Klitzke, D.O., Butler Hospital, 345 Black Stone Blvd, Providence, RI 02906; Steven A. Rasmussen, M.D., Charles Zeanah, M.D., Daniel Stern, M.D.

Educational Objectives:

To define the developmental antecedents of obsessive compulsive disorders in order to identify children at risk and discuss possible preventative treatment strategies.

Summary:

Childhood personality traits associated with behavioral inhibition have been shown to be more common in the offspring of probands with panic disorder and agraphobia than in the offspring of age and sex-matched controls. There has been no recent study of the developmental antecedents of obsessive-compulsive disorder. We have systematically gathered developmental histories, with special attention to personality features, from ages three to 12 from 92 OC probands and their relatives. Each proband completed a semistructured interview developed by the authors that was designed to elicit the presence or absence of 18 different childhood personality traits. Mean age of the probands at interview was 28.1 ± 7.7. There were no significant differences in demographics, clinical features, and course of illness between this group of probands than of 250 probands previously described by our group. Nine personality traits were found to be present in over half the sample including: risk aversion (52 percent), separation anxiety (56 percent), resistant to change or difficulty with novelty (72 percent), hypermorality (62 percent), and perfectionism (82 percent). These were two distinct clusters of traits, those associated with behavioral inhibition and those associated with completeness or perfection. A 30 item observer rated scale with anchor points (Kiddie Brown Obsessive Compulsive Scale (KBOCS) has been developed on the basis of our retrospective study. Preliminary data from a prospective study of the offspring of OCD probands using this scale will be presented. The further characterization of these childhood antecedents of OCD is important in order to identify children at risk as well as for developing preventive treatment strategies.

Reference:

[1]Rosenbaum, J.F., Biederman, J., Gershen, M., Hirschfield, D.R., Meninger, S.R., Herman, S.B., Kagan, J., Resmick, J.S., Snidman, N. Behavioral Inhibition in Children of Parents with Panic Disorders and Agoraphobia. *Arch. Gen. Psych.* 45:463–471 1988.

NR94 **Tuesday, May 9 9:00 a.m.–10:30 a.m.**

PHENELZINE AND ATENOLOL IN SOCIAL PHOBIA

Franklin R. Schneier M.D., Psychiatry, NY State Psych Inst., 722 West 168th St. Box 13, New York, NY 10032; Jack M. Gorman, M.D., Eric Hollander, M.D., Raphael Campeas, M.D., Michael R. Liebowitz, M.D.

Educational Objectives:

To present findings comparing the efficacy of phenelzine, atenolol and placebo in the treatment of social phobia, and to discuss implications for the pharmacotherapy of social phobia.

Summary:

Sixty-seven patients meeting DSM-III criteria for social phobia completed eight weeks of double-blind randomized treatment with the monoamine oxidase inhibitor phenelzine, the cardioselective beta-adrenergic blocker atenolol, or placebo. After eight weeks of treatment, 67 percent of patients on phenelzine demonstrated moderate or marked improvement, compared to 33 percent on atenolol and 24 percent on placebo. Phenelzine was significantly more effective than atenolol or placebo, but efficacy of atenolol and placebo did not differ significantly.

Patients who were rated moderate or marked responders after eight weeks continued on the same treatment in double-blind fashion during a 16-week maintenance phase. Nineteen (86 percent) of these 22 responders at week 8 maintained their response at week 24.

Patients were also prospectively divided into generalized (n=50) and discrete (n=17) subtypes of social phobia. Within the generalized subtype, rate of response to phenelzine (72 percent) was significantly superior to atenolol (29 percent) or placebo (22 percent). Within the discrete subtype there were no significant differences in rates of response to phenelzine (50 percent), atenolol (50 percent) or placebo (40 percent).

Phenelzine appears to be an effective treatment for social phobia, particularly for the generalized subtype.

References:

[1]Liebowitz MR, Gorman JM, Fyer AJ, Campeas R, et al: Pharmacotherapy of social phobia: An interim report of a placebo-controlled comparison of phenelzine and atenolol. J. Clin Psychiatry 1988;49:252–257.

[2]Liebowitz MR, Gorman JM, Fyer AJ, Klein, DF: Social phobia: Review of a neglected anxiety disorder. Archives of General Psychiatry 1985;42:729–736.

NR95 **Tuesday, May 9 12 noon–2:00 p.m.**

FRONTAL HYPOPERFUSION IN DRUG NAIVE SCHIZOPHRENICS

Jorg Pahl, M.D., Univ of Iowa Coll of Med, 500 Newton Road, Iowa City, IA 52242; Nancy C. Andreasen, M.D., Greg A. Cohen, M.S., K. Rezai, M.D., P.K. Kirchner, M.D.

Summary:

Ingvar and Franzen were the first to document reduced cerebral blood flow (CBF) in the frontal lobes of chronic schizophrenics during resting conditions using the Xenon-133 cortical probe method. The finding of "hypofrontality" has remained controversial, however, primarily for methodological reasons. Of central concern has been the drug status of patients. Most imaging protocols have scanned patients while on medications or in the drug-free but not drug-naive state.

Regional cerebral perfusion (rCP) was measured with a Gamma SPECT camera and [I^{123}] Iodoamphetamine (IMP) in 11 neuroleptic-naive DSM-III diagnosed schizophrenics (age=33.6±11.1; disease duration=8.45±12.0, [mean±S.D.]) and 14 normal controls (age=31.9±6.1) during a resting baseline state (eyes and ears open state). Regions of interest (ROI) were defined for 12 cortical and subcortical areas: left and right superior, middle and inferior frontal corticies, tempero-parietal cortex, basal ganglia, and cerebellum. Cerebral perfusion values are reported here as ROI/cerebellum ratios. The data were analyzed for significance with the Mann-Whitney two-tailed t-test.

Significantly decreased resting cerebral perfusion values were detected in both frontal lobes in the drug-naive schizophrenics. The other cortical regions and the basal ganglia demonstrated normal blood flow patterns.

Our findings are consistent with previous Xenon-133 cortical probe CBF data showing "hypofrontality." The data are, however, still considered quite preliminary for a number of methodological reasons. First, ROIs were defined on the functional SPECT study rather than on high resolution MRI images. Transcription of MRI defined ROIs to corresponding SPECT scans would result in improved anatomical localization of brain regions. Second, the relative (ROI/reference structure) cerebral perfusion ratios reported here use the cerebellum as denominator. The use of such a ratio would clearly be inaccurate if the cerebellum were affected functionally in schizophrenia. Lastly, the small number of drug-naive subjects (n=11) preclude the evaluation of correlations between symptoms and flow patterns.

NR96 **Tuesday, May 9 12 noon–2:00 p.m.**

LACK OF VENTRICULOMEGALY BY MRI IN SCHIZOPHRENIA

Stephen C. Olson, M.D., Psychiatry, Ohio State University, Rm 065 Upham Hall 473 W 12th, Columbus, OH 43210; Jeffrey A. Coffman, M.D., Steven B. Schwarzkopf, M.D., Judy A. McLauglin, M.S., Henry A. Nasrallah, M.D.

Summary:

Despite more than a decade of research first using CT and now magnetic resonance imaging (MRI) to elucidate the nature of structural brain abnormalities in schizophrenia, the issue is far from resolved. Kelsoe et al (1988) utilized the multiplanar capability of MRI to demonstrate that ventriculomegaly is more apparent in coronal slices in the posterior region of the lateral ventricle than in the anterior horns. We report here results of a similar study in male schizophrenics compared to controls.

DSM-III-R diagnoses of schizophrenia (SZ) were made based on all available data, including structured interview and medical records. Subjects were 18–50 years of age and were excluded for significant substance abuse, neurologic disease, head injury, or metallic implants. Controls (CTL) were recruited from the community by advertisement and had no personal history of psychiatric disorder by SCID-R interview. MR images were acquired using a GE 1.5 tesla system with inversion recovery imaging parameters. Area measurements of the ventricles and cerebrum were made on five coronal cuts 5 mm thick: two cuts through anterior horns, and three cuts at the splenium corresponding to the region found by Kelsoe et al to show the maximal increase in ventricle area.

No differences were found in any measure of ventricular area or ventricle-brain ratio (VBR) between SZ (n=35) and CTL (n=14) males. Mean$\pm$SD VBR averaged across all slices was 3.11$\pm$1.6 percent in SZ and 3.05$\pm$1.3 percent in CTL groups. Ventricular area in each cut was nearly identical in both groups, and exhibited the same pattern observed by Kelsoe, i.e., posterior VBR $>$ anterior. It appears that our control group has larger VBR than the hospital employee group reported by Kelsoe, suggesting that this is the source of the discrepancy between the two studies. Another source of difference may have been that our SZ group were largely outpatients stable enough to complete electrophysiologic and neuropsychological testing.

Methodological issues in the design of imaging studies in schizophrenia will be discussed in relation to these findings.

NR97 **Tuesday, May 9 12 noon–2:00 p.m.**

FRONTAL LOBE SIZE IN SCHIZOPHRENICS BY MRI

Anand K. Pandurangi, M.D., Psychiatry, Medical College VA, Box 170 MCV Station, Richmond, VA 23298; Anthony L. Pelonero, M.D., Jay M. Otero, B.S., Lyn Nadel, M.D., Jae Y. Lee, B.A.

Summary:

Magnetic resonance imaging of the brain reveals gross anatomic information previously obtainable by postmortem examination. Reduced frontal and cranial size was reported in schizophrenics by MRI (1). If replicated this could provide major support for a neurodevelopmental theory of schizophrenia advanced recently (2).

We present findings of a study of MRI in schizophrenics. Unlike previous studies, extensive scanning was performed in the coronal and saggital planes (multiecho, 12–15 slices each). Thirty subjects with schizophrenia by RDC prospectively underwent MRI. Fifteen patients with headache/dizziness scanned in a comparable fashion were used as controls. Outlines of the left and right frontal lobes are traced on every coronal slice. Maximum width of the inner table of the skull is measured. Three indices of frontal lobe size are calculated; (a) maximum width of the frontal lobe (b) area of the biggest slice of frontal lobe and (c) volume of the three biggest slices. High interrator reliability has been established for these measures. Blind measurements have so far been completed for ten subjects and ten controls by two raters for each tracing.

Mean age of subjects is 29 years. There are five males and five females in each group. Until now there is no significant difference in frontal lobe size between schizophrenics (Sch) and controls (Cntrl). Mean max frontal width: Sch = 13.30 cms, Cntrl = 12.38 cms; Mean area of biggest slice of frontal lobe: Left, Sch = 34.65 sq cms, Cntrl = 35.14 sq cms; Right, Sch = 36.09 sq cms, Cntrl = 36.01 sq cms; Mean volume (three slices): left, Sch = 64.65 cc, Cntrol = 60.98 cc, Right, Sch = 62.80, Cntrl = 62.15 cc. Data on all subjects will reduce the possibility of a type II error and will be presented. The use of MRI for detailed in-vivo examination of gross anatomy in schizophrenics and the implications of negative findings in this study will be discussed.

NR98 **Tuesday, May 9 12 noon–2:00 p.m.**

SUICIDAL BEHAVIOR IN SCHIZOPHRENIA

Gretchen L. Haas, Ph.D., Psychiatry, Payne Whitney Clinic,
525 East 68th Street, New York, NY 10021; John Lauriello, M.D., Lisa Dixon, M.D., Margaret Rea, Ph.D., John Sweeney, Ph.D., Peter Weiden, M.D.

Summary:

Although as many as 10 to 15 percent of schizophrenic patients die by suicide, there is a gross clinical underrecognition of suicide risk in schizophrenia—in part because little is known about the predictors of suicide in this population. Study aims were to: (1) assess incidence of serious suicidal behavior in a sample of consecutive admission schizophrenic disorder patients, and (2) identify clinical and psychosocial correlates of serious suicidal behavior.
METHODS: Study 1. Chart review of 321 consecutive admission DSM-III-R schizophrenic disorder patients was conducted to assess report of serious suicidal ideation/behavior at time of hospitalization. *Study 2.* Follow-up interviews were conducted with 65 DSM-III-R (SCID) Schizophrenic Disorder patients to assess incidence and lethality of suicidal behavior, symptomatology, and psychosocial functioning. Data on family attitudes (Expressed Emotion) and interpersonal communication in a problem-solving task were also available for a subset ($n = 20$) of cases. *RESULTS: Study 1.* Serious suicidal ideation and/or attempts were documented at admission to hospital in 38 percent of cases. *Study 2.* Follow-up interviews revealed that 26 percent of cases had history of serious suicidal behavior during three years prior to interview. Substance abuse was common at time of suicide attempts—more common than at time of suicidal ideation ($p < .05$). Lifetime history of drug abuse ($p < .03$), and family history of psychiatric treatment ($p < .005$) were more common among attempters than non-suicidal patients. Interpersonal problem-solving deficits were also associated with occurrence of lethal attempts ($r = .51$, $p < .04$). *SIGNIFICANCE:* Suicidal behavior is common among schizophrenic patients and serious suicidal behavior may be associated with such factors as substance abuse, problem-solving deficits, and family history variables.

NR99 **Tuesday, May 9 12 noon–2:00 p.m.**

NEUROENDOCRINE EFFECTS OF CLOZAPINE IN SCHIZOPHRENIA

Carmen Z. Lemus, M.D., Research, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004; Jeffrey A. Lieberman, M.D., Celeste A. Johns, M.D., Simcha Pollack, Ph.D., Bruce L. Saltz, M.D.

Summary:

Clozapine is a neuroleptic considered atypical on the basis of its low incidence of extrapyramidal side effects and its proven efficacy in the management of treatment-refractory schizophrenic patients. In contrast to typical antipsychotics, clozapine does not produce sustained hyperprolactinemia.

One of the neurochemical mechanisms proposed to explain clozapine's unique profile is a combined effect on both dopamine and serotonin.

We studied two groups of chronic schizophrenic patients. They were all physically healthy. None had a history of endocrinopathy and all were alcohol and drug-free for at least six months. They underwent a two to four week medication wash-out period prior to clozapine treatment. One group (15 subjects, mean age 30.3 years, 80 percent male) had blood samples collected weekly for prolactin and cortisol levels, starting on the last week of drug wash-out through the first six weeks of clozapine treatment. The second group (14 subjects, mean age 27.8 years, 80 percent male), in addition to weekly blood collections, received an acute haloperidol challenge (0.07 mg/kg I.V.) while drug-free and after five weeks of clozapine treatment. When compared to a control group of schizophrenic patients treated with fluphenazine, preliminary results indicate that chronic clozapine treatment does not significantly elevate prolactin levels but does alter pituitary lactotroph response to an acute haloperidol challenge. These results will be discussed, focusing on the possible actions of clozapine on the serotonergic and dopaminergic systems.

NR100 **Tuesday, May 9 12 noon–2:00 p.m.**

CHOLINERGIC EXCESS AND NEGATIVE SCHIZOPHRENIA

Rajiv Tandon, M.D., Psychiatry, Univ of Mich Med Center, 1500 E. Med Ctr Dr UH 9C9150, Ann Arbor, MI 48109; Kenneth R. Silk, M.D., James E. Shipley, M.D., John F. Grenden, M.D.

Summary:

Although negative schizophrenic symptoms represent the most debilitating and treatment-refractory aspect of schizophrenic psychopathology, their pathophysiological basis remains obscure. While several mechanisms have been implicated in the production of negative symptoms, a satisfactory model of negative schizophrenic symptoms has still to be developed. Based on the phenomenological similarity between the behavioral profile of physostigmine infusion in humans and the negative syndrome, preliminary reports of improvement in negative symptoms with anticholinergic agents, and other related findings, increased central cholinergic activity has been proposed as a mechanism in the production of negative schizophrenic symptoms.[1] To further study the role of cholinergic mechanisms in schizophrenia, we studied the sleep EEG of 15 medication-free schizophrenic patients (SADS-RDC and DSM-III-R) and analyzed the sleep findings in relationship to ratings of positive, negative, and depressive symptoms and global severity of illness. Since central cholinergic mechanisms significantly influence REM latency and minutes of slow-wave sleep (SWS), these were used as measures of cholinergic activity. Decreased REM latency and reduced SWS (both suggestive of increased cholinergic activity) were both found to be significantly associated (p 0.01) with the severity of negative symptoms, but not with any other clinical parameter. These data provide support for the implication of cholinergic hyperactivity in the production of negative schizophrenic symptoms.

[1]Tandon R, Greden JF: Cholinergic hyperactivity and negative schizophrenic symptoms: a model of dopaminergic/cholinergic interactions in schizophrenia. Arch. Gen. Psychiatry. In press, 1988.

NR101 **Tuesday, May 9 12 noon–2:00 p.m.** **NEGATIVE SYMPTOMS: RELATIONSHIP TO FAMILY HISTORY**

Frederic J. Sautter, Ph.D., Psychiatry, Tulane Univ Medical Ctr., 1430 Tulane Avenue, New Orleans, LA 70112; Barbara E. McDermott, Ph.D., David L. Garver, M.D.

Summary:

A preliminary way of identifying some of thse factors that influence the evolution of negative symptoms is to differentiate between patients with and without a family history of schizophrenia and to compare them for differences in negative symptomatology. Families with familial schizophrenia may be used to study negative symptoms closely related to genetic etiology; families with nonfamilial (i.e. "sporadic") schizophrenia may be used to study environmental factors.

In this longitudinal study, the first degree relatives of 32 RDC schizophrenics were diagnosed using SAD-L procedures or the Family History Method. Patients were assigned either to a group with a family history ($n=14$) or without a family history ($n=18$) of schizophrenia. These two groups were then reevaluated for negative symptoms on four occasions over a two-year period. A one between, one within repeated measures ANOVA was performed using family history as the between factor, with time as the within factor. The results indicate that: (1) patients with familial schizophrenia show a higher level of negative symptoms than sporadics ($p<.06$), (2) negative symptoms changed over time ($p<.005$), and (3) time and family history show a significant interaction ($p<.02$) indicating that negative symptoms change over time in familial schizophrenics and remain stable in sporadics. The data indicate that patients with familial schizophrenia show negative symptoms that are both more intense and less stable over time than negative symptoms seen in patients with a nonfamilial illness.

NR102 **Tuesday, May 9 12 noon–2:00 p.m.**

PREDICTING OUTCOME OF SCHIZOPHRENIA: NEW FINDINGS

Stanley R. Kay, Ph.D., Psychiatry, Albert Einstein Col Med, Bronx Psy Ctr 1500 Waters Pl, Bronx NY 10461; Lisa M. Murrill, M.A.

Summary:

Psychiatric hospitals are increasingly populated by chronic refractory patients who cannot be transitioned to community living. To clarify the antecedents of poor long-term outcome in schizophrenia, we followed up 58 DSM-III diagnosed schizophrenic inpatients, mostly chronic, for one–four years (M = 2.7). The group was prospectively assessed on psychopathology and syndrome scales and on psychiatric and family history. At followup, the 46 patients (79.3 percent) who could be relocated were measured on the Strauss-Carpenter Multidimensional Outcome Scale and days of subsequent hospitalization.

The results indicated that, contrary to popular assumption, a baseline negative syndrome was unrelated to later outcome. A baseline positive syndrome, however, carried ominous implications for followup quantity of useful work, fullness of life, and continuous hospitalization. Whereas the "thought disturbance" cluster predicted the poorest outcome, the baseline "depression" cluster forecasted significantly better occupational adjustment, self-care, and fullness of life. Multiple regression and analysis revealed that (a) nine of the ten outcome measures could be reliably predicted by combinations of three–five baseline variables (R's from .49 to .61); (b) clinical, genealogical, and historical dimensions separately contributed to outcome prediction; and (c) different sets of variables predicted social vs. occupational adjustment. The findings carry implications toward prognosis, selection for rehabilitation programs, and understanding the basis for successful outcome in schizophrenia.

NR103 **Tuesday, May 9 12 noon–2:00 p.m.**

DIFFERENTIATING NEGATIVE AND DEFICIT SYMPTOMS

Barbara E. McDermott, Ph.D., Psychiatry, Tulane Univ Medical Ctr., 1430 Tulane Avenue, New Orleans, LA 70112; Frederic J. Sautter, Ph.D.

Summary:

It has been proposed that the negative syndrome of schizophrenia be reconceptualized as consisting of two separate types of symptoms: deficit and negative symptoms. Negative symptoms may be secondary to pharmacologic and psychological factors and are transitory in nature; deficit symptoms are primary enduring symptoms that result from the interaction of unremitting negative symptoms. If the distinction between negative symptoms and the deficit state is valid, a different pattern of predictors should emerge for each one. To determine if this was true, a variety of instruments were administered to 60 DSM-III schizophrenic-spectrum disorder patients, including measures of negative symptoms, the deficit state, and self- regulation variables. The results of multiple regression analysis revealed that a combination of negative symptoms, positive symptoms, length of illness, and a perceived inability to effectively manage social situations contributed to the deficit state (R^2= .5121, $F_{(4,54)}$ = 14.17, p– .0001). In contrast, education, medication, length of illness, and an inability to manage positive symptoms predicted negative symptoms (R^2= .2711, $F_{(4,54)}$ = 5.02, p– .01). The results of this study strongly support the construct validity of Carpenter's reconceptualization of negative symptoms. These results also indicate that psychosocial treatments may be useful in ameliorating some of the detrimental effects of these syndromes.

NR104 **Tuesday, May 9 12 noon–2:00 p.m.**

SCHIZOPHRENIA AND CORRELATES OF FAMILY ATTITUDES

Eugenia T. Randolph, Ph.D., Research, Brentwood VAMC, 11301 Wilshire Boulevard B151J, Los Angeles, CA 90073; Shirley M. Glynn, Ph.D., Spencer Eth, M.D., Andrew L. Shaner, M.D., Walter B. Van Vort, M.D., Denise H. Paz, Ph.D.

Summary:

Studies of family attitudes have provided some insights into the problems of living with a schizophrenic relative. Falloon et al (1984), in a study of 36 families with a schizophrenic member, found that a large proportion of the families were experiencing significant stress. Kreisman et al (1988) reported that negative family attitudes, especially rejection, were found to predict time to relapse in patients on low dose medication. The present study examined the relation of family attitudes, psychological distress, and patient functioning in a sample of 35 patients with DSM-III diagnoses of schizophrenia. Family factors were assessed with the Social Adjustment Scale: Family Version (SAS III), Patient Rejection Scale, and the SCL-90. Patient functioning was assessed with the BPRS and Social Adjustment Scale: Patient Version (SAS II). Two components of family attitudes emerged. *Attitudes of rejection* toward the patient were significantly correlated with BPRS total score. More symptomatic patients had relatives with stronger attitudes of rejection (r=.43). *Family subjective burden* was not related to BPRS ratings or social functioning as measured on the SAS II. However, family members reporting more burden reviewed their ill relatives as more impaired (r=.49). These family members also exhibited significantly more symptoms of psychological distress as measured on the SCL-90 and were rated by the interviewer as having made a poorer adjustment to patient needs and behavior (r=.38). Rejection and subjective burden were not significantly related suggesting that they may be independent expressions of family stress. These findings suggest that in working with schizophrenic patients and their families it is important to monitor patients' symptoms and signs of family distress closely to minimize rejection and burden.

NR105 **Tuesday, May 9 12 noon–2:00 p.m.**

HYPOPLASIA OF VERMAL LOBULES VI AND VII IN SCHIZOPHRENIA

Henry A. Nasrallah, M.D., Psychiatry, Ohio State University, 473 W. 12th Avenue, Columbus, OH 43210; Stephen B. Schwarzkopf, M.D., Jeffrey A. Coffman, M.D., Stephen C. Olson, M.D.

Summary:

Introduction: Several CT studies of the cerebellum in schizophrenia have suggested evidence of vermal "atrophy." The significance of this finding has remained obscure. More recently, pregnancy and delivery complications (which tend to occur with a higher frequency in schizophrenia) have been increasingly implicated as important factors in enlarged cerebral ventricles. A recent report of hypoplasia of a developmentally specific cerebellar vermal region (lobules VI and VII in autism (Courchesne et al, 1988) prompted us to hypothesize that schizophrenic subjects with history of perinatal brain insult should have smaller cerebellar vermal lobules VI and VII compared to schizophrenic subjects with no history of perinatal complications. *Methods:* Thirty schizophrenic males (DSM-III-R) consented to participate in the study. MRI scans were done on a 1.5 Tesla scanner, using a T_1-weighted pulse sequence. Perinatal complications were obtained using a structured interview with the patients' mothers. The patients were divided into 13 perinatally "damaged" and 17 "undamaged" subjects. The midsagittal MRI scan was used to trace and digitally measure the areas of three vermal regions of the cerebellum; lobules I-V, lobules VI and VII, and lobules VIII to X. The data were analyzed with one-tailed t-test. *Results:* The perinatally "damaged" schizophrenics had significantly smaller lobules VI and VII ($2.75 \pm .50$) than in the undamaged group (3.33 ± 1.15) ($p=.041$). The other lobules were not different between the groups. *Discussion:* The results suggest that perinatal injury in schizophrenia may selectively impair vermal lobules VI and VII. Perinatal events that interrupt Purkinje cell migration to the posterior vermis may also disrupt neurogenesis in the hippocampus and amygdala which have been reported to be hypoplastic in schizophrenia.

NR106 **Tuesday, May 9 12 noon–2:00 p.m.**

REMOXIPRIDE IN SCHIZOPHRENIA: A HALOPERIDOL CONTROLLED MULTICENTRE DOUBLE-BLIND DOSE-FINDING CLINICAL TRIAL

Yvon D. Lapierre, M.D., Research, Royal Ottawa, 1145 Carling Avenue, Ottawa Ontario, Canada K1Z 7K4

Summary:

Remoxipride is a selective dopamine D2-receptor blocking agent with virtually no effect in vitro on dopamine D1-receptors or on a series of other neurotransmitters receptors (e.g. adrenergic, cholinergic, histaminergic, serotoninergic) in brain tissue. Furthermore, remoxipride shows in animal studies selective action for limbic areas compared to striatum. Accordingly, it is hypothesized that a compound with the pharmacological profile of remoxipride would be less likely than classical neuroleptics to produce side effects including those that are extrapyramidal. *Method:* A multicenter dose-finding clinical trial was conducted wherein three nonoverlapping dose ranges of remoxipride (30–90 mgs., 120–240 mgs., and 300–600 mgs. daily) were compared over six weeks in hospitalized acutely ill schizophrenic patients. The study design included an active control group treated with haloperidol in doses of 15 to 45 mgs. daily. *Results:* 204 patients contributed data to the main efficacy analyses. Assessment of change based on BPRS scores (baseline versus last valid evaluation) OGI of severity of illness and NOSIE revealed either significant or strong trends in favor of REM 120–240, REM 300–600 and haloperidol over REM 30–90. Furthermore, in the analysis of the BPRS subscale reflecting negative symptoms, significant (P=.043) between-drug differences were observed between REM 120–240 versus haloperidol in favor of remoxipride while a trend (P=.07) was observed in favor of REM 300–600 over haloperidol. Finally, treatment emergent extrapyramidal checklist symptoms were significantly more frequent and more severe in the haloperidol group then in any of the three remoxipride groups. Also haloperidol treated patients required significantly greater usage of anticholinergic medication than remoxipride treated patients. *Discussion:* This study's results provide evidence that remoxipride is an effective therapeutic agent for the treatment of patients in the acute phase of schizophrenia and may offer significant overall therapeutic advantages by inducing significantly less side effects than drugs such as haloperidol, particularly extrapyramidal symptoms.

NR107 **Tuesday, May 9 12 noon–2:00 p.m.**

AUTOANTIBODIES AND SCHIZOPHRENIA

Anthony L. Pelonero, M.D., Psychiatry, Medical College of VA, Box 710 MCV Station, Richmond, VA 23298; Anand K. Pandurangi, M.D., Vincent P. Calabrese, M.D.

Summary:

Reports on autoantibodies in persons with schizophrenia are contradictory. Many previous studies have utilized homogenate brain and the less sensitive immunofluorescence and complement-fixing techniques to detect antibrain antibody. The Enzyme-Linked Immunosorbent Assay is a well-established procedure which can detect small amounts of antibody and antibody which would not be detected by other tests. We report a study of IgG autoantibodies in schizophrenics and matched controls to two brain antigens: GM-1 ganglioside, a synaptosome marker, and cerebroside, a neuronal membrane marker.

Serum was collected from 38 patients with a research diagnosis of schizophrenia (DSM-III-R). Twenty-two healthy controls were screened using a modified SADS-L to rule out psychiatric morbidity and matched for age, sex, and race. All patients and controls were free of medical illness. The 38 subjects' mean age was 30 years, 27 male and 11 females. Mean duration of illness was 8.7 years. Subjects were on neuroleptics at the time of blood drawing. An indirect ELISA method was used to determine concentration of antibody bound to antigen and measured by a Flow Multiskan ELISA Reader. Serum was also tested in "blank" culture media for laboratory control.

Results show no significant differences between subjects and controls. Implications of testing specific brain antigens vs. homogenate brain will be discussed.

NR108 **Tuesday, May 9 12 noon–2:00 p.m.**

NEW VIEWS ON AMINE METABOLITIES IN SCHIZOPHRENIA

P. Eric Konicki, M.D., NSB, NIMH Bldg10 RM 4N212, 9000 Rockville Pike, Bethesda MD 20892; Alan Breier, M.D., ALlen R. Doran, M.D., Owen M. Wolkowitz, M.D., Carlos N. Pato, M.D., David Pickar, M.D.

Summary:

Disturbances of CNS dopaminergic function have been putatively associated with psychosis in schizophrenia. This study examines the relationship between cerebrospinal fluid (CSF) and plasma amine metabolites and clinical phenomenology. Twenty-two medication-free schizophrenics and thirty-three normal controls underwent inpatient lumbar puncture. Patients were diagnosed by DSM-III criteria and rated blindly. Metabolites were assayed by high pressure liquid chromatography. CSF HVA/5-HIAA ratio was significantly ($p < .05$) lower in male schizophrenics as compared to male controls. Moreover, CSF HVA was lowest in the most symptomatic patients. These data might be consistent with emerging evidence suggesting diminished dopaminergic function in distinct brain regions in schizophrenic patients. Stepwise multiple regression analysis revealed that both CSF and plasma HVA correlated with global psychosis ratings and positive symptom measures. Plasma HVA levels appear to provide clinically relevant information about dopamine metabolism that complement CSF measurements. These data are presented in the context of a dynamic model of dopaminergic function in schizophrenia which invokes differential involvement of several dopaminergic systems in the genesis of psychotic symptoms.

NR109 **Tuesday, May 9 12 noon–2:00 p.m.**

NEGATIVE SYMPTOMS IN EARLY PHASE OF SCHIZOPHRENIA

Joseph Ventura, M.A., Psychiatry, UCLA NPI, 760 Westwood Plaza Box 18, Los Angeles, CA 90024; Keith H. Nuechterlein, Ph.D., Michael Green, Ph.D., Jim Mintz, Ph.D.

Summary:

Frequency and course of negative symptoms in the early phase of schizophrenia are virtually undocumented. Symptom ratings were obtained on the Brief Psychiatric Rating Scale every two weeks for at least one year for 55 recent-onset RDC schizophrenic outpatients. Based on outpatient symptoms: (1) 22 (40 percent) had episodes of positive symptoms and relatively few negative symptoms, (2) three (5 percent) had periods of negative symptoms and relatively few positive symptoms, (3) 13 (24 percent) had both positive and negative symptom periods, (4) 11 (20 percent) had neither as prominent features. To examine temporal relationships in symptom onset, negative symptoms of mild severity were included, increasing the number in the category of mixed positive and negative symptoms to 29. Six times periods were defined in relationship to the psychotic onsets, e.g., prodromal, concurrent, post-psychotic, etc. The expected frequency of negative symptom onsets occurring in each period based on the relative duration of the six time periods and the total number of negative symptom periods was found to differ from the observed frequency ($X^2 = 14.41$, $df = 5$, $p < .02$). Negative symptom onsets occurred with significantly higher frequency ($x^2 = 12.66$, $df = 1$, $p < .01$) simultaneously with positive symptom onset than expected by chance. The low number of expected negative symptom onsets in the concurrent period prompted an additional analysis utilizing the Poisson distribution with results again significant at $p < .02$.

These findings indicated that, in the early outpatient phases of schizophrenia, only 36 percent of patients showed prominent negative symptoms. The negative symptoms had their onset concurrently with psychotic symptoms to a disproportionate degree.

NR110 **Tuesday, May 9 12 noon–2:00 p.m.**

GATING AND HABITUATION IN SCHIZOPHRENIA

David L. Braff, M.D., Psychiatry, Univ of California, M-003, La Jolla, CA 92093; Mark A. Geyer, Ph.D., Robert W. Butler, Ph.D., Robert S. Mansbach, Ph.D., Neal Swerdlow, M.D., Christian Grillon, Ph.D.

Summary:

The startle response (SR) is a cross-species reflex reaction to strong sounds (eg, 116dB(A)0 or to tactile stimuli (eg, strong air-puffs). The SR is measured in humans by monitoring the eye blink reflex; in rats, the SR is measured by monitoring whole body startle. The utility of the SR in human research stems from its plasticity: 1) If preceeded by a weak prepulse, the SR is "gated" or inhibited. This prepulse inhibition (PPI) reflects CNS inhibition or sensorimotor gating. This inhibition is deficient in some schizophrenic patients and in rats with nucleus accumbens dopamine overactivity. The most common interpretation of deficient PPI is that it can lead to sensory overload and cognitive fragmentation in schizophrenic patients. 2) The SR also "habituates" or shows a decrement in amplitude over multiple trials. This habituation is also deficient in some schizophrenic patients and in rats treated with LSD or other 5HT agonists. The most common interpretation of deficient habituation is that it also leads to stimulus inundation and overload.

Over 50 schizophrenic and 50 normal control subjects have now been tested in a new electromyographic (EMG) blink reflex paradigm that assesses both SR gating and habituation. There is evidence that both gating and habituation are defective in schizophrenic patients and that the abnormalities in both processes occur selectively in certain chronic "Kraepelinian" subgroups. Data from this new, integrated paradigm offer important information about the neurobiology of schizophrenia.

NR111 **Tuesday, May 9, 12 noon–2:00 p.m.**

HYPOFRONTALITY, NEUROPSYCHOLOGY AND SCHIZOPHRENIA

David L. Braff, M.D., Psychiatry, Univ of California, M-003, La Jolla, CA 92093; Sidney Zisook, M.D., Munro Cullum, Ph.D., Robert Heaton, Ph.D., Lewis L. Judd, M.D., Igor Grant, M.D.

Summary:

Hypofrontality has long been invoked as a major factor in understanding schizophrenic psychopathology. Evidence of hypofrontality includes data from electrophysiological, brain imaging, and neuropsychological (eg, Wisconsin Card Sorting Test or WCST) methods. The WCST data have evoked considerable interest since the NIMH group have shown selective activation of the dorsolateral prefrontal cortex (DLPFC) during the WCST in normal subjects.

We have tested 40 chronic schizophrenic outpatients at the UCSD Schizophrenic Clinical Research Center (CRC) utilizing clinical, neurophysiological, MRI brain imaging, and an extensive neuropsychological battery, the expanded Halstead-Reitan Battery (HRB). These patients, mostly with normal MRIs, are on maintenance antipsychotic medications. While they show extensive deficits on complex learning and memory tasks, their WCST results are in the normal range compared to a matched group of normal control subjects and to normative data on over 400 normal subjects.

These results support the hypothesis that, while chronic, deteriorted "Kraepelinian" schizophrenic patients have abnormal WCST results, a chronic, outpatients schizophrenic sample has normal range WCST scores. The important implications of these data for understanding transient versus fixed frontal lobe dysfunctions in schizophrenia will be discussed.

NR112 **Tuesday, May 9, 12 noon–2:00 p.m.**

NEURAL IMPLANTS IN PARKINSON'S DISEASE: IMPLICATIONS FOR SCHIZOPHRENIA

Barry D. Jones, M.D., Research, Royal Ottawa Hosp., 1145 Carling Avenue, Ottawa, Ontario, Canada K1Z 7K4; Alain Labelle, M.D., David Grimes, M.D.

Summary:

Introduction: Schizophrenia and Parkinson's Disease are progressive illnesses that can present in treatment resistant forms. They both are related to disturbances of dopamine activity and both show some impairment of frontal lobe function in their symptomatology. Until recently patients suffering from the most severe forms of Parkinson's Disease had little hope for control of the progression of the disorder. Recently, microsurgical autografting of adrenal medullary tissue to the right caudate nucleus has been used to treat some of those with severe motor symptoms. Fetal substantia nigra and fetal adrenal medulla transplants have also been used. Initial results show some objective improvement of motor symptomatology of the patients treated with these procedures. Among temporary phenomena observed post-operatively, transient psychotic symptoms in a clear sensorium and decreased frontal cognitive deficit are most relevant to our understanding of schizophrenia. *Case Reports:* Two patients that underwent autograft of adrenal medullary transplant to their right caudate nucleus will be presented. They both experienced psychotic symptoms post-operatively that cleared after a few weeks. The appearance of these symptoms did not clearly associate in time with motor improvement or dyskinesias as might be expected from a nonspecific release of dopamine from the transplanted chromaffin cells. This fact combined with other patients showing improvement in frontal cognitive deficits after surgery suggests that the neurophysiology of both the therapeutic effects and side effects of implants in Parkinson's Disease is complex. *Conclusion:* We propose that future patients receiving neural implants for Parkinson's Disease be studied carefully to determine the quantity, quality, and time course of symptom change, both motor and cognitive-psychiatric. In this way we may improve our understanding of not only Parkinson's Disease but also schizophrenia and related psychiatric disorders.

NR113 **Tuesday, May 9, 12 noon–2:00 p.m.**

VENTRAL TEGMENTAL PATHOLOGY IN SCHIZOPHRENIA

Manuel F. Casanova, M.D., NIMH Neurosciences, Center at St. Elizabeth, 2700 Martin Luther King Ave SE, Washington, DC 20032; Thomas M. Hyde, M.D., Terry E. Goldberg, Ph.D., Daniel R. Weinberger, M.D., Joel E. Kleinman, M.D.

Summary:

The ventral tegmental area (VTA) is the major dopaminergic (DA) center responsible for innervation of the prefrontal cortex, striatum (especially nucleus accumbens and head of the caudate), and entorhinal cortex. All of the areas comprising the terminal fields of the VTA have been implicated in schizophrenia. Interestingly, both the distribution of DA terminals from the VTA and the recently described cytoarchitectural abnormalities of the entorhinal cortex in schizophrenic patients follow the same laminar distribution. Thus, the existence of VTA pathology could explain, in part, some of the abnormal findings previously described in schizophrenic patients. In order to examine this possibility, we studied serial coronal Nissl stained sections of the VTA at the level of the interpeduncular nucleus in seven schizophrenic patients and 13 controls, all from the Yakovlev collection. Using a computer image analysis system (LOATS), we found differences in neuronal cell area ($p = .0001$), shape (as determined from a Fourier expansion series) ($p = .01$) and orientation ($p = .07$) (as determined from the circular variance of its second phase angle) in the lateral VTA (parabrachialis pigmentosum) of schizophrenic patients as compared to controls. The abnormalities were greatest for the larger neuronal cell subpopulation, the same putative DA cells with cortical projects. The importance of this finding in terms of the dopaminergic hypothesis of schizophrenia will be discussed.

NR114 **Tuesday, May 9, 12 noon–2:00 p.m.**

CORRELATES OF PREFRONTAL ATROPHY IN SCHIZOPHRENIA

Jeffrey L. Peters, M.D., Psychiatry, VA Medical Center, Highland Drive, Pittsburgh, PA 15206; Jeffrey K. Yao, Ph.D., David Shaw, Ph.D., Thomas C. Neylan, M.D., Doris McAdam, R.N., Daniel P. van Kammen, M.D.

Summary:

Prior computed tomography (CT) and functional brain-imaging studies have shown changes in schizophrenia in the prefrontal cortex. In this study, 81 physically healthy, male schizophrenic patients (RDC and DSM III criteria) consented to a head CT scan without contrast, medication withdrawal, and lumbar punctures. Patients had a mean age of 39.4 +/ – 8.33 years and a mean duration of illness of 12.6 +/ – 7.48 years. Prefrontal atrophy (PFA) was scored in 0.5 increments from 0 to 3 (Doran et al., 1987) by rater blind to other information. Patients were maintained on a low monoamine, alcohol and caffeine restricted diet. CSF norepinephrine (NE), homovanillic acid (HVA), 3-methoxy-4-hydroxyphenylethylene glycol (MHPG) and 5-hydroxy-indoleacetic acid (5HIAA) were determined by HPLC with electrochemical detection from a L.P. performed in standard fashion at six weeks drug-free in stable patients. Preliminary data analysis show a mean PFA score of 1.25 (n = 81, S.D. = 0.72, range = 0 – 2.5). PFA correlates with age (r = 0.48, p 0.001) and duration of illness (r = 0.31, p 0.01). Twenty-two patients received a drug-free L.P. at six weeks while clinically stable. There was no correlation between PFA and CSF NE (n = 21, r = 0.11, p = NS), CSF HVA (n = 22, r = – 0.15, p = NS), CSF MHPG (n = 21, r = 0.10, p = NS), or CSF 5HIAA (n = 19, r = 0.25, p = NS). The relationship between PFA, other clinical variables, and other CT atrophy measures will be presented. This study fails to replicate the findings of other investigators.

NR115 **Tuesday, May 9, 12 noon–2:00 p.m.**

NEUROLEPTIC NONCOMPLIANCE IN SCHIZOPHRENIA

Peter Weiden, M.D., Payne Whitney Clinic, 525 East 68th Street, New York, NY 10021; Alan Manevitz, M.D., Lisa Dixon, M.D., Neal DeChillo, M.S.W., Bruce Rapkin, Ph.D., Allen J. Frances, M.D.

Summary:

Goals: Neuroleptic noncompliance is common and often limits prevention of relapse in schizophrenia. We have attempted to 1) identify the scope and course of outpatient neuroleptic noncompliance, and 2) assess factors associated with noncompliance. *Methods:* A cohort of 70 SCID-diagnosed DSM-III schizophrenic patients were retrospectively assessed for neuroleptic noncompliance and related phenomenon following discharge from an index hospitalization. Noncompliance was conservatively defined as a one week period of complete neuroleptic refusal during a three month interval. *Results:* Using survival curve estimates, 48 percent of patients become noncompliant within the first year (n = 65) and 74 percent within two years (n = 37). Within any three month interval, 30 to 40 percent of patients are noncompliant. The most prominent predictors of noncompliance were denial of illness (r = – .54, p<.0001) and stigma (r = – .41, p<.0001). Feeling "recovered" and no longer needing medication (r = – .30, p<02) and family ambivalence about neuroleptic (r = .29, p<.03) were also significant factors. Predictors of compliance included a good (perceived) doctor/patient relationship (r = .51, p<.0001), perception of ongoing symptom relief (r = .41, p<.0001), and perceived fear of relapse (r = .28, p<.02). *Significance:* Neuroleptic noncompliance is very common and is a "steady state" phenomena where outpatient compliance status goes back and forth. Stigma seems to be an important—and potentially treatable—predictor of noncompliance.

NR116 **Tuesday, May 9, 12 noon–2:00 p.m.**

WORK ADJUSTMENT AND SYMPTOMS OF SCHIZOPHRENIA

Shirley M. Glynn, Ph.D., UCLA Research, Camarillo St. Hospital, Box A, Camarillo, CA 93011; Eugenia T. Randolph, Ph.D., Spencer Eth, M.D., Gregory B. Leong, M.D., George G. Paz, M.D., Denise H. Paz, Ph.D.

Summary:

Research associating psychiatric symptoms with vocational functioning has yielded conflicting results. Many studies have found no relation, while others have established isolated associations between variables such as anxiety, thought disorder, or global psychopathology and work adjustment. We examined the prospective relation between psychiatric status at discharge and subsequent work functioning in 40 male veterans diagnosed with schizophrenia or schizoaffective disorder. Psychiatric symptoms were assessed using the Brief Psychiatric Rating Scale (BPRS) and the Scale for the Assessment of Negative Symptoms (SANS). Work adjustment was assessed one month post-discharge using patient reports of time spent working or in job searching activity, friction at work, and performance adequacy. Patient reports were corroborated with family members using the patient and family versions of the Social Adjustment Scale.

BPRS factor scores were unrelated to one-month work adjustment. However, the SANS global avolition and alogia items significantly predicted work adjustment ($\underline{rs} > -.36$)and number of hours worked/week ($\underline{rs} > -.39$) at one-month follow-up. Not surprisingly, negative symptoms at discharge were significantly associated with lack of desire for work at follow-up. The global SANS affective flattening, alogia, avolition, and attentional impairment items were all significantly related ($\underline{rs} > .33$) with lack of employment interest. These results suggest the need for a comprehensive assessment of negative symptoms when evaluating work capacity as well as for vocational programs which emphasize the development of motivation concurrent with job skills.

NR117 **Tuesday, May 9, 12 noon–2:00 p.m.**

EFFECTS OF THE D1 AGONIST SKF38393, COMBINED WITH HALOPERIDOL, IN SCHIZOPHRENIC PATIENTS: A PRELIMINARY REPORT

Michael Davidson, M.D., Psychiatry, Mt. Sinai Med School, One Gustave L. Levy P1 Box 1230, New York, NY 10029; Phil Harvey, Ph.D., Peter Powchik, M.D., Rami Kaminski, M.D., Linsey Bergman, B.S., Kenneth L. Davis, M.D.

Summary:

Recent elaboration of the dopamine hyphothesis in schizophrenia and result of cerebral blood flow (CBF) studies suggest hypoactive dopaminergic neurotransmission of frontocortical brain areas. Results of the CBF studies together with studies indicating increase receptor densities in subcortical brain areas and activate dopamine receptors in frontocortical areas. This effect can be best achieved by combining a selective D-2 antagonist with a selective D-1 agonist since in the frontal cortex D-1 rather than D-2 receptors are predominant. Patients who failed to respond to four weeks of treatment with 20mg haloperidol daily, were randomly and blindly assigned to SKF 38393, 250mg BID *combined* with haloperidol 20mg daily or placebo *combined* with haloperidol for a period of four weeks. During the following four weeks patients who received SKF 38393 and haloperidol were crossed over to placebo and haloperidol while patients who received placebo and haloperidol were crossed to SKF 38393 and haloperidol. Wisconsin Card Sort Test (WCST), a test reflective of prefrontal function was administered during treatment with SKF 38393.

To date, 4/9 patients who completed the study showed moderate clinical improvements and reductions in BPRS scores (ranging between 7 percent and 20 percent) which reversed when SKF 38393 was discontinued. 3/4 patient whose symptoms also showed improvements in WCST scores, similar to the symptomatic improvements of the WCST scores, reversed when the D-1 agonist drug was discontinued. Present efforts directed at increasing the sample size will help to establish if SKF 38393 has a role in the treatment of schizophrenia.

NR118 **Tuesday, May 9, 12 noon–2:00 p.m.**

CSF NPY IN SCHIZOPHRENIA

Daniel P. van Kammen, M.D., Chief of Staff, VA Medical Center, Highland Drive, Pittsburgh, PA 15206; Jeffrey L. Peters, M.D., Joel Gelernter, M.D., David Shaw, Ph.D., Thomas C. Neylan, M.D.

Summary:

Neuropeptide Y (NPY), a 36-aminopeptide, has recently been discovered in the CNS. NPY is co-released with norepinephrine from some monoadrenergic neurons as well as with somatostatin. We measured NPY with NPY specific antibody radioimmunoassay in the CSF of 35 male schizophrenic patients (DSM-III) with mean age of 34 ± 7.8 years and 10.5 ± 6.83 years of illness. They had been drug-free for at least two weeks. Thirty-one patients were withdrawn from chronic haloperidol treatment (12 ± 8.9 mg/day). Eleven patients relapsed and 19 did not within six weeks of placebo replacement. They received an LP within days of relapse or after having been drug-free for six weeks. CT scans of the brain were obtained. *Results:* CSF NPY correlated negatively with age and duration of illness. Haloperidol withdrawal was associated with a significant increase in CSF NPY ($p = 0.002$). CSF NPY was not significantly different between relapsers and nonrelapsers. Positive correlations with schizophrenic symptomatology were only observed in the nonrelapsers. CTR scan measures such as VBR, cerebellar atrophy, and sulcal widening correlated negatively with CSF NPY. The data suggest that CSF NPY is a stable trait marker in drug-free patients. The implications of these findings for a potential role of NPY in schizophrenia will be discussed.

NR119 **Tuesday, May 9, 12 noon–2:00 p.m.**

MANAGEMENT OF RISK OF RELAPSE IN SCHIZOPHRENIA

William C. Wirshing, M.D., Psychiatry, West LA BVAMC, Wilshire & Sawtelle Blvds, Los Angeles, CA 90073; Kathleen Johnston-Cronk, B.S., Stephen R. Marder, M.D., Robert P. Liberman, M.D., Than Ekman, Ph.D.

Summary:

Several recent studies have indicated that schizophrenic prodromal symptoms may 1) be valid and reliable markers for predicting subsequent relapse and 2) provide identifiable junctures to begin early neuroleptic intervention. In an ongoing prospective study of these factors, of 54 patients meeting DSM-III-R criteria for schizophrenia, 20 developed prodromes (as defined by pre-established and operationalized criteria) during two years of formalized evaluation. This cohort received low dose neuroleptics (i.e. 5-10 mg of fluphenazine decanoate every two weeks) and was randomized to receive (double-blind) either placebo or supplemental fluphrenazine HCL at the first sign and for the duration of each prodromal period. Included in the monitored outcome measures were number and length of prodromal episodes and exacerbations, degree of life disruption of exacerbations, and total amount of open label neuroleptics required to stabilize following an exacerbation. The active supplementation group demonstrated significantly shorter exacerbations than the placebo group (mean 23 days vs. 43 days, $\underline{p} = 0.013$) and a trend toward less total neuroleptic required to stabilize following an exacerbation (mean 219 mg. vs. 317 mg, $p = 0.19$). These interim results suggest that neuroleptic supplementation before the development of overt psychotic worsening may reduce the length and perhaps the severity of the ensuing exacerbation.

NR120 **Tuesday, May 9, 12 noon–2:00 p.m.**

SEX DIFFERENCES IN OLFACTORY FUNCTION IN SCHIZOPHRENIA

Lili C. Kopala, M.D., Psychiatry, Univ of British Columbia, 2255 Wesbrook Mall, Vancouver, BC, Canada V6T 2A1; Campbell Clark, Ph.D., Trevor Hurwitz, M.D.

Summary:

Besides replicating our previous finding of deficits in olfactory identification in subjects with schizophrenia, the results of the current study suggest that this deficit is confined to male patients with schizophrenia. In contrast, the male and female schizophrenic subjects performed almost equally on a test for olfactory acuity. These findings will be discussed with respect to other reported sex differences in schizophrenia including the frequency of specific neurological signs and structural brain abnormalities, response to neuroleptic medication, and long term outcome. *Method:* The University of Pennsylvania Smell Identification Test (SIT) and a test of olfactory acuity were administered to 26 male and 18 female patients meeting DSM-III and ICD-9 criteria for schizophrenia, and receiving neuroleptic medication. Normal controls were also tested. Subjects were examined neurologically and biochemically to rule out any other causes for an olfactory disturbance. *Results:* The male subjects with schizophrenia had a significantly lower mean SIT score ($X = 33.8$) than did the female schizophrenia subjects ($X = 37.1$) and male and female controls ($X = 37.8$). The latter three groups performed at equivalent levels. Olfactory acuity for the male and female patients were not significantly different. In fact, the male patients performed slightly better than the females. *Discussion:* The data clearly indicate that the olfactory deficits in odor identification were confined to a significant proportion of the male patients with schizophrenia and that these disturbances were not related to abnormal olfactory acuity. The finding of a striking deficit on a relatively primitive sensory identification task in a subsample of male patients with schizophrenia further buttresses the hypothesis that sex may be a critical variable in understanding the developmental processes leading to schizophrenia.

NR121 **Tuesday, May 9, 12 noon–2:00 p.m.**

OCULOMOTOR IMPAIRMENTS IN SCHIZOPHRENIA

John A. Sweeney, Ph.D., Psychiatry, Cornell Univ Med., 525 East 68th Street, New York, NY 10021; Gretchen Haas, Ph.D., Brett Clementz, M.A., Peter Weiden, M.D., James Hill, M.A., Allen J. Frances, M.D.

Summary:

Eye movement abnormalities in schizophrenia are a promising familial marker and a potentially informative neurophysiological abnormality. However, the specific forms of oculomotor impairment that occur in 50 percent to 85 percent of schizophrenic patients remain poorly characterized. To describe these impairments and to evaluate their diagnostic specificity, we studied the pursuit tracking performance of 52 recently admitted inpatient schizophrenics (18 unmedicated), 19 bipolar patients (all off lithium), and 25 normal controls. In comparison with normals, schizophrenics demonstrated low velocity pursuit ($p < .02$), more frequent ($p < .05$) and larger ($p < .02$) corrective saccades, and more large intrusive saccadic eye movements (anticipatory saccades and macro square-wave jerks). Differences between medicated and unmedicated schizophrenic patients were minimal, with medicated patients performing slightly better. The reduced pursuit gain was associated with negative symptoms and ventricular enlargement. Saccade abnormalities were associated with neuropsychological tests sensitive to frontal lobe dysfunction. Bipolar patients, though less acutely disturbed when tested, demonstrated impairments similar to those observed in schizophrenic patients. The results provide one of the first detailed characterizations of eye movement impairments in a large sample of schizophrenics, and raise concern about the diagnostic specificity of these abnormalities for schizophrenia.

NR122 **Tuesday, May 9, 12 noon–2:00 p.m.**

TEMPORAL LOBE CHANGES IN SCHIZOPHRENIA

Patrick E. Barta, M.D., Psychiatry, Johns Hopkins, 600 N. Wolfe St. Meyer 3-166, Baltimore, MD 21205; Godfrey D. Pearlson, M.D., Richard E. Powers, M.D., Larry E. Tune, M.D.

Summary:

Temporal lobe structures, including hippocampus, parahippocampal gyrus, and entorhinal cortex, have been implicated in the pathology of schizophrenia in several post-mortem studies(1,2). We compared MRI data for 10 schizophrenics and 10 normal controls, group matched on age, sex, education, SES, and race. All subjects received thin (3mm) T1-weighted coronal cuts, archived on magnetic tape to avoid potential differences due to film processing. Volumes of anatomic structures were rated blind to subject diagnosis by an experienced neuropathologist using a DEC Microvax III-based graphics workstation. Volumes were sampled (3 contiguous cuts) from superior temporal gyrus (STG) at the level of the amygdala, from hippocampus (H), amygdala (AM), and parahippocampal gyrus (PHG) at the level of the midhippocampus and from entorhinal cortex (ERC) at the level of the pes hippocampi.

Rate-rerate reliability for STG was .90 (L) and .97 (R). All structures tended to be smaller in schizophrenics. However, after correction for overall brain volume, schizophrenics showed no evidence of net volume reduction in ERC, AM, PHG, or HP, but a striking reduction of $\simeq$20 percent in STG volume ($p<.01$ bilaterally). The area of STG sampled corresponds to auditory association cortex, and its stimulation in humans is reported to produce auditory hallucinations. Data will be available on 20 patients individually matched to normal controls. Supported by NIH MH43375 to G. Pearlson

NR123 **Tuesday, May 9, 12 noon–2:00 p.m.**

UNCONSCIOUS PROCESSING OF EMOTIONAL STIMULI

Bruce E. Wexler, M.D., Psychiatry, Yale University, VA Medical Center 116A1, West Haven, CT 06516; Gary E. Schwartz, Ph.D., George Bonano, B.A., Stephen Warrenburg, Ph.D., Larry Jamner, Ph.D., Jon Michaelis, Ph.D.

Summary:

Emotion-evoking and neutral stimuli differing only in their initial consonants (e.g. kill-till) were presented simultaneously, one to each ear. Because of the high degree of their spectral and temporal overlap, stimuli in each of these dichotic pairs fused into a single auditory percept. Even when informed that they would receive two different stimuli on each trial, subjects were able to identify both stimuli on fewer than 5 percent of trials. Trace recognition tests, however, indicated significant recognition of words that subjects were unaware of hearing ($p<.01$). Moreover, emotion-specific EEG ($p<.03$) and facial EMG ($p<.008$) responses were evident to emotion-evoking stimuli processed out of conscious awareness. Both EEG and facial EMG data indicated that left hemisphere response was greater with conscious processing than with unconscious processing while right hemisphere response did not differ as a function of consciousness ($p<.01$). Subjects defined as repressors by personality scales showed lower trace recognition of, but greater physiological response to unconsciously processed stimuli than did nonrepressors ($p<.05$). Differences as a function of personality were greatest when stimuli were presented to the left rather than the right hemisphere ($p<.008$).

NR124 **Tuesday, May 9, 12 noon–2:00 p.m.**

EFFECTS OF A PROGRAM FOR SCHIZOPHRENIC RELATIVES

Hughes J. Cormier, M.D., Sante Mentale, Center Hosp Univ Laval, 2705 Boul Laurier Bureau 4211A, Sainte-Foy, QC, Canada G1V 4G2; Gaston Guimond, M.D., Real Morin, M.D., Sylvie Vaillancourt, M.A., Christian Gingras, B.Sc., Suzanne Ricard, M.Ps.

Summary:

The purpose of this paper is to describe an intervention program aimed at the family members living with a schizophrenic person, and to present the results of an evaluation of the effects of such a program. Its main objective being the improvement of the family members' quality of life, the program consists of eight two-hour meetings and favors a psychoeducational approach. The two first meetings aim for the acquisition of knowledge necessary to understand schizophrenia as well as its treatment. The six others are centered around the development of the following abilities: communication skills, learning how to establish one's limits, to develop self-esteem and personal confidence, to establish realistic expectations, to be able to turn to necessary help, and finally, to establish and maintain a social network. The program, which was administered to three groups of families (N = 28) was evaluated on level of acquisition of knowledge, family burden (quantitative evaluation), and on the acquisition of expected behavior (qualitative evaluation). The results reveal the degree of satisfaction and presence of participants to be high. There was a significant improvement of the level of knowledge as measured by an objective questionnaire with the mean going from 52,7 at pretest to 60,7 at posttest ($p = .0024$). The family burden evaluation as measured by the Social Behavior Assessment Scale (Platt, 1983) showed that the burden elements expressed by families went from 55 elements to only 20 after the program ($p = .0001$). Also, the burden mean for each element went from 1,24 to 1,10 ($p = .0542$). As for the expected behavior acquisition, the comments which were collected reveal that the intervention program has achieved the desired objectives. (Grant froom CQRS)

NR125 **Tuesday, May 9, 12 noon–2:00 p.m.**

SCHIZOPHRENIA: P300 TOPOGRAPHY AND POSITIVE SYMPTOMS

Martha E. Shenton, Ph.D., Psychiatry, Harvard-Brockton VA, 940 Belmont Street 116A, Brockton, MA 02401; Steven F. Faux, Ph.D., Robert W. McCarley, M.D., Michael Colemna, M.A., Virginia Penhune, A.B., Amy Ludwig

Summary:

Positive symptoms (including thought disorder) are among the hallmark symptoms of schizophrenia and may be linked to dysfunctions at the neurophysiological level. Our earlier studies showed 1) a left temporal scalp region P300 decrement in schizophrenics (Sz) (Morstyn et al, 1983; Faux et al, 1987) and 2) an association of this feature with positive symptoms in Sz (Shenton et al, in press). We here report a topographic analysis of the auditory P300 recorded from a 28 electrode montage in chronic, neuroleptic-medicated Sz ($n = 20$) and age-matched normal controls (NC; $n = 20$) that replicates and extends our earlier studies. Sz were diagnosed by Feighner and DSM-III-R criteria; for comparison, separate P300 procedures were run on each subject for both nose and linked ears reference electrodes. Both t-Statistic Mapping and "protected" Hotellings T-Squared contrasts of the integrated voltages showed that the left temporal scalp region (T3) produced the greatest separation between Sz-NC groups ($p < 0.05$). Although present with nose reference, Sz-NC difference was greatest for the linked ears reference, which was used for correlations between P300 amplitude at T3 and measures of negative and positive symptoms (Scale for the Assessment of Negative Symptoms- SANS; Scale for the Assessment of Positive Symptoms- SAPS; and the Thought Disorder Index- TDI). Statistically significant Spearman rank order correlations ($p < 0.05$) ranged from .42 to .50 for the SAPS and from .54 to .79 ($n = 11$) for the TDI. Correlations with the SANS were not significant. These data provide evidence for a neurophysiological abnormality in schizophrenia observable in the left temporal scalp region P300 that is correlated with the positive symptoms of schizophrenia. Our previous findings are thus replicated in a new and larger group.

NR126 **Tuesday, May 9, noon–2:00 p.m**

MEG AUDITORY EVOKED FIELDS IN SCHIZOPHRENIC WOMEN

Martin L. Reite, M.D., Center for Adv. Study in the Behav. Sciences, 203 Junipero Serra Blvd., Stanford, CA 94305; Dana Scheuneman, B.A., Peter Teale, M.S.E.E., Steven Linnville, Ph.D., Leigh Goldstein, M.D.

Summary:

We recorded magnetoencephalographic (MEG) auditory evoked fields (EF) in response to 128 1KHz tone pips from the left hemisphere of four female controls (ages 22-46) and four medicated female patients (ages 35-41, three schizophrenic, one schizoaffective), and from the right hemisphere in four controls and a subset of two patients. We used a second order gradiometer with DC SQUID operated in an aluminum room providing 50dB attenuation at 60 Hz. Recordings were made using a 2 cm grid. Averaged waveforms were digitally filtered from 1-20 Hz, and the 100msec latency EF component (M100) identified and topographically mapped. M100 source locations were estimated using a simple dipole model in a spherical conductor and a least squares best fit routine to all data points. The normal subjects did not exhibit the same type of interhemispheric asymmetry of M100 sources previously described in normal males. M100 sources tended to be more anterior in the schizophrenic patients over both hemispheres. While preliminary due to the small N and possible medication effects, the findings are compatible with altered temporal lobe structure and/or function in schizophrenia. Supported by MH46335 and MH 41396.

NR127 **Tuesday, May 9, 12 noon–2:00 p.m.**

TRANSDERMAL NICOTINE IN PSYCHIATRIC PATIENTS

Neil Hartman, M.D., WLA VA Medical Ctr., Brentwood Div., 11301 Wilshire Blvd., (209C), Los Angeles, CA 90073; Gregory B. Leong, M.D., Shirley M. Glynn, Jeffery N. Wilkins, M.D., Murray E. Jarvik, M.D.

Summary:

Psychiataric patients have difficulty with nicotine detoxification. Response to transdermally applied nicotine was studied in fourteen male psychiatric patients using two separate double blind procedures. The subjects reported smoking an average of 21.6 cigarettes per day for a mean of 17.3 years. Thirteen subjects completed the study, smoking an average of 11.8 (SD = 4.1) cigarettes while wearing the placebo patch and 9.9 (SD = 2.7) with the nicotine patch, yielding an average reduction in smoking of 1.8 (SD = 2.6) cigarettes over a six hour period. A matched pairs t-test revealed this difference to be significant ($t(12) = 2.55$, $p < 0.02$, one-tailed). The efficacy of the nicotine patch in reducing smoking was significantly related to baseline placebo smoking levels ($r = 0.68$, $p < 0.02$). No subject who smoked less than an average of two cigarettes or more while wearing the placebo patch reduced his smoking with the nicotine patch. The heaviest placebo smokers achieved the most benefit from the nicotine patch with a 27% reduction. The data suggest that transdermally administered nicotine can be a useful adjunct in assisting psychiatric patients in smoking cessation, especially as more institutions regulate smoking.

NR128 **Tuesday, May 9, 12 noon–2:00 p.m.**

SHORTENED T2 OF CAUDATE IN MRI STUDY OF TARDIVE DYSKINESIA

George Bartzokis, M.D., Psychiatry, VA Med Center W. LA, 11301 Wilshire Blvd B210C RM15, Los Angeles, CA 90073; H. Jordan Garber, M.D., Virginia J. Griswold, M.D., Stephen R. Marder, M.D., William H. Oldendorf, M.D.

Summary:

Nuclear magnetic resonance (NMR) relaxation times (T1 and T2) can provide biochemical data on the living human brain. We used magnetic resonance imaging (MRI) to measure T2 of the basal ganglia and thus examine if iron accumulation (believed to shorten T2) is involved in the pathophysiology of tardive dyskinesia (TD). We studied 14 male DSM-III diagnosed schizophrenic patients with a minimum cumulative exposure to neuroleptics of one full year. Nine of these patients had, and five had not developed TD as diagnosed using the Schooler and Kane criteria for persistent TD, and rated using the Abnormal Involuntary Movement Scale. Axial images of the head (6 mm slice thickness) were obtained at 1.5 Tesla using inversion-recovery (IR) sequencing (TR = 2500, TI = 600, TE = 40) and multiple spin-echo (MSE) sequence (TR = 2500, TE = 40,80). Spin-spin relaxation times (T2) were calculated by an automated algorithm for each voxel from the MSE signal intensities to produce grey-scale encoded T2 maps of the brain. A single rater who was blind to the TD diagnosis obtained the mean T2 values for a standard 30 voxel (0.3 sq cm) area within the left and right caudate, putamen and globus pallidu. The preliminary data analysis on the calculated T2 values showed a significantly shorter T2 in the left caudate nucleus of the TD patients (mean = 50 msec) when compared to the patients without TD (mean = 54 msec), using a two-tailed t-test ($t = 4.19$, $p = 0.0012$). This difference remained significant after making a covariance adjustment for age ($t = 3.47$ $p = 0.005$). Shortening of T2 in the caudate nucleus of schizophrenic patients with TD may reflect increased iron deposition which could contribute to the risk of developing TD.

NR129 **Tuesday, May 9, 12 noon–2:00 p.m.**

VULNERABILITY AND PRESENTATION OF NMS

Pavlos Sakkas, M.D., Research, ISPI, 1601 Taylor Street, Chicago, IL 60612; John M. Davis, M.D., Hva Jin, M.D.

Summary:

We present our data after a review of 481 NMS cases reported in 254 publications in the international literature over the last 30 years. We analyzed data on 55 parameters which may influence the occurrence, clinical and laboratory findings, treatment, and outcome of NMS.

Men (59 percent) and elderly patients are more vulnerable to reveal NMS. The use of high doses of neuroleptic treatment (42 percent), the concomitant use of lithium (11 percent), or the exposure of the patients to high environmental temperatures are some of the factors that facilitate NMS.

The severity of NMS was correlated with the rise in body temperature, the drop in blood pressure, the cloudiness of the sensorium, or the presence of agitation ($p < .01$). Fever was correlated with leukocyte count, CPK, and hepatic enzyme values. Overall mentally retarded patients had the most unfavorable outcome (40 percent).

Treatment with dantrolene and bromocriptine was effective in half of the cases used. ECT was used with controversial results. The reinstitution of neuroleptics in a patient after an NMS episode was related with the symptoms relapse in 48 percent of the cases.

NR130 **Tuesday, May 9, 12 noon–2:00 p.m.**

CROSS-CULTURAL SURVEY OF TARDIVE DYSKINESIA PREVALENCE AMONG THREE ETHNIC GROUPS OF CHRONIC PSYCHIATRIC PATIENTS

John Sramek, Ph.D., Research, Metropolitan State, 11400 Norwalk Blvd, Norwalk, CA 90650; Swati Roy, Ph.D., Tom Ahrens, Ph.D., Edmond H. Pi, M.D.

Summary:

There is little information currently available on cross-cultural comparisons of the prevalence of tardive dyskinesia (TD). Gardos et al (1980) reported a lower prevalence among Hungarian schizophrenics, but Binder et al (1987) found a similar prevalence between U.S. reports and schizophrenic patients in Japan. We reviewed the chronic population of a 900-bed psychiatric hopital (US) to determine whether there were any differences in TD prevalence among the three largest ethnic groups: Caucasian, Black, and Hispanic patients. Over a six month period, AIMS ratings were administered to 491 psychiatric inpatients (280 Caucasians, 112 Blacks, and 99 Hispanics). The mean age of this group was 36.4 years (range 17-84). All patients were hospitalized at this facility for at least one year and received neuroleptics continuously for the length of the hospitalization. The three ethnic groups did not differ from one another in age, sex, use of high versus low potency neuroleptics, neuroleptic dosage in CPZ-equivalents at the time of rating, use of antiparkinson drugs, or psychiatric diagnosis. The majority of patients were schizophrenic (352), followed by schizoaffective (69), mania or depression (45), and organic brain syndromes (25). The distribution of the three ethnic groups was similar among these diagnoses. Probable TD was defined as an AIMS score of 2 in two separate body areas or a score of 3 in one body area. According to this definition, TD was present in 87 patients (17.7 percent), but there was no significant relationship to ethnic background (Chi Square 1.78, $df = 6$, $p = 0.94$).

NR131 **Tuesday, May 9, noon–2:00 p.m.**

BRAIN CHOLINERGIC REDUCTION IN NMS OR FATAL CATATONIA

Stephen J. Kish, Ph.D., Human Brain Lab, Clarke Inst. Psychiatry, 250 College Street, Toronto, Ontario, Canada M5T 1R8; J. Gilbert, M.D., R. Kleinert, M.D., G.F. Walter, M.D., M. Minauf, M.D., O. Hornykiewcz, M.D.

Summary:

To our knowledge, no information is available concerning the behavior of the major neurotransmitter systems in the brains of patients with neuroleptic malignant syndrome (NMS) or fatal catatonia. We examined neuropathologically and neurochemically the autopsied brains of three patients (aged 16, 24, and 54) who received neuroleptic drugs and developed a severe and fatal hyperthermia with extrapyramidal features. No neuropathological changes were observed in hypothalamus or basal ganglia. We found, in the two young adult cases, a widespread and almost total loss of activity of the cholinergic marker enzyme cholineacetyltransferase (ChAT) in cerebral cortex, limbic brain and basal ganglia. This was associated with a severe loss of large neuronal cell bodies in the nucleus basalis of Meynert, the brain area which provides the cholinergic innervation to cerebral cortex and limbic brain. The older patient showed a mild to moderate brain ChAT reduction without significant nucleus basalis loss. We suggest that a brain cholinergic dysfunction could represent one of the predisposing factors in the pathogenesis of neuroleptic malignant syndrome or fatal catatonia. (Supported by The Ontario Mental Health Foundation.)

NR132 **Tuesday, May 9, 12 noon–2:00 p.m.**

INCIDENCE OF AKATHISIA IN PATIENTS ON CLOZAPINE

Paul E. Keck, Jr., M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Bruce M. Cohen, M.D., Andrew Satlin, M.D., Jonathan O. Cole, M.D.

Summary:

It is well-documented that clozapine, which is a weak dopamine antagonist, is associated with a lower incidence and severity of extrapyramidal side effects of the Parkinsonian type. However, recent reports involving small numbers of patients suggest that akathisia, often thought to be extrapyramidal and often overlooked during antipsychotic drug treatment, may be present as frequently in patients receiving clozapine as in patients receiving typical neuroleptic antipsychotic drugs. We blindly rated akathisia using a standard scale (derived from the extrapyramidal rating scale of Chouinard) with scores from 0-3 for subjective experience and 0-5 for objective evidence of akathisia in 23 patients receiving clozapine and in a demographically and diagnostically similar group of 29 patients receiving standard neuroleptics. Akathisia was both as common and as severe in patients receiving clozapine (incidence = 39 percent for total score of three or greater, mean score = 2.17 ± 1.80) as in patients receiving other antipsychotic drugs (incidence = 45 percent for total score of three or greater, mean score = 2.41 ± 2.55). For patients receiving clozapine, clinical state was rated as part of an ongoing protocol. BPRS and akathisia scores correlated $r = 0.551$, $p < 0.01$. The results suggest that the production of akathisia is a common property of all antipsychotic drugs, including the atypical drug clozapine, and that, as in patients receiving standard treatment, the presence of akathisia is associated with a worse overall outcome. Patients receiving clozapine should be monitored for the presence of akathisia.

NR133 **Tuesday, May 9, 12 noon–2:00 p.m.**

THE ACUTE EFFECTS OF SMOKING ON TARDIVE DYSKINESIA

William C. Wirshing, M.D., Psychiatry, West LA BVAMC, Wilshire and Sawtelle Blvds, Los Angeles, CA 90073; Jeremy Engle, B.A., Edward Levin, Ph.D., Jeffrey L. Cummings, M.D., Jed Rose, Ph.D.

Summary:

Epidemiologic data have suggested that smokers are less likely to develop idiopathic Parkinson's disease (PD) and more likely to develop tardive dyskinesia (TD) than nonsmokers. Such a relationship among smoking, TD, and PD might be expected given nicotine's known dopamine stimulating effects. To further explore the relationship between TD and smoking, 16 subjects with mild to severe TD were studied after two hours of smoking abstinence and again immediately after smoking a single cigarette. Measures obtained included Abnormal Involuntary Movement Scale (AIMS) ratings and quantified measures of bucco-oral movement utilizing an ultrasonic device. Both the rate and subjects were blind to the experimental hypothesis. Compared to the nonsmoking condition, smoking a single cigarette significantly increases both the total AIMS rating ($p < 0.01$ using a two-tailed t test) and the ultrasonic measures ($p < 0.01$ using a two-tailed t test). The magnitude of the change, however, was small; the average increase in total AIMS score was 1.4, and the average change in the ultrasound measures was a 35 percent increase above the nonsmoking condition. These results 1) demonstrate the utility of ultrasonic devices in quantifying the movements of TD, and 2) suggest that the small, acute exacerbation of TD by smoking does not account for all of the reported differences in the prevalence of TD between smoking and nonsmoking groups.

NR134 **Tuesday, May 9, 12 noon–2:00 p.m.**

CIRCADIAN ACTIVITY RHYTHM IN ALZHEIMER'S DISEASE

Andrew Satlin, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Martin H. Teicher, M.D., Harris Lieberman, Ph.D., Ross Baldessarini, M.D., Ladislav Volicer, M.D., Yvette Rheaume, R.N.

Summary:

Patients with Alzheimer's disease (AD) commonly develop changes in normal patterns of behavior in addition to cognitive declines. Hyperactivity, disorders of the sleep-wake cycle, and "sundowning" suggest the possibility of a disordered circadian pacemaker in AD.

We studied the circadian rhythm of locomotor activity in 17 patients with probable AD and in nine healthy elderly controls using a portable piezoelectric activity monitor. Six of the patients were clinically classified as persistent "pacers." AD patients had significantly higher percent nocturnal activity than controls, corresponding to the clinical picture of fragmented sleep. AD pacers had 39 percent more overall activity than controls.

A computer cosinor analysis found that the circadian activity pattern of AD patients was well fit by a cosine curve. However, the amplitude of the curve in AD pacers was only 63 percent that of controls, suggesting a weakened circadian oscillator in this subgroup. Also, AD patients had a prominent circadian phase delay of their peak activity compared to controls (2:47 PM vs. 1:02 PM, $p = .0026$). This further suggests a pacemaker abnormality and may correspond clinically to "sundowning."

Our findings document the feasibility of activity monitoring for clinical assessment in AD. Locomotor activity rhythm abnormalities suggest dysfunction of the circadian oscillator in this disease.

NR135 **Tuesday, May 9, 12 noon–2:00 p.m.**

DYSKINESIA IN THE DEMENTED ELDERLY

Andrew Satlin, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Gudarz Davar, M.D., Jonathan O. Cole, M.D., Ross J. Baldessarini, M.D., David W. Marby, B.A.

Summary:

Dyskinetic movements in the demented elderly are poorly characterized and may include both spontaneous and drug-induced dyskinesias. The role of neuroleptics in the etiology of such movements is not well understood.

We examined a demented elderly population for dyskinesia and attempted to identify risk factors for the the development and severity of these involuntary movements. Residents in a nursing home with a diagnosis of dementia, a history of neuroleptic treatment, and no previous psychiatric history were studied ($n = 60$, mean age = 89). Subjects were rated for dyskinesia using the AIMS, and for parkinsonism using a standard rating scale. Dental status and medication history were obtained from medical records.

Forty-five percent of this population met Schooler and Kane criteria for tardive dyskinesia. The total lifetime dose of neuroleptic in chlorpromazine equivalents, problems with teeth or dentures, and the number of drug-free intervals were positively correlated with total AIMS. Bradykinesia was negatively correlated with total AIMS. Together these variables accounted for 50 percent of the variance. This degree of predictive power is greater than that previously reported for any combination of risk factors in dyskinesia studies.

When orofacial dyskinesia was analyzed separately, the presence of one or more teeth predicted a lower score on orofacial items on the AIMS, suggesting protective effect.

Gary L. Gottlieb, M.D., Psychiatry, Univ of Penn, HUP 3 Piersol 3400 Spruce St, Philadephia, PA 19104; Raquel E. Gur, M.D., Barbara L. Malamut, M.A., Andrew J. Saykin, Psy. D., Barbara A. Kamholz, M.D., Ruben C. Gur, Ph.D.

Summary:

The application of standard clinical rating scales to patients with dementia may help quantify symptom severity and relate disease progression to neurobehavioral dysfunction. We estabished the reliability of such scales in patients with probable dementia of the Alzheimer's type (DAT). One measure, the Global Deterioration Scale (GDS) is useful in rapid description of phenomenology and progression of DAT. This study evaluates the validity of GDS in relation to neuropsychological function. We studied 71 normal aging (NA) control subjects and 116 patients who met NINCDS/ADRDA criteria for possible and probable DAT. The GDS and neuropsychological evaluation were administered at enrollment. The neuropsychological battery included measures of attention, abstraction, IQ, memory, language, spatial ability, and sensory and motor functions. The GDS showed systematic relations with neuropsychological measures. These relations supported current hypotheses on the pattern of neurobehavioral deficits associated with DAT: memory is impaired even in patients with mild DAT ($F[1,191] = 255.41$, $p < .0001$), whereas intellectual functions assessed by WAIS-R subscales show relatively less deterioration in mild DAT (GDS 1e 3 vs NC X memory vs intelligence interaction, $F[1,189] = 110.46$ $p < .0001$), but decline with more advanced stages. We will also present relationships between neuropsychological measures of depression and other behavioral ratings. By linking neurobehavioral measures to clinical symptomatology it is possible to characterize the pattern of deficits associated with the progression of DAT. This can lead to better understanding of the pathophysiology underlying dementing illness.

NR137 **Tuesday, May 9, 12 noon–2:00 p.m.**

THE SCREENING CEREBRAL ASSESSMENT OF NEPPE: A BEDSIDE SCREENING TOOL

Vernon M. Neppe, M.D., Psychiatry, Univ of Washington, Dept of Psych RP-10, Seattle, WA 98195

Summary:

The Screening Cerebral Assessment of Neppe, a new screening instrument to evaluate higher cortical functions, attempts to fill the void in adequate short bedside clinical measures of higher cerebral cortical functioning. The data on the first hundred patients will be presented. At present the correlations of this test, with neuropsychiatrist rating, MRI, and neuropsychological testing, and also of interrater reliability range from .89 to .93. The test is statistically significantly better than the Folstein Mini Mental Status Exam ($p < 0.001$). The SCAN measures ten major areas: recall, recognition, orientation, organization, concentration, calculation, agnosia, apraxia, speech, and sensory-motor-reflex, and compares these with behavior measured on a modified Brief Psychiatric Rating Scale. It has been used in focal cerebral deficits, dementias, schizophrenia, depression, epilepsy, and other neuropsychiatric conditions.

NR138 **Tuesday, May 9, 12 noon–2:00 p.m.**

CHANGES IN SELECTIVE FREE CSF AMINO ACIDS IN ALZHEIMER'S DISEASE

Nunzio Pomara, M.D., Clinical Division, Nathan S. Kline Inst., Orangeburg, NY 10962; Dennis Deptula, Ph.D, Rajkumar Singh, M.D., Peter A. LeWitt, M.D., Miriam Banay-Schwartz, Ph.D.

Summary:

While decreases in CSF and brain concentrations of transmitter amino acids in their receptors have been associated with end stage Alzheimer's disease (AD), these findings might not be generalizable to early stage AD. Therefore, we examined amino acid levels in CSF of ten patients meeting DSM-III and NINCDS/ADRDA criteria for probable AD (6f,4m:age 59.7 ± 10.8) and ten age matched controls (6f,4m:63.8 ± 11.2). AD subjects were mildly to moderately impaired (mean GDS = 4.7, SD = 4.7, SD = 0.4; mean WAIS – R = 79.4, SD = 10.9) unmedicated outpatients. LP's were performed in the lateral decubitus position between 8 and 9 AM after an overnight fast. CSF was stored at $-70°C$. Aliquots from a pooled specimen of the 3rd-17th ml were used for determination of free amino acids using precolumn derivatization with 1-naphthylisocyanante, and separation by reverse-phase HPLC on a C_{18} silica column. *Results:* The concentration (nmol/ml) of glutamate in the CSF of AD patients (mean = 7.44; SD = 1.54) was higher than that of controls (mean = 5.57; SD = .71) ($t[18] = 3.49$, $p < .005$). Proline concentrations were also increased ($p < .05$). In contrast, AD patients showed a reduction in taurine ($p < .01$), ornithine ($p < .05$), and lysine ($p < .05$) relative to controls. Glutamate correlated with aspartate ($r = .83$, $p < .001$). *Conclusion:* These preliminary findings, if confirmed, raise the possibility of additional mechanisms in the pathophysiology of Alzheimer's disease.

NR139 **Tuesday, May 9, 12 noon–2:00 p.m.**

PARKINSON'S DISEASE, DOPAMINE AND PERSONALITY

Matthew A. Menza, M.D., Psychiatry, RWJ Univ Med School, 1 RWJ Place CN19, New Brunswick, NJ 08903; Nancy Forman, M.D., Harris Goldstein, M.D., Lawrence Golbe, M.D.

Summary:

For many years clinicians have been of the opinion that patients with Parkinson's disease (PD) have many personality traits in common, both premorbidly and after the onset of the illness. There are many studies to this effect in the literature and with few exceptions the described personality characteristics cluster around descriptors such as industriousness, rigid moral attitudes, stoicism, and seriousness.

Recent work indicates that personality varies along three independent axes which may have biochemical and neuroanatomical correlates. Utilizing this work we attempted to determine if the personalilty associated with Parkinson's disease was related to the associated dopaminergic deficits. Twenty PD patients and 20 matched orthopedic patients were given Cloninger's Tri Personality Questionnaire (TPQ). PD patients had significantly ($P<.05$) lower scores on the novelty seeking scale (which is thought to be dopamine-related) but there were no differences on the scales thought to be related to NE and serotonin. This work indicates that the personality long associated with PD is due to a reduction in dopamine-dependent novelty seeking behaviors. Further, it supports the suggestion that dopamine is related to a group of behaviors, defined by the TPQ, described as novelty seeking.

NR140 **Tuesday, May 9, 12 noon–2:00 p.m.**

LIMITATIONS OF THE MINI-MENTAL STATE EXAMINATION

William O. Faustman, Ph.D., Psychiatry, Stanford VA MHCRC, VA Medical Center Unit 4B2, Palo Alto, CA 94304; James A. Moses, Jr., Ph.D., John G. Csernansky, M.D.

Summary:

The Mini-Mental State Examination (MMSE) represents a frequently administered screening instrument. Despite the widespread use of the MMSE in psychiatric research, little work has examined the concurrent validity of the MMSE in samples exclusively containing psychiatric patients.

We compared the outcome of the MMSE and the Luria-Nebraska Neuropsychological Battery (LNNB) in a diagnostically mixed sample of of 111 psychiatric inpatients. A majority of the sample met Research Diagnostic Criteria for either Schizophrenia (N = 54, 48.6 percent), schizoaffective disorder (N = 13, 11.7 percent), or major depression (N = 27, 24.3 percent). LNNB performance was expressed as the number of clinical scales (excluding the C7 & C9 scales) in addition to the S1 scale that exceeded critical cutoff levels for each patient.

The correlation between the MMSE score and the global performance measure of the LNNB was modest (rho = -0.26). The MMSE was *not* able to classify global performance on the LNNB among patients who did and did not show significant deficit (i.e., five or more scales above critical level) on the LNNB. The overal results suggest serious limitations of the MMSE in estimating the presence and degree of cognitive impairment in psychiatric samples.

NR141 **Tuesday, May 9, 12 noon–2:00 p.m.**

CHARACTERIZING ORGANIC DELUSIONAL SYNDROME

Jack R. Cornelius, M.D., Psychiatry, Western Psychiatric, 3811 O'Hara St. Room 874, Pittsburgh, PA 15213; Juan E. Mezzich, M.D., Horacio Fabrega, M.D., Marie D. Cornelius, Ph.D., Richard F. Ulrich, M.S.

Summary:

A research task force of the NIMH (1975) 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 category of "organic delusional disorder," among other changes. However, the descriptions of this disorder did not include such basic information as the average age, gender distribution, frequency of associated features, average level of impairment, prevalence in a large evaluation sample, or distribution of associated medical diagnoses.

A total of 39 cases of this syndrome presented at our institution out of a total of 14,889 patients evaluated between January 1, 1983, and December 31, 1987. They represented 0.26 percent of all cases and 7.6 percent of cases with organic brain syndromes. Of these 39 cases, 24 (61.5 percent) were male and 15 (38.5 percent) were female. The mean age was 61.8 years. The four most common symptoms listed on the Initial Evaluation Form (1981) were lack of insight, suspiciousness, acquired intellectual impairment, and delusions. They demonstrated moderate to marked impairment in functioninng in all areas measured. Twelve symptoms distinguished this syndrome from schizophrenia. The most common group of medical diagnoses associated with this syndrome consisted of a variety of neurological disorders, of which idiopathic Parkinson's disease and convulsions were most common.

NR142 **Tuesday, May 9, noon–2:00 p.m**

AURA PREDICTS PSYCHOPATHOLOGY IN SEIZURE PATIENTS

Edward K. Silberman, M.D., Psychiatry, Medical College of PA, 3200 Henry Avenue, Philadelphia, PA 19129; Neil Sussman, M.D., Gerald Skillings, Ph.D., Mimi Callanan, M.S.N.

Summary:

The clinical observation that seizure patients are at increased risk for psychiatric illness or personality pathology has been difficult to verify. While previous studies have attempted to relate psychopathology to seizure type, the present pilot project investigates the relationship between aura symptoms and interictal psychopathology.

Fifteen patients with well documented complex partial and generalized seizures were surveyed for paroxysmal sensory, cognitive, affective, and motoric symptoms occurring with seizures and interictally. They were independently assessed with a SADS-L diagnostic interview, an MMPI, and the Washington Psychosocial Seizure Inventory.

Sensory, affective, and cognitive, but not motoric aura symptoms were associated with higher MMPI scale scores and more psychiatric disorders (DSM-III), symptoms, and treatment. Significant correlations ($P<.05$) between aura and psychopathology variables occurred at three times the rate expected by chance, and had a mean magnitude of $r = .565$.

This preliminary survey suggests that occurrence of psychosensory aura symptoms may be an important factor in predicting interictal psychopathology. Similar symptoms have recently been found in patients with mood and anxiety disorders.[1] Their presence may reflect subictal neuronal irritability, which has been hypothesized to play a role in the development of both organic and "functional" psychopathology.[2]

NR143 **Tuesday, May 9, 12 noon–2:00 p.m.**

DEPRESSION IN ALZHEIMER'S DISEASE: DIAGNOSIS BY PSYCHIATRY AND OTHER MEDICAL SPECIALTIES

Barbara C. Black, M.H.S., Wien Center, Mt. Sinai Medical Center, 4300 Alton Road, Miami Beach, FL 33140; David A. Loewenstein, Ph.D., Carl Eisdorfer, M.D.

Summary:

Depression is frequently diagnosed in patients with Alzheimer's Disease[1,2]. Since most patients with dementia are initially seen by community-based internists, it is of interest to determine whether additional psychiatric consultation is necessary to detect depression in this patient population. Fifty (50) patients meeting NINCDS-ADRDA criteria for probable AD were assessed by a team of psychiatrists, internists, and neurologists who saw the patients independently for diagnostic evaluation of their dementia. The psychiatrists utilized DSM-III-R criteria for the diagnosis of depression while internists and neurologists used clinical ratings to estabish the presence and severity of depression. Results indicate that the internists correctly identified (82 percent) of those patients whom psychiatrists judged as meeting DSM-III-R criteria for depression. However, of the 26 patients who were identified by internists as depressed, only 46 percent met DSM-III-R criteria for depression according to psychiatrists. Of those patients deemed by internists as depressed, only 54 percent evidenced dysphoric mood as assessed by the examining psychiatrists. Similar concordance rates were found between psychiatrists and neurologists. These findings suggest the importance of an extensive psychiatric evaluation to establish the presence of potentially treatable depression. Further, these results have implications for the assessment of the dementia patient in the general community.

NR144 **Tuesday, May 9, 12 noon–2:00 p.m.**

PSYCHIATRIC ILLNESS IN WOLFRAM SYNDROME PATIENTS

Ronnie Gorman Swift, M.D., Psychiatry, Univ of N. California, BSRC CB#7250, Chapel Hill, NC 27599; Debra B. Sadler, B.A., Diana O. Perkins, M.D., Michael Swift, M.D.

Summary:

Patients with the autosomal recessive Wolfram syndrome (WS) have diabetes mellitus and progressive optic atrophy, usually diagnosed asynchronously in childhood or adolescence. Many WS homozygotes develop diabetes insipidus, nerve deafness, neurogenic bladder, ataxia, or vertigo. We now report evidence for psychiatric disorder, often severe, in 47 of 70 (67 percent) of WS patients in their teens, 20s, and 30s.

Review of hospital records for 70 living or recently deceased WS patients in the U.S. revealed that the most common psychiatric manifestation of WS was depression. WS patients also had episodes of organic brain syndrome, violent behavior, and psychosis. The severity of the disorder is demonstrated by the 11 patients who required psychiatric hospitalization one or more times and the nine who attempted suicide at least once. Thus, allowing for the overlap in the two groups, 15 (21 percent) of the 70 WS patients had such severe symptoms. This proportion of psychiatric hospitalizations and suicide attempts is much greater than that observed in severe diabetes with psychiatric illness in homozygotes. These data evidence that the single metabolic abnormality determined by the WS gene predisposes to mental illness.

NR145 **Tuesday, May 9, 12 noon–2:00 p.m.**

DEPRESSION AND COGNITION IN PARKINSON'S DISEASE

Sergio E. Starkstein, M.D., Psychiatry, JHU Sch of Medicine, 600 North Wolfe Street, Baltimore, MD 21205; John Paul Fedoroff, M.D., Thomas Preziosi, M.D., Robert G. Robinson, M.D., Helen S. Mayberg, M.D.

Summary:

Neuropsychiatric problems, including cognitive impairments and depression, are among the most frequent and important mental disorders found in patients with PD. It has never been determined, however, whether there is a causal relationship between cognitive impairments and depression. In the present study, we examined a consecutive series of 78 patients with PD for the presence of depression and neuropsychological impairment. Using a stepwise regression analysis, we found that severity of depression was the single most important factor associated with the severity of cognitive impairment ($R^2 = .17$, $F = 15.3$, $p < .01$). When neuropsychological test scores in patients with PD and major depression ($n = 15$) were compared with scores in an age- and stage of PD-matched group of nondepressed controls ($n = 15$), major depressed patients performed significantly worse than the nondepressed patients ($f(1,11) = 34.8$, $p < .01$). These impairments were most pronounced on frontal-lobe tasks (i.e., Wisconsin Card Sorting Test). On the other hand, no significant group differences on neuropsychological performance were found between patients with minor depression ($n = 19$), and stage of PD-matched nondepressed controls ($n = 19$). These results suggest that *major* but not minor depression may lead to a particular pattern of cognitive impairments in patients with PD.

NR146 **Tuesday, May 9, 12 noon–2:00 p.m.**

EFFECT OF DEPRESSION ON LONGITUDINAL SYMPTOM CHANGE IN ALZHEIMER'S DISEASE

Elisse Kramer-Ginsberg, Ph.D., Psychiatry, Mount Sinai Med Center, 1 Gustave Levy Place Box 1229, New York, NY 10029; Blaine S. Greenwald, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

Summary:

Depression complicating Alzheimer's Disease (AD) may: (1) reversibly worsen cognitive status; (2) relate to family history of depression; and (3) correlate with dopaminergic and noradrenergic markers. Typically, affective symptoms develop earlier in AD, whereas other behaviors (e.g. hallucinations, delusions, agitation) appear later. Little is known about the predictive value of depressive symptomatology on clinical course of AD.

Sixty-four NINCDS-diagnosed "probable AD" patients are participants in a longitudinal study. Symptom evaluations were completed by reliable (icc = 0.98) raters at successive six-month intervals for up to three years on at least three occasions, employing the Alzheimer's Disease Assessment Scale (ADAS). This instrument assesses cognitive (language, praxis, orientation, memory) and non-cognitive (depression, psychoticism, motor, vegetative) functioning. A depressive subscore was derived. *Hierarchical linear analyses* estimated rate of change in performance over time. This method avoids pitfalls (e.g. baseline performance differences, variable timing, and number of observances) encountered when comparing simple difference scores to assess change. Individual slope values were obtained. Subsequent regression analyses revealed that higher (worse) baseline depression scores predicted *better* ADAS noncognitive performance over time ($p < .01$).

These findings lend data-based support to the prior intimation that early depression confers a protective effect on rate of AD deterioration. Implication will be discussed.

NR147 **Tuesday, May 9, noon–2:00 p.m**

REACTION TIME EVALUATION AS A NEUROPSYCHIATRIC TOOL

Angelo Bosio, M.D., Clinical Pharmacol., Assoc. Advan Neurosci., Viavivanti 9, Brescian Mompiano 25060, Italy; Rosangela Rosola

Summary:

The evaluation of reaction time of a subject has been considered as a realistic method to determine his clinical answer to psychopharmacological treatments inducing sedation or alertness modifications. The development of a computerized tachistoscope in our laboratories three years ago allows the evaluation of the reaction time to a luminous stimulus as a separate count for the "time of thinking" and the "time of movement." The difference among the times has been obtained through an electronic device measuring the starting movement after the luminous stimulation.

The possibility to split the central and peripherical reaction time induces our group to build the normal tables with the distribution of percentiles in a sample of control subjects. The study was carried out on a population of 24,000 normal subjects with an age ranging from five to 85 years. The reaction time in normal subjects is a function of aging, with a minimum at about 25 years and an increasing value after this age.

The reaction time of right and left handed persons has a similar distribution during aging. The data collected in this three-year trial on control subjects represent a fundamental point of reference for clinical studies in which the measuring of reaction time may be considered an objective criterion to establish the degree of clinical symptoms or the valid method to monitor the pharmacological response to a specific treatment.

The results obtained during various double-blind clinical trials are shown, with particular regard to pathological cerebral aging evaluation, parkinsonian syndromes, and iatrogenic extrapyramidal side effects.

NR148 **Tuesday, May 9, 12 noon–2:00 p.m.**

REACTION TIME EVALUATION AS A NEUROPSYCHIATRIC TOOL

Anastasios Georgotas, M.D., Psychiatry, NYU Medical Center, 560 First Avenue, New York, NY 10016; Robert E. McCue, M.D., Thomas B. Cooper, M.A.

Summary:

One of the important unanswered questions facing clinicians treating depressed patients is how long to continue a patient on an antidepressant once he or she has responded to it. The value of long-term maintenance therapy with antidepressants is an especially important issue with elderly patients, but may also have a greater sensitivity to the side effects of antidepressants and may not be able to tolerate extended treatment with them.

The present study was a placebo-controlled comparison of the efficacy of nortriptyline and phenelzine in preventing recurrences of major depression in elderly patients. Fifty-one elderly depressed outpatients who had responded to antidepressants and completed continuation therapy were observed under double-blind conditions for one year. Twenty-three had been switched to placebo while 13 and 15 were kept on nortriptyline and phenelzine, repectively. Patients on phenelzine did significantly better with 13.3 percent recurrences than patients on either nortriptyline (53.8 percent recurrences) or placebo (65.2 percent recurrences). In addition, patients who had higher Hamilton scores and who had an earlier age of onset of the first depressive episode were significantly more likely to have recurrences.

NR149 **Tuesday May 9, 12 noon–2:00 p.m.**

COMBINED ECT AND TRICYCLICS IN ELDERLY PATIENTS

John P. Nelson, M.D., Geriatrics, Western Psychiatric, 3811 O'Hara Street, Pittsburgh, PA 15213; Lloyd Benjamin, M.D.

Summary:

Electroconvulsive therapy (ECT) remains the most potent treatment for severe depression, but the mechanism of its action is unknown and onset of its effects is gradual. Recent data from rat experiments suggests that ECT and tricyclic antidepressant (TCA) therapies may be addictive in their effects on receptors, both in rapidity of onset and in amount of change (1,2). In order to see if similar addictivity might be seen in clinical treatment of depression, we retrospectively reviewed the outcome of 84 hospitalized patients over age 60 with a diagnosis of unipolar depression who had been treated with ECT alone or concomitantly with tricyclic antidepressants. The patients were in three treatment groups: ECT alone (n = 44), ECT plus ongoing low-dose TCA treatment (n = 23), and ECT plus full TCA treatment (n = 17). Outcome was scored from the discharge summary (while blind to the patient identity and treat group) on a four-point scale of improvement. The number of ECT needed to achieve maximal benefit was also noted. Seizure times were measured by both cuff and EGG methods. Patients in the combined ECT and TCA treatment groups had significantly greater overall improvement (2.53 vs. 2.02, $p<0.01$), as well as a reduction in average number of ECT treatments need for that improvement in the combined group (9.75 vs. 8.07 $p<.01$). No differences were seen in side effects.

NR150 **Tuesday May 9, 12 noon–2:00 p.m.**

LATE LIFE DEPRESSIVE PSEUDODEMENTIA

Blaine S. Greenwald, M.D., Psychiatry, Mt. Sinai Medical Center, 1 Gustave Levy Place Box 1229, New York, NY 10029; Elisse Kramer, Ph.D., Eileen Wachter, M.D., Miklos F. Losonczy, M.D., Paul Aisen, M.D.

Summary:

Reversible cognitive impairment ("pseudodementia") may accompany major depression, especially in the elderly. The prevalence of this phenomenon is uncertain. Several investigations have compared pseudodementia and dementia patients. This study is unique in (1) comparing geriatric non-cognitively impaired *depressives* and pseudodementia patients, whose inclusion was dependent upon antidepressant response *and* posttreatment cognitive improvement as diagnostic validators; and (2) examining family history of dementia, and markers of medical illness. Sixty-two consecutively admitted, elderly, unipolar, DSM-III major depressed psychiatric inpatients with (MMSE adm = 20, posttreatment = 28) and without (MMSE adm and posttreatment = 28) reversible cognitive impairment were prospectively compared. Twenty-nine percent (18/62) met criteria for pseudodementia. Pseudodementia patients had higher Cumulative Physical Illness Ratings ($p<.02$), number of medical illnesses ($p<.01$), number of subspecialty consultations ($p<.06$), hallucinosis (SADS rating, $p<.02$), and length of hospital stay ($p<.03$); and fewer number of prior depressive episodes ($p<.04$). Family history of dementia and depression, mean age, age at onset of first depression, sex ratio, Hamilton depression score (adm, posttreatment, change), delusionality; and number of nonpsychotropic and psychotropic medications were similar between groups. In patients who underwent CT scans (n = 25), quantitative measures of brain atrophy will also be reported.

NR151 **Tuesday May 9, 12 noon–2:00 p.m.**

DRUG TREATMENT OF DEPRESSION IN THE FRAIL AGED

Ira R. Katz, M.D., Psychiatry, Medical Coll of PA, 3200 Henry Avenue, Philadelphia, PA 19129; George M. Simpson, M.D., Vijay Jethanandani, M.D., Thomas Cooper, Cathy Muhly, R.N., Patricia Parmelee, Ph.D.

Summary:

Recent studies have shown that DSM-III-R Major Depression is common among the institutional elderly. To validate the diagnosis in this setting, we have conducted a double-blind, placebo-controlled study of the effects of nortriptyline among a population of frail elderly institutional residents, average age 85. Even in this population, we find that nortriptyline exhibits linear pharmacokinetics. The mean for the ratio of plasma level to dose was 1.18 ng/ml/mg/day. Measurement of plasma levels 24 hours after a test dose remains a reliable approach for predicting an individual's steady state dosage requirements. Among the first 30 patients treated in this study, seven experienced adverse effects necessitating early termination (1/12 placebo treated, and 6/18 drug treated patients; Fishers exact probability = 0.11). Among the completers, we observe drug-placebo differences favoring nortriptyline on Clinical Global Improvement ($p<0.002$), Hamilton Depression Rating Scale ($p<0.02$), and Raskin Scale ($p<0.05$). On the Hamilton Rating Scale, baseline was $23.7 +/- 4.1$ for drug patients and $21.7 +/- 2.5$ for placebo; final scores were $21.7 +/- 2.5$ and $13.1 +/- 6.7$. These findings suggest that DSM-III-R symptoms of Major Depression predict nortriptyline response, even in the frail elderly and that nortriptyline remains a reasonable approach for treatment.

NR152 **Tuesday May 9, 12 noon–2:00 p.m.**

B VITAMINS IMPROVE MEMORY IN GERIATRIC DEPRESSION

Iris R. Bell, M.D., Psychiatry, McLean Hospital, 115 Mill St. Geriatric Service, Belmont, MA 02178; Frank Morrow, Ph.D., Stephanie Mirages, M.A., Gayle Perrone, B.S., Joel Edman, M.S., David Marby, B.A., Michele Greenwald, R.N.

Summary:

This study evaluated cognition and depression in 14 depressed geriatric inpatients (mean age 75.3 ± 7.0, 4M/10F) during double-blind, placebo-controlled, between-group ($n_{act} = 7$, $n_{p1} = 7$) treatment with vitamins B1, B2, and B6 (all 10 mg. q.d.) concomitant with a four-week open nortriptyline trial (titrated to the therapeutic blood levels). The only baseline deficiency was B2 in one placebo subject; three placebo Ss were deficient in one or more vitamins (B1, B2, B12) by the end of the study. RBC enzyme assays showed better improvement within the normal range in the active than in placebo group for B2 ($p = .08$) and B6 ($p = .002$) at four weeks. Without supplementation, B12 increased in the active Ss and decreased in the placebo Ss (p .05). On the initial free-recall task of the Buschke Memory Test, active Ss performed better than placebo Ss (week w, $p = .09$; week 3 = .08; week 4, $p = .02$). Baseline Buschke correlated with B12 ($r = .64$, $p = .01$) and folate ($r = .58$, $p = .02$); Week 4 Buschke correlatedc with B2 ($r = .67$, $p = .04$). Depression lessened in both groups but Montgomery-Asberg Depression Scale score did not differ significantly between groups. The previously reported interference of tricyclics and phenothiazines in B2 metabolism and the interaction of B vitamins with each other's absorption and coenzyme function may have clinical implications. These data suggest that low dose B vitamin supplementation may improve cognitive function in depressed geriatric inpatients.

NR153 **Tuesday, May 9, noon–2:00 p.m**

PREDICTORS OF DEPRESSION IN THE URBAN ELDERLY

Gary J. Kennedy, M.D., Psychiatry, Montefiore Medical Center, 111 E. 210 Street, Bronx, NY 10467; Howard Kelman, Ph.D., Cynthia Thomas, Ph.D.

Summary:

The reciprocal relationship between depression and disability confounds current efforts to estimate the significance of depressive symptoms in the elderly. As a result both the design and feasibility of mental health interventions that might extend the older individual's independence and survival in the community remain problematic. In previous work with 1,855 adults aged 65 and older, we found that health and disability outranked demographic and psychosocial characteristics in their association with depressive symptoms in 361 individuals at baseline. In the present study we examined characteristics among 79 of 1,354 individuals who did not meet Center for Epidemiologic Studies Depression scale criteria at baseline but were judged depressed 24 months later. Health and disability again outranked demographic and psychosocial characteristics in predicting the incidence of depression at 24 months although the magnitude of effect was smaller. The analysis of mortality in our population offers hope of clarifying the interaction and modifiability of depression and disability in late life.

NR154 **Tuesday May 9, 12 noon–2:00 p.m.**

VITAMIN B12 AND COGNITION IN GERIATRIC DEPRESSION

Joel S. Edman, M.S., Psychiatry, McLean Hospital, 114 Mill St. Geriatric Service, Belmont, MA 02178; Iris R. Bell, M.D., Richard Linn, Ph.D., Nancy Hebben, Ph.D., Diane Ray, Ph.D.

Summary:

This study examined the relationship between admission serum vitamin B12 and a standard battery of neuropsychological tests in 21 depressed geriatric inpatients with and without dementia (3M/18F, mean age 75.4, range 62-91). The DSM-III-R diagnoses included: unipolar depression 57 percent (n = 12); bipolar disorder 24 percent (depressed n = three, mixed n = two); and dementia with depression 19 percent (SDAT n = two, multi-infarct n = one and unspecified n = one). All Ss had normal B12 levels (mean = 479 ± 240 pg/ml, range = 190-980, normal = 150-950). B12 correlated significantly with numerous raw and peer-adjusted scores, especially those of verbal retrieval; (a) WAIS-R Subscales (Vocabulary r = .65, p = .001; Digit Symbol r = .58. p = .007); (b) Wechsler Memory Subscales (Memory Passages Immediate r = .60, p = .004 and Delayed r = .44, p = .047; Visual Reproduction Delayed r = .60, p = .004); (c) Boston Naming Test (r = .71, p = .003). B12 did not correlate with age or Hamilton depression scores. Ss with above average WAIS-R peer-adjusted Vocabulary scores (>10) had significantly higher serum B12 (551.1 ± 210.2) than those with below-average scores (B12 = 333.7 ± 95.8). The data suggest the possibility of a B12 threshold within the normal range for optimizing cognitive function in geriatric depression. The relationship of B12 status to cognitive deficits associated with depression merits further investigation.

NR155 **Tuesday May 9, 12 noon–2:00 p.m.**

GENDER DIFFERENCES IN CAREGIVER COPING

William Borden, Ph.D., Psychiatry, Univ of Illinois, MC309 P.O. 4348 JAC SW, Chicago, IL 60680; Rhoda R. Frankel, M.A., Ben Gierl, M.D., Sharon Berlin, Ph.D.

Summary:

While men and women appear to experience comparable levels of strain in caring for spouses with chronic dementia, a number of studies suggest that women are more likely to report signs of psychological distress than are men. One interpretation of such findings holds that gender-related differences in coping lead to variance in adaptational outcomes, which, in turn, result in differential rates of symptomatology. In order to test this hypothesis, the present study examined the relationships between 1) gender and selection of coping strategies, 2) classes of coping strategies and psychological well-being, and 3) gender and psychological well-being in spousal caregivers of older adults with chronic dementia. Fifty-one subjects completed standardized instruments assessing eight classes of coping strategies and levels of psychological well-being. Results of multiple regression analyses indicate that women rely more frequently on tension reduction and support seeking as coping strategies, and show higher levels of psychological distress than do men. Contrary to cultural stereotypes, no gender-related differences were found in use of problem-focused coping strategies. Developmental and clinical implications of findings are examined, and emergent issues in future research are summarized.

NR156 **Tuesday May 9, 12 noon–2:00 p.m.**

LATE LIFE PSYCHOSIS AND STRUCTURAL BRAIN INJURY

Ira M. Lesser, M.D., Psychiatry, Harbor UCLA Medical Ctr, 1000 West Carson Street, Torrance, CA 90509; Bruce L. Miller, M.D., Kyle B. Boone, Ph.D., Elizabeth Hill, R.N., C. Mark Mehringer, M.D.

Summary:

Twelve patients who had the onset of their first non-affective psychotic disorder after the age of 45 and nine patients with a psychotic depression first presenting after the age of 45 were studied with psychiatric, neurologic, magnetic resonance imaging (MRI), and neuropsychological (NP) evaluations and compared to healthy, nonpsychiatrically ill age, sex, education, and ethnicity matched control subjects who were studied similarly. The patients demonstrated more structural brain injury both by clinical diagnoses from MRI (e.g. stroke, tumor) and by quantitatively assessing the amount of white matter lesions on MRI. On NP testing, even after controlling for differences in IQ, the patients did more poorly than matched controls on many tests measuring frontal lobe functions. Findings from MRI and performance on NP tests were essentially comparable between the two patient groups. We conclude that there is a strong association between brain injury, especially silent stroke, and the late onset of psychosis. When patients experience a psychosis for the first time later in life, clinical investigations must include evaluations including imaging techniques to explore this possibility of structural brain injury.

NR157 **Tuesday May 9, 12 noon–2:00 p.m.**

DELAYED ANTIDEPRESSANT EFFECT IN THE ELDERLY

Robert E. McCue, M.D., Psychiatry, NYU Medical Center, 560 First Avenue, New York, NY 10016; Anastasios Georgotas, M.D., Thomas B. Cooper, M.A., Narmada Nagachandran, M.D.

Summary:

Although it is widely recognized that there is a delay in the onset of the therapeutic effect after antidepressants are begun, little is known about it. In the past, a two- to four-week trial of an antidepressant was felt to be adequate but some recent studies suggest that the delay in the antidepressant effect may be more variable than previously thought and that some patients may take much more time to respond. The purpose of the present study was to analyze the delay before response in elderly depressed patients who received optimal treatment. Seventy-six elderly depressed patients who had responded to either nortriptyline or phenelzine after trial of up to three months were examined. The mean week of response was nearly six weeks. Patients who were more severely depressed took longer to respond. Patients with endogenous depression responded sooner on nortriptyline than did patients with nonendogenous depression. For patients on nortriptyline, lower plasma levels in the early weeks of treatment may delay response while differences in platelet MAO inhibition in the early weeks of treatment do not appear to affect week of response for patients on phenelzine.

NR158 **Tuesday May 9, 12 noon–2:00 p.m.**

BRAIN CT AND OUTCOME OF GERIATRIC DEPRESSION

George S. Alexopoulos, M.D., Psychiatry, Cornell Univ Med College, 21 Bloomingdale Road, White Plains, NY 10605; Robert C. Young, M.D., Charles A. Shamoian, M.D.

Summary:

Brain CT abnormalities have been reported in depression[1] and appear to be more prominent in depressed patients with onset in late life.[1,2] In this study, the hypothesis was tested that brain CT abnormalities are associated with the outcome of geriatric depressive disorder.

Brain CT was was performed in 45 psychiatrically hospitalized elderly (mean age 74.7 years, SD: 6.3) subjects who met DSM-III criteria for unipolar major depression (Cornell Depression Scale mean: 20.6, SD: 3.4). Linear and surface measures of ventricular size were obtained and sulcal widening was assessed using reference pictures. The number of previous depresssive episodes was correlated with sulcal widening ($r = -0.30$, $P<0.05$) and ventricular-brain-ratio ($r = 0.31$, $P<0.04$). The subjects and an informant were contacted 38.1 months (mean; SD: 17.1) after the initial evaluation. Weak correlations were observed between sulcal widening the length of the index depressive episode ($r = 0.18$, $P<0.2$), and the total time in depression during the follow-up period ($r = 0.22$, $P<0.1$). Subjects who developed irreversible dementia during the follow-up period had greater sulcal widening (mean = 76.2 years, SD: 6.6) ($t = 3.08$, $df = 41$, $P<0.01$) and later age of illness onset (mean = 76.2 years, SD: 6.6) ($t = 3.08$, $df = 41$, $P<0.01$) than subjects who remained non-demented. At entry, there were no significant differences in age, severity of depression, cognitive dysfunction, or measures of ventricular size between subjects who developed dementia and those who did not. The findings suggest a relationship between age of depression onset, sulcal widening, and later development of dementia.

NR159 **Tuesday, May 9, noon–2:00 p.m**

L-DEPRENYL TREATMENT OF OLDER DEPRESSIVES

Trey Sunderland, M.D., SCN LCS, NIMH Bldg 10 RM 3D41, 9000 Rockville Pike, Bethesda, MD 20892; Robert M. Cohen, M.D., Karen E. Thompson, B.S., Brian A. Lawlor, M.D., Alan M. Mellow, M.D., Paul A. Newhouse, M.D., Pierre N. Tariot, M.D., Edward A. Mueller, M.D., Dennis L. Murphy, M.D.

Summary:

L-deprenyl, a selective monoamine oxidase-B (MAO-B) inhibitor, is a potentially interesting antidepressant for elderly depressives because it has few anticholinergic effects and is thought to be free of the troublesome "cheese effect," at least at low doses. However, we have previously shown that L-deprenyl loses its MAO-B selectivity at doses above 10 mg/day. We therefore questioned whether L-deprenyl is an effective antidepressant at low MAO-B selective doses or whether higher nonselective doses are needed. Sixteen treatment-resistant older subjects (63.2 ± 9.7 years) with DSM-III-R depression participated in this double-blind study. Subjects received placebo and one or more doses of L-deprenyl (10, 30, or 60 mg/day) each for three-week periods in a serial design. Platelet MAO-B was reduced more than 95 percent from placebo levels by each deprenyl dose tested ($p<0.01$). Objective measures of mood and behavior including the Hamilton Depression Scale, Global Depression Scores, and the BPRS all revealed significant improvement ($N = 12$, $p<0.02$), but only at the 60 mg/day dose. There was a trend for objective improvement in selected depression scores at the 30 mg/day dose ($N = 6$, $p = 0.09$). Side effects with high-dose deprenyl were minimal, except for a statistically significant lowering of systolic blood pressure on standing (17 mmHg, $p<0.01$). In a subgroup of patients treated with 60 mg/day, cerebrospinal fluid measures revealed a significant decrease from placebo values in MHPG and HVA ($N = 6$, $p<0.05$) but not 5HIAA. These results suggest that L-deprenyl can be an effective antidepressant, even in a group of treatment-resistant older depressives, but that the dose required has nonselective MAO effects and would thus not be free of the tyramine "cheese effect."

NR160 **Tuesday, May 9, 12 noon–2:00 p.m.**

ADJUNCTIVE LITHIUM CARBONATE IN NORTRIPTYLINE RESISTANT ELDERLY DEPRESSIVE

Ben Zimmer, M.D., Psychiatry, WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213; Charles F. Reynolds III, M.D., Joe E. Thorton, M.D., Carolyn C. Hoch, Ph.D., James M. Perel, Ph.D., Mary A. Schlernitzauer, R.N.

Summary:

In recent years, several investigators have reported on the efficacy of lithium carbonate (Li^+) as an adjunct to tricyclic antidepressants (TAD) for the treatment of refractory depression. Limitations of these studies have included the absence of consistent TAD in the groups studied, as well as the failure to establilsh a constant therapeutic serum range of Li^+. In addition, elderly patients, a particularly problematic group with TAD refractory depression, have not been systematically addressed. In an open trial conducted at the University of Pittsburgh School of Medicine Geropsychiatric Clinical Research Unit from 1/88 to 12/88, we added Li^+ ($\bar{x}$ serum level .5-.7mEq/L) to nortriptyline (NTP) for at least three weeks to 18 elderly (14F/M; $\bar{x}$ age $73.6 \pm$ SD 8.2) depressed ($\bar{x}$ Hamilton Depression Rating Scale (HDRS) 25.8 SD 6.5, $\bar{x}$ Folstein Mini-Mental State 25.4 SD 4.5) patients. All patients had failed at least a four-week trial of therapeutic NTP (serum range 50-150ng/mx4 weeks). $\bar{x}$ HDRS score after four weeks of NTP was 22.7 SD7.7) consistent with previous claims in non-geriatric resistant depressives. After lithium augmentation, we found a $\bar{x}$ HamD drop of 7.7 points (22.7 to 15.0 SD7.1) (paired $T = 3.119 P < 0.01$). Eight of 18 patients had a partial response to the Li^+ adjunct (HDRS 10-18); five had a complete response (HamD 10). These data are one of the first set which has prospectively and systematically looked at nortriptyline resistant late life depression and suggest that lithium as an adjunct of time on a therapeutic nortriptyline can be an efficacious treatment. Because of questions related to appropriate length of time on a therapeutic antidepressant regimen particularly nortriptyline), a controlled trial is now in order.

NR161 **Tuesday, May 9, 12 noon–2:00 p.m.**

ZK 112 119: A NOVEL B-CARBOLINE ANXIOLYTIC

David N. Stephens, Ph.D., Schering AG, Mullerstrasse 170, Berlin 65, West Germany; Ralph Schmiechen, Ph.D.

Summary:

ZK 112 119 is a novel B-carboline partial agonist at central benzodiazepine (BZ) receptors undergoing clinical trials in generalized anxiety disorder. In vitro, ZK 112 119 displaces ^{3}H-lormetazepam from rat cortical membranes (IC50 0.85nM); displacement was increased 1.2-fold in the presence of 50 M GABA. Binding of ^{35}S-TBPS to brain membranes was enhanced by ZK 112 119 by a factor 1.3, suggesting weak partial agonist properties. ZK 112 119 increased punished activity in mice and conflict activity in rats about ten times more potently than diazepam, suggesting anxiolytic properties. In tests of side effects, ZK 112 119 did not impair motor coordination of mice in the chimney or rotarod tests at doses up to 100 mg/kg (diazepam ED50 values of 1.5 and 4 mg/kg, respectively), and was about ten times less potent than diazepam in potentiating threshold dose of ethanol, in these tests. Rats trained to discriminate chlordiazepoxide from saline in drug-discrimination procedures, generalized to diazepam (ED50 1.5), ZK 112 119 (ED50 0.5 mg/kg), and a range of other BZ receptor ligands. Rats trained to discriminate ZK 112 119 (0.5 mg/kg, i.p), however, failed to generalize to chlordiazepoxide and and to other B-carbolines, and only partially generalized to diazepam. Together with the paucity of side effects, these results predict that ZK 112 119 will be a potent anxiolytic in the clinic, acting via an established mechanism, but with other properties differing from those of conventional BZs.

NR162 **Tuesday, May 9, 12 noon–2:00 p.m.**

ENDOCRINE RESPONSES TO APOMORPHINE IN SCHIZOPHRENIA

Fabrice Duval, M.D., Psychiatry, C.H. SPecialise, Service Du Dr Macher, Rouffach 68250, France; Luc-Andre Granier, M.D., M-Claude Mokrani, Ph.D., Juarez Oliveira Castro, M.D., Jean-Paul Macher, M.D.

Summary:

We studied serum prolactin (PRL) and growth hormone (GH) responses to apomorphine (APO) (0.75 mg subcutaneously), a short acting dopamine (DA) receptor agonist, after a ten day washout period in 37 schizophrenic (DSM-III-R) inpatients (23 M, 14F; mean 30.9 $\pm$ 10.2 SD yrs) and 19 controls (12 M, 7 F; mean 34.1 $\pm$ 8.4 SD yrs). Both GH stimulation (area under the curve: AUC) and PRL suppression (percentage of change from baseline obtained from AUC) were significantly blunted in schizophrenics compared to controls ($\leq$0.01 and p 0.05 respectively). The blunting of GH and PRL responses to APO in schizophrenics could not be explained by differences in age, body weight, and sex distribution. Furthermore, GH response did not seem to be dependent on a stress effect: cortisol variations, expressed as COR AUC, did not differ significantly between groups and did not correlate with GH response. However, GH AUC correlated inversely with age (rho = $-$0.46; n = 56, p$\leq$0.001). The intensity of PRL suppression correlated with negative symptoom scores (SANS) (rho = 0.4; n = 0.4; n = 37; p$\leq$0.025). The blunting of PRL and GH responses suggest a DA receptor hyposensitivity in a subgroup of schizophrenics. However, this subgroup could not be characterized in terms of disorganized or paranoid subtypes, or chronicity of illness.

NR163 **Tuesday, May 9, 12 noon–2:00 p.m.**

AN AUGMENTED TEST OF RESPONSE TO TRH

Fabrice Duaval, M.D., Psychiatry, C.H. Specialise, Service Du Dr Macher, Rouffach 68250, France; M-Claude Mokrani, Ph.D., Luc-Andre Granier, M.D., Marc-Antoine Crocq, M.D., Jean-Paul Macher, M.D.

Summary:

An examination of the thyroid-stimulating hormone (TSH) response to thryotropin-releasing hormone (TRH) challenge (200 μg I.V.) was made at 8AM and 11PM after a minimum ten day washout in 80 euthyroid hospitalized subjects: 34 with a Major Depressive Episode (DSM-III-R) (13 M, 21 F; mean 38.6 ± 10.5 yrs), 23 schizophrenics (DSM-III-R) (14 M, 9 f; mean 33.8 ± 8.9 SD yrs), and 23 controls (11 M, 12 F; mean 35.5 ± 9.2 SD yrs). In each group, after TRH adminstration, the maximum increment in TSH above baseline (ΔTSH) was significantly greater at 11 PM than 8AM ($p<0.001$). The difference between 11PM ΔTSH minus 8AM ΔTSH ($\Delta\Delta$TSH) was significantly lower in major despressives (mean $\Delta\Delta TSH = 1.3 \pm 1.8$ SD μU/ml) compared to schizophrenics (mean $\Delta\Delta TSH = 5.7 \pm 2.4$ SD μU/ml; $p \leq 0.00001$) and controls (mean $\Delta\Delta TSH = 4.8 \pm 1.8$ SD μU/ml: $p \leq 0.00001$). The lower $\Delta\Delta$TSH found in depressives could not be explained by differences in age, bodyweight, sex distribution, or thyroid function. In the whole population, there was a correlation of $\Delta\Delta$TSH with circadian parameters (i.e. mesor: rho = .55, $p \leq 0.0001$; and amplitude: rho = .54, $p \leq 0.0001$). Blunted $\Delta\Delta$TSH, defined as a value of less than 3 μU/ml, discriminates best major depressives from schizophrenics and controls (diagnostic sensitivity: 88 percent, specificity: 96 percent). $\Delta\Delta$TSH offers a better diagnostic value than ΔTSH measured only at 8AM (sensitivity: 23 percent; specificity: 93 percent; threshold for blunted response: 5 μU/ml) or 11PM (sensitivity: 41 percent; specificity: 98 percent; threshold: 8 μU/ml). It is suggested that the $\Delta\Delta$TSH test has the merit of taking into account the complex dysregulations, notably chronobiological, that affect the HPT axis in major depression.

NR164 **Tuesday, May 9, noon–2:00 p.m**

DYSREGULATED CSF POMC PEPTIDES IN DEPRESSION

Samuel Craig Risch, M.D., Psychiatry, Emory University, P.O. Box AF, Atlanta, GA 30322; Ned H. Kalin, M.D.

Summary:

We[1] and others2 have previously described a highly significant correlation in cerebrospinal fluid (CSF) concentrations of the peptides ACTH, B-endorphin, and B-lipotropin presumably reflecting their common derivation from the parent Pro-opiomelanocortin (POMC) supra-peptide. Recently, Young, Akil, and colleagues have described abnormalities in peripheral plasma concentrations of these POMC-derived peptides in human and animal models of stress and depression, possibly related to severity and chronicity. In the present study, we report a possible disruption in the *central* processing of POMC-related peptides in major depressive disorder patients.

Twenty-three research volunteers, nine normal controls, and 14 inpatients meeting Research Diagnostic Criteria for major depressive disorder or bipolar depression, received research lumbar punctures. Subjects were medication-free for at least two weeks and had normal physical and laboratory examinations.

In agreement with some studies, but discrepant with others, CSF concentrations of ACTH and corticotropin releasing factor (CRF) did not differ between the normals and the affective disorder subjects. Within the normal control subjects, there was a highly significant ($r = 0.79$, $p = 0.01$) correlation between CSF concentration of CRF and ACTH. However, within the subjects with major affective disorders or bipolar depression, there was no significant correlation ($r = 0.16$, $p = .58$) between CSF concentrations of CRF and ACTH.

These results parallel a previous preliminary report of Berrettini and colleagues[2] suggesting a CNS disruption of POMC peptide processing in depression. These results will be discussed with respect to the role of POMC-related peptides in affective illness.

NR165 **Tuesday, May 9, 12 noon–2:00 p.m.**

MELATONIN AND HOUR OF SUICIDE

Paul A. Kettl, M.D., Psychiatry, MS Hershey Med Ctr, P.O. Box 850, Hershey, PA 17033; Tracey Collins, M.S., Edward O. Bixler, Ph.D

Summary:

A variety of evidence links low melatonin to suicide. Melatonin levels in pineal glands of suicide victims are lower than in nonsuicide controls.[1] Seasonal rates of suicide negatively correlate with circannual rhythms of plasma melatonin and correlate with seasonal daylight length.[2] Depressed patients have lower nocturnal melatonin levels while treatment with antidepressants increases circulating melatonin levels. Given the clear diurnal daily pattern of melatonin secretion, we decided to compare hourly death rate from suicide to existing data of the hourly curve of plasma melatonin levels for both depressed patients and their normal controls.[3]

Death certificate data from all 6,859 Pennsylvania suicides from 1981 to 1985 were examined for time of death. Each year produced virtually the same diurnal pattern of hourly suicide death rates (intercorrelation coefficients among the yearly curves ranged from 0.83 to 0.90, $p<0.001$). The lowest death rate occurred at 4 AM (1.7 percent of all deaths) closely corresponding to the peak melatonin level, and rates then gradually rose to the peak death rate at 2 PM (6.0 percent of all deaths). Hourly death rates then gradually declined until 4AM. Most deaths occurred during daylight, which shuts off melatonin production.

The hourly suicide death rate curve showed an extremely strong negative correlation with th daily pattern of circulating plasma melatonin in depressed patients[3] ($r = -0.82$ $p<0.001$) and with the normal daily melatonin curve ($r = -0.78$ $p<0.001$).

While suicide is a behavior with a wide variety of pathologic, personal, and social antecedents, this finding adds additional evidence that low melatonin levels are associated with suicide potential.

NR166 **Tuesday, May 9, 12 noon–2:00 p.m.**

ALZHEIMER'S DISEASE ALPHA2 ADRENERGIC RECEPTORS

Grant N. Ko, M.D., Psychiatry, Mount Sinai, 1 Gustave Levy Place, New York, NY 10029; Murray A. Raskind, M.D., Daniel M. Dorsa, Ph.D., J. Smood, B.S., K.L. Davis, M.D.

Summary:

The widespread clinical deficits of Alzheimer's disease (AD) and the modest results of attempts to improve clinical function with pharmacologic augmentation of CNS cholinergic activity suggest that a single neurochemical lesion hypothesis in AD may be insufficient. Several lines of evidence detail a disturbance of CNS norepinephrine (NEI function in AD, including reduced frontal cortex NE and dopamine beta hydroxylase, diminished locus coeruleus cell counts, and elevated CSF and plasma NE and 3-methoxy-4-hydroxyphenylglycol. The purpose of the present study was to compare alpha ± adrenergic receptors in the frontal cortex of postmortem brains from patients with AD and control subjects. Unfixed frontal cortex material from Brodmann's Area 8 and 9 was obtained, cut and mounted on brass microtome chucks. Coronal cryostat sections were thaw mounted on subbed microscope slides and allowed to air dry at room temperature before being stored. ($_3$H) para-aminoclonidine was used to label alpha ± adrenergic binding sites in the mounted tissue sections. Binding appeared most dense over layers three and four. At 0.5 nM PAC, AD samples (n = eight had a mean density of 0.83uC/gm compared with a control mean of 1.56uC/gm (p 0.05). The present data lend support to a pathophysiologic role of NE in AD and suggest alpha ± adrenergic receptor loss in cortex may be another marker for NE system degeneration in AD.

RN167 **Tuesday, May 9, 12 noon–2:00 p.m.**

DOPAMINE FUNCTION IN COCAINE WITHDRAWAL

Joseph M. Palumbo, M.D., Psychiatry, Yale University, 34 Park Street, Third Fl. CNPU, New Haven, CT 06519; Lawrence H. Price, M.D., John H. Krystal, M.D., Scott w. Woods, M.D., Dennis S. Charney, M.D., Thomas Kosten, M.D., Herbert Kleber, M.D.

Summary:

The effects of cocaine abuse have been monumental. To date, there have been few systematic descriptions of the characteristics of withdrawal from cocaine as observed in an inpatient setting. We present preliminary data describing the neurochemistry, neurophysiology, and behavior of individuals in such a setting.

Method: Ten patients with a minimum cocaine intake of four grams per week were observed drug-free during a four-week period. All patients had positive urine toxicology screens for cocaine, and negative toxicology for other drugs at the time of admission. Patients were administered behavioral ratings twice daily, and were routinely screened for urine toxicology three times a week. Serial blood samples were obtained at 8 AM on Monday, Wednesday, and Friday for assays of growth hormone, prolactin, and homovanillic acid (HVA). Single photon emission computerized tomographic scan studies of brain metabolic rates were performed within 24 hours of admission, and again three weeks after admission.

Results: In preliminary comparisons with AM baseline levels in normal controls, there were no significant differences between the pooled data of the cocaine patients and normal baseline values at either admission, days five-seven, days 12-14, days 19-21, or days 26-28 for growth hormone or prolactin. A trend appears to exist which differentiates normal subjects from cocaine patients by plasma HVA levels. Minimum and maximum HVA values for individual cocaine patients, as well as their pooled means at the above intervals, remained below those of normal control subjects. Correlative studies of behavioral change and brain metabolism are being conducted and will be presented, as will data from additional normal controls.

Discussion: These data suggest that chronic abuse of cocaine may produce decreases in the turnover of dopamine as measured by plasma HVA. Cocaine, like amphetamine, inhibits the presynaptic reuptake of dopamine and enhances presynaptic dopamine release. A recent study of intermittent amphetamine administration in an animal model show long-term (30 days) increases in D-2 receptor sensitivity. Such observed increases in postsynaptic receptor sensitivity are consistent with evidence of decreases in presynaptic release of neurotransmitter at the synapse. This is consistent with our preliminary finding of decreased plasma HVA. Prolonged decreases in HVA may be associated with chronic cocaine abuse. Our data fail to replicate the findings of Mendelson, et al (1988), who found that serum prolactin levels were increased in chronic cocaine users relative to normative values.

NR168 **Tuesday, May 9, 12 noon–2:00 p.m.**

ASYMMETRICAL HEMISPHERIC CONTROL OF HEART RATE

Richard D. Lane, M.D., Psychiatry, Chicago Medical School, 3333 Green Bay Road, North Chicago, IL 60064; Robert Novelly, Ph.D., Carol Conell, M.A., Sharon B. Zeitlin, M.S., Gary E. Schwartz, Ph.D.

Summary:

Land and Schwartz have proposed that the brain regulates cardiac activity in a lateralized manner. Since heart rate is under right autonomic control, we determined whether heart rate was differentially influenced by intracarotid injection of sodium amobarbital into each hemisphere (the Wada test) prior to neurosurgery.

Thirteen patients with intractable epilepsy ranged in age from ten to 38 years ($x = 23.5$). Seven patients had right-sided lesions, six had left-sided lesions. In 12 cases the dosage of sodium amobarbital was identical on the two sides and ranged from 100 to 130 mg. ECG tracings were obtained for 30 seconds just before injection and for 2.5 minutes after injection. HR was measured every ten seconds.

Baseline HRs did not differ on the two sides. Mean HR after left injection was significantly greater than baseline HR prior to left injection ($p = .018$). This finding was observed in patients with left-sided ($p = .02$) but not those with right-sided lesions. Significant changes in HR after right injection or in patients with right-sided lesions were not observed.

These findings suggest that an intact right hemisphere or an inhibited left hemisphere drives the right-sided autonomic fibers controlling heart rate, and supports the hypothesis that asymmetry of both brain function and neural innervation of the heart are linked.

NR169 **Tuesday, May 9, 12 noon–2:00 p.m.**

CONTRIBUTION OF MDD AND BPD TO 5-HT RESPONSIVITY

Michael D. De Meo, M.D., Psychiatry, Cornell Medical Center, 525 East 68th Street, New York, NY 10021; P. Anne McBride, M.D., Jaw-Sy Chen, Ph.D., Katherine Johnson, R.N., J. John Mann, M.D.

Summary:

Introduction: Abnormalities in central 5-HT activity have been found in both mood and personality disorders and implicated in the regulation of impulsive aggressive behaviors. *Methods:* To explore relationships between central 5-HT function, major depressive disorder (MDD), and personality traits, the PRL response to the 5-HT releaser/agonist fenfluramine (FEN), a measure of "net" 5-HT responsivity, was assessed in 23 patients with MDD (11 with co-morbid DSM-III-R borderline personality disorder; MDD + BPD) and matched controls (CTRL). *Results:* MDD alone and CTRL subjects exhibited a similar age-related decline in PRL responses, and differed from the MDD + BPD group who did not exhibit this age-related decline ($F(2,37) = 8.9$, $p = .001$). Different patterns of correlation of personality traits with PRL responses were found in the MDD + BPD group compared to the MDD alone group and will be discussed. The data suggest that abnormalities in central 5-HT function may be confined to patients with comorbid personality disorders characterized by impulsive aggressive behaviors and unstable interpersonal relationships, for which diminished 5-HT function may have a causal relationship.

NR170 **Tuesday, May 9, 12 noon–2:00 p.m.**

DIFFERENCES BETWEEN 3H COCAINE AND 3H GBR-12935 BINDING

Paul Berger, M.D., NSB, NIMH Bldg 10 RM 4N212, 9000 Rockville Pike, Bethesda, MD 20892; David Tanen, Frank Vocci, Ph.D., John Elsworth, Ph.D., Robert Roth, Ph.D., Martin Reith, Ph.D.

Summary:

Recently we and others have reported that a variety of tritiated dopamine uptake inhibitors, including GBR-12935, cocaine, mazindol, nomifensine, and methylphenidate, bind to the dopamine uptake carrier. Despite the preclinical similarity that all of these dopamine uptake inhibitors are self-administered in rodents, only cocaine is associated with major abuse liability in man. When administered blindly, oral anorectic doses of mazindol are reportedly dysphoric. In an open trial of mazindol's efficacy in treating cocaine craving, although craving for cocaine was reduced, we did not observe any abuse potential of mazindol or augmentation of cocaine euphoria. We therefore have analyzed the kinetics of mazindol's interaction with both cocaine and GBR- 12935 binding to the dopamine carrier in order to evaluate whether cocaine interacts with the same receptor on the dopamine carrier as other dopamine uptake inhibitors. In the presence of 100 nM mazindol the Bmax of striatal cocaine binding was reduced by approximately 50 percent with no change in the Kd; yet 100 nM mazindol increased by approximately 50 percent the Kd of GBR-12935 binding with no change in the Bmax. The Ki for cocaine's inhibition of GBR-12935 binding is substantially higher than its Kd for cocaine binding when both assays are performed under similar conditions. The sodium curves of tritiated GBR-12935 binding and tritiated cocaine binding differ in that high sodium concentrations (500 MM) inhibit only cocaine binding. Our preliminary impression is that most dopamine uptake inhibitors are competitive inhibitors of GBR-12935 binding but non- competitive inhibitors of cocaine binding. This data raises the possibility that dopamine uptake inhibitors may interact with different allosterically linked regions of the dopamine carrier.

NR171 **Tuesday, May 9, 12 noon–2:00 p.m.**

THE INFLUENCE OF h-CRH UPON DST-OUTCOME

Klaus B. Wiedemann, M.D., Psychiatry Klinik, Univ of Freiburg, Haupstrasse 5, Freiburg 7800, West Germany; Flortan J. Holsboer, M.D.

Summary:

In depressed patients nonsuppression during the dexamethasone suppression test (DST) can be explained by an impaired feedback control mediated presumably by an enhanced secretion of corticotropin releasing hormone (h-CRH) from the hypothalamus. It is knows that the time around 12.00 pm is the period of maximum sensitivity of the pituitary corticotrophic cells to feedback regulation. Therefore, we conducted the following study to investigate the effects of h-CRH administration during the DST upon test outcome. Ten healthy male volunteers were enrolled in the study. At 11.00 pm 1.5 mg dexamethasone was administered orally and blood samples were drawn every full hour until 9.00 am. H-CRH (increasing dosages from 10 ug to 70 ug) or saline were injected repeatedly between 11.00 pm and 7.00 am. After saline all volunteers remained DST suppressors, after h-CRH seven out of ten subjects changed to DST-nonsuppressor status (cortisol levels at 8.00 am above 40 ng/ml plasma). Recent studies from our laboratory demonstrated that the DST outcome remains unaffected by h-CRH application 16 hours after administration of dexamethasone. In contrast, h-CRH application during the hours around midnight can overcome the suppressive action of dexamethasone.

NR172 **Tuesday, May 9, 12 noon–2:00 p.m.**

BRAIN NEUROPEPTIDES: MODIFICATION BY INDOCIN AND ECT

Aleksander A. Mathe, M.D., Psychiatry, Karolinska Institute, St. Gorans Hospital, S-1128 Stockholm, Sweden; Elvar Theodorsson, M.D., Carina Stenfors, M.Sc., Orsolya Hoffman, M.D.

Summary:

The right-left brain distribution and effects of indomethacin treatment as well as electroconvulsive treatment (ECT) on the tissue concentrations of three neuropeptides: substance P (SP), neurokinin A (NKA), and vasoactive intestinal polypeptide (VIP) were investigated in the rat. Neuropeptides were measured by specific radioimmunoassays after tissue extraction. Concentrations of SP and NKA were 69 percent and 46 percent lower, respectively, in the left compared to the right brain. In contrast VIP distribution was even. The uneven peptide distribution is of potential relevance in view of the linkage of several brain functions to predominantly one hemisphere and the hypothesized association of depressive and schizophrenic disorders with dysfunction of primarily one side of the brain. Pretreatment with indomethacin (indocin), an inhibitor of eicosanoid [7]"prostaglandin") synthesis, decreased the levels of SP and NKA both in the right (69 percent and 62 percent, respectively) and left brain (49 percent and 52 percent, respectively). The tissue concentrations of VIP were not changed. The effect of indomethacin was limited to the tachykinin family (SP and NKA), lending support to the hypothesis of specific eicosanoid-neuropeptide interaction in the CNS. Single ECT did not change the concentrations of SP, NKA, or VIP. Since a series of ECTs is necessary for the therapeutic effect in human, it is possible that repeated ECT animal model is required to elucidate the effects of ECT on CNS neuropeptides. The present data, taken together with the findings of modification of regional brain tachykinins by major classes of psychoactive drugs, indicate that tachykinins may play a role in mental disorders.

NR173 **Tuesday, May 9, 12 noon–2:00 p.m.**

AMINO ACID MARKERS IN PSYCHIATRIC DISORDERS: A PRELIMINARY STUDY

Vance Norum, M.D., P.O. Box A 487, Camarillo, CA 93011; James B. Roufs, M.S.R.D.

Summary:

At present, there are various psychiatric "hypotheses" attempting to explain the etiology and/or psychopathogenesis of psychiatric disorders. Plasma amino acid levels were measured in forty-seven individuals diagnosed as "classical cases" of the following psychiatric disorders; Chronic Paranoid Schizophrenia (13), Schizoaffective Disorder (13), Chronic Undifferentiated Schizophrenia (8), Bipolar Disorder, Manic Type (6), as well as seven additional diagnoses, including Obsessive Compulsive, Major Depressive, and Chronic Disorganized Schizophrenia. The purpose of this investigation was to identify the presence of "biochemical markers" indicative of psychiatric disorders utilizing 42 measured plasma amino acids and amino acid analogues. Preliminary data revealed that all test groups demonstrated significantly high plasma phosphoserine levels and low plasma aspartic acid, proline, and ornithine levels when compared to reference standards. Increasing the populations may increase the number of statistically significant amino acid anomalies as plasma taurine and tryptophan levels were reaching statistical significance. Although the use of amino acids has not been a major approach in the treatment of the psychiatric disorders listed above, the question remains as to whether normalizing amino acid imbalances (as detected by plasma amino acid analysis) would improve clinical symptoms, particularly in the nonresponsive individual.

NR174 **Tuesday, May 9, 12 noon–2:00 p.m.**

DO SERUM DEXAMETHASONE LEVELS IMPROVE THE DST?

Douglas Mossman, M.D., Psychiatry, Univ of Cincinnati, 231 Bethesda Ave ML 559, Cincinnati, OH 45267; Eugene Somoza, M.D.

Summary:

As a practical diagnostic tool, the utility of the dexamethasone suppression test (DST) remains limited. Several investigators have suggested that variations in dexamethasone bioavailability may influence DST outcome and that the accuracy of the DST might be improved by quantification of serum dexamethasone concentrations. Recent reports describe an inverse relationship between dexamethasone and cortisol levels, and claim that DST accuracy is improved when drug levels are factored in. These claims, however, are based on inadequate measures of test accuracy.

We have suggested that receiver operating characteristic (ROC) analysis be used to characterize and evaluate proposed improvements in the DST. Using recently-developed ROC techniques, we evaluated data from four published studies totaling 135 depressed and 158 control subjects in whom serum cortisol and dexamethasone levels were measured at one or two times post-ingestion. There was enormous inter-study variability in ROC indices or performance and accuracy for the conventional DST, with areas under the ROC curves (AUCs) ranging from 0.55 to 0.95 (p 0.001). We compared DST accuracy using cortisol levels alone with test results that employed either the product or the quotient of cortisol and dexamethasone levels. In none of the 14 comparisons did including dexamethasone significantly alter AUC, suggesting that incorporating drug levels does not enhance DST accuracy.

NR175 **Tuesday, May 9, 12 noon–2:00 p.m.**

MAOIS, HYPOTHERMIA, HYPERACTIVITY AND THE 24 HOUR CLOCK

Wallace C. Duncan, Ph.D., CPB, NIMH Bldg 10 4S239, 9000 Rockville Pike, Bethesda, MD 20892; Bo Gao, M.Ms.

Summary:

We have proposed that monoamine oxidase inhibitors (MAOIs) alter the regulation of the mammalian circadian system. The clinical antidepressant mechanism as well as some of the reported side effects of these drugs, such as disrupted sleep, may be related to their effects on the circadian system. The effects of chronic clorgyline (CLG), a selective type A MAOI, on 24 hour motor activity, peritoneal body temperature (Tb), EEG sleep, and light responsiveness were studied. CLG (2 mg/kg/day) or saline (SAL) was administered to Syrian hamsters housed at 22°C, using mini-osmotic pumps for over one month. Motor activity and Tb were monitored using the Mini-Mitter telemetry system. Twenty-four hour EEG sleep patterns were recorded and visually scored for waking (W), slow-wave sleep (SWS), and REM sleep. Light responsiveness was determined by measuring the capacity for brief light exposure to shift the onset of wheel-running. Compared to SAL, CLG increased W and decreased REM sleep during the four-week drug trial. During the first week of drug treatment, CLG hamsters became hypothermic during both the active and rest phases of the circadian cycle. Following the first week of CLG treatment, Tb normalized and motor activity showed a 300 percent increase *during the active phase*. In contrast CLG hamsters remained hypothermic, activity levels were similar to SAL, and SWS increased *during the rest phase*. These results suggest that CLG treatment produces hypothermia which then activates behavioral thermogenic mechanisms possibly to compensate for the drug induced hypothermia. In a separate experiment, the daily clock that controls the timing of the activity-rest cycle relative to the light-dark cycle became less responsive to environmental light following CLG treatment. CLG's capacity to alter the response of the daily clock to light may be related to the temporal disorganization of the sleep-wake cycle produced by MAOI's. CLG's capacity to alter thermoregulation may be part of the drug's antidepressant mechanism.

NR176 **Tuesday, May 9, 12 noon–2:00 p.m.**

MESOLIMBIC DOPAMINE NEURONS IN CELL CULTURE

Stephen Rayport, M.D., Psychiatry, Columbia University, NYSPI Box 62, 722 West 168th St., New York, NY 10032; David Sulzer, Ph.D.

Summary:

Reconstruction of neural circuits in tissue culture offers unparalleled access to neurons and in particular their synaptic connections. Understanding of the role of the mesocorticolimbic dopamine system in schizophrenia and drug dependence has been limited by the inability to study the synaptic connections where therapeutic agents or drugs of abuse might act. As a necessary first step, we have utilized retrograde labeling with fluorescent latex microspheres as a way of identifying mesolimbic dopamine neurons. When isolated and grown in culture, labeled cells show many of the known properties of the mesolimbic cells in intact animals. Electrophysiologically, the cells have characteristically broad action potentials, after-hyperpolarizations, rapid spike accommodation, time-dependent anomalous rectification, and responsiveness to exogenous dopamine application. Over 90 percent of the identified cells stain for dopamine or tyrosine hydroxylase (the rate-limiting enzyme in the dopamine synthetic pathway). We are currently asking whether the cultured cells utilize, in addition to dopamine, their known co-transmitters cholecystokinin and neurotensin. Ultrastructurally, the cells show characteristic catecholaminergic vesicle accumulations in axonal varicosities and evidence of dopamine uptake. Subsequent steps in the work will focus on co-cultures of identified mesoaccumbens dopamine cells with known limbic and frontal cortical target cells. Examining the cellular actions of neuroleptics and drugs of abuse on the synapses formed should enhance both mechanistic understanding of the dopamine system and its role in disease states.

NR177 **Tuesday, May 9, 12 noon–2:00 p.m.**

RHYTHMS OF PLATELET PROTEIN AND 3H-IMI BINDING

Edward DeMet, Ph.D., Psychiatry, Univ of California, Medical Science I D435, Irvine, CA 92717; Aleksandra Chicz-DeMet, Ph.D.

Summary:

Decreased platelet 3H-imipramine (3H-IMI) binding has been suggested as a potential diagnostic marker of major depression. However, results from various laboratories are divided as to whether or not binding is actually decreased. A number of previous studies have reported seasonal fluctuations in binding which could obscure patient control differences. The present study examined platelet binding in 20 normal controls for one year, and a subset of ten controls for two years, at six week intervals. Significant seasonal rhythms of the number of binding sites (Bmax) were found in each of the two years. However, the results of the two years were not well correlated. Rather Bmax values were much better fit by a two year, than by a one year rhythm. Platelet membrane protein also cycled with a similar amplitude, but inverted phase, relative to apparent 3H-IMI binding. Since the binding measures were expressed on a per protein basis, the results chow that non-binding proteins were responsible for the apparent seasonal change. While the reason for a biyearly rhythm in platelet protein is unclear, the results indicate that changes in membrane protein may represent a major confounding variable in platelet measures.

NR178 **Tuesday, May 9, 12 noon–2:00 p.m.**

SEVERITY OF OFFENSE AND DISORDER RATES

Emil R. Pinta, M.D., Psychiatry, Ohio State Univ, 473 West 12th Avenue, Columbus, OH 43210; Gerald Bean Jr., Ph.D.

Summary:

A probability two-stage, sampling design was utilized to determine the prevalence rates of psychiatric disorders within Ohio's prison system. Five hundred nine inmates from 12 correctional facilities were randomly chosen to receive the Psychiatric Epidemiology Research Instrument (PERI). Two hundred fifty seven of these were screened into the second stage and received the Structured Clinical Interview for DSM-III-R (SCID), utilizing modules for psychotic, mood, and anxiety disorders. Forty five subjects were lost to parole before completion of the study.

The Ohio justice system ranks felonies from first to fourth degree according to severity, with first degree felonies representing the most serious. The final sample size for inmates with these classifications was 433. When lifetime and past month disorder rates for the most serious felonies (first and second degree, n = 307) were compared to those for the least serious felonies (third and fourth degree, n = 126), no significant differences were found (chi-square test). Lifetime anxiety disorders demonstrated the widest variability among disorders tested, with 7.8 percent and 4.0 percent rates, respectively for most and least serious oFfenses. Psychotic disorder rates showed the least variability with rates of 3.3 percent and 3.2 percent for most and least serious felonies for both lifetime and past-month diagnoses. Mood disorders were the most frequent diagnoses occurring at lifetime rates of 17.6 percent and 19.8 percent and past-month rates of 8.1 percent and 11.1 percent for most and least serious felonies.

The presence of a psychotic, mood, or anxiety disorder among prisoners did not distinguish between the type of felony committed on the basis of severity of offense.

NR179 **Tuesday, May 9, 12 noon–2:00 p.m.**

DIAGNOSES IN ADOLESCENT SEX OFFENDERS

William Huckaby, Ph.D., Child Psychiatry, Stanford University, 1618 Seward Way, Stockton, CA 95207; Hans Steiner.

Summary:

Adolescent male sexual offenders (SO,N = 87) confined to the California Youth Authority were examined using demographics, self-report, standard psychiatric interview, and psychometric data. The purpose was to assess the presence of psychiatric disorder as well as adaptive style in contrast to a group of non-sex offenders (NSO, N = 42). Both groups were comparable in terms of age, IQ, race distribution, and length of stay. Percentile distribution for race was .51 Caucasian, .31 Black, .16 Hispanic, .02 Asian/Indian. Mean scores were determined for the following: commitment = 15.3 (SD = 1.1); IQ = 92 (SD = 17); length of stay = 18.6 months ; +/− 10. Wards were evaluated using clinical casework summaries (educational achievement and intelligence data), clinical interviews, standard psychiatric examination, Carlson Psychological Survey (CPS), Minnesota Multiphasic Personality Inventory (MMPI), and Weinberger Adjustment Inventory (WAI). Results indicate that SO are significantly more likely to suffer from substance use, attention deficit disorder, posttraumatic stress disorder and pedophilia (chi square = 22.9, DF = 7, P = 0.002). They are more likely to have committed previous offenses against persons (t = 1.89, p = 0.03) rather than property. On psychometric exam, they appear significantly more distressed, less restrained, and less defensive than age-matched norms (82nd, 34th, and 43rd percentile, respectively). Our findings argue for the establishment of specialized intervention programs for sex offenders.

NR180 **Tuesday, May 9, 12 noon–2:00 p.m.**

MORNING INCREASE IN THE RISK OF INPATIENT BATTERY

John J. Mooney, M.D., Mass Mental Health, 74 Fenwood Road, Boston, MA 02115; Doris Pearsall, Ph.D., John Orav, Ph.D.

Summary:

We examined the times of seclusion for battery on adult inpatient units in two data sets: 1) apparently unprovoked batteries at Mass. Mental Health Ctr. (MMHC), 1/78-12/80 (n = 1,474), and 2) all batteries in 17 non-forensic Mass. Dept. Mental Health (MDMH) facilities (including MMHC), 7/85-7/87 (n = 9, 993). In both cases the distribution of these events was nonrandom over the 24-hr day with major and minor cyclic peaks occurring at approximately 9-10am and 6-8pm, respectively. Incidence of battery seclusion during the three-hr period 8-11am was about two-fold greater than the mean three-hr incidence rate during the rest of the day. The significance of the observed bimodal behavior was established by double-harmonic regression equations which showed, significant 24-hr (sin,p = .0001; cos,p = .0001) and 12-hr (sin,p = .0001; cos,p = .069) oscillations in the MMHC data. Similar significant results were obtained for the MDMH data, and also for each data set when fit over only the waking day. The morning and evening peaks coincide with the morning and evening wake maintenance zones (Strogatz, et al., *Am. J. Physiol. 253:* R172-R178, 1987), and the 9-10 am peak coincides with similar increases in stroke, sudden death, and nonfatal myocardial infarction (Muller, et al., *Circulation 75:* 131-138, 1987). These and other chronobiological features of inpatient battery suggest the usefulness of particular treatment and staffing strategies.

NR181 **Tuesday, May 9, 12 noon–2:00 p.m.**

NADOLOL TO TREAT AGGRESSION IN AUTISTIC ADULTS

John J. Ratey, M.D., Research, Medfield State Hospital, 45 Hospital Road, Medfield, MA 02052; Gillian O'Driscoll, Miriam Blumenkrantz, Karen J. Lindem, James R. Fletcher.

Summary:

There is currently a large literature on the beta-blockers to treat aggression in psychiatric diagnoses. Autism is a disorder of particular interest as it is accompanied by severe behavioral dyscontrol that has remained refractory to traditional and nontraditional pharmacotherapies despite nationwide studies (for example, of fenfluramine). Neuroleptics in this group are often ineffective except at sedating doses that impair the patient's limited capacities for adaptive functioning. We have published numerous case reports extending the efficacy of beta-blockers to the autistic population; this is the first double-blind placebo-controlled report available.

The entire study involves 50 autistic adults in New York and California. The site reported, the first completed of three, involves 14 highly aggressive adults. Subjects were tracked for four weeks with the Modified Overt Aggression Scale (M-OAS) to determine eligibility for the study. They then received placebo for four weeks and baseline measures were taken of aggression, language, adaptive functioning, social behavior, and blood pressure. After one month, patients were randomly assigned to either placebo or nadolol (target dose 120mg) and were assessed weekly with the NOSIE and the M-OAS for 16 weeks. After 16 weeks patients were assessed again for language, adaptive functioning, and social behavior.

Over a four month period, subjects on nadolol showed a 50 percent decrease in aggression, including significant decreases in assaultiveness, property destruction, and screaming. Subjects receiving placebo showed no change. Side effects were minimal; decreases in blood pressure were addressed by reducing dosage. In this first sample, previous reports of improvements in language, sociability, and adaptive functioning were not substantiated.

This blinded study confirms earlier case reports of the efficacy of beta-blockers in treating the aggressive autistic adult, without the suppression of adaptive behaviors or the negative side-effects associated with neuropleptics.

NR182 **Tuesday, May 9, 12 noon–2:00 p.m.**

NADOLOL TO TREAT AGGRESSION IN PSYCHIATRIC PATIENTS

John J. Ratey, M.D., Research, Medfield State Hospital, 45 Hospital Road, Medfield, MA 02052; Paul Sorgi, M.D., Karen Lindem, Gillian O'Driscoll, James fletcher, Maria Daehler, et. al.

Summary:

We have completed a double-blind placebo controlled study investigating the effects of nadolol on aggressive behaviors in an adult psychiatric population. Forty-five patients from four hospitals, most with a diagnosis of schizophrenia and all with a history of aggressive behaviors, completed the 18-week protocol which included four weeks of placebo lead-in and 12 weeks of blinded treatment. Twenty-five subjects had randomly been assigned to the treatment group and 20 to the control group. Frequency and severity of aggressive behaviors were tracked by incident with the Overt Aggression Scale (OAS). Overall ward behavior was followed weekly with the NOSIE. Psychiatric impairment was rated monthly on the BPRS and overall response to treatment was rated also monthly, using the CGI. Depressive symptoms were followed on an in and out basic with the HAM-D.

Subjects receiving nadolol scored consistently better than the placebo group in the measurements evaluated. The treatment group demonstrated a 69 percent decrease in the frequency and 62 percent decrease in severity of aggressive behaviors while the control group dropped 41 percent in frequency and 39 percent in severity. Frequency and severity of aggressive behavior in the control group decreased, however, not consistently or as dramatically. total scores obtained on the NOSIE indicated overall ward behavior of the treatment group was also seen to improve over time ($p = .0001$) but no significant changes in the control group were found ($p = .2397$).

The treatment group was shown to decrease in the severity of illness as recorded on the CGI ($p = .0294$), demonstrating a greater mean change than the control group throughout each month. The overall comparison of mean scores on the BPRS indicated a significant difference in psychiatric impairment between the control and treatment groups, $p = .0075$. The depression rating based on the HAM-D indicated a drop of 41 percent for the treatment group and 19 percent for the control group. Individual comparison showed that all but four treatment group subjects obtained a lower depression rating.

The results obtained indicate some improvements with both nadolol and placebo, however, patients treated with nadolol showed more immediate, consistent, and greater improvements supporting the efficacy of beta-blocking agents in the treatment of aggression.

NR183 **Tuesday, May 9, 12 noon–2:00 p.m.**

5-HT POST-SYNAPTIC FUNCTION IN AGGRESSION

Emil F. Coccaro, M.D., Psychiatry, Bronx VA Med Center, 130 West Kingsbridge Road, Bronx, NY 10468; Larry J. Siever, M.D., Richard Kavoussi, M.D., Paul Rinaldi, M.A., Debbie Morrison, M.A., Luana Howard, R.N.

Summary:

Central 5-HT activity is implicated in the regulation of aggressive impulses in patients with mood and/or personality disorder. In order to explore relationships between 5-HT function and aggressive impulses in patients with personality disorder (PD), neurochemical [i,e., lumbar CSF 5-HIAA; a pre-synaptic measure) and/or neuroendocrine (i.e., pharmaco-challenge with: a) the 5-HT releaser/uptake inhibitor, fenfluramine (FEN), a pre- and post-synaptically active agent; and, b) the 5-HT post-synaptic receptor agonist: m-chlorophenylpiperazine (m-CPP)] indices of central 5-HT function were examined in male patients with DSN-III PD. PRL responses to both FEN and m-CPP were inversely correlated with clinician- and self-rated measures of impulsive aggression in two partially overlapping samples of male PD patients (e.g. Buss-Durkee "Assault + Irritability": FEN: $r = -0.77$, $n = 20$, $p = 0.0002$; m-CPP: $r = -0.66$, $n = 10$, p 0.05). In addition, PRL responses to FEN and m-CPP were highly correlated in a preliminary sample of patients with both measures ($r = 0.91$, $n = 5$, $p < 0.05$). In contrast, lumbar CSF 5-MIAA concentrations did not correlate with impulsive aggression in 17 of the PD patients for which this data were available (e.g. Buss-Durkee "Assault + Irritability": $r = 0.10$, $n = 17$, ns). These data suggest that central 5-HT function is reduced in male PD patients with prominent histories of impulsive aggressive behavior and that reduced responsiveness of hypothalamic post-synaptic 5-HT receptors may contribute to this deficit in 5-HT function in these patients.

NR184 **Tuesday, May 9, 12 noon–2:00 p.m.**

EFFECTS OF A SCHOOL SHOOTING ON MENTAL HEALTH: MEDICAL AND PUBLIC SAFETY

Ira H. Sloan, M.D., Psychiatry, Evanston Hospital, 2650 Ridge Avenue, Evanston, IL 60201; Ronald H. Rozensky, Ph.D., Robert McSay, M.D., Leslie Kaplan, A.C.S.W., Stephen Saunders, M.S.

Summary:

This ongoing research is designed to assess the effects of a traumatic incident, a shooting within an elementary school, upon nonschool personnel. This incident involved a home fire, school invasion, five wounded children, one dead child, a hostage taking, and the suicide of the assailant. The subjects evaluated included those involved in the initial crisis intervention and treatment of children and teachers. This included a total of 250 individuals (police, firemen, paramedics psychiatrists, psychologists social workers, and medical, and nursing personnel in the ER and OR). The Impact of Events Schedule (Horwitz, Wilner, and Alveraz, 1979) and a graphic self-rating of the effects of this trauma were collected from each subject. An overall return rate of over 66 percent of the questionnaires indicated both interest and involvement of those affected. Results will show effects of the trauma on post-traumatic stress disorder (PTSD) variables both within professional cohort and across all subject. Proximity to the incident, time involved with victims, and overall intensity of the experience were found to be predictive of PTSD symptoms. Discussion will focus upon research problems with this population and applicability of findings to future work with those involved with the treatment of victims of such trauma.

NR185 **Tuesday, May 9, 12 noon–2:00 p.m.**

THE EFFICACY IN SPECT IN GERIATRIC DEMENTIA EVALUATION

Gary r. Horowitz, D.O., Neurology, Albert Einstein Med Ctr., 5401 Old York road, Suite #300, Philadelphia, PA 19141; Alice Scheff, M.D., Gretta Leopold, M.D., Jacqueline Nemec, M.D.

Summary:

Twenty patients were referred to a geriatric neuropsychiatric program for evaluation of change in behavior. Patients were examined by a neurologist, psychiatrist, and a neuropsychologist. The patient's social milieu was assessed by a nurse practitioner and a psychiatric social worker. In addition to routine laboratory studies, patients were evaluated per MRI scan, EEG, and SPECT. Of the patients evaluated, 12 were diagnosed as suffering with SDAT, one with multi-infarct state, three mixed dementia, one SDAT plus depression, two with alcoholic dementia, and one with parkinsonism and dementia. Of the studies obtained, there was particularly high correlation with SPECT, psychometrics, and the clinical diagnosis. The SPECT was particularly sensitive to early SDAT. In four patients it demonstrated classical biparietal deficits. Neuropsychological testing and neuropsychiatric examination suggested cortical dementia, while both EEG and MRI scan were unremarkable. More extensive SPECT abnormalities were noted in patients with more advanced SDAT. Significantly, there was correlation in asymmetric cases with left-sided preponderant deficit relating to language abnormalities and right-sided deficits with visuospatial problems. Patients with other forms of dementia failed to demonstrate biparietal deficits. Our results suggest the efficacy of SPECT along with multi-disciplinary approach in the early diagnosis of dementia.

NR186 **Tuesday, May 9, 12 noon–2:00 p.m.**

SPECT PATTERN OF SLEEP APNEA AND ALZHEIMER DISEASE

Bruce L. Miller, M.D., Neurology, Harbor-UCLA Medical Ctr. 1000 W. Carson Street, Torrance, CA 90509; Ismael Mena, M.D., Robert Giombetti, M.D., James Daly, M.D., Steve L. Read, M.D., Karen Garrett, C.P.T.

Summary:

Sleep Apnea (SA) is not uncommon in the elderly and occurs with even higher frequency in patients with Alzheimer Disease (AD). A variety of neuropsychological (NP) deficits have been described in patients with SA, including memory disturbance. However, it is not clear whether SA is a risk for AD or occurs secondary to AD. Therefore, to further understand the relationship of SA to AD we studied AD patients utilizing HMPAO SPECT.

We have analyzed cerebral blood flow in five patients with SA, 22 AD patients, and four normal controls. The SA group had mild NP impairment with a mean Mini-Mental-State-Exam of 27 compared to 21 for the AD group and 30 for the norms. In the SA and AD groups SPECT demonstrated bilateral temporo-parietal (TP) hypoperfusion and diminished total CBF while in the controls SPECT was normal. In two patients the SA was treated and the abnormal pattern of bilateral TP hypoperfusion disappeared or improved.

This work suggests that SA can lead to selective hypoperfusion of TP neocortex and that treatment of the SA can normalize CBF. It strengthens the hypothesis that TP neocortex is selectively vulnerable to hypoxic insults and suggests that SA may be a risk factor for developing AD.

NR187 **Tuesday, May 9, 12 noon–2:00 p.m.**

MRI IN OBSESSIVE COMPULSIVE DISORDERS

Charles H. Kellner, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; Richard Holgate, M.D., Bob R. Jolley, M.D., Linda Austin, M.D., Bruce Lydiard, M.D., James C. Ballenger, M.D.

Summary:

A link between obsessive-compulsive disorder (OCD) and a neurological lesion has been postulated.(1) A recent CT study demonstrated decreased caudate volume in OCD(2). We performed MRI brain scans on twelve OCD patients and age- and sex- matched normal controls using a GE Signa 1.5 tesla scanner. Images were obtained in sagittal, coronal, and axial planes. Additional images were obtained in an oblique axial plane determined by a line through the anterior and posterior commissures. These anatomic landmarks were used to ensure comparability of images among subjects.

We measured 1) caudate nucleus head area (patient mean (n = 11), right 1.41, control mean (n = 11), 1.40, P = N.S., patient mean left 1.49, control mean 1.48, p = N.S.); 2) Cingulate thickness (patient mean (n = 12), right 12.92; control mean (n = 10), 14.16, p = N.S., patient mean left 12.88, control mean 12.26, p = N.S.); 3) intracaudate/frontal horn ratio (patient mean (n = 12) 0.57, control mean (n = 11) 0.57, p = N.S.); and 4) callosal area (patient mean (n = 12) 6.29, control mean (n = 11) 6.45, P = N.S.). No differences between patients or controls were found on these measures using paired and grouped t-tests. Clinical readings by a neuroradiologist were abnormal in 75 percent (9/12) of patients and in 50 percent (6/12) of normal controls. Increased white matter signal intensity and cerebral atrophy accounted for most of the abnormalities in both groups. These data do not support the presence of a gross brain structural abnormality in OCD. Imaging techniques which demonstrate differences in brain *function* will likely be necessary to elucidate the neurobiology of OCD.

NR188 **Tuesday, May 9, 12 noon–2:00 p.m.**

INCREASED PET DA D2 RECEPTORS ACROSS PSYCHOSES

Godfrey D. Pearlson, M.D., Psychiatry, Johns Hopkins, 600 N. Wolfe St. Meyer 3-166, Baltimore, MD 21205; Christopher Ross, M.D., Dean F. Wong, M.D., Jonathan Links, Ph.D., Robert Dannals, Ph.D., Larry E. Tune, M.D.

Summary:

PET studies using 11 C-Nmethylspiperone have found elevated caudate dopamine D2 receptor Bmax values in schizophrenics compared to controls. We have now extended these studies to affective disorder.

Affective patients either had never received neuroleptic medication (N = 14) or had been neuroleptic-free for 6 months (N = four) and met DSM-III-R criteria for currently symptomatic affective disorder. All patients received two PET scans, the second preceded by 5 - 7.5 mg p.o. haloperidol, to permit the calculation of D2 Bmax. D2 Bmax values in the four groups were as follows: Affective Psychotic: N = nine, Bmax = 29.2 ± 12.5, age = 43.1 ± 14.2; Schizophrenics: N = 20, Bmax = 33.1 ± 20.5, age = 42.5 ± 22.0; Affective Non-Psychotic: N = 13, Bmax = 20.6 ± 10.9, age = 48.8 ± 17.9; Normal Controls: N = 14, Bmax = 14.4 ± 8.6, age = 33.6 ± 17.5. Diagnostic groups differed in Bmax by ANOVA ($p < .01$). Post hoc tests indicated higher Bmax values ($p < .05$) for both psychotic groups compared to normals, and for schizophrenics compared to nonpsychotic bipolars. Among affective disorder patients, Bmax correlated significantly with severity of psychotic symptoms (r = .63) derived from the PSE, but not nonpsychotic affective symptoms.

We conclude: 1) like schizophrenics, psychotic affective patients have elevations of D2 Bmax values 2) elevation of D2 Bmax in affective disorder is more closely associated with psychosis than with mood abnormality. **Research supported by NIMH Grants -MH43775, 40362 and 40391 to GDP and LET.**

NR189 **Tuesday, May 9, 12 noon–2:00 p.m.**

EFFECTS OF MEMORY ON CEREBRAL METABOLISM IN NORMAL SUBJECTS

Robert P. Rose, M.D., Psychiatry, Univ of Chicago, 5841 S. Maryland Box 411, Chicago, IL 60637; John T. Metz, Ph.D., Lester I. Debbold, M.D., Daniel J. Luchins, M.D., Malcolm D. Cooper, M.D.

Summary:

The use of Positron Emission Tomography (PET) to study memory has been relatively unexplored. Previous studies reveal conflicting results due, in part, to difficulties in design of unambiguous control conditions. In this study we compare PET scans from two provocative cognitive tasks; a verbal "memory intensive" task and a "memory minimized" control, specifically designed to duplicate the nonspecific aspects (sensory, attentive, motor, etc. . .) of the memory task while minimizing the memory component.

Six healthy males were studied on two occasions using a PETT VI scanner. Five slices (14mm each) were collected simultaneously with a special resolution of 8mm. Subjects received injections of 18-F-2-deoxy-2-fluoro-D-glucose (2FDG). Tasks were assigned using a balanced, randomized schedule. Regions of interest were placed by a technician blind to subject condition. Response measures indicated that subjects were comparably attentive to both tasks.

Metabolic rates over the whole brain were significantly higher during the memory task (p less than .02). All regions examined were higher during the memory task as well. These findings suggest a diffuse brain activation in healthy subjects performing a verbal memory task. Despite methodological and technical limitations this study emphasizes the value of psychometrically controlled, provocative cognitive tasks and PET to study memory and other higher cognitive functions.

NR190 **Tuesday, May 9, 12 noon–2:00 p.m.**

MEMORY INFLUENCES ON HUMAN CEREBRAL METABOLISM

Robert P. Rose, M.D., Psychiatry, UCLA VAMC West LA, B151 Wilshire & Sawtelle Blvds, Los Angeles, CA 90073; Lester I. Debbold, M.D., John T. Metz, Ph.D., Daniel J. Luchins, M.D., Malcolm D. Cooper, M.D.

Summary:

The use of Positron Emission Tomography (PET) to study human memory has been relatively unexplored. In the present study we compare PET scans obtained while subjects performed two provocative cognitive tasks; a verbal "memory intensive task" (involving acquisition and recall of serial word lists) and a "memory minimized control task" designed to duplicate many of the nonspecific cognitive aspects of performing the "memory intensive task" such as attentional, sensory perceptual, and motor function, while minimizing the memory component. Six healthy, non-impaired males (aged 21-34 years) were studied on two occasions. In each session subjects received an injection of 18-F-2-deoxy-2-fluoro-D-glucose (FDG) followed immediately by performance of the cognitive task which continued throughout the 40 minute 2FDG equilibration period. Images were reconstructed with the autoradiographic model. Regions of interest were placed by a technician blind to subject's identity or condition. Average metabolic rate over the whole brain was significantly higher when the subjects performed the "memory" task versus the "control" task (9.98 ± 1.08mg; $F = 11.74$, $p < .02$), All of the 14 brain regions examined (frontal, parietal, temporal, and occipital cortices, basal ganglia, thalamus, and cerebellum bilaterally) were markedly higher during the "memory" task. These findings suggest a diffuse activation of the brain in healthy young subjects performing a verbal memory task.

NR191 **Tuesday, May 9, 12 noon–2:00 p.m.**

LINKAGE ANALYSIS OF THE 11PTR REGION IN MDI

Charles D. Mellon, M.D., Psychiatry, Univ of Utah Medical Ctr., 50 North Medical Drive RM 5R278, Salt Lake City, UT 84132; William F. Byerley, M.D., John J. Holik, B.A., Mark Leppert, Ph.D., Ray White, Ph.D.

Summary:

As part of the University of Utah Molecular Genetic Study of manic-depressive illness and schizophrenia, we have identified five multigenerational pedigrees affected with manic-depressive illness. Each family has multiple affected members. Accepted phenotypes for strict linkage analysis are bipolar type I or II (n = 36) and recurrent major depression (n = 40), while broad linkage analysis also includes cyclothymia (n = 2). Diagnoses are made according to modified Research Diagnostic Criteria. Linkage analysis is focused on the 11ptr region. This region is of interest for several reasons: (1) it contains the tyrosine hydroxylase gene (the rate limiting enzyme for dopamine and norepinephrine synthesis which is considered a candidate gene for bipolar disorder; (2) linkage has been reported to the 11pter region in one Amish family (Egeland et al 1987); and, (3) two case reports show an association between thalassemia minor and manic-depressive illness (B-hemoglobin is located at 11p15.5) (Joffe et al 1986). Preliminary work using several DNA markers does not yield evidence of linkage between this chromosomal region and manic depressive illness in our families. We will discuss the significance of these findings.

NR192 **Tuesday, May 9, 12 noon–2:00 p.m.**

PSYCHIATRIC FEATURES IN FIFTY HUNTINGTON'S DISEASE AT-RISK SUBJECTS

Jorg J. Pahl, M.D., College of Medicine, The Univ of Iowa, 500 Newton Road, Iowa City, IA 52242; Lewis R. Baxter Jr., M.D., John C. Mazziotta, M.D., Michael E. Phelps, Ph.D.

Summary:

In a previous examination we demonstrated caudate nucleus hypometabolism in 31 percent of subjects (n = 58) at risk (AR) for Huntington's disease (HD) using the 18-FDG PET method (ref 1). Fifty of the 58 subjects completed psychiatric evaluations including SADS-L and Hamilton depression ratings. Eighteen of the AR subjects were members of a single HD family on whom DNA linkage results are available.

Sixty percent 60 percent of AR subjects met RDC life-time criteria for psychiatric illness. Of the 50 AR individuals 27 percent suffered from major depression and 10 percent from minor depression.

We found that caudate nucleus hypometabolism (and genetic linkage results) in AR subjects did not correlate with a lifetime diagnosis of major or minor depression. Our combined PET and DNA linkage results do not favor a genetic etiology as a cause of depression in HD. These findings are in variance with those of Folstein et al who reported that major affective disorder in HD offspring may be a harbinger of the illness (ref 2).

NR193 **Tuesday, May 9, 12 noon–2:00 p.m.**

GENETIC DATABASE IN MOOD DISORDERS

Ronald Allan Remick, M.D., Psychiatry, University of BC, Univ Hospital UBC Site, Vancouver, BC Canada V6T 2A1; Patricia A. Baird, M.D., Adele D. Sadovnick, Ph.D., A. P. Zis, M.D., Marlene J. Huggins, M.Sc.

Summary:

The Departments of Medical Genetics and Psychiatry have collaborated to set up a genetic database for research on mood disorders. *All* patients attending our Mood Disorders Service have a detailed family history taken during initial assessment by a full-time genetic associate, thus avoiding many of the biases inherent in genetic studies when families are identified either through a genetics clinic or by volunteer solicitation. The caseload is representative of those seen by university psychiatric departments which tend to more severe cases. From a genetic counseling point of view, this population is very relevant since the more severely affected the patient, the greater the concern of relatives with respect to recurrence risks. The protocol for collecting genetic data for analysis will be described. Specific information on several degrees of relatives is recorded as gathered from the patient and at least one co-informant. All reportedly affected relatives are classified using the Family History Research Diagnostic Criteria (FHRDC) (Endicott et al, 1975). Accurate classification is ensured by a biennial intra-rater and inter-rater reliability evaluation. The data presented are for the first six months of the study. To date, well documented family histories are available for 383 consecutive, unrelated index cases. Of these, 303 (79.1 percent) have a mood disorder (DSM-III-R and Spitzer et al, 1978); 66 (17.2 percent) clearly do not have this diagnosis; and the diagnosis is pending in the remaining 14 (3.7 percent). Of the 303 index cases with a mood disorder, 97 (32.0 percent) have at least one first degree relative with a mood disorder according to FHRDC criteria. The database will be collected over a two year period with an estimated total sample of 1,200 cases, offering a valuable resource for ongoing clinical and research studies.

NR194 **Tuesday, May 9, 12 noon–2:00 p.m.**

FAMILY STUDY OF LITHIUM RESPONSE

Martin Alda, M.D., Research, Royal Ottawa Hospital, 1145 Carling Avenue, Ottawa, Ontario Canada K1Z 7K4; Paul Grof, M.D., Petr Zvolsky, M.D., Eva Grof, M.D., Mary Walsh, M.S.W.

Summary:

A relation between family history and response to lithium stabilization treatment was investigated. The study involved 121 patients with recurrent affective and schizoaffective disorders and 941 first-degree relatives and spouses. The probands in this study have been followed for three to 20 years and the pobands' and the relatives' diagnoses and the assessment of lithium response were based on all available lifelong information (SADS-L/SADS-FH interviews, medical records, and family questionnaires). The RDC diagnoses of the relatives were assigned by a group of investigators blind to the proband's diagnosis and lithium response. The families were grouped according to the proband's response to stabilizing lithium treatment, assessed by the change of recurrence rate. The results revealed significantly higher frequency of bipolars in relatives of Li responders (3.7 ± 1.0 percent vs. 0 percent, $p = 0.008$). The morbidity risk for major depression in relatives of responders was also higher but the difference was not significant (6.9 ± 2.1 percent vs. 3.6 ± 1.5 percent in nonresponders' relatives). There was a significantly higher risk of major depression in female relatives of responders than in male relatives (10.9 ± 4.0 percent vs. 3.5 ± 1.9 percent, $p = 0.017$), however, this sex effect was not observed in the relatives of nonresponders (3.9 ± 2.2 percent vs. 3.5 ± 2.0 percent). On the other hand, schizophrenia was more common in the families of nonresponders (2.6 ± 1.1 percent vs. 0.3 ± 0.3 percent, $p = 0.005$). There were no significant differences in the rates of other psychiatric disorders. The results confirm that the family history of bipolar illness, but not of other disorders, is associated with a favorable outcome of lithium treatment. The values of risks do not suggest any simple mode of inheritance in either group.

NR195 **Tuesday, May 9, 12 noon–2:00 p.m.**

MOLECULAR GENETIC STUDIES USING D2 DOPAMINE RECEPTOR

William F. Byerley, M.D., Psychiatry, Univ of Utah Med Center, 50 North Med. Dr. RM 5R278, Salt Lake City, UT 84132; Charles Mellon, M.D., John J. Holik, B.A., Angela M. Lubbers, B.A., Mark Leppert, Ph.D., Ray White, Ph.D.

Summary:

Alterations in dopaminergic neurotransmission have been implicated in the pathogenesis of schizophrenia and manic-depression. As such, genes that are involved in the function or regulation of dopamine in the brain are good candidate genes for genetic linkage investigations. Civelli and associates have recently cloned the rat D_2 dopamine receptor gene. In addition, this group has isolated a partial human D_2 dopamine receptor clone that reveals a 2 allele Taq I polymorphism. Using this RFLP, we are currently testing for linkage between the human D_2 dopamine receptor and six multigenerational families segregating schizophrenia as well as five multigenerational families segregating manic-depressive illness. We will report whether the D_2 dopamine receptor gene is of etiological importance in the pathogenesis of schizophrenia or manic-depression in our families.

NR196 **Tuesday, May 9, 12 noon–2:00 p.m.**

MOLECULAR GENETICS OF SCHIZOPHRENIA

James L. Kennedy, M.D., Human Genetic, Yale School Medicine, I-310 SHM 333 Cedar Street, New Haven, CT 06510; Luis A. Giuffra, M.D., Lennart Wetterberg, M.D., L.L. Cavalli-Sforza, M.D., Hans W. Moises, M.D., Kenneth K. Kidd, Ph.D.

Summary:

Recently, Sherrington et al have reported linkage of schizophrenia to two RFLP markers on chromosome 5 in five Icelandic and two British families. Employing the same RFLP markers as Sherrington et al, plus five additional markers, our group has excluded linkage of genes in the 5q11.2-13.3 area to schizophrenia in our large kindred from northern Sweden. Using the data published by Sherrington et al, we have performed a statistical test of genetic heterogeneity (K test, p 0.05) and the results support the hypothesis that the chromosome 5 locus implicated in the etiology of schizophrenia in the families of Sherrington et al, is not involved in the north Swedish kindred. With specific comparison between the two groups of families a desirable goal, we have begun compiling a more detailed description of the clinical symptoms. We have typed an additional system, D5S6 (lod score < -4); the data strengthen our exclusion (lod scores < -4) which encompasses the entire trisomic segment noted to segregate with schizophrenia in an uncle-nephew pair (Bassett et a), Lancet i:799, 1988). Our genetic map of the trisomic segment and its vicinity is as follows: D5S76—D5S6—D5S39—HEXB—D5S78—DHFR. We have typed a total of 65 markers to date in the Swedish kindred, covering segments of 16 autosomes. Areas where other psychiatric disorders have shown evidence of linkage have been excluded (the HLA region, 11p). The HLA DQ alpha locus was probed with allele-specific oligonucleotides (ASO). Weakly positive lod scores (between 1 and 2) have been found with markers in two different chromosomes—we are pursuing these results to determine whether they are spurious or representative of true linkage.

NR197 **Wednesday, May 10, 9:00 a.m.–10:30 a.m.**

BIPOLAR DISORDER IN THE ELDERLY

Andrew Satlin, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178; David W. Marby, B.A., Iris R. Bell, M.D., Benjamin Liptzin, M.D.

Summary:

Bipolar affective disorder in the elderly has received little study. Controversy exists about the prevalence of mania arising late in life, and about whether this disorder is distinct from early-onset illness. We surveyed all admissions to the geriatric unit at McLean Hospital over a one-year period. Of 103 admissions, 85 had major affective illness, and 25 of these had bipolar disorder (29 percent). Bipolars and unipolars did not differ in rates of family history of affective illness. Patients with a later age of onset had less family history of affective illness ($p = .029$), suggesting the importance of nongenetic factors in the etiology of late-onset illness.

Patients with bipolar disorder had earlier ages of first affective episode than patients with unipolar disorder (40 vs. 59 ($p = .0001$). However bipolars had a late age of onset of mania (mean age = 57), and thus a long latency of 15.7 years between the first episode of depression and the appearance of mania. Mania preceded the first depression in three of the four patients whose mania started before age 40, but followed the first depression in 20 of the 21 whose mania started after age 40. These data suggest that mania appearing, for the first time in late life may be associated with a factor due to aging. Late-onset mania develops frequently among patients with affective illness, but may represent a distinct disorder from early-onset bipolar illness.

NR198 **Wednesday, May 10, 9:00 a.m–10:30 a.m.**

EFFECT OF REARING ON CSF NOREPINEPHRINE IN MONKEYS

Michael H. Ebert, M.D., Psychiatry, Vanderbilt Med Center, A2215 MCN, Nashville, TN 37232; Gary W. Kraemer, Ph.D., Dennis E. Schmidt, Ph.D., William T. McKinney, M.D.

Summary:

Many forms of human psychopathology have been linked to changes in brain biogenic amine systems. The present study determined whether disruption of early social attachment, thought to be important in the development of vulnerability to psychopathology, produced changes in cerebrospinal fluid (CSF) measures of brain catecholamine and indoleamine metabolism in rhesus monkeys (Macaca mulatta). Male rhesus monkey infants were deprived of maternal interaction, peer interaction, or both, over the course of the first 22 months of life. Cisternal CSF was collected under controlled conditions approximately every month and assayed for levels of norepinephrine, its major metabolite (MHPG), and the major metabolites of dopamine (HVA) and serotonin (5HIAA).

Mother deprived infants had significantly lower levels of CSF norepinephrine than mother reared infants over 22 monthly observations. CSF levels of HYA and 5HIAA did not significantly differ with regard to early rearing experience. Mother-deprived infants failed to develop the pattern of positive correlations between CSF amine metabolites and month-to-month stability in level of a particular CSF amine metabolite or CSF norepinephrine that characterized mother-reared infants. Finally, there were changes in CSF norepinephrine levels associated with social separation and social group formation. The level of activity in brain noradrenergic systems appears to be influenced by both prevailing social environment and the prior rearing environment.

NR199 **Wednesday, May 10, 9:00 a.m–10:30 a.m.**

BIOLOGICAL ABNORMALITIES IN PREMENSTRUAL DYSPHORIA

Uriel Halbreich, M.D., Psychiatry, State Univ of NY, 462 Grider St. K-Annex, Buffalo, NY 14215; Nathan Rojansky, M.D., Amiram Barkai, Ph.D., John Piletz, Ph.D., James Perel, Ph.D., Frank Barbarossa, Ph.D.

Summary:

It has been proposed that premenstrual syndromes (PMS) might be caused by a multi-factorial process involving vulnerability, hormonal imbalance, and changes in neurotransmitters and neuromodulators, We performed a series of studies involving women who sought treatment for PMS, women with PMS who did not seek treatment and women with no PMS. The role of fluctuations of gonadal hormones and ovulation was elucidated by studies of normal cycles as well as suppression of ovulation by danazol. Thyroid functions were studied by determination of the TSH response to TRH; in vitro ir TSH levels in lymphocytes in response to TRH and SEA; as well as thyroid antibodies and thyroid hormones. Serotonergic mechanisms were studied by determination of imipramine receptors binding and serotonin uptake in platelets and behavioral and hormonal responses to challenges with the serotonergic precursor tryptophan and the serotonergic agonist m-CPP. α_2 adrenoreceptors were studied by binding to 3H-para amino clonidine. All studies were performed at least twice—during the mid follicular and late luteal phases of the menstrual cycle and included over 120 women. Results suggest that increased luteal phase fluctuations of gonadal hormones are involved in the pathophysiology of PMS and their elimination is associated with improvement in symptoms. Subclinical hypothyroidism is probably a trait in a subgroup of women and might contribute to the vulnerability to PMS but is not a major factor in most cases. A serotonergic impairment is demonstrated which probably is a estradiol dependent defect of synaptic responsiveness. Upregalation of α_2 adreno receptors is also related to severity of dysphoric PMS. These findings are integrated into a partial explanation of the pathophysiology of PMS and its association with affective disorders.

NR200 **Wednesday, May 10, 9:00 a.m–10:30 a.m.**

MAPPING AND CLONING IN REGION OF X-LINKED BPD GENE

Sue Klapholz, M.D., Biochemistry, Stanford University, Stanford Univ Medical Center, Stanford, CA 94305; Chris N. Traver, M.S., Richard Hyman, Ph.D., Ronald W. Davis, Ph.D.

Summary:

There is compelling evidence that in a subset of families a gene for bipolar disorder (BPD) is located on the long arm of the human X-chromosome (Xq28). Classical linkage analysis has revealed close linkage to both the color blindness (CB) and glucose-6-phosphate dehydrogenase (G6PD) deficiency loci. We have initiated a study to clone a large part of the Xq28 region, including the CB to G6PD interval (about two million base pairs (Mb) in size) using yeast artificial chromosome (YAC) vectors. Our goals are: (1) to derive a detailed physical map of the Xq28 region, (2) to generate new probes to detect restriction fragment length polymorphisms that flank the BPD locus, and, ultimately, (3) to identify a candidate BPD gene. We have examined a human (46, XY) genomic DNA library containing inserts of approximately 0.1 Mb cloned into YAC vectors (C. Traver, R. Hyman, R. Davis, unpublished) for the presence of Xq28 sequences. We have screened 25,000 yeast colonies with six different Xq28 probes and have identified two clones that contain Xq28 DNA sequences. We are in the process of isolating the ends of the human DNA inserts to use for "walking" within the library. This library will be rescreened with additional Xq28 probes, and another YAC library, enriched for X-chromosome sequences, will be constructed.

NR201 **Wednesday, May 10, 9:00 a.m–10:30 a.m.**

NORMALIZATION OF LYMPHOCYTE BETA-RECEPTORS BY ECT

John C. Mahler, M.D., Psychiatry, NY Hospital Cornell, 525 East 68th Street, New York, NY 10021; Phillip J. Wilner, M.D., Kathryn S. Johnson, R.N., James P. Halper, M.D., Richard P. Brown, M.D., J. John Mann, M.D.

Summary:

Introduction: Animal studies have demonstrated that both repeated electroconvulsive shocks and chronic administration of most antidepressant medications produce desensitization of central beta-adrenergic receptors. Investigators have postulated that if this effect may mediate the antidepressant action of somatic antidepressant treatments. We and others have previously reported decreased responsivity of lymphocyte beta-adrenergic receptors in patients with major depressive disorder (MDD), endogenous subtype. This study examines the effects of ECT in lymphocyte beta-adrenergic receptor function in patients with MDD. *Methods*: Physically healthy patients with MDD, endogenous subtype were studied one to two days prior to ECT and two to five days after a course of ECT. Lymphocyte beta-adrenergic receptor responsivity was measured as isoproterenol-induced cyclic AMP generation. *Results*: ECT had a significant therapeutic effect with the mean baseline HAMD score of 37.4 ± 1.7 decreasing to 12.0 ± 2.2 ($p = 0.001$) post-treatment. When compared to healthy controls ($n = 24$), pre-ECT patients ($N = 19$) had significant blunting of the cyclic AMP response to isoproterenol stimulation (group = isoproterenol interaction; $F_{6,246} = 6.85$); $p = 0.0001$). Following the course of ECT, isoproterenol-stimulated cyclic AMP levels in the post-ECT patient group were significantly increased (treatment = isoproterenol interaction; $F_{6,108} = 4.12$; $p = 0.001$) and were no longer different from those of the controls (group X isoproterenol interaction; $F_{6,102} = 1.04$; $p = 0.533$). *Conclusion*: This is the first report that a course of ECT can produce a significant resensitization of lymphocyte beta-adrenergic receptors in patients with MDD, endogenous subtype such that isoproterenol generated cyclic AMP levels no longer differ from those of control subjects.

NR202 **Wednesday, May 10, 9:00 a.m–10:30 a.m.**

COGNITIVE THERAPY OF ENDOGENOUS DEPRESSION

Michael E. Thase, M.D., Psychiatry, WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213; Anne D. Simons, Ph.D.

Summary:

Recent research has demonstrated the efficacy of several short-term psychological treatments of major depression, including cognitive behavioral therapy (CBT). Moreover, preliminary data from some centers suggest that CBT may be effective in endogenously depressed outpatients. If correct, these observations suggest that CBT also may be effective in depressions characterized by psychobiologic disturbances, including sleep electroencephalographic (EEG) abnormalities such as shortened REM latency. We present findings from an ongoing protocol evaluating three-night EEG sleep profiles before and after CBT treatment of 38 outpatients ($\bar{x}$ age: 38.5; $\bar{x}$ HAM-D: 21.3) with nonbipolar endogenous (RDC) major depression. All patients were psychotropic medication-free throughout the 16 week protocol. A treatment response rate of 68 percent (26/38) was observed, with significant within-subjects reductions on the HAM-D ($\Delta = -16.3$ is. and Beck ($\Delta = -18.9$ pts.) scores and improvements in global functioning (ΔGAS $= +32.9$) (all p .0001). A similar percentage of patients with either normal or shortened rapid eye (REM) sleep latency responded to CBT [11/17 (65 percent) vs. 15/21 (71 percent)]. Post-treatment sleep studies revealed normalization of sleep revealed normalization of sleep continuity disturbances, but persistence of shortened REM latency and diminished slow wave sleep time in affected patients. Thus, CBT effectively treated endogenous depression but did not rapidly reverse all psychobiological features. Implications of these findings for the differential therapeutics of nonbipolar depression and for the longitudinal study of biological markers in depression will be discussed.

NR203 **Wednesday, May 10, 9:00 a.m–10:30 a.m.**

THERAPIST INTERVENTIONS WITH BORDERLINE PATIENTS

Harold W. Koenigsberg, M.D., Psychiatry, NY Hosp West Division, 21 Bloomingdale Road, White Plains, NY 10605; Otto F. Kernberg, M.D., Ann Appeobaum, M.D.

Summary:

During psychotherapy sessions, the therapist is engaged in a continuous process of deciding which thematic material to address and how to intervene using the material. Interventions may take the form of eliciting more information, confronting puzzling inconsistencies, delivering interpretations, setting limits, and offering advice, among others We have developed a computer based method for analyzing therapist responses to patient material to identify the extent to which the therapist responds to patient introduced themes, and to categorize the type of interventions employed by the therapist. This method, which has been designed to measure therapist adherence to a specific operationally defined psychotherapy for borderline patients, also has application in the teaching of psychotherapeutic technique and in measuring parameters of therapist skill. We have assessed the interrater agreement achievable and, with category kappas of up to 0.85 obtainable, have demonstrated the feasibility of the method. We have applied this session analysis program to psychotherapy sessions of 20 borderline patients treated by experienced and inexperienced therapists, and will present the session profiles generated by the method. We will discuss the application of this approach to training psychotherapists and to manual-based psychotherapy research.

NR204 **Wednesday, May 10, 9:00 a.m.–10:30 a.m.**

PLASMA HVA IN SCHIZOTYPAL PERSONALITY DISORDER

Richard J. Kavossi, M.D., Psychiatry, MT. Sinai Medical Center, Box 1228 One Gustave Levy Pl., New York, NY 10029; Larry J. Siever, M.D., David Bernstein, Ph.D., Emil F. Coccaro, M.D., Michael Davidson, M.D., Kenneth L. Davis, M.D.

Summary:

Abnormalities in dopaminergic functioning as measured by plasma levels of the dopamine metabolite homovanillic acid (pHVA) have been found to correlate with psychotic symptoms in schizophrenia and changes in pHVA have been associated with therapeutic response to neuroleptics. While schizotypal personality disorder (SPD) is phenomenologically and genetically related to schizophrenia, the relationship between pHVA and psychotic-like symptoms in SPD has not been evaluated.

Plasma HVA concentrations were obtained at 10 A.M. via indwelling I.V. catheter in three groups: normal controls (n = 6), SPD (n = 8), and other personality disorders (n = 7). Subjects were medication free for two weeks , and on low monoamine diets for three days. Mean pHVA was significant) higher in SPD (14.96 ng/ml) than in other personality disorders (9.22 ng/ml) or normals (7.77 ng/ml) (F = 15.49 p .0001). Plasma HVA correlated significantly with the sum of psychotic-like schizotypal traits (magical thinking, ideas of reference, illusions, suspiciousness) (r = .56, p .05) but not with the sum of "negative" traits (inadequate rapport, social anxiety, social isolation). Plasma HVA also significantly correlated with two individual psychotic-like schizotypal criteria: magical thinking (r = .56, p .05) and illusions (r = .57, p .05) but not with any individual "negative" a criteria.

These results suggest that dopamine dysfunction is associated with psychotic-like symptoms in SPD. Comparisons with dopamine dysfunction in schizophrenia require further investigation.

NR205 **Wednesday, May 10, 9:00 a.m.–10:30 a.m.**

SMOKING CESSATION, DEPRESSION, AND ANTIDEPRESSANTS

Alexander H. Glassman, M.D., Clin Psychopharm, NYS Psychiatric Inst., 722 West 168th Street, New York, NY 10032; Lirio S. Covey, Ph.D., Fay Stetner, M.S.

Summary:

We have recently demonstrated that clonidine significantly improves success rates in smoking cessation. During the course of the study we made two unexpected observations: a markedly elevated frequency of previous major depression among our sample of heavy smokers and strong evidence that such a history predicts failure in efforts to stop. These trends have been replicated using ECA data. We now report two new findings. Although depression is not listed as a withdrawal symptom in DSM-III-R, among smokers with a history of major depression, its occurrence upon smoking abstinence is both very common and predictive of failure. In an attempt to modify the high failure rate in this group, we pretreated with antidepressant drugs, seven heavy smokers who had a clear history of depression, and had developed depressive symptoms on prior attempts to quit smoking, Pretreatment with either nortriptyline (3) or fluoxetine (4) resulted in complete smoking cessation with no recurrence of depression in six of the seven cases. All subjects have been followed more than six months.

NR206 **Wednesday, May 10, 9:00 a.m.–10:30 a.m.**

REDUCED PLASMA GABA ACTIVITY IN MEN AT RISK FOR ALCOHOLISM

Howard B. Moss, M.D., Psychiatry, Univ of Pitts Sch of Med, 3811 O'Hara Street, Pittsburgh, PA 15213; Jeffrey Yao, Ph.D., Mark Burns, Ralph E. Tarter, Ph.D.

Summary:

Sons of alcoholic fathers (HR and matched control men from families without alcoholism (LR) were administered in a randomized double-blind fashion either a placebo beverage or an isovolemic beverage containing ethanol 0.8 gm/kg). Serial blood sampling for determination of plasma GABA-like activity, mood, and intoxication ratings were performed. The HR subjects were found to have significantly less plasma GABA-like activity than LR during the placebo condition. The alcoholic beverage condition washed out the differences in plasma GABA between groups. Significant interactions between risk group status and beverage conditions were found with respect to plasma GABA-like activity. Plasma GABA-like activity also had a significant inverse correlation with self-reports of perceived tension in the placebo condition, and tension, confusion, and intoxication in response to the alcoholic drink. Since previous investigators have reported reduced plasma GABA levels in individuals, reduced plasma GABA-like activity may be a biological marker for vulnerability to alcoholism or for heightened tension as a behavioral factor which predisposes to alcoholism.

NR207 **Wednesday, May 10, 9:00 a.m.–10:30 a.m.**

A FAMILY STUDY OF PSYCHIATRIC DISORDER ASSOCIATED WITH BULIMIA NERVOSA

Joy Kassett, M.S.W., DIRP/CNE, NIMH Bldg 10 35231, 9000 Rockville Pike, Bethesda, MD 20892; E. M. Maxwell, M.D.W., Elliot S. Gershin, M.D., Harry A. Brandt, M.D., David C. Jimerson, M.D.

Summary:

In addition to adoption and twin studies, family studies help to identify the involvement of genetic and/or familial-environmental influences in the etiology of a psychiatric disorder. Research findings from family studies may not only have an impact on clinical treatment but also on prevention through identification of an"at-risk" population. A family study of psychiatric disorders associated with bulimia nervosa was conducted at the National Institute of Mental Health. Forty probands with bulimia were recruited from a consecutive series of patients admitted to an eating disorders program. Utilizing the family interview method, the probands and their first degree relatives were studied with systematic interviews (SADS-L diagnosed by modified RDC criteria), information from relatives (RPHQ), and medical records where appropriate. Our results indicate significantly higher rates of major affective disorders, eating disorders, and alcoholism in the families of bulimics when compared to controls. Note importantly, the data show higher rates of major affective disorder (BP + UP), and of BP alone in relatives of bulimics who themselves had no history of major affective disorder when compared to controls. This significant finding indicates a familial relationship between bulimia and major affective disorder which suggests the possibility of a common diathesis.

NR208 **Wednesday, May 10, 9:00 a.m.–10:30 a.m.**

EFFECT OF WEIGHT LOSS ON BRAIN NEUROPEPTIDE mRNAs

Mark A. Smith, M.D., Clin. Neuroendocrinology, NIMH/NIH, Bldg 36 Room 2D-15, Bethesda, MD 20892; Linda S. Brady, Ph.D., Philip W. Gold, M.D.

Summary:

Clinical studies have implicated neuropeptides in eating disorders as evidenced by decreased concentrations of proopiomelanocortin (POMC) products such as B-endorphin, and increased levels of corticotropin releasing hormone (CRH), arginine vasopressin (AVP), and neuropeptide Y (VPY) in the CSF of patients with anorexia nervosa. The question remains, however, whether this endocrine profile is specific to eating disorders or simply represents the normal compensatory response to weight loss. We addressed this question by using in situ hybridization to quantitate brain neuropeptide mRNA levels (reflecting neuropeptide secretion) in male and female rats placed on a 10 gram/day diet for 14 days during which time they lost 35 percent of their body weight relative to the control groups which fed ad libitum. Frozen brain sections were thaw-mounted onto slides and ^{35}S-oligonucleotide probes used for hybridization to the neuropeptide mRNAs. Results indicated that POMC mRNA decreased by 50 percent whereas NPY mRNA levels increased by over 100 percent in the arcuate nucleus of both male and female rats placed on the diet. These changes were specific to the arcuate nucleus as POMC mRNA in the pituitary and NPY mRNA in the locus ceruleus were unchanged. No changes in hypothalamic CRH, dynorphin, or vasopressin mRNA levels occurred in the underweight rats of either sex. These results indicate that increased NPY and decreased B-endorphin CSF concentrations in anorexia nervosa may represent normal physiological consequences of weight loss. However, increased secretion of CRH and vasopressin in anorexia nervosa may represent a pathological response to weight loss. In particular, CRH, which is an appetite suppressant, may be important in the pathophysiology of anorexia nervosa.

NR209 **Wednesday, May 10, 12 noon–2:00 p.m.**

THIN AND THICK BOUNDARIES: A NEW PERSONALITY DIMENSION

Ernest L. Hartmann, M.D., Sleep Lab, Lemuel Shattuck Hospital, 170 Morton Street, Jamaica Plain, MA 02130; Robert Harrison, Ph.D., Judith Bevis, Ph.D., Deirdre Barrett, Ph.D., Stephanie Beal, M.A., Robert Kunzendorf, Ph.D.

Summary:

A new, or rather old but little investigated, dimension of personality is "thin and thick boundaries." The mind encompasses a group of processes, functions, mental states, representations. The degree of separateness between these is considered thickness of boundaries. People with thick boundaries keep things separate; they are rigid, defended, armored, "thick-skinned." Persons with thin boundaries are open, undefended, vulnerable. A 138-item Boundary Questionnaire (BQ), developed to examine many aspects of thin and thick boundaries, has been taken by over 1,000 persons. Factor analysis produces 13 orthogonal factors, of which 12 are clearly understandable as aspects of thin or thick boundaries—for instance, a tendency for primary process thinking; fragility; interpersonal openness.

Persons with frequent nightmares and art students score very "thin", while naval officers score very "thick" on the BQ. People who score extremely thick usually have no DSM-III-R diagnosis; some have compulsive personality disorder. People who score thinnest have borderline or schizotypal personality disorder, if they have any diagnosis. Creative artists—sculptors and composers—score thinner than interpretive artists. "Thinness" on the BQ is correlated with three scores of hypnotizability, with influence of emotion on perception, and with biological sleep measures such as amount of phasic REM activity (PIPs) found *outside* REM sleep.

NR210 **Wednesday, May 10, 12 noon–2:00 p.m.**

RHYTHMS IN DEPRESSION: TEMPERATURE AND CORTISOL

Charles P. Pollak, M.D., Chronobiology, New York Cornell Med Ctr, 21 Bloomingdale Road, White Plains, NY 10605; George S. Alexopoulos, M.D., Margaret L. Moline, Ph.D., Daniel R. Wagner, M.D.

Summary:

Several circadian rhythms have been found to be abnormal in Major Depressive Disorder. The properties of the circadian timing system were therefore investigated in depressives living in isolation from all time cues.

Subjects were eight drug-free outpatients with primary, major depression (Hamilton 20-38), and eight age and sex matched normal controls. The studies consisted of four to six days of entrainment to a 24 hour schedule followed by eight to 17 days without a schedule (free-running, FR).

Plasma cortisol levels of the depressed subjects were significantly higher (mean difference 2.6 uq/dl) and more variable at nearly all times of the circadian day. Rectal temperature of the depressives was also significantly higher (mean difference 0.16 deg C) at all circadian times. The circadian peaks and troughs of the FR body temperature rhythm of the depressives, as well as the troughs of the cortisol rhythm, were significantly delayed with respect to the time of mid-sleep. This was attributable to a shorter FR period of the sleep-wake rhythm, since the FR periods of the temperature and cortisol rhythms did not significantly differ between the depressives and controls.

These results suggest that depressed subjects have an elevated "setpoint" for cortisol and temperature than controls and possibly a shorter sleep-wake period. No evidence was found in support of the phase-advance hypothesis of depression.

NR211 **Wednesday, May, 10, 12 noon–2:00 p.m.**

MIGRAINE AND DEPRESSION: THE ZURICH COHORT STUDY

Kathleen R. Merikangas, M.D., Psychiatry, Yale University, 40 Temple Street Lower Level, New Haven, CT 06510; Jules Angst, M.D., Hansreudi Isler, M.D.

Summary:

This paper will present data regarding the association of psychiatric syndromes and migraine headache from a prospective epidemlologic cohort study of 27-28 year olds in Zurich, Switzerland. The prevalence of a migraine of 13.3 percent, approximates estimates from previous epidemiologic studies in other regions of the world.

Consistent with previous reports, there was a strong association between migraine and depression. However, this is the first study to demonstrate this association in an unselected epidemiologic sample with standardized assessment of psychiatric diagnoses. The association between migraine and the anxiety disorders was even stronger than that for the affective disorders. Both the combination of anxiety disorder plus major depression, and pure anxiety disorders, but *not* pure depression, were significantly associated with migraine.

Our data suggest that migraine with anxiety and depression may comprise a distinct syndrome comprised of anxiety, often manifested in early childhood, followed by the occurrence of migraine headaches, and then by discrete episodes of depressive disorder in adulthood. Because of the prospective longitudinal design of this study, future assessments of this cohort will provide further information on the stability of these findings and the course of this cohort as they proceed through adulthood.

NR212 **Wednesday, May 10, 12 noon–2:00 p.m.**

COGNITION IN ENDOGENOUS AND ORGANIC DEPRESSION

Bruce Cohen, M.D., Psychiatry, Johns Hopkins Sch of Med, 600 North Wolfe Street, Baltimore, MD 21205; Sergio E. Starkstein, M.D., Robert G. Robinson, M.D., John R. Linsey, M.D., Peter V. Rabins, M.D.

Summary:

Using the Mini-Mental State Exam (MMSE), cognitive performance was examined in three groups of patients: group one consisted of 13 patients with major depression following stroke and 13 non-depressed stroke patients matched for age, lesion location, and lesion volume; group two consisted of 15 patients with Parkinson's disease and major depression and 15 non-depressed patients with Parkinson's disease matched for age, education, and stage of disease; group three consisted of 14 patients with functional major depression (no clinical or CT evidence of neurologic disease) and 14 age-matched normal controls. All three groups of major-depressed patients had significantly lower (i.e., more impaired) MMSE scores than their respective non-depressed counterparts ($F=10.1$, $df=1,72$, $p<.01$). There were no significant interactions of neurological diagnosis and depression (i.e., the effect of depression was not greater or less in the patients with and without neurological disorder) ($F=.72$, $p=NS$). Their lower scores were due primarily to significantly ($p<.05$) lower scores in the delayed recall task in the MMSE. Although we did not do a detailed neuropsychological assessment in these patients, we did control for age, education, and lesion variables. The results suggest that depression associated with a specific neuropathology has the same magnitude of effect on cognition as depression without known neuropathology. In addition, the major impairment tested by the MMSE that is adversely affected by depression is delayed recall. These findings are also consistent with the suggestion that the pathophysiology of depression in organic and function conditions may be similar.

NR213 **Wednesday, May 10, 12 noon–2:00 p.m.**

ABNORMAL VISUAL EVOKED POTENTIAL IN MELANCHOLIA

Russell G. Vasile, M.D., Psychiatry, NEDH, 110 Francis Street Ste 4A, Boston, MA 02215; Frank Duffy, M.D. Gloria McAnulty, Ph.D., John J. Mooney, M.D., Kerry Bloomingdale, M.D., Joseph J. Schildkraut, M.D.

Summary:

In a previous pilot study (1) utilizing a computer based quantified neurophysiologic technique with mapping to measure brain electrical activity (2), we found abnormalities in the flash visual evoked potential (FVEP) in nine elderly, medically healthy patients with a DSM-III diagnosis of major depression with melancholia when compared to age matched normative control subjects. The major group finding was a large increase of late FVEP epochs (msec) attributable to latency delay and amplitude augmentation seen symmetrically in the posterior quadrants, mid-parietal, and occipital regions. There was no clear medication effect. Again utilizing quantitative mapping techniques we performed a replication study on a new group of 30 hospitalized patients with melancholia ranging in age from 59 to 85 years (mean age 68 years). Clinical computerized EEG and EP reports demonstrated that of the 30 melancholic patients, 18 displayed a clearly abnormal FVEP, five a questionable FVEP, and seven a normal FVEP. The aberrant FVEP was consistently found in the posterior quadrant as in the pilot study. We are currently conducting computer based statistical analyses of the data from this group of elderly melancholic patients in comparison to a group of 15 elderly patients with major depression without a melancholia and an age matched normative control group. In this presentation we shall review the findings from these analyses to characterize more precisely the nature of the FVEP abnormalities as well as lesser abnormalities in EEG background and auditory evoked potentials in the melancholic patients. The relationship of the FVEP abnormalities to psychiatric diagnosis, medication status, age, gender, and catecholaminergic neuronal function will be discussed.

NR214 **Wednesday, May 10, 12 noon–2:00 p.m.**

TRH TEST IN TREATMENT OF DEPRESSION

Paul J. Goodnick, M.D., Medical, Fair Oaks Hospital, 5440 Linton Boulevard, Delray Beach, FL 33484; Irl L. Extein, M.D., Mark S. Gold, M.D.

Summary:

Thyroid insufficiency may exist in patients with normal thyroid hormones and TSH but augmented TSH response to TRH (Extein & Gold, 1986). Thirty-nine patients (8M, 31F; 45.0 SD 15.7 yrs) meeting DSM-III-R criteria for major depression, completed FTI, TSH, and TRH testing. Patients completed the Beck Depression Inventory (BDI) and the General Behavior (manic-depression) Inventory (GBI). They were separated by their Δ TSH results into normal (N), Δ TSH$<$20 [n = 23], and "high" (H), Δ TSH$>$20 [n = 16], groups. Eight "H" patients who were treated with thyroid hormone alone for eight weeks, completed BDI forms at each visit. There was no placebo group. *Results:* The 2 Δ TSH groups showed the expected mean differences in FTI [N = 7.9 $>$ H = 6.2, p = .01]. TSH (N = 2.0 $<$ H = 3.7, p = .06], and Δ TSH [N = 11.6 $<$ H = 27.6, p .001]. The high Δ TSH group had no significant correlation between baseline TSH and Δ TSH [r = .29]. The two groups did not differ in mean BDI or CGI. The eight patients who were treated with thyroid alone for depression had baseline FTI of 6.7, TSH of 4.0, and Δ TSH of 28.0. They had a baseline lifetime GBI of 24.8 and past month GBI of 23.0. In eight weeks, their mean BDI dropped from 21.4 to 4.9 [t = 7.15, p = .0004]. *Thyroid insufficiency may only be revealed by TRH testing, and those depressed patients with high Δ TSH may freguently respond to synthetic thyroid without antidepressants.*

NR215 **Wednesday, May 10, 12 noon–2:00 p.m.**

WELLBUTRIN AND PROZAC IN DEPRESSIVE SUBTYPES

Paul J. Goodnick, M.D., Medical, Fair Oaks Hospital, 5440 Linton Boulevard, Delray Beach, FL 33484; Irl L. Extein, M.D.

Summary:

An eight week study contrasted a dopamine-specific antidepressant, bupropion (Wellbutrin, WB:max, 450 mg/day], to a serotonin-specific antidepressant, fluoxetine [Prozac, PZ;max, 40 mg/day]. Patients were included who met DSM-III-R criteria for major depression; they were not chosen by symptom profile. Patients were subclassified as "atypical" (AD) if hypersomnic/hyperphagic; as bipolar (BD), by history of mania/hypomania; or as typical (TD). At baseline, patients completed the General Behavior Inventory (GBI) of subclinical mood disorder. At every visit, patients completed the Beck Depression Inventory (BDI). Fifty-seven patients (20M, 37F; 44.0 SD 14.0 yrs) included 10BD, 23AD, and 24TD. Thirty-four received WB; 23 received PZ. Baseline BDI ratings were quite similar: WB = 28.2, SD 11.7; PZ = 27.7 SD 11.5. IN AD, WB dropped BDI 12.3 (53 percent) ($t = 4.63$ $p < .001$], but PZ Dropped BDI 3.1 (6 percent) ($t = 0.73$, $p = NS$]. Significant improvement (fall of >50 percent in BDI) was seen for WB in 9/14 but for PZ in 2/9 (Chi-sq = 3.88, $p = .04$]. In TD, WB dropped BDI 6.0 (20 percent) ($t = 1.84$, $p = .09$], but PZ dropped BDI 11.8 (43 percent) ($t = 3.91$, $p = .002$]. Significant improvement was seen for WB in 2/11 but for PZ in 7/13 [Chi-sq = 3.23, $p = .06$]. Furthermore, in BP, WB dropped BDI significantly in 8/9 patients (16.2, 66 percent) ($t = 4.37$ $p < .003$]. Larger numbers are needed for replication, but there may yet be a role for biochemical specificity of treatment of depression; Wellbutrin was effective for bipolar and atypical depression while Prozac was shown to be effective for standard depression.

NR216 **Wednesday, May 10, 12 noon–2:00 p.m.**

SODIUM VALPROATE TREATMENT OF BIPOLAR PATIENTS

Jeffrey Clothier, M.D., Psychiatry, Harris Co Psych Center, 2800 S. Mac Gregor Way, Houston, TX 77025; Thomas Freeman, M.D., Peggy Pazzaglia, M.D., Michael D. Lesem, M.D., Alan Swann, M.D.

Summary:

Sodium valproate (VPA) may represent an alternative for resistant bipolar patients. Seventeen patients with bipolar-manic and schizoaffective disorders were treated in an open-label, escalating fixed dose study. The study design allowed for dosage adjustments every fifth to seventh day until the patient responded or developed toxic manifestations. Patients were monitored with plasma levels and weekly scores of the Brief Psychiatric Rating Scale (BPRS). All patients achieved plasma levels of at least 50ng/ml on 1500 to 4500mg/ day. Eight of the patients had failed lithium; five had failed carbamazepine treatment prior to VPA. Gastric distress, the most common side effect, resolved with the use of an enteric dosage form.

BPRS scores were inversely correlated to the VPA plasma concentrations. Average BPRS score prior to the administration of VPA was 37.7, with a range of 21 to 60. Average change in BPRS was 70 percent, with a standard deviation of 15 percent. Eight patients failed to achieve final BPRS scores of less than 10 and one patient worsened with VPA.

Valproic acid appears to be useful in the treatment of many lithium-resistant or lithium-intolerant patients. The characteristics of VPA responders and pattern of response will be presented.

NR217 **Wednesday, May, 10, 12 noon–2:00 p.m.**

SEROTONIN-2 RECEPTOR BINDING SITES IN DEPRESSION

Ghanshyam Pandey, Ph.D., Illinois State Psych Inst, 1601 W. Taylor Street, Chicago, IL 60612; Subhash Pandey, Ph.D., Philip Janicak, M.D., Robert C. Marks, M.D., John M. Davis, M.D.

Summary:

Reports of decreased imipramine binding sites and serotonin uptake in platelets of depressed patients and increased 5MT-2 receptor binding sites in the post-mortem brain of suicide victims provide evidence for the involvement of the serotonergic system in the pathophysiology of depression. In order to examine the role of serotonin receptors in the etiology of depression, we studied platelet serotonin-2 receptor binding sites in drug-free hospitalized depressed patients and nonhospitalized norma] control volunteers by binding techniques using ^{125}-LSD as the binding ligand. The maximum number of binding sites (B_{max}) and apparent dissociation constant (K_D) was calculated by Scatchard Analysis in each subject. We observed that the mean B_{max} (68.5 ± 7.9 fmole/mg protein) in 16 depressed patients was significantly higher as compared to the mean B_{max} (46.5 ± 5.1) in 19 normal control volunteers. The mean K_D ($1.5 \pm .32$ nM) in the depressed patients was not significantly different from the mean K_D ($1.5 \pm .24$ nM) in normal controls. We did not find any significant correlation between baseline B_{max} and K_D with the baseline HDRS or BPRS scores and there were no significant correlations between the HDRS or BPRS change score and the baseline B_{max} or K_D of ^{125}I-LSD binding. These results thus indicate increased 5HT-2 receptor binding sites in the platelets of depressed patients as compared to normal control subjects. Our studies are consistent with the previous reports of increased 5HT-2 receptor binding in the post-mortem brain of suicide victims and thus indicate that increased 5HT-2 receptor number and function may be associated with the pathophysiology of depression.

NR218 **Wednesday, May 10, 12 noon–2:00 p.m.**

PRO-GAMMA-MSH LEVELS IN DEPRESSION

Murray A. Morphy, M.D., Psychiatry, VA Medical Center, 3495 Bailey Avenue, Buffalo, NY 14215; Giovanni A. Fava, M.D., Robert C. Pedersen, M.D., Maria Zielezny, Ph.D., Nicoletta Sonina, M.D., Alexander C. Brownie, Ph.D.

Summary:

There is current controversy over the mechanisms underlying hypothalamic-pituitary-adrenal (HPA) axis hyperactivity in depression. Pro-gamma-MSH, a portion of the terminal region of POMC, has been shown to act synergistically with ACTH in stimulating corticosteroid secretion both in vitro and in vivo. Pro-gamma-MSH and ACTH plasma levels were measured in 30 drug-free male patients with a DSM-III-R diagnosis of major depression and in 21 healthy control subjects. Baseline levels, measured by RIA, were similar in the two groups. After single-dose metyrapone stimulation the night before, both a.m. hormones increased, but pro-gamma-MSH was significantly higher (P 0.05) in control subjects(mean = 70.6; SD = 37.9 pg/ml) than in depressives (52.2 ± 24.1). After overnight dexamethasone (1 mg), a.m. ACTH was significantly ($P <= 0.05$) less suppressed in depressives (34.5 ± 20.8 pg/ml) than controls (20.1 ± 28.2), whereas there were no significant changes in pro-gamma-MSH levels. These results suggest that HPA axis dysregulation in depression may involve pituitary peptides other than ACTH and may thus be more complex than previously reported.

NR219 **Wednesday, May 10, 12 noon–2:00 p.m.**

PREMENSTRUAL DYSPHORIC CHANGES IN DEPRESSED PATIENTS

Joseph E. Malikian, Ph.D., Psychiatry, Four Winds Hospital, Four Winds 800 Cross River Rd, Katonah, NY 10536; Stephen Hurt, Ph.D., Jean Endicott, Ph.D., Jeanne R. Delaney, R.N.

Summary:

While most studies have investigated retrospectively the occurrence and recrudescence of psychiatric symptoms during the premenstruum in women with a lifetime history of depressive syndromes, to date there are virtually no prospective longitudinal studies investigating premenstrual worsening of continuously experienced depressive and associated depressive symptoms in hospitalized females with either major or minor depressive episodes. The degree to which the premenstruum impacts on the course of existing depressive symptomatology is an area which remains relatively unexplored.

For the duration of one menstrual cycle, changes in depressive mood, behavior, and somatic functioning of 33 hospitalized patients with major and minor depressive disorders were analyzed retrospectively and prospectively to determine whether psychological and physical symptoms were exacerbated during the five days preceding the onset of menstruation [premenstruum] as compared to a hormonally stable baseline period of five days during the postmenstrual phase.

The results indicate that major and minor depressives were manifested significant premenstrual exacerbation of depressive mood, suicidal ideation, social withdrawal, hostility/anger, and somatic functioning.

NR220 **Wednesday, May, 10, 12 noon–2:00 p.m.**

INSULIN RECEPTOR BINDING IN DEPRESSED PATIENTS

Keith Caruso, M.D., Psychiatry, Cornell Univ Med Center, 525 E. 68th Street Room P277, New York, NY 10021; Robert Rees-Jones, M.D., Peter E. Stokes, M.D., James H. Kocsis, M.D.

Summary:

Insulin receptor function in patients with major depression has thus far been studied by indirectly measures such as the insulin tolerance test (ITT). ITT studies have demonstrated that depressed patients are less sensitive to the effects of an exogenous insulin challenge than normal controls.[1] It is likely that this insulin insensitivity is due to down-regulation of insulin receptor binding. In order to test this hypothesis, we are studying in vitro binding of ^{125}I radiolabeled insulin to insulin receptors on erythrocytes from nondiabetic patients with major depression and normal controls using a method developed by Gambhir et a1.[2] Pilot data from six patients with unipolar major depression and five normal controls indicate that there is a 40 percent decrease in insulin binding to receptors on erythrocytes of depressed patients (6.6 ± 2.9 percent) compared to normal controls (11.0 ± 0.6 percent). These findings are significant ($t = 3.67$, $df = 9$, $p < 0.01$). Because adrenocortical hyperactivity is known to affect carbohydrate metabolism, we also studied subjects using the dexamethasone suppression test (DST). Our findings were even more impressive when we included only the DST nonsuppressors ($N = 5$) among the depressed patients (5.7 ± 0.5 percent binding) and compared them to normal controls ($t = 5.95$, $df = 8$, $p < 0.001$). Our findings suggest that previous findings of insulin insensitivity on the ITT in depressed patients are secondary to down-regulation of insulin receptor binding. We will also discuss the relationship of insulin receptor binding to cortisol measures in plasma and urine and the role of insulin receptor down-regulation to weight loss in patients with major depression.

NR221 **Wednesday, May 10, 12 noon–2:00 p.m.**

MEDICAL ADRENAL SUPPRESSION IN MAJOR DEPRESSION

Beverly E. Pearson Murphy, M.D., Psychiatry, McGill University, 1650 Cedar Avenue, Montreal, Canada H3G 1A4; Veena Dhar, M.D., A. Missagh Ghadirian, Guy Chouinard, M.D., Robert Keller, M.D.

Summary:

We present the first clinical trial of medical adrenal suppression in the treatment of major depression in the absence of Cushing's syndrome. All six patients satisfied the DSM-III-R criteria for major depression; two were psychotic and two melancholic; in addition patients were considered to have failed to respond to conventional antidepressant drugs. All had hypercortisolemila, and four had a positive DST. Patients entered into the trial after a three-day drug washout period. Patients were rated regularly using the Hamilton Depression Scale (HAM-D) and the Zung self-rating scale. So far four patients have completed an eight-week course of treatment using aminoglutethimide $\pm$ metyrapone (well known adrenal suppressing drugs), the dose being increased according to the response in cortisol and dehydroepiandrosterone (DHAS) levels. No psychotropic drugs other than chloral hydrate and/or benzodiazepines prn were permitted. All patients were considered to respond to the treatment; however two patients, after six weeks, started to escape—their cortisols and DHAS's rose, along with the HAM-D's; these two patients are considered partial responders. Mean HAM-D before treatment (24.5 ± 1.1, $n = 6$) fell to 11.3 ± 2.3 ($n = 6$, each value being the mean of available ratings for each patient) during treatment ($P < 0.005$). The first two patients have continued to do well off all drugs for seven months and two months, respectively. These results suggest that steroid suppression may offer an alternative treatment in major depression and that, if adequate, may permit a readjustment of the hypothalamic-pituitary-adrenal axis to occur, leading to a lasting remission.

NR222 **Wednesday, May 10, 12 noon–2:00 p.m.**

AFFECTIVE DISTURBANCES IN PRECLINICAL HYPERTHYROIDISM

Dr. Siegfried Kaumeier, Psychiatry, AISG, J 5, Mannheim 06800, West Germany; Dr. Martina Rockel, Prof. Klaus H. Usadel, Dr. Josef Teuber, Dr. Reinhold Schmidt, Prof. Heinz Hafner

Summary:

The study reported here was undertaken to establish the degree to which a person in a preclinical state of hyperthyroidism, with (by definition) euthyroid T3 and T4 levels but suppressed TRH on testing, already exhibits psychological changes and clinical symptoms. Two groups of 20 patients each, with clear clinical and preclinical hyperthyroidism were studied, as well as a group of 20 controls. The subjects' psychological state of mind was investigated using self-rating scales. Cognitive achievments were evaluated using the d2 test. Subjects were examined for somatic symptoms in accordance with Crooks' index of hyperthyroidism. In both patient groups, a significant increase in anxiety, a sense of not feeling well, and emotional irritability were found, as well as a tendency toward depressiveness, and an increased lack of vitality and activity. Attentiveness and concentration in both patient groups were lower than in the control group. Both patient groups showed the same prevalence of symptoms, such as palpitations, preference of cold over heat, excessive sweating, nervousness, fine digital tremor, and increased heart rate. With regard to the results, the diagnosis "preclinical hyperthyroidism" thus gains clinical importance.
Key words: Preclinical hyperthyroidism—Psychological changes—Clinical symptoms.

NR223 **Wednesday, May 10, 12 noon–2:00 p.m.**

COGNITIVE IMPAIRMENT AND BRAIN STRUCTURE IN BIPOLARS

Jeffrey A. Coffman, M.D., Psychiatry, Ohio State University, RM 071 Upham Hall 473 W 12th, Columbus, OH 43210; Henry A. Nasrallah, M.D., Robert A. Bornstein, Ph.D., Stephen C. Olson, M.D., Steven B. Schwarzkopf, M.D.

Summary:

Introduction: In contrast to schizophrenia, there are no systematic studies of brain structure versus cognitive function in patients with bipolar affective disorders. We report here a study of neuropsychological performance and magnetic resonance imaging (MRI) brain structural measurements in bipolar patients. *Method*: Thirty patients with bipolar disorder (ten males, 14 females) and 52 control volunteers (ten males, 18 females) consented to participate in the study. Diagnosis was done with a structured interview (SCID). The neuropsychological test battery included the WAIS-R, and an expanded Halstead-Reitan Battery. Twenty-seven of each group completed MRI scores which were performed on a 1.5 T GE Sigma instrument. The midsagittal, cranial, cerebral, frontal, and callosal areas were measured with computerized planimetry. Data analysis included ANOVA covarying for age, symptom level and education, and correlation between MRI variables and neuropsychological variables having discriminatory power. *Results*: ANOVA and ANCOVA, where appropriate, showed bipolars to perform poorly across multiple neuropsychological measures including Wisconsin Card Sort, Knox Cube, and Pegboard tests. IQ did not differ. Cerebral MRI measures, especially frontal and cerebral areas correlated significantly with neuropsychological performance in the expected direction (smaller structure, poorer performance). The data suggest that bipolar patients have significant cognitive deficits and structural brain difference from controls and that bipolar illness may be associated with significant cognitive impairment in contrast to the uniformly favorable outcome Kraepelin observed. These results are similar to our previous findings in schizophrenics, and suggest cognitive impairment and altered brain structure in bipolar disorder.

NR224 **Wednesday, May, 10, 12 noon–2:00 p.m.**

ALTERED SYMPATHOMEDULLARY RESPONSIVITY IN MDD

Philip J. Wilner, M.D., Psychiatry, New York Hospital, 525 East 68th Street, New York, NY 10021; Katherine Johnson, R.N., Jaw-Sy Chen, Ph.D., John A. Sweeney, Ph.D., J. John Mann, M.D.

Summary:

Goals: Elevated plasma norepinephrine (NE) levels have been reported in patients with Major Depressive Disorder (MDD) after postural challenge. We have further evaluated sympathetic nervous system (SNS) function by measurement of epinephrine (EPI) release in addition to NE, heart rate (HR), and blood pressure (BP) responses to postural challenge. *Methods:* Patients (N=40) and healthy controls (N=30) rested supine for 30 minutes after insertion of an IV catheter. NE, EPI, HR, and BP were measured supine, three and five minutes after standing. Patients met RDC criteria for MDD, endogenous subtype, were on no medications, and had no active medical illnesses. *Results:* Patients had significantly higher levels of EPI at rest and at three minutes of standing ($p<.05$) than controls. There was no difference after five minutes of standing. We did not find significant differences in NE levels. HR was significantly higher in the depressed group at three minutes (p .05), paralleling the EPI rise. BP was comparable in both groups. EPI release correlated with NE release in the control group, but not in the depressed group ($p<.05$). *Significance:* (1) These findings suggest that patients have elevated resting sympathomedullary function and faster sympathomedullary response to a postural challenge; (2) There is a dissociation of sympathomedullary responses from other SNS responses in MDD; (3) These findings may be due to heightened adrenomedullary reactivity or altered central regulation of the SNS.

NR225 **Wednesday, May 10 12 noon–2:00 p.m.**

SPEM ABNORMALITY IN MAJOR DEPRESSION, ECT EFFECTS

Dolores Malaspina, M.D., Psychiatry, Columbia University, 722 W. 168th Street Box 58, New York, NY 10032; Xavier F. Amador, Ph.D., Harold Sackeim, Ph.D., Eliza A. Coleman, B.A., Sukdeb Mukherjee, M.D.

Summary:

Smooth pursuit eye movement (SPEM) abnormality is associated with schizophrenia but it has not been well described in other groups of seriously ill psychiatric patients, nor has the effect of ECT treatment of SPEM been well characterized. In this study SPEM was evaluated by EOG in 27 RDC depressed patients (age = 55 + 15 yr) 30 RDC chronic schizophrenic patients (age = 34 + 7 yr), and 20 normals (age = 30 + 6 yr). Study aims were to (1) determine rates of SPEM abnormality, (2) examine effects of ECT treatment of depression on SPEM, and (3) to characterize the nature of SPEM abnormality specific to schizophrenia.

The depressed patients had been admitted for an ECT research protocol, and they were free of psychotropic medications for at least ten days execpt for prm doses of lorazepam in 23 patients to control agitation. SPEM was abnormal in 5 percent of controls, 60 percent of schizophrenics, and 67 percent of pre-ECT depressives. Explanations for the high rate of abnormality in depression in this study include effects of age, lorazepam, and state effects of depression. Correlations to the impaired tracking were; r = .35 for advancing age, r = .14 for increasing lorazepam dose, and, of note, r = .50 for Hamilton Depression scores. ECT did not appear to worsen SPEM performance. Of 13 patients evaluated a two month follow up after treatment, only four evidenced abnormal SPEM.

Abnormal SPEM in the schizophrenic and depressed patient groups did not differ with regard to the degree of abnormality, the quantity of large saccadic intrusions ($\geq 5°$), and a measure of variability in tracking during the evaluation. Thus, these measures failed to distinguish characteristics of SPEM abnormality specific to schizophrenia.

NR226 **Wednesday, May 10, 12 noon–2:00 p.m.**

DISRUPTION OF NORADRENERGIC RHYTHM IN DEPRESSION

Larry J. Siever, M.D., Psychiatry, Bronx VAMC, 130 West Kingsbridge Road, Bronx, NY 10468; Martin Teicher, M.D., Emil Coccaro, M.D., Kim Owen, M.D., Ren Kuy Yang, M.D., Steven Gabriel, Ph.D.

Summary:

Dysfunction of the monoamine/neuroendocrine systems in depression has been conceptualized as reflecting:

1) alterations in net activity, 2) phase shift in the circadian rhythm, or 3) dysregulation of their activity. The last hypothesis implies disruption of normal dominant circadian rhythms with replacement by higher frequency ultradian harmonics, resulting in an "erratic," inefficient system. Newly developed non-linear multioscillator cosinor analyses of serial determinations of neurotransmitter/hormone concentrations offer a new tool to empirically test the dysregulation hypothesis. Concentrations of plasma 3-methoxy-4-hydroxyphenylglycol (MHPG), were sampled at one hour intervals and plasma norepinephrine and pituitary hormones were sampled at half-hour intervals for either an eight hour or 24 hour period in 41 acutely depressed patients, 22 remitted depressed patients, and 24 age-and sex-matched controls. While mean concentrations of plasma MHPG did not significantly differ between groups, the peak plasma MHPG concentration occurred significantly earlier in the day ($p<0.01$) and showed significantly more variance ($p<0.05$) in the acute depressed patients compared to the controls. Cosinor analyses of individual patients serial MHPG samples revealed an absence of a circadian rhythm but the presence of 12, six, and four hour ultradian rhythms in the acute depressed patients, which tended to normalize in the remitted depressed patients. These results as well as results of cosinor analyses of the other variables suggest this strategy may be useful in the evaluation of neuromodulator rhythms and support a dysregulation hypothesis of the noradrenergic system in depression.

NR227 **Wednesday, May 10, 12 noon–2:00 p.m.**

B-ENDORPHIN RELATED SYMPTOMS IN LATE LUTEAL DISORDER

A. James Giannini, M.D., Psychiatry, Neoucom, P.O. Box 2169, Youngstown, OH 44504; David M. Martin, M.D.

Summary:

Fifty-three women who met DSM-III R criteria for late luteal phase disorder were studied. All ranged in age between 21 and 32. Thirty-five were white, one was Oriental, and seven were black. All signed consent forms to participate in the study. Responses were measured by Brief Psychiatric Rating Scale and a daily caloric diary.

Serum levels of β -endorphin were measured on the first, tenth, fifteenth, twentieth, and twenty-fifth day of each two menstrual cycles. Twenty-one women had significant decline in β -endorphin ($p<0.02$) on the twentieth day as compared to 32 women without β -endorphin decline.

This drop was associated with increased anxiety ($p<0.01$), increased physical discomfort ($p<0.01$), decreased concentration ($p<0.05$), and increased caloric consumption (p 0.05).

NR228 **Wednesday, May 10, 12 noon–2:00 p.m.**

TRANSDERMAL AND ORAL CLONIDINE IN LATE LUTEAL PHASE DISORDERS

A. James Giannini, M.D., Psychiatry, Neoucom, P.O. Box 2169, Youngstown, OH 44504; David M. Martin, M.D.

Summary:

Forty women who met DSM-III R criteria for late luteal phase dysphoric disorder syndrome were included in this study. All were white, middle class, aged from 24 to 31, and had significant declines in plasma β-endorphin prior to the luteal phase. Clonidine, an β-agonist, has been reported effective in treating preluteal symptoms associated with a significant β-endorphin decline.

Twenty subjects each were randomly assigned to groups A or B and signed consent forms. Group A patients adhered to the following protocol; clonidine 0.1 mg. b.i.d., p.o. with sham patches for the first two months, placebo and sham patches for the next two months, then clonidine 0.2 mg. q.d. via transdermal patches with placebo for the last two months. Group B subjects received this medication schedule in reverse order. Responses were scored blindly with the Brief Psychiatric Rating Scale by two researchers. There were no significant differences between researchers' scores ($p<0.05$).

Both oral and transdermal systems were superior to placebo ($p<0.01$). Neither system was superior to the other ($p<0.05$). Also, order of delivery did not change outcome. Transdermal clonidine treatment may be useful in treating these dysphoric patients with significant drops in β -endorphin.

NR229 **Wednesday, May 10, 12 noon–2:00 p.m.**

PSYCHOBIOLOGIC EFFECTS OF BETA-ADRENERGIC BLOCKADE

Robert N. Golden, M.D., Psychiatry, Univ of Carolina, CB #7160, Chapel Hill, NC 27599; Terry Brown, D.O., Manuel Tancer, M.D., George Mason, Ph.D., Lillie Burnett, M.S.N., Dwight L. Evans, M.D.

Summary:

We examined the role that dysregulation of noradrenergic systems might play in the pathogenesis of affective illness by studying the effects of acute and chronic beta-adrenergic receptor blockade on several of the psychobiologic "stigmata" of depression in healthy volunteers: mood state, HPA axis activity, and cognitive functioning. Ten male subjects (mean age: 25.8 years) who were free of medical disease and who had negative personal and family histories of psychiatric illness participated after giving informed consent. Each subject was evaluated with a series of clinical, cognitive, and biologic assessments at baseline; these tests were repeated one week later after acute (24 hour) exposure to 80 mg bid propranolol (PROP), and again after chronic (14 day) exposure.

Chronic, but not acute PROP led to a statistically significant increase in mean Hamilton Depression Rating Scale scores, although the magnitude of the increase was not clinically significant. Self-reports of feelings of hopelessness increased significantly following acute and chronic PROP, and there were similar trends toward increased feelings of guilt and sadness.

Twenty-four hour urinary free cortisol excretion decreased after acute and chronic PROP. Performance on effortful" cognitive tasks improved following acute and chronic beta-blockade; in contrast, performance on effortless" cognitive tasks declined following acute PROP, with a return to baseline levels after chronic PROP. The implications of these findings regarding the role of noradrenergic dysregulation in depressive symptomatology will be discussed.

NR230 **Wednesday, May 10, 12 noon–2:00 p.m.**

CHOLECYSTOKININ SECRETION IN DEPRESSIVE SUBTYPES

Thomas D. Geracioti, M.D., Neuroendocrinology Branch, NIMH Bldg 10 RM 35231, NIH Clinical Center, Bethesday, MD 20892; Jean R. Joseph-Vanderpool, M.D., Norman E. Rosenthal, M.D., Mitchell A. Kling, M.D., Themis Kamilaris, M.D., Phillip W. Gold

Summary:

Cholecystokinin is a peptide hormone produced both by the CNS and the gastrointestinal tract. CCK is normally secreted into the plasma immediately upon commencement of feeding and may, via receptors in the vagus nerve and nucleus tractus solitarius, send satiety signals to hypothalamic feeding circuits. We have recently shown that meal-related CCK secretion correlates positively with a subjective sense of satiety in volunteers. We have also found that bulimics have both an impaired sense of postprandial satiety and impaired meal-related CCK secretion.

We report here further investigations of CCK secretion in melancholic and seasonally depressed patients. It is well known that hyperphagia is a major component of atypical and seasonal depressives and the cardinal symptom of bulimia nervosa, while anorexia nervosa and melancholia show restricted food intake and weight loss. Compared to controls, winter depressives with hyperphagia have significantly reduced integrated CCK secretion following test meal administration, while preliminary evidence shows robust meal related CCK secretion in melancholics with anorexia.

We have also begun to explore the dynamics of cholecystokinin secretion into the cerebrospinal fluid utilizing an indwelling lumbar catheter. In studies with volunteers, we note that this pepetide is secreted into the CSF in large (ng/ml) quantities in an episodic fashion which may bear some relationship to food ingestion. Further study of this paramter in volunteers and patients is now underway.

NR231 **Wednesday, May 10, 12 noon–2:00 p.m.**

THE CORNELL DYSTHYMIA RATING SCALE

Barbara J. Mason, Ph.D., Psychiatry, Cornell Medical College, 525 East 68th Street, New York, NY 10021; James H. Kocsis, M.D., Allen J. Frances, M.D.

Summary:

Chronic depressive syndromes (DSM-III Dysthymic Disorder) have recently been shown to respond to antidepressant medications. Traditional scales for measuring change and outcome such as the Hamilton, were developed using samples of acute recurrent and episodic depressives, were heavily weighted toward somatic and vegetative symptoms, and were cued to comparisons with recent, normal premorbid periods. Dysthymic disorders have an insidious onset, run a chronic course, and have prominent cognitive and behavioral symptoms. Thus for rating severity and measuring change in dysthymia, it would be useful to develop a scale more specifically designed for assessment of this syndrome.

As part of an ongoing drug treatment study, ratings were made on 43 items measuring depressive symptoms in 56 subjects having DSM-III Dysthymic Disorder, 24-items from the Hamilton, plus 19 additional items derived from the DSM-III list of associated symptoms for Dysthymic Disorder.

Frequency distributions and correlation matrix were generated. Items were eliminated if they were seldom endorsed or were redundant. A factor analysis indicated that the dysthymic sample was described by a body energy factor and an affective factor. Items were included to represent the major factors.

Twenty items were selected to comprise the Cornell Dysthymia Rating Scale. Anchor points were established for each item using the format from the SADS (Spitzer et al, 1978). Preliminary results of the use of this scale in patients undergoing treatment for dysthymia will be presented.

NR232 **Wednesday, May, 10, 12 noon–2:00 p.m.**

PROGESTERONE AND PROVERA IN THE TREATMENT OF MRMD

Peter J. Schmidt, M.D., BPB, NIMH Bldg 10 3N238, 9000 Rockville Pike, Bethesda, MD 20892; Christine Hoban, M.S.W., Gay N. Grove, M.S.N., George M. Merriam, M.D., David R. Rubinow, M.D.

Summary:

We compared the efficacy of progesterone suppositories and of the oral synthetic progestin, Provera, with placebo in 12 women with prospectively confirmed diagnoses of menstrual-related mood disorder (MRMD). Patients also met DSM-III-R criteria for late luteal phase dysphoric disorder (LLPDD). Following a three month baseline period on no medication all subjects received an initial month of placebo (single blind). Patients then received a double blind and randomized sequence of three month trials of progesterone (400 mg), provera (10 mg), and placebo. Patients took both tablets and suppositories throughout the study to maintain the blind. Subjects ccmpleted daily self-ratings of a variety of affective and physical symptoms during the baseline pericd and for the duration (ten months) of the treatment study. For the ten patients who completed the study, ANOVA showed no evidence of significant improvement in any of the affective or physical symptoms measured on either progesterone or provera compared with placebo or no drug (baseline evaluation). Further, none of the subjects showed individual evidence of significant improvement in any of the symptoms measured on either progesterone or Provera ccmpared with placebo or baseline. Our results suggest that prior demonstrations of the efficacy of progesterone in MRMD and of high placebo response rates appear to reflect methodological problems (addressed by this study) including diagnostic heterogeneity, brief trial length, and the use of only inactive control medication.

NR233 **Wednesday, May, 10, 12 noon–2:00 p.m.**

LONGITUDINAL SLEEP ENDOCRINE STUDY IN DEPRESSION

Axel Steiger, M.D., Psychiatry, Univ of Freiburg, Hauptstrasse 5, Freiburg 07800, West Germany; Isabella Heuser, M.D., Florian Holsboer, M.D.

Summary:

Sleep structure and endocrine activity are known to be changed in depressed patients. The simultaneous examination of both phenomena enables investigation of interactions between several biological axes. We performed a longitudinal sleep endocrinological study in 12 male inpatients (mean age 46 years) with major depression. Sleep-EEG and nocturnal hormonal profiles (cortisol, growth hormone (GH), prolactin, and testosterone) were examined under drug-free conditions (1) before treatment (t_1) and (2) after recovery (t_2). At t_1 sleep-EEG showed characteristical changes as decreased slow wave sleep and shortened REM-latency. At t_2 most sleep variables remained unchanged, while sleep-stage 4 percent decreased. The cortisol concentration decreased at t_2, cortisol nadir and rise shifted to a later clocktime. GH concentration was blunted at t_1 at t_2. The testosterone concentration increasedd at t_2. Prolactin variables showed no differences between both examinations. Our data demonstrate that an enhanced cortisol secretion and a blunted testosterone concentration are state markers of acute depression. Cortisol secretion normalizes independently from sleep structure. Prolactin concentration is not affected by depression. We suggest that the persistence of a disturbed sleep structure and a blunted GH release in remitted patients represent a biological scar, due to the metabolic aberrancies during acute depression.

NR234 **Wednesday, May, 10, 12 noon–2:00 p.m.**

RELIABILITY OF RECALL OF PAST DEPRESSIVE SYMPTOMS

Delbert G. Robinson, M.D., Psychiatry, Hillside Hospital, Box 38, Glen Oaks, NY 11004; Jose Alvir, Ph.D.

Summary:

When evaluating a depressed patient not known to him or her previously, clinicians frequently have to rely on the patient's report of past symptoms in order to make a longitudinal diagnosis. To assess the accuracy of this information, forty-one former patients of an cutpatient research mood disorders clinic were interviewed two to six years after they initially applied for treatment in the clinic. The interview consisted of two parts. In the first part, subjects were interviewed about the symptoms they had when they first applied to the clinic. The second part of the interview consisted of an Interval ADS-L to assess clinical status since discharge from the clinic. Ratings of individual RDC depression criteria and of overall RDC diagnoses based on subjects' recollections of their past symptoms were then compared to the ratings on these same items made by research staff When the subject first applied to the clinic. Kappa statistic for RDC depression criteria ranged from 0.77 for loss of interest to -0.21 for diminished concentration. Kappa for RDC major depression was 0.68 and 0.28 for intermittent depressive disorder. Sex, course of illness both before and after initial clinic visit, or diagnosis at recall did not effect reliability.

NR235 **Wednesday, May 10, 12 noon–2:00 p.m.**

ATYPICAL FORMS OF RECURRENT MAJOR DEPRESSION

Michael E. Thase, M.D., Psychiatry, WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213; Linda Carpenter, B.A., David J. Kupfer, M.D.

Summary:

Recent work by Liebowitz, Quitkin, Klein, and colleagues indicates that atypical depressions (AD) respond preferentially to MAOIs such as phenelzine. Such findings provide the strongest evidence to date concerning the diagnostic significance of depressive syndromes characterized by mood reactivity, anergia, *and* reversed neurovegetative features (hypersomnia and/or hyperphagia). We report an investigation of the prevalence and significance of atypical depressions in a sample of 211 patients with DSM-III/RDC recurrent major depressive disorder (mean age:39.2; mean HAM-D score: 22). Twenty eight patients (13 percent) met modified Columbia criteria for AD, a prevalence significantly greater than expected by the chance aggregation of criteria ($X^2 = 9.4$, $p = .002$). An additional 101 patients (48 percent) with unreactive mood had at least two of the remaining symptom criteria; this subgroup was named Pittsburgh Anergic Depression (PAD). Few differences emerged in demographic and pretreatment symptom - variables (beyond those dependent upon the selection criteria) when the AD and PAD groups were compared with the remaining "typical" depressions. However, response to a standardized 16 weeks pretreatment protocol with imipramine (mean dose:226mg) and interpersonal psychotherapy was significantly poorer in the AD and PAD groups on both the HAM-D (repeated measures ANOVA: $F = 2.41$, df^{16}, $p = .003$) and life table analysis of time to remission ($X^2 = 10.0 = 007$). Nearly 80 percent of the AD and PAD nonresponders subsequently responded to an MAOI. Overall results support the value of separately grouping depressive episodes characterized by reversed vegetative features and broadening the spectrum of AD to include some episodic major depressive disorders with loss of mood reactivity.

NR236 **Wednesday, May, 10, 12 noon–2:00 p.m.**

CSF NEUROPEPTIDE CHANGES IN DEPRESSION AND SUICIDE

Mihaly Arato, M.D., Research, Hamilton Psych Res Ctr, P.O. Box 585, Hamilton, Ontario, Canada L8J 2N6; Csaba Banki, M.D., Laszlo Tothfalusi, Ph.D., Garth Bissette, Ph.D., Charles B. Nemeroff, M.D., Huda Akil, Ph.D.

Summary:

Neuroendocrine investigations of depressed patients have indicated some association between neuroendocrine dysregulation and suicidal behavior. To further explore this possible relationship we have measured the concentrations of neuropeptides and hormones (corticotropinreleasing factor, CRF; thyrotropin-releasing hormone, TRH; ACTH; cortisol and beta-endorphin) in the cerebrospinal fluid (CSF) of suicide victims as well as of depressed patients with and without previous suicide attempt. CSF samples from suicide victims were obtained in the first ten hours after death, and the possible influence of various factors (age, sex, postmortem interval, and clock-time of death) on the neuropeptide levels have been also analyzed. We have found elevated CSF, CRF, and TRH levels in the suicide victims compared to the controls (acute cardiac death). There was no difference in the ACTH, cortisol, and beta-endorphin levels. The depressed patients also showed higher CRF and TRH levels than the neurologic controls; however, patients with and without a suicide attempt did not show any difference. It suggests that the elevated neuropeptide levels found in suicide victims may be related to the underlying affective disorder and not to the suicidality. The measurement of the hypothalamic neuropeptides in the CSF can better incidate the endocrine dysfunctions in depression than the peripheral hormone measurements.

NR237 **Wednesday, May 10, 12 noon–2:00 p.m.**

BRIGHT LIGHT BENEFIT UNRELATED TO REM LATENCY

Univ of Calif San Diego, V116A, La Jolla, CA 92093; J. Christian Gillin, M.D., Daniel J. Mullaney, M.S.

Summary:

To determine the benefits of bright light treatment on hospitalized veterans with *nonseasonal* major depressive disorders, 51 depressed patients were treated with light for one week. Considering Hamilton, Beck, and circadian mood ratings combined into a common z score, and contrasting the last three days of treatment with both pretreatment baseline and posttreatment recovery, bright light was significantly superior to placebo in reducing depression scores ($p = 0.023$, using pretreatment depression scores as the covariate). For 19 subjects treated with three hours of evening bright white light and 19 subjects treated with evening dim red light placebo, baseline polysomnographic data were available. The degree of benefit with bright light was *not* significantly correlated with baseline REM latency, REM percent, or REM onset time. The only significant polysomnographic correlation was a negative relationship ($r = -0.48$, $p < 0.05$) between the amount of baseline slow wave sleep and the amount of Hamilton rating improvement. Further, there was no significant difference in benefit between evening bright light and morning/evening treatment. Thus, the data do *not* support the hypothesis that evening bright light works by differentially delaying circadian rhythms in patients with a evidence of phase advance. There were no significant polysomnographic correlates of improvement in the placebo-treated group.

NR238 **Wednesday, May 10, 12 noon–2:00 p.m.**

THE CLINICAL USE OF ANTICHOLINERGIC DRUGS TO CONTROL EXTRA- PYRAMIDAL SIDE EFFECTS

Angelo Bosio, M.D., Clinical Pharmacol., Assoc. Advan Neursci, Viavivanti 9, Brescian Mompiano 25060, Italy; Rosangela Rosola

Summary:

The current clinical use of anticholinergic drugs to prevent and treat extrapyramidal side effects after neuroleptic administration is well known. The patients' compliance to this oral treatment may be improved by reducing the number of daily administration. In this light a comparative trial has been performed on a group of 20 patients with a diagnosis in accord with DSM-III-R suggesting the chronic administration of haloperidol decanoate. The patients received biperidene 4 mg u.i.d. or orphenadrine 150 mg t.i.d. per os during a period of three weeks. The trial was in double-blind, crossover with a washout period of one week before every treatment. The evaluation of extrapyramidal side effects was performed by a clinical rating scale and by the measuring of reaction time to luminous stimulations (tachi-test). This method has been standardized during previous clinical trials; the use of a computerized tachistoscope allows an objective evaluation of tremor and rigidity due to extrapyramidal system pathological involvement.

The results obtained with this trial clearly indicate that the use of anticholinergic drugs u.i.d. may be of therapeutical efficacy in treating iatrogenic extrapyramidal symptoms. Biperidene use may improve the quality of life of patients under neuroleptic treatments by reducing the side effects and improving their compliance to therapy with a simple daily scheduled drug administration.

NR239 **Wednesday, May 10, 12 noon–2:00 p.m.**

ULTRA BRIEF PULSE ECT CLINICAL TRIAL

Vaclav Hyrman, M.D., Psychiatry, Royal Columbian Hospital, 260 Sherbrooke Street, New Westminster BC, Canada V3L 3M2; Lancelot L. Patrick, M.D., Laurence K. Weldon, Ph.D.

Summary:

Ultra Brief Pulse (<0.1ms) ECT stimuli have been considered unreliable in producing therapeutic seizures (Cronholm & Ottoson, 1963). Animal experiments hinted that ultra brief pulses may have an unexpected potential for seizure induction (Hyrman et al, 1985). A pilot clinical trial of an ultra brief pulse instrument was undertaken to investigate the potential of these pulses to induce therapeutic seizures with less stimulus power and energy, in order to minimize side effects, especially cognitive dysfunction. Treatment and hospital records of 64 patients treated with ultra brief pulses over the past three years were examined and compared with 28 patients treated with a reference brief pulse instrument. No significant differences were found in the therapeutic effectiveness between the two ECT tecnniques, the ultra brief pulse treated patients presented significantly less complaints of confusion and memory loss.

NR240 **Wednesday, May, 10, 12 noon–2:00 p.m.**

LLPDD: INTERACTION OF CIRCADIAN RHYTHMS

Sally K. Severino, M.D., Psychiatry, NYH Cornell Med WD, 21 Bloomingdale Road, White Plains, NY 10605; Daniel R. Wagner, M.D., Margaret L. Moline, Ph.D., Stephen W. Hurt, Ph.D.

Summary:

Three women with and three women without a prospectively confirmed diagnosis of LLPDD (and no present psychiatric disorder) were studied at four segments of one menstrual cycle. On each occasion, ambulatory monitors recorded 72 hours of core body temperature and activity rhythms.

The LLPDD group experienced a progressive two-hour phase delay in temperature nadir from days five to seven to days 19-21, with a two-hour phase advance from days 19-21 to premenses, Women without LLPDD shcwed a small phase delay from days five to seven to days 12-14, an equivalent phase advance from days 12-14 to days 19-21, and a small phase delay from days 19-21 to premenses. These patterns of phase shift were significantly different with the most marked difference occurring at days 19-21.

Analysis of activity data showed that the onset of low activity associated with preparing for sleep occurred significantly earlier in the women with LLPDD and remained stable over the entire menstrual cycle. Later, but also stable, bedtimes characterize the women without LLPDD.

These data suggest that LLPDD is associated with an abnormal internal phase shift (of approximately 2 hours) across the first 3/4 of the menstrual cycle and, a much later temperature nadir relative to bedtime compared to women without LLPDD.

NR241 **Wednesday, May 10, 12 noon–2:00 p.m.**

CAN NEUROPHYSIOLOGIC MEASURES PREDICT ANTIDEPRESSANT RESPONSE?

Jonathan W. Stewart, M.D., Psychiatry, NYS Psychiatric Inst., 722 West 168th Street, New York, NY 10032; Gerard Bruder, Ph.D., Frederick Quitkin, M.D.

Summary:

Sixty depressed outpatients tested with visual and auditory laterality tasks were then randomly treated with imipramine, phenelzine, or placebo. Patients with normal right visual field advantage on the nonsense syllable visual task had a 33 percent (3/9) response to imipramine, 92 percent (11/12) to phenelzine ($p = .005$), while in patients showing minimal laterality, or abnormal left visual field advantage, 68 percent (17/25) responded to imipramine and 63 percent (15/24) to phenelzine (ns). On the complex tones auditory task, patients with normal left ear advantage had a 31 percent (5/16) response to imipramine, 74 percent (14/19) to phenelzine ($p = .01$); in patients with the abnormal right ear advantage, 81 percent (13/16) responded to imipramine, 75 percent (12/16) to phenelzine. On both tests, patients with normal results had an imipramine response barely better than our placebo results, with fairly robust response to phenelzine. Abnormal results were associated with good response to both antidepressants.

If replicated in a larger sample, these tests may help to identify subtypes of depressive disorder and predict treatment response.

	visual field asymmetry		
	TCA response	*MAOI response*	
normal	33 percent (3/9)	92 percent (12/13)	$X^2 = 7.88$, $p = .005$
abnormal	68 percent (17/25)	63 percent (15/24)	ns
	$X^2 = 3.28$ $p = .07$	$X^2 = 3.39$ $p = .07$	
	auditory asymmetry		
	TCA response	*MAOI response*	
normal	31 percent (5/11)	74 percent (14/19)	$X^2 = 6.30$, $p = .012$
abnormal	81 percent (13/16)	75 percent (12/16)	ns
	$X^2 = 8.13$ $p = .0044$	ns	

NR242 **Wednesday, May 10, 12 noon–2:00 p.m.**

DEPRESSION, PERSONALITY DISORDER AND CSF 5-HIAA

Barbara Stanley, Ph.D., Neuroscience, NYS Psychiatric Inst., 722 West 168th St. Box 28, New York, NY 10032; Lil Traskman-Benz, Ph.D., J. John Mann, M.D., Allen J. Frances, M.D., Michael Stanley, Ph.D.

Summary:

The dual diagnosis of personality disorder and depression has been identified in clinical studies as increasing the risk for suicidal behavior above and beyond the diagnosis of either personality disorder or depression. Furthermore, altered serotonergic function (decreased 5-hydroxyindoleacetic acid (5-HIAA) in the cerebrospinal fluid (CSF)) has been found in suicide attempters. The purpose of this study is to determine whether CSF 5-HIAA is significantly lower in suicide attempters with a dual diagnosis of personality disorder and depression than 1) suicide attempters without a personality disorder; 2) nonattempters. A one-way analysis of variance examining CSF 5-HIAA concentrations in the three groups was significant ($F = 4.27$; $p < .05$). However, in examining the mean scores, it was found that a diagnosis of personality disorder was not associated with lower CSF 5-HIAA in the suicide attempters (PD and Affective — $\bar{x} = 17.8$ ng/ml; Affective without PD — $\bar{x} = 16.2$ ng/ml). The major difference in CSF 5-HIAA values resulted from the comparison of nonattempters with affective illness ($\bar{x} = 23.1$ ng/ml). Thus, it may be that dual diagnosis and altered serotonergic function provide independent sources of risk for suicidal behavior. Findings will be discussed as they relate to evaluation of suicide risk.

NR243 **Wednesday, May, 10, 12 noon–2:00 p.m.**

CSF FINDINGS IN ELDERLY SUICIDE ATTEMPTERS

J. Sidney Jones, M.D., Neuroscience, NYS Psychiatric Inst., 722 West 168th St. Box 28, New York, NY 10032; Barbara Stanley, Ph.D., J. John Mann, M.D., Allen J. Frances, M.D., Ronald Winchel, M.D., Michael Stanley, Ph.D.

Summary:

Suicide is particularly alarming in the elderly, 50 percent higher than the rate of suicide in young individuals. Biological studies in suicide attempters have reported differences in the amount of 5-hydroxyindoleacetic acid (5-HIAA), the major metabolite of serotonin in the cerebrospinal fluid (CSF), of attempters in comparison with controls in a range of psychiatric diagnoses. This study involves analysis of CSF metabolites in an aged population of suicide attempters, controls, and normals.

Twenty-six patients (11 nonattempters, 15 attempters) with a mean age of 63.27 were included in the study. There was a significant difference in CSF 5-HIAA levels in aged suicide attempters in comparison with age matched controls. CSF 5-HIAA levels in the attempter group were lower ($x = 18.96$) than the nonattempter group ($x = 25.68$) ($p < .04$). Lower levels of CSF 5-HIAA were characteristic of aged attempters in comparison with aged diagnostic controls, and compared with age-matched normals ($p < .02$). Levels of the dopamine metabolite, homovanillic acid (HVA) in CSF were also significantly different in older patients with a history of suicide attempts ($x = 29.93$) than diagnostic controls with no history of attempts ($x = 49.00$) ($p < .02$). The relationship between behavioral measures (eg. impulsivity) and biochemical indices will be reported.

NR244 **Wednesday, May 10, 12 noon–2:00 p.m.**

LONGITUDINAL IMI BINDING IN ADOLESCENT SUICIDE ATTEMPTS

Lee S. Cohen, M.D., Psychiatry, NYS Psychiatric Inst., 722 W. 168th St. Box 78, New York, NY 10032; Michael Stanley, Ph.D., Paul D. Trautman, M.D., Alyssa Morishima, M.S., Erica Wilheim, B.A., David Shaffer, M.D.

Summary:

Serotonin's (5HT) role in suicide and aggression has been suggested by studies showing low CSF 5HIAA and decreased brain ^{3}H IMI binding sites in individuals manifesting these behaviors with varied diagnoses as compared with controls. Platelet ^{3}H IMI binding sites have been used as a peripheral measure of presynaptic serotonergic functioning and have been found to be reduced in adult depressed patients and children/adolescents with conduct disorder and ADDH. Significant increases in the density of platelet ^{3}H IMI binding (B_{max}) have been demon strated after treatment of adult depressed patients with tricyclic antidepressants implicating this measurement as a possible state dependent marker. To investigate the role of 5HT in adolescent suicide, we examined platelet ^{3}H IMI binding density in 24 female and three male outpatient suicide attempters ($N = 27$, age range 12-18, mean 15.35, S.D. 1.60, 19 adjustment disorders, six major depressions, one separation anxiety disorder, one dysthymic disorder) within 14 days of their attempt [Time 1(T1)] and then 8-12 weeks after their initial visit [Time 2(T2)]. No psychopharmacologic interventions were made during this interval. Platelets were sampled and ratings for depression, anxiety, psychosis, hopelessness, and conduct factors were done at T1 and T2. Significant decreases in the Hamilton rating scale for depression ($t = 3.00$, $df = 19$ $p<.01$), children's manifest anxiety scale ($t = 2.76$, $df = 19$, $p<.02$) and delinquent scores ($t = 3.68$, $df = 10$, $p<.01$) were found from T1 and T2. No significant difference between B_{max} or Kd at T1 and T2 were found [(Mean: $B_{max}1 = 711.4$, $B_{max}2 = 7.309$, $t = .09$, $df = 18$, NS) (Mean: $Kd1 = 1.177$, $Kd2 = 1.192$, $t = -.09$, $df = 18$, NS)]. Furthermore, no correlation between Bmax at TI and T2 was found ($r = .140$, $p = .568$); however, Kd remained stable over time ($r = .552$, $p = .014$). No significant correlations were found between changes in Bmax and changes in behavioral ratings from TI to T2. Further research should be considered with regard to the role of 5HT in mediating behaviors of this type.

NR245 **Wednesday, May 10, 12 noon–2:00 p.m.**

NEUROPEPTIDES AND SUICIDE

Csaba M. Banki, M.D., Psychiatry, Reg. Neuropsych Inst., P.O. Box 37, Nagykallo, Hungary H-4321; Garth Bissete, Ph.D., Mihaly Arato, M.D., Charles B. Nemeroff, M.D.

Summary:

Corticotropin-releasing factor (CRF), thyrotropin-releasing hormone (TRH), somatostatin (SRIF), and neurotensin (NT) were measured by specific radioimmunoassay (RIA) methods in subsequent groups of recently hospitalized psychiatric patients with DSM-III-R diagnoses of major depression, schizophrenia, anxiety, or adjustment disorders. Immunoreactive peptide levels were compared between patients with and without suicide attempts within one month prior to admission. NT and SRIF levels did not discriminate among the diagnostic subgroups although there was a weak, nonsignificant tendency for SRIF to be lowered in schizophrenia and major depression; similarly, suicidal patients had closely similar mean NT and SRIF levels than the nonsuicidal ones within the respective diagnostic groups. CRF levels were significantly higher in depression, but again there was no difference between suicidal and nonsuicidal subjects; finally, TRH levels were the highest in violent suicidal depressed patients. Postmortem analysis of suicide victims corroborated these findings: both CRF and TRH levels were found to be significantly elevated as compared with victims of sudden cardiac or accidental death. The results suggest that violent suicidal behavior may be related to elevated central CRF and/or TRH production at least in patients suffering from major depression.

NR246 **Wednesday, May 10, 12 noon–2:00 p.m.**

PREDICTION OF SUICIDE BY MULTIPLE INDICATORS

William A. Scheftner, M.D., Psychiatry, Rush Medical Center, 1653 W. Congress Parkway, Chicago, IL 60612; Michael Young, Ph.D., Louis Fogg, M.D., Jan Fawcett, M.D.

Summary:

A total of 955 affectively disordered probands within the NIMH Collaborative Study of the Psychobiology of Depression were followed for a minimum of five years for cause of death. Several univariate predictors of suicide emerged: hopelessness, cycling within an episode for bipolars, a lifetime diagnosis of both alcohol and substance abuse disorder, and not having a child under 18 living with you. Since these appear to come from independent domains, we investigated the predictive power of combining these indicators. A monotonic increasing relationship was demonstrated. None of the 121 probands without any predictors committed suicide. Of the 436 probands with any single predictor, 1.4 percent committed suicide. Of the 314 with any two predictors, 5.1 percent committed suicide. Combining the 78 with any three, and the six with all four predictors because of small cell sizes, 9.5 percent committed suicide. Further analyses investigating the relative strengths and patterns of predictors will be presented.

NR247 **Wednesday, May 10, 12 noon–2:00 p.m.**

EMPIRICAL ESTIMATION OF NEAR-TERM SUICIDE RISK

Jerome A. Motto, M.D., Psychiatry, Univ of Calif Sch of Med, 401 Parnassus Avenue, San Francisco, CA 94143; Alan G. Bostrom, Ph.D.

Summary:

Estimation of suicide risk remains a critical task that largely determines the management of suicidal persons. Empirical instruments developed to aid in this task have generally considered a risk period of two a years following assessment. Clinical needs call for an objective estimate of risk over a much shorter time span.

In a prospective study examining 101 variables in 3,005 persons hospitalized for a depressive or suicidal state, 38 subjects suicided within 60 days of discharge from the hospital. From a statistical analysis employing a screening procedure followed by a backwards stepwise logistic regression nine variables were identified as contributing most to the discrimination between suicides and nonsuicides. These were: a history of psychiatric hospitalization, contemplation of suicide by jumping or hanglng, the presence of suicidal impulses, divorced status, threat of financial loss, feeling a burden to others, a negative reaction to the person by the interviewers, extremes of crying, and ideas of persecution or reference. Two approaches to validation were employed, using jacknife techniques to examine variable selection and fitting of the model.

Both gave a degree of validation to the findings. With an estimated risk of .01 or greater, the sensitivity was 79 percent and the specificity 67 percent.

NR248 **Wednesday, May 10, 12 noon–2:00 p.m.**

PITUITARY POMC GENE EXPRESSION FOLLOWING SUICIDE

Juan F. Lopez, M.D., Psychiatry, Univ of Michigan, MHRI 205 Washtenaw Place, Ann Arbor, MI 48109; Stanley J. Watson, M.D., Alfred Mansour, Ph.D., Miklos Palkovits, Ph.D., Mihaly Arato, M.D., Huda Akil, Ph.D.

Summary:

Studies of the hypothalamic-pituitary-adrenal axis have provided an important biological link betwen stress and psychiatric illness. Most illness research relies on the measurement of the secreted peptides in plasma or cerebrospinal fluid, either at baseline or after pharmacological challenges. However, secretion is only the final of several cellular and biochemical events that include receptor activation, mRNA transcription, translation, and peptide storage. In fact, accumulation of mRNA may be a better indicator that the system has been under chronic stress. We have studies the accumulation of Pro-opiomelanocorton (POMC) mRNA, the molecule coding for the ACTH/β-endorphin precursor, in human anterior pituitaries.

Pituitaries from seven suicide victims and 11 cardiac deaths (controls) were sectioned and processed for *in situ* hybridization. A radioactive nucleic acid, complementary to human POMC mRNA, was used to detect and quantify POMC message. To correct for possible postmortem cell loss, P1B15, a nucleic acid probe against a non-regulated membrane protein, was used in sections adjacent to the POMC slides. Quantification of the resulting radioactives images was performed with a computerized image analysis system (ICC/LOATS).

Suicide victims showed a 25 percent increase in POMC message (<0.01, 2-tail t-Test) compared to controls. This increase was mostly noticed in male suicides. No correlation with age or postmortem time were detected. There were no differences in P1B15 message between the two groups. A preliminary radioimmunoassay of pituitary β-endorphin content also showed a modest increase in suicides. We conclude that: 1) *in situ* hybridization is suitable for studying neuroendocrine regulation in psychiatric illness and 2) suicide victims show an increase in POMC gene expression, perhaps related to psychogenic stress. The relationship of Corticotropin Releasing Hormone receptors and human glucocorticoid receptor message to these changes is currently under investigation in the same pituitaries and will be reported.

NR249 **Wednesday, May 10, 12 noon–2:00 p.m.**

SUICIDE IN LATE-LIFE: PSYCHOLOGICAL AUTOPSY FINDINGS

Yeates Conwell, M.D., Psychiatry, Univ of Rochester, 300 Crittenden Boulevard, Rochester, NY 14642; Kurt H. Olsen, M.A., Eric D. Caine, M.D., Catherin Flannery, M.D.

Summary:

The elderly commit suicide at a higher rate, make fewer attempts, but use more lethal methods than any other age group. Despite the frequency and malignancy of this behavior, only one study has used the psychological autopsy method to describe a sample of 30 suicides in late life.

We shall present preliminary results of our ongoing psychological autopsy study of all suicides 50 years of age and over in Monroe County, New York. Of 18 cases studied thus far, 16 had diagnosable psychopathology. Twelve had a primary diagnosis of unipolar major affective disorder, usually of recent onset and short duration. The terminal depressive episode was the first for nine of these 12 subjects, and had been present for less than one year in six. Substance use disorders were diagnosed in eight victims.

Physical health problems were the most common precipitant, including the belief held by seven of the 15 male suicides that they were dying of cancer. Whereas only three of the 18 victims had received psychiatric care within the last month, nine had seen their primary care provider. These data imply that suicide in the elderly is associated with treatable psychopathology, but that many of those at highest risk will not present to psychiatrists. Additional data regarding the victims' premorbid symptoms and behaviors will be presented.

NR250 **Wednesday, May 10, 12 noon–2:00 p.m.**

STRESS AND THE BIOLOGY OF AFFECTIVE EPISODES

Alan C. Swann, M.D., Psychiatry, Univ of Texas, P.O. Box 20708, Houston, TX 77225; Jack Croughan, M.D., Steven K. Secunda, M.D., Stephen H. Koslow, Ph.D., James W. Maas, M.D., Peter E. Stokes, M.D.

Summary:

Despite considerable interest, there is little information about relationships between stressful events and clinical or biological characteristics of depressive or manic episodes. Therefore, we investigated relationships between the perceived role of stress and clinical and biological features in 84 unipolar depressed, 46 bipolar depressed, and 18 manic patients (SADS-RDC) in the NIMH CRB Collaborative Program on the Psychobiology of Depression (Biological Studies). Patients had comprehensive clinical and biochemical studies before and during a drug treatment protocol. Patients with high stress had fewer previous episodes and a longer index episode. There were no differences between patients with high and low perceived roles of stress by age, gender, diagnosis, severity of illness, or eventual treatment outcome. Biological findings varied across diagnostic groups. Unipolar depressed patients with high stress had lower CSF 5-HIAA than low-stress patients did. Bipolar depressed patients with high stress had lower excretion of epinephrine and metanephrine, and of 0-methylated metabolites metanephrine and normetanephrine relative to their metabolic products or to total amine excretion. Manic subjects with high stress had increased excretion of the parent amines, norepinephrine and epinephrine, relative to their metabolites and to total amine excretion. These findings suggest that affective episodes may become progressively more independent of environmental events, regardless of diagnosis. Differences in monoamine function associated with high stress varied with diagnosis. Patients with high stress generally had characteristics resembling those previously found to predict treatment response in their diagnostic group.

NR251 **Wednesday, May 10, 12 noon–2:00 p.m.**

SOCIAL DOMINANCE, DEPRESSION AND IMMUNITY

Donna J. Holmes, Ph.D., Psychiatry, UMDNJ-NJ Medical School, 185 South Orange Avenue, Newark, NJ 07103; Elizabeth Pinner, B.A., Steven J. Schleifer, M.D., Jacqueline A. Bartlett, M.D., Steven E. Keller, Ph.D.

Summary:

Psychosocial factors, including dominance, have been shown to mediate immune function in animals, including humans. Previous research by this group has shown age-related relationships between stress, depression, otner psychosocial factors, and immunity. In this study we examined the relationships between a composite self-reported measure of dominance and age, sex, lifetime incidence of depression, Perceived Stress Scale scores, scores on the UCLA Loneliness Scale, and a battery of immune parameters in inner city adolescents. Subjects consisted of 55 healthy adolescents between 11 and 22 years of age who did not meet DSM-III-R criteria for psychiatric illness other than depression. Hierarchical multiple regression analysis controlling for effects of age and sex showed significant relationships between dominance and natural killer cell activity, numbers of helper and suppressor cells, and lymphocyte responses to pokeweed mitogen and ConA challenge. Significant interactions between sex and dominance suggest a relationship between dominance and heightened levels of these immune variables in boys, but not in girls. Stress and lifetime depression also explained a significant amount of the variability in several immune measures. These findings suggest that age- and sex-related coping skills play an important role in mediating immunity in this population.

NR252 **Wednesday, May 10, 12 noon–2:00 p.m.**

DOES STRESS RELATED AMENORRHEA REALLY EXIST?

Stephanie D. Jofe, M.D., Psychiatry, Mass General Hospital, Fruit Street BHX-5, Boston, MA 02114; Dara K. Lee, B.A., Joanne F. Waldstreicher, M.D., David A. Schoenfeld, Ph.D., Gloria S. Mok, M.A., Janet E. Hall, M.D., William F. Crowley Jr., M.D.

Summary:

To determine whether stress is an important factor in the development of hypothalamic amenorrhea, women medical students, physicians and Ph.D.s at Harvard Medical School were studied to ascertain the one-year prevalence of amenorrhea and the possible associated factors. Eighteen hundred anonymous questionnaires were sent to all female medical students and doctorate level faculty members at the medical school. Seven hundred fifty responses were received (42 percent); 657 of these were not pregnant, lactating, menopausal, or taking oral contraceptives, and were analyzed. The one-year prevalence of amenorrhea for this group was 4.5 percent, consistent with the prevalence of amenorrhea in the largest general population study to date. The prevalence among the 135 medical students was high (10.4 percent) compared to the remainder of the group (2.9 percent). Excluding students with a serious illness, none of the 59 students who reported little or no exercise had amenorrhea, while 15 percent (11/73) of the moderate-to-serious exercisers had amenorrhea. The binge eating was also significantly associated with amenorrhea. Factors associated with amenorrhea in the nonmedical student group were serious illness and low weight for height. Stresses traditionally associated with medical training and practice and Type A personality features were not found to be associated wtih amenorrhea. Conclusions: (1) idiopathic or stress-related hypothalamic amenorrhea may not be as common as has been previously thought; and (2) serious illness, exercise, and dietary histories may explain many cases of amenorrhea that were previously thought to be idiopathic or stress related, even in a highly stressed population.

NR253 **Wednesday, May 10, 12 noon–2:00 p.m.**

STRESS PREVENTION FOR MEDICAL STUDENTS

M. Bruce Sarlin, M.D., Psychiatry, NYS Psychiatric Inst., 722 West 168th Street Box 51, New York, NY 10032; James T. Halper, M.D., Harlow T. Fischman, Ph.D., Keith W. Sedlacek, M.D., Donald C. Ross, Ph.D., Eric Marcus, M.D., Henrietta Wolland, M.P.H., Samuel Perry III, M.D.

Summary:

This study was designed to assess the relative impact of psychosocial interventions in alleviating examination stress and their effects on lymphocyte function in medical students. Biofeedback (1) and emotional disclosure (2) have been reported to increase lymphocyte function. A group of 30 students at Columbia University College of Physicians and Surgeons were randomized into: 1) an experiential dream group (n=10), 2) a biofeedback group (n=10), and 3) a control group (n=10). A psychological test (SCL-90) was administered and blood was drawn for mitogen stimulated lymphocyte proliferation assays, (mitogenesis, an in vitro measure of lymphocyte function) and Sister Chromatid Exchanges (SCE), a test of DNA damage. Assays were performed at a relatively stress free time (baseline) and on the days before final examinations in Anatomy and Physiology, two and three months later. Weekly dream group meetings and biofeedback training were begun one month before the first examination. All data were subjected to an analysis of variance of repeated measures: orthogonal components were tested individually for significance. During the course of the study all three groups showed significant reduction on the interpersonal sensitivity scale of the SCL-90, diminished mitogenesis, and a significant decline in SCE's. There were no significant inter-group differences in these measures, although the dream group showed a trend toward the least impaired lymphocyte function. Significantly greater decreases ($p < .05$) were noted on the anxiety, hostility, and depression scales of the SCL-90 in the dream group as compared with the biofeedback and control group. In the dream group those reporting dreams showed greater reduction in five of nine subtests and total scores of the SCL-90 ($p < .05$). This study suggests that uncovering unconscious emotional conflicts in an experiential dream group of medical students significantly reduces stress as measured by psychological tests, compared with a biofeedback and control group. Future study will further investigate the interrelationship between the stress reduction and psychosoci intervention reported here, as well as other assays of lymphocyte function.

NR254 **Wednesday, May 10, 12 noon–2:00 p.m.**

FAMILIAL TRAUMATIC INJURY AND IMMUNITY

Steven J. Schleifer, M.D., Psychiatry, UMDNJ-NJ Medical School, 185 South Orange Avenue, Newark, NJ 07103; Steven E. Keller, Ph.D., Barbara J. Scott, Cheryl H. Cottrol, M.D., Thomas J. Valente

Summary:

Exposure to chronic stressful life experiences such as the death of a spouse and the occurrence of depressive states have been associated with decrements in immune functions. Immune effects immediately following acute unanticipated major life stress in man have not been investigated. We have been studying psychiatric and immune consequences in relatives of patients admitted to a trauma service with life threatening disorders. Fourteen otherwise healthy family members have been studied within seven days of the traumatic episode (eight motor vehicle accident, three gunshot, three other) concurrent with 14 matched controls. Five trauma family members showed symptoms consistent with major depression and two showed signs of minor depressive states. The mean Hamilton Depression Score for the family members (12.5±6.1) was substantially elevated (controls: 2.1±2.4). Preliminary analysis revealed significantly higher levels of natural killer cell (NK) function in trauma families compared with the controls (p 0.05), while mitogen responses (Con A and Pokeweed mitogen) tended to be lower. These data are consistent with prior observations that psychoimmunologic effects on NK responses are dissociated from those of mitogen response and that NK function may be elevated following acute life stress. Elevated NK function may be among the adaptive nonspecific short term responses to stress.

NR255 **Wednesday, May 10, 12 noon–2:00 p.m.**

ECT AND MEMORY: THE ROLE OF TREATMENT SCHEDULE

Baruch Shapira, M.D., Research, Ezrath Nashim Hospital, P.O. Box 140, Jerusalem, Israel 91001; Avraham Calev, Ph.D., Bernard Lerer, M.D., Doron Niual, B.A., Nurith Tubi, B.A., Heinz Drexler, M.D.

Summary:

Memory impairment is the most important drawback of ECT. An ongoing, double-blind study has examined the impact of ECT schedule on memory function and therapeutic efficacy. Consenting drug-free, depressed patients have been randomly assigned to three times (3×) weekly bilateral ECT or twice (2×) weekly treatment plus one simulated ECT (anesthesia and muscle relaxant only) per week. Extensive cognitive testing has included a memory battery administered pretreatment, after four weeks (eight real ECT's in the 2× group and 12 in the 3× group) and at six month follow-up. Data from the first 25 subjects to complete the protocol have been examined. Across treatment groups, the results provide a convincing cross-cultural replication of previously reported patterns of ECT-induced anterograde (Paired Associate Recall, Word List Recall, and Complex Figure Reproduction) and retrograde (Famous Events Recall and Personal Memory) memory deficits. By six month follow-up recovery exceeds pretreatment levels although subjects still report subjective memory impairment. Preliminary comparison between 2× and 3; weekly schedules reveals a trend toward better performance by the 2× group on most at the tasks. In the context of equivalent therapeutic efficacy, these findings could, if robust, necessitate a significant revision of current ECT practice. (Supported in part by NIMH Grant #40734.)

NR256 **Wednesday, May, 10, 12 noon–2:00 p.m.**

GRADUAL SUNRISE ILLUMINATION FOR TREATMENT OF SAD

David Schlager, M.D., Psychophysiology, NYS Psychiatric Inst., 722 W. 168th Street Box 50, New York, NY 10032; Michael Terman, Ph.D.

Summary:

Recurrent wintertime depression associated with atypical neurovegetative changes in Seasonal Affective Disorder can be quickly reversed by exposure of the eyes to bright, artificial light.[1] Seasonal variation in actual light exposure, due in part to annual cycles of changing light-dark patterns, is presumed to be etiologic but has been incompletely and imprecisely studied. Using a new bedside apparatus capable of delivering precise, naturalistic illumination[2], we exposed ten winter depressives to late-Spring, early-morning light profiles, initiated during sleep in 14-day home trials. Structured ratings of clinical state, objective measures of sleep and activity, and overnight plasma melatonin profiles were collected. Naturalistic patterns of dawn twilight exposure, mainly during sleep, to maximum intensities of 500 lux, were associated with full clinical remission in most subjects; all subjects showed earlier awakening and increased morning energy and activity. Phase advances of dim-light melatonin onset and immediate supression of early-morning melatonin secretion were also observed under twilight exposure. The demonstration of human clinical and physiologic sensitivity to naturalistic, indoor-level light exposure, even during sleep, provides a new line of evidence supporting a phase-shift hypothesis in Seasonal Affective Disorder. It further suggests a role for light, perhaps mediated by melatonin, in circadian regulation of sleep.

NR257
WITHDRAWN

NR258 **Wednesday, May, 10, 12 noon–2:00 p.m.**

FLUOXETINE-TCA COMBINED FOR RESISTANT DEPRESSION

Jeffrey B. Weilburg, M.D., Psychiatry, Mass General Hospital, 15 Parkman Street Acc 715, Boston, MA 02114; Jerrold F. Rosenbaum, M.D., Gary S. Sachs, M.D., Mark H. Pollack, M.D., Maurizio Fava, M.D., Jonathan Worth, M.D.

Summary:

We openly initiated fluoxetine treatment in depressed patients poorly responding to ongoing adequate trials of various antidepressants.

Retrospective open review of our first 30 cases indicated that 28/30 (93.3 percent) demonstrated a positive response to the combination of agents, including 13 of 15 patents (86.6 percent) with a diagnosis of major depressive disorder (MDD), 12 of 12 patients with MDD plus dysthymic disorder, two of two patients with dysthymic disorder alone, and one patient with manic-depressive disorder, depressed.

The heterocyclic antidepressant was stopped in 12 responders, and response was subsequently lost in eight of these. Response was recovered in all eight when the heterocyclic was restarted along with continued fluoxetine treatment.

There may be a synergistic effect when fluoxzetine is combined with a heterocyclic antidepressant. Baron[1] found that the combination of fluoxetine and desipramine acted synergistically, producing more rapid and extensive down regulation of central Beta receptors in the rat than that produced by either agent alone. This possible synergism may be related to augmentation of central serotonergic mechanisms when flouxetine, a serotonin uptake inhibitor, is combined with a norepinephrine inhibitor (desipramine).

NR259 **Wednesday, May, 10, 12 noon–2:00 p.m.**

LOW DOSE TRAZODONE REDUCES MAOI SLEEP DISTURBANCES

Frederick Jacobsen, M.D., 1301 20th Street, N.W., Washington, DC 20036

Summary:

Sleep disturbances are a frequent and troublesome side effect of treatment with monoamine oxidase inhibitors (MAOIs). MAOI-induced sleep disturbances include difficulty falling asleep (DFA) and middle night awakening (MNA), and often lead to the prescription of sedative-hypnotic agents, particularly benzodiazepines. Unfortunately, tolerance to sedative-hypnotics often develops and drug dependence may occur. The antidepressant trazodone is a triazolopyridine derivative which is reported to have serotonin agonist activity at standard doses and serotonin antagonist activity at lower doses. Sedation is a commonly observed side effect of treatment with trazodone, perhaps due to its serotonergic and/or alpha blocking activity. This uncontrolled study investigated whether low dose trazodone might be useful for treating nocturnal MAOI-induced sleep disturbances.

Sixteen patients with RDC major depression who had been successfully treated with MAOIs but subsequently developed persistent MNA and/or DFA were given Desyrel® (or trazodone) 25-50 mg PO at bedtime. Ten subjects reported complete elimination of sleep disturbance and six reported partial improvement of sleep with trazodone. Negative interactions with the MAOIs were not observed and side effects were minimal. The improvement in sleep has continued for up to 18 months without development of tolerance. Low dose trazodone appears to be a safe and effective agent for reducing MAOI-induced sleep disturbances. The theoretical basis for this finding is discussed.

NR260 **Wednesday, May, 10, 12 noon–2:00 p.m.**

PROPRANOLOL IN NEUROLEPTIC-INDUCED AKATHISIA: A DOUBLE-BLIND PLACEBO CONTROLLED STUDY

Mark S. Kramer, M.D., Psychiatry, Thomas Jefferson Univ, 10th & Walnut Streets, Philadelphia, PA 19107; Robert A. Gorkin, M.D., Celeste DiJohnson, B.S., Patricia Sheves, B.S.N.

Summary:

Neuroleptic induced akathisia (NIA), estimated to occur in 20-75 percent of patients treated with neuroleptics is sometimes refractory to standard anti-akathisia treatments. Case reports, a controlled single-blind, and a another controlled double-blind study suggest that propranolol may be an efficacious alternative in NIA. The study reported herein is the second controlled double-blind investigation of the effect of propranolol in NIA. Twenty DSM-III diagnosed schizophrenic patients completed a randomized double-blind placebo controlled two to five day trial of 60mg/day of propranolol. Patients had been treated for an average of 29 days with benztropine without demonstrating appreciable clinical improvement in akathisia. Patients were rated on a detailed Akathisia Rating Scale based on the results of Braude et al, 1983. Propranolol was well tolerated by all patients. Propranolol treatment as compared with placebo suggested improvements in 18 of 26 measures, worsening in four of 26, and no change in four of 26 measures. A priori two-tailed Student's t tests suggested that after five days of treatment, propranolol was superior to placebo on two of three targeted items. These data support previous reports of propranolol's beneficial effect in patients who suffer from NIA. It also appears that propranolol's effect may not be persuasive prior to three to five days of treatment.

NR261 **Wednesday, May, 10, 12 noon–2:00 p.m.**

ANTIDEPRESSANT EFFECT OF ORAL S-ADENOSYL-METHIONINE

Bruce L. Kagan, M.D., Psychiatry, Univ of California, 760 Westwood Plaza, Los Angeles, CA 90024; David Sultzer, M.D., Nicholas Rosenlicht, M.D., Robert H. Gerner, M.D.

Summary:

Methylation has long been implicated in the etiology of psychiatric illness. Parenterally administered S-adenosyl-methionine (SAM), a biological important methyl group donor, has previously been shown to be an effective antidepressant. We studied the antidepressant effects of oral SAM in a double-blind, placebo controlled trial of 15 inpatient with major depression. Our results indicate that *oral* SAM, like parenteral SAM, appears to be a safe and effective antidepressant with few side effects and a rapid onset of action. We suggest that SAM may have potential for use in a broad spectrum of patients who cannot tolerate tricyclic antidepressants. We also find that SAM can induce mania in a patient with no previous history of bipolar illness. These findings lend credence to the idea that methylation may play a role in the etiology of affective disorders.

NR262 **Wednesday, May, 10, 12 noon–2:00 p.m.**

FOUR CASES OF CHLOROQUIN INDUCED PSYCHOSES

Gayle Bigelow, M.D., Psychiatry, McMaster University, 1200 Main Street West, Hamilton, Ontario, Canada L8N 3Z5; Nahum Spinner, M.D.

Summary:

It is not well known that the antimalarial drug Chlorcquin can induce psychoses, even though its use has increased as North Americans increasingly travel to tropical areas. Only twenty case reports, mainly from third-world Countries, exist in the literature from 1958 on. We had the opportunity to investigate an "outbreak of psychoses" from Oct '82-Dec '83 in four Canadians teaching in various parts of Nigeria, with a university volunteer service. Illness initially was presumed to be due to "psychological stress." We directly treated one of the teachers. In April '84, we investigated all four with in-depth interviews, and review of past medical and organizational records. The follow-up EEGs, neuropsychological testing, and CTT scans conducted have never been reported in the literature. The patients were two male and two female university educated teachers between ages 23-27, with no previous personal or family medical or psychiatric history. In all cases the episode began with fever, presumed malaria, and a loading dose of Chloroquin. Symptoms of insomnia, visual hallucinations proceeding to a manic-like state, and paranoid disorganization, began 12 hours to 12 days after ingestion of 1.5-10.4 grms of chloroquin. There was no evidence of malaria or other cerebral infection on investigation. All responded to low dose antipsychotics within one week, but two relapsed. Follow-up EEGs were normal. The implication of mild abnormalities on some neuropsychological testing and mild bilateral frontal atrophy on 2 CTT scans are unclear. A follow-up questionnaire to 69 other university volunteer service workers in Nigeria in May 1984 detected four other probable cases. This drug effect may be much more common than is reported.

NR263 **Wednesday, May 10, 12 noon–2:00 p.m.**

DISCONTINUATION OF LITHIUM IN REMITTED BIPOLAR ILLNESS

Ehud Klein, M.D., Psychiatry, Rambam Medical Center, Haifa 35254, Israel; Rami Meiraz, Peretz Lavie, M.D., Albert Hefez, M.D., Robert H. Lenox, M.D.

Summary:

Lithium is the treatment of choice for prohylaxis of manic depressive illness. Optimal length of treatment with this drug has not been established and while some workers think that lithium theraphy, once established, has to be lifelong, others believe that a discontinuation trial after several years of treatment, is appropriate. The number of adequately controlled lithium discontinuation studies in the literature is surprisingly small and these have suggested relapse rates of 30-50 percent over one year following discontinuation. Ten patients with remitted bipolar affective illness who were followed in our clinic and received lithium for a mean duration of nine years, gave informed consent to participate in a double-blind lithium discontinuation study, which was approved by the "Helsinki Committee" at our institute. Clinical status was assessed using behavioral ratings and in addition, motor activity and sleep-wake activity were recorded using computerized wrist actigraphs. Seven of ten patients became manic or hypomanic within one to three months following lithium discontinuation, with rapid control of their symptoms following readministration of lithium. Marked changes in motor activity and-sleep-wake activity as shown by the actigraphic recordings, were associated with the clinical changes. The high relapse rate over a short period of time is higher than expected by the course of illness prior to lithium treatment, and these findings might suggest a rebound phenomenon, althrough other explanations should be considered. Our findings and their clinical implication for the treatment of bipolar affective illness, will be discussed.

NR264 **Wednesday, May 10, 12 noon–2:00 p.m.**

HYPNOTIC-NEUROLEPTICS IN THE CONTROL OF AGITATION

Enrique S. Garza-Trevino, M.D., Psychiatry, UT Medical School, P.O. Box 20708, Houston, TX 77225; Leo E. Hollister, M.D., John E. Overall, Ph.D.

Summary:

In a previous report (1), we concluded that haloperidol-lorazepam combined was superior to either drug alone in agitated psychotics. This study was carried out to see if the effectiveness of a hypnotic-neuroleptic acombination could be generalized to either members of each drug class.

Fifty-two psychotic, agitated patients were randomized to either of the following treatments: haloperidol-phenobarbital (5-130mg), or thiothixene-lorazepam (5-4mg). The degree of agitation was rated in a visual analog scale of 100mm. A 100mm mark represented the highest degree of agitation, and a 0-20mm mark referred to a calm or sleeping patient. Ratings and treatment on fixed doses (5-130, 5-4mg) were carried out every 30 minutes. A patient was considered a failure if the rating remained greater than 2Omm after 90 minutes. Psychiatric diagnosis in both groups were comparable. Twenty-seven patients, with a median age of 31 years, were treated with the haloperidol-phenobarbital combination. Twelve patients needed more than one dose to attain control. The median time to control was 30 minutes an median doses were 5-130mg. Three patients were treatment failures and one developed hypotension.

Twenty-five patients, with a median age of 34 years, were treated with thiothixene-lorazepam (5-4mg). Eleven patients needed more than two doses to reach a level of 20mm or lower. The median dose Was 5-4mg. One patient was considered a treatment failure. None of the patients developed side effects. Both combinations were effective, compatible, and safe. These results support the notion that the degree of effectiveness of a hypnotic-neuroleptic combination can be generalized to either members of each drug class.

NR265 **Wednesday, May 10, 12 noon–2:00 p.m.**

MILACEMIDE IN THE TREATMENT OF MAJOR DEPRESSION

Ann K. Morrison, M.D., Psychiatry, University Hospital, 600 Highland Avenue, Madison, WI 53792; Kenneth A. Kobak, M.S.W., John H. Greist, M.D.

Summary:

Milacemide (2-n-pentylaminoacetamide) is a selective MAO-B inhibitor. This selectivity is of interest for two reasons: development of inhibitors without the potential to cause hypertensive crisis when tyramine is ingested, and development of inhibitors which may target specific monoamine oxidases in specific tissues. In addition, certain MAO inhibitors have shown superiority over tricyclic antidepressants in patients with atypical depression or history of panic attacks.

As part of a multicenter study, we evaluated 23 outpatients. One week of placebo washout preceded and followed four weeks of double-blind treatment with one of four doses (1,200, 2,400, 3,600 or 4,800 mg/d) of milacemide or placebo. Demographic and tretreatment variables were comparable across groups.

Results of a two-tailed Kruskal-Wallis analysis showed a significant main effect ($p < .04$) on Hamilton Depression scores, but not on physician or patient global ratings. Mann-Whitney U tests of the main effect showed only the 4,800 mg dose was significantly different than placebo ($Z = -1.96$, $p < .049$). History of Panic attacks did not predict treatment response ($X^2 = .818$, $p < .366$). Elevated liver enzymes occurred in one of our patients and in ten of 64 patients overall, resulting in discontinuation of the trial.

NR266 **Wednesday, May, 10, 12 noon–2:00 p.m.**

EFFECTS OF HCTZ VERSUS FUROSEMIDE ON SERUM LITHIUM

Brian L. Crabtree, Ph.D., Medical Center, Univ of Mississippi, 2500 N. State Street, Jackson, MS 39216; James E. Mack, Ph.D., Cynthia D. Johnson, M.S.N., Barry A. Amyx, M.D.

Summary:

Effects of a distal tubular diuretic (hydrochlorothiazide-HCTZ) and loop diuretic (furosemide - FUR) on serum lithium levels were compared in 13 normal male volunteers. Thiazide diuretics are well known to increase serum lithium levels, predisposing patients taking lithium to increased side effects; but effects of drugs which work at different sites in the renal tubule have been poorly studied. The study used a double-blind, placebo controlled, crossover design. All subjects took lithium 300 mg. twice daily for 42 days. Diuretic or placebo was given in random order during weeks two, four, and six. Blood for serum lithium and renal function indices was drawn after the fifth and seventh day of each week. Blood pressure, weight, urine volume, and adverse effects were monitored.

Results showed HCTZ significantly increased serum lithium after five but not seven days) when compared to placebo and FUR ($p<0.05$). There was no difference between FUR and placebo. These data suggest that when combined lithium-diuretic treatment is indicated, FUR may be a better choice than HCTZ. No lithium dosage adjustment is routinely needed when given with FUR.

NR267 **Wednesday, May 10, 12 noon–2:00 p.m.**

FLUOXETINE TREATMENT OF BIPOLAR II DEPRESSION

Sylvia Simpson, M.D., Psychiatry, Johns Hopkins University, Meyer 4-181 Johns Hopkins Hosp, Baltimore, MD 21205; J. Raymond DePaulo, M.D.

Summary:

We have previously reported on the familial aggregation of Bipolar (BP) II affective disorder and have speculated that new treatment approaches might be required for this difficult disorder. Reimherr and his associates, in a clinical trial comparing imipramine and fluoxetine, reported that fluoxetine-responders were more likely to have poor prior responses to tricyclics and to have chronic depressions with "atypical" clinical features. Since the depressive phase of BP II disorder often has the features of chronicity, atypicality, and poor response to tricyclics, we describe in this paper our preliminary experience using fluoxetine in selected BP II patients. In our series of 13 BP II patients, all had been depressed for an average of ten or more years and had had poor responses to tricyclics, MAOIs, and lithium. All but one have had some response to fluoxetine and the eight who have been on it for four or more months have had a good response. Only one patient had side-effects severe enough to require discontinuation of fluoxetine. These findings should encourage further treatment research using fluoxetine and other serotonin reuptakeblockers as well as research into the genetic and pathophysiologic identity of BP II as a possible distinct form of affective disorder.

NR268 **Wednesday, May 10, 12 noon–2:00 p.m.**

EVALUATION OF A NEW STEADY-STATE LITHIUM PREDICTION METHOD

Mary A. Gutierrez, Pharm.D., School of Pharmacy, Univ of South California, 1985 Zonal Avenue, Los Angeles, CA 90033; Neal R. Walker, Pharm.D., Barry A. Kramer, M.D.

Summary:

Patients randomly admitted to two adult psychiatric wards and treated with lithium were studied to evaluate a new method for predicting steady-state lithium levels within +/– 0.1 mEq/L. This method, which uses simple ratio mathematics instead of complicated pharmacokinetic formulas, assumes a 24-hour half-life, normal renal function, and a 0.15 to 0.35 mEq/L increase in steady-state levels for each increase in lithium dose of 300 mg/d. There are two steps to this method: 1) After the first reported level, a calculation is made for steady-state level at that given dose and a range is predicted for steady-state levels for any subsequent increase in dose. 2) After two or more levels, an individualized calculation is derived to predict the amount of change at steady-state for each change of 300 mg/d in dose. Steady-state levels can then be predicted as one single point instead of a range. Analysis of the data from 114 patients using Step 1 resulted in 153 predictions (114 predictions based on the first reported level, and 39 predictions based on the second level without a change in dose): 107 (70 percent) fell into the accuracy criteria of within +/– 0.1 mEq/L; 134 predictions (88 percent) fell within +/– 0.2 mEq/L; 149 (97 percent) within +/– 0.3 mEq/L. There were 238 predictions based on Step 2: 135 (57 percent) were within +/– 0.1 mEq/L of the single point prediction; 179 (75 percent) within +/– 0.2 mEq/L; 236 (99 percent) within +/– 0.3 mEq/L. Examples will be presented to demonstrate how this prediction method is calculated. The authors believe this prediction method provides a safe, accurate, and practical technique that can be easily utilized by clinicians.

NR269 **Wednesday, May 10, 12 noon–2:00 p.m.**

MOOD VARIABILITY IN NORMAL SUBJECTS ON LITHIUM

Denise Dufer, M.D., Psychiatry, Johns Hopkins Hospital, 600 N. Wolfe St. Meyer 4-181, Baltimore, MD 21205; Rachel Monderer, M.D., Mitchell Cohen, M.D., Dennis Barton, A.B., Harold Fuller, M.D., Michael Clark, M.D., J. Raymond DePaulo, M.D.

Summary:

Thirty normal volunteer subjects were randomly assigned to four weeks each of lithium or placebo treatment with crossover at mid-study. Subjects were maintained during the lithium treatment period at serum levels ranging 0.4 to 0.8.[1] All subjects completed visual analog mood scales daily throughout the study period. The delta squared (i.e. mean squared successive difference) of the mood self-ratings did not differ in lithium and placebo conditions. However, the self-rated mood variability declined significantly in both experimental conditions as a function of time in the study.

These data suggest that lithium does not have a substantial mood stabilizing effect in normal subjects given the drug in modest doses over a four-week period. The mode of action of lithium has been thought by some to be a non-specific, mood-stabilizing effect. The theoretical significance of study data will be discussed in relationship to issues of mode of action and specificity of lithium carbonate.

[1]units: mEq/L

NR270 **Wednesday, May 10, 12 noon–2:00 p.m.**

OPTIMAL ESMOLOL DOSE FOR HEART RATE AND BLOOD PRESSURE CONTROL IN ECT

Anthony L. Kovac, M.D., Anesthesiology, Kansas Univ Medical Ctr, 39th and Rainbow Boulevard, Kansas City, KS 66103; Manuel P. Pardo, M.D., Jane S. Lauchland, M.D.

Summary:

Electroconvulsive therapy (ECT) normally causes a transient but significant hyperactivity of the sympathetic nervous system resulting in tachycardia and hypertension potentially harmful to the patient with coronary artery disease. Esmolol (Brevibloc®) is a short acting beta blocker. In this study, all patients (N = 12) received esmolol bolus doses (100 and 200 mg) and placebo in a randomized, double-blind crossover design. Anesthesia was induced with methohexital 1 mg/kg and succinylcholing 0.75 mg/kg. ECT began two minutes after bolus injection. HR and BP were recorded pre-bolus and every minute for ten minutes following bolus injection, then at 12, 15, 20, 25, and 40 minutes following bolus injection. Both 100 and 200 mg bolus doses significantly blunted the maximum increase in HR by 35 percent ($p<0.05$, ANOVA), mean arterial pressure by 17 percent and rate pressure product by 39 percent. Seizure duration (seconds $\pm$ SEM) measured by EEG decreased 15 percent with esmolol 100 mg (45 $\pm$ 4 sec) and 25 percent with esmolol 200 mg (40 $\pm$ 3 sec) compared to placebo (53 $\pm$ 5 sec). Since hemodynamic effects between the two esmolol doses were similar and esmolol 100 mg exerted a smaller decrease in seizure duration, we conclude esmolol 100 mg to be the optimal bolus dose.

NR271 **Wednesday, May, 10, 12 noon–2:00 p.m.**

DEPIPRAMINE EFFECTS ON RESTING METABOLIC RATE

R. Bruce Lydiard, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; Michele Laraia, M.S.N., Gail W. Stuart, Ph.D., Joseph J. Zealberg, M.D., W. Alex Morton, Pharm.D.

Summary:

Psychotropic drugs which affect weight may do so by affecting resting metabolic rate (RMR). We report here the first double-blind study of the effects of desipramine and placebo on RMR and weight in nondepressed panic disorder patients. Fourteen (14) patients with panic disorder entered a double-blind, placebo-controlled study. Seven (7) patients received desipramine (DMI) and seven placebo. RMR was measured on a Sensormedics Nutritional Evaluation Unit prior to and after eight weeks' treatment.

Results: Baseline RMR (mean $\pm$ SD) was 1448 $\pm$ 212 Kcal/day for the DMI group and 1602 $\pm$ 328 Kcal/day for the placebo (Pbo) group (p 0.47, ns). Post-treatment RMR was 1495 $\pm$ 218 Kcal/day (DMI) vs. 1543 $\pm$ 334 Kcal/day (Pbo). Weight change was not different between the groups. However, the change in RMR and weight were highly correlated in the DMI group ($r = 0.96$, $p<0.0001$) but not in the Pbo group ($r = 0.54$, ns). Dose and RMR were correlated in the DMI group ($r = -0.77$, $p<0.41$) but not in the Pbo group ($r = -0.41$, ns). These data suggest that unlike other antidepressants, DMI has little effect on RMR or weight. We are currently extending this study to a larger group of panic patients.

NR272 **Wednesday, May, 10, 12 noon–2:00 p.m.**

EFECTS OF FLUVOXAMINE ON CATECHOLAMINE FUNCTION

R. Bruce Lydiard, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; Lyle K. Laird, Pharm.D., W. Alex Morton, Pharm.D., Thomas E. Steele, M.D., Charles H. Kellner, M.D.

Summary:

Chronic treatment with TCA or MAOI has been shown to reduce 24-hour urinary catecholamine (CA) output in depressed patients. Fluvoxamine (FLU), one of several newer antidepressants, has been reported to be a relatively specific inhibitor of serotonin (5HT) uptake and to have no significant effects on uptake of other neurotransmitters, norepinephrine (NE) in particular.

The effects of imipramine (IMI, n = 13), fluvoxamine (FLU, n = 13), and placebo (PBO, n = 12) Jon 24-hour urinary catecholamine (CA) output were studied in depressed outpatients meeting DSM-III-R criteria for major depression before and after six weeks' double-blind treatment. IMI treatment resulted in a significant reduction ($p<0.05$) in total CA output and shift in the pattern of metabolites suggesting an increase in extraneuronal metabolism ($p<0.01$). FLU and PBO had no significant effects on any CA measure and were not different from each other. These findings support the relatively serotonin-selective effects of FLU, at least as reflected by a lack of effect on 24-hour urinary CA measures.

NR273 **Wednesday, May 10, 12 noon–2:00 p.m.**

COMPARISON OF CLONAZEPAM AND LORAZEPAM IN MANIA

Jacques Bradswejn, M.D., Psychiatry, McGill University, 3830 Lacombe Avenue, Montreal PQ, Canaca H3T 1M5; Greg B. Meterissian, M.D., Christian Shriqui, M.D., Diana Koszycki, M.A.

Summary:

Benzodiazepines have shown therapeutic action on symptoms of mania. Their action might be antimanic or symptomatic and they might differ among themselves with regard to this action. The present study compared the effects of clonazepam and lorazepam in acute mania. A double-blind, randomized design was used with either clonazepam (n=11) or lorazepam (n=12) alone for 14 days. Mean daily dosages (± SEM) to tolerance or up to a maximum of 24 mg were 13.3 mg (±2.5) for clonazepam and 12.8 mg (±1.4) for lorazepam. The Inpatient Multidimensional Psychiatric Scale (IMPS) and Clinical Global Impression Scale of severity and improvement were used on days 0, 7, and 14. Clonazepam did not produce significant changes at days 7 and 14, with two drop-outs (therapeutic failure), but two patients showed much improvement. Lorazepam showed significant improvement at day 7 ($p< .001$, $p< .001$) and at day 14 ($p< .02$, $p< .004$, $p < .05$) on the scales, respectively, with one drop-out, three patients much improved, and five near remission. Lorazepam showed significant superiority over clonazepam at day 7 and 14 ($p< .02$ to $p< .05$) on the measures. This study supports the antimanic effect of benzodiazepines in mania, with superiority of lorazepam. This difference might be dose related.

NR274 **Wednesday, May 10, 12 noon–2:00 p.m.**

LIMITED ACCESS TO ECT FOR PUBLIC PATIENTS (CALIF)

Barry B. Kramer, M.D., Psychiatry, LAC/USC Medical Center, 1934 Hospital Place, Los Angeles, CA 90033

Summary:

Availability of ECT in the United States often has been greater in the private sector than in the public sector. This is especially true in California where ECT is heavily regulated. In 1986, ECT was available in 29.6 percent of the public hospitals and 42.9 percent of the private hospitals with psychiatric units. Public hospital patients accounted for 8.5 percent of all ECT in the state while private hospital patients accounted for 91.5 percent. Of those patients unable to give informed consent, 34.1 percent came from public hospitals vs. 65.9 percent from private hospitals. Two university affiliated county hospitals accounted for 43 of 52 patients (82.7 percent) treated in the six county hospitals with psychiatric units. White patients account for 92.4 percent of ECT, leaving minorities undertreated.

Private patients have a greater degree of choice regarding changing physician or hospital if ECT is needed but unavailable. The choices for public patients are limited. Possible causes and potential solutions to this problem will be discussed.

NR275 **Wednesday, May, 10, 12 noon–2:00 p.m.**

PREDICTORS OF TRICYCLIC FAILURE IN DEPRESSION

J. Craig Nelson, M.D., Psychiatry, Yale University, 20 York Street, New Haven, CT 06504; Carolyn Mazure, Ph.D., Peter I. Jatlow

Summary:

Prediction of tricyclic failure in major depression is important for optimizing drug selection and for understanding mechanisms of drug resistance. We determined predictors of resistance to desipramine (DMI). Since inadequate dose or blood levels have been a common reason for treatment failure, we used 24-hour blood levels to adjust dose and insure that adequate plasma levels were attained. Inpatients with DSM-III nonpsychotic unipolar major depression, who failed to respond to one week of hospitalization without antidepressants, began a four-week desipramine (DMI) trial. The dose was rapidly adjusted (50-500 mg/day) to achieve a therapeutic blood level (*J Clin psychopharm* 1987; 7:72- 77). CGI ratings were used to define response (no/minimal improvement vs much/very much improvement) and a complete four-week trial was required for nonresponse. Fifty patients (34 females and 16 males) completed the trial. Mean age was 48 ± 15 years, mean HDRS was 24.6 ± 4.8, and 20 had DSM-III melancholia. Thirty-five were responders and 15 failed to respond. Five variables significantly correlated with nonresponse. Multiple regression indicated that these 5 variables were each significantly and independently associated with response and accounted for 60 percent of the variance. The predictors of DMI failure were definite personality disorder, age ≤ 35, prior drug failure in this episode, and duration ≥ 2 years. Paradoxically, response to somatic treatment in a prior episode also correlated with non-response but may reflect problems rating this item. These variables appear to be clinically valuable for prediction of outcome. patients with two or more predictors had an 85 percent failure rate while 89 percent of those with one or no predictors responded.

NR276 **Wednesday, May 10, 12 noon–2:00 p.m.**

NICOTINE POTENTIATES HALOPERIDOL IN TOURETTE CASES

Brian J. McConville, M.D., Psychiatry, Univ of Cincinnati Med Ct, 231 Bethesda Avenue, ML #0599, Cincinnati, OH 45267; Andrew B. Norman, Ph.D., Harold M. Fogelson, M.D., Karen W. Parker, R.N., William M. Klykylo, M.D., Paul S. Sanberg, Ph.D.

Summary:

Low doses of nicotine markedly potentiate haloperidol-induced hypokinesia in rats (Manderscheid et al, 1988) and may potentiate haloperidol effects in Tourette's Syndrome (T.S.) (Sanberg et al, 1988). Ten child patients aged seven to 17 with both Tourette's Syndrome and attention deficit problems initially received haloperidol in doses of 1.0 to 3.0mg daily; all had inadequate response with dose related side effects. One 2.0mg chewing piece of Nicorette® was then administered to each child three times daily for a two week trial. Parent reported changes in severity of tics and attention-concentration problems after nicotine administration were globally assessed by two raters, using the criterion definitions of the Yale Global Tic Severity Scale and the Conner's Abbreviated Parent-Teacher Rating Scale. Fifteen to 20 minutes after beginning chewing the gum, a diminution in intensity and severity of tics was noted in all cases, with increased concentration and attention in eight cases. The effect lasted 45 - 60 minutes with a subsequent return to the previous clinical state. However, 70 percent of children subsequently discontinued using the nicotine gum because of side-effects including bitter taste and nausea. Two children with T.S. given Nicorette® gum only, and two children with T.S. given ordinary chewing gum only, without prior haloperidol, showed no effect on tics or attention span. Increased cholinergic activity by haloperidol plus nicotine may increase the inhibitory influence of the striatum on motor behavior, thereby increasing hypokinesia in rats, while decreasing tics in Tourette patients.

NR277 **Wednesday, May, 10, 12 noon–2:00 p.m.**

LORAZEPAM TREATMENT OF CATATONIA: A STUDY OF SEVEN CASES

Patricia I. Rosebush, M.D., Psychiatry, McMaster University, 1200 Main Street West, Hamilton, Ontario, Canada L8N 3Z5; Ann Hildebrand, M.D., Brian Furlong, M.D., Michael Mazurek, M.D.

Summary:

It has recently been reported that psychogenic catatonia may respond dramatically to lorazepam. It has been proposed that this response to lorazepam might help to distinguish psychogenic from organic causes of catatonia. We have had the opportunity to study this response in seven instances involving five patients. Catatonic syndrome was diagnosed if four or more of the following were present: stupor, akinesia, mutism, waxy flexibility, stereo typy, echolalia, echopraxia, staring, grimacing, negativism, flat affect. Each patient was treated with lorazepam 1-2 mgs with no other medication change and was re-evaluated one to three hours later. On six-occasions there was dramatic and complete resolution of the catatonic syndrome within 2 hours. One patient with classic psychogenic catatonia, displaying all features of the syndrome with normal CT, EEG, and laboratory investigations, showed no response. At the same time, two patients with clear-cut organic illnesses—one with an NMS-like syndrome, another with cocaine induced psychosis and decreased striatal dopamine function on PET scan—showed dramatic responses to the lorazepam. These results confirm that lorazepam can produce dramatic resolution of catatonia in some cases, but suggest that the response to lorazepam is not a useful indicator of whether the etiology is psychogenic or organic. It remains unclear which factors are predictive of a therapeutic response.

NR278 **Wednesday, May 10, 12 noon–2:00 p.m.**

CIGARETTE SMOKING AND NEUROLEPTICS

Rakesh K. Bansil, M.D., Psychiatry, CMHC at Newark C 44, 215 South Orange Avenue, Newark, NJ 07103; Norman Hymowitz, Ph.D., Steven Keller, Ph.D., Anwar Y. Ghali, M.D.

Summary:

The dose of neuroleptic medication received by smoker (N = 32) and nonsmoker (N = 27) schizophrenic patients was compared. The smokers group received significantly more medication as compared to the nonsmokers a ($P < 0.01$).The present findings are consistent with previous reports in the literature; however our study extends the previous research in that we statistically controlled the severity of illness as an influencing factor. By doing a heirarchical multivariate regression analysis we are also able to conclude that the differences in age, weight, sex, alcohol intake, and tea/coffee intake between the smokers and nonsmokers group did not account for the differences in the neuroleptic dose. The stimulant effects of nicotine on the the release of dopamine in the central nervous system is proposed as another possible explanation for the higher neuroleptic dose received by the smokers.

NR279 **Wednesday, May, 10, 12 noon–2:00 p.m.**

EFFECTS OF DIFFERENT LIGHT WAVELENGTHS IN SAD

Dan A. Oren, M.D., Clinical Psychobiology, NIMH Bldg 10 RM 4S239, 9000 Rockville Pike, Bethesda, MD 20892; George C. Brainard, Ph.D., Jean R. Joseph-Vanderpool, M.D., Elizabeth Sorek, R.N., Scott Johnston, B.A., Norman E. Rosenthal, M.D.

Summary:

Although the eye has been implicated in the antidepressant effects of phototherapy in seasonal affective disorder (SAD), the form of light needed and its mechanism of action is unclear. We randomly assign SAD patients to red or green light treatments for one week in a crossover design. During treatment, patients are exposed to light for two hours each morning. Patients are off light for one week between treatments. Therapies consist of equal quanta exposures (2.3×10^{15} photons/sec/cm^2) of colored light comparable to that achieved by standard, bright, full-spectrum phototherapy. Light sources are Philips F40R (half-peak bandwidth, 615-685 nm) and F40G (half-peak bandwidth, 505-555 nm) lamps, filtered through a clear pyramidal diffuser, an ultraviolet filter, and a yellow gelatin filter to remove light emitted below 450 nm. Eleven patients have been treated to date with a total of seventeen conditions. Mean decreases ($\pm$ S.D.) in Hamilton Depression Rating scores for red and green lights are 5 ± 7 and 10 ± 5 respectively, despite patients' similar expectations. It appears that green light has efficacy similar to full-spectrum lights, whereas red resembles placebo. The study is ongoing and the final results and their implications will be discussed.

NR280 **Wednesday, May, 10, 12 noon–2:00 p.m.**

SUDDEN DEATH: A COMPLICATION OF TCA THERAPY

Sheldon H. Preskorn, M.D., Psych. Research Inst., 929 North St Francis, Wichita, KS 67214; Pamel K. Widener, B.S.

Summary:

Sudden death has long been associated with tricyclic antidepressant (TCA) pharmacotherapy. Coroners are now quantitating the TCA concentration in postmortem blood samples from such cases and have found elevated concentrations. The results from 13 cases are as follows:

	Age (yrs)	*Dose*	*Concentration (mg/L)*	*Sex*	
Mean ± SD	45 ± 18	212 ± 145	3.44 ± 2.96	Males	8
Range	5-77	50-375	.50-10.0	Females	5

In all cases, autopsy revealed no cause of death other than drug toxicity. There was no evidence of acute overdose. Of the 13 cases, eight (62 percent) were being treated with amitriptyline, three (23 percent) with imipramine, and one (8 percent) with desipramine. Cognitive deterioration or other side-effects were noted in several cases prior to death but were attributed to problems other than the drug therapy, including worsening of the psychiatric disorder. In eight cases, the medication was dispensed in a supervised setting. In the case of tertiary TCAs, a ratio of parent drug to active metabolite indicated chronic accumulation and was incompatible with a sudden overdose. This conclusion was further supported in cases in which tissue concentrations were also determined and compared to blood concentrations. Based on data from these cases and parallel animal and *in vitro* studies, TCA concentration in blood can increase up to five-fold within 20 hours of death but then plateaus. Even considering such postmortem changes, these cases of sudden death were associated with obvious supratherapeutic concentrations of TCA. Therapeutic drug monitoring had not been employed to guide dosage adjustment so that antemortem values were not available for comparison.

NR281 **Wednesday, May, 10, 12 noon–2:00 p.m.**

USING PLASMA LEVELS TO ADJUST IMIPRAMINE DOSING

Steven J. Bupp, M.D., Research, Psychiatric Inst., 929 North St. Francis, Wichita, KS 67214; Sheldon H. Preskorn, M.D.

Summary:

Patients on standard doses of imipramine (IMI) demonstrate large interindividual variability in steady-state plasma levels. Calculating dosing requirements based upon clinical impressions is imprecise. Adjustments based on predictions from single-dose or steady-state plasma levels may provide a useful alternative, but prior reports of dose-dependent kinetics for IMI need further investigation.

We studied 17 medically healthy, hospitalized depressed patients (eight male, nine female, average age 28 ± 12.4 years, range 14-48 years), who had steady-state levels of IMI and its primary metabolite desipramine (DMI) measured, and then underwent a dosage change with repeat steady-state plasma levels. A positive correlation was observed between percent change in total plasma level (IMI + DMI) and percent change in dose ($y = 1.4x - .293$; $r = .71$, $F = 15$;$df = 1,15$; $p < .005$).

The slope of 1.4 indicates that the relationship is not linear and suggests that levels 40 percent higher than expected may be encountered in a similar clinical population. Separate analysis of change in IMI or DMI alone versus change in dose revealed the DMI (slope 1.33) rather than IMI (slope 1.17) is the prime contributor to this non-linearity. Increasing age was correlated with higher plasma level changes per change in dose ($r = .65$;$p < .005$). Thus, non-linearity may be due to an age related decrease in 2-hydroxylation capacity which would account for the disproportionate rise in DMI with increased dose.

NR282 **Wednesday, May 10, 12 noon–2:00 p.m.**

CLINICAL USE OF LOADING DOSE HALOPERIDOL DECANOATE

Tram K. Tran-Johnson, Pharm.D., Child Pharmacy, Univ of Texas, 7703 Floyd Curl Drive, San Antonia, TX 78284; Larry Ereshefsky, Pharm.D., Stephen R. Saklad, Pharm.D., Jerome Tilles, M.D., Robert C. Lyman, M.D., Davis M. Chester, Ph.D.

Summary:

We evaluated the efficacy and safety of a novel, "two-step" pharmacokinetic-based loading dose regimen of haloperidol decanoate (HD). The total monthly dose was calculated using a conversion factor of 20 times the oral haloperidol (HL) dose (16.0 ± 5.4 mg/day) and given in consecutive divided doses of 100-150 mg q three to seven days until the full amount was administered (370 mg±64.3 mg). No overlapping oral therapy was used. HL plasma concentrations (Cp) was obtained as part of a therapeutic drug monitoring program. Diagnoses were chronic schizophrenia (n=12), bipolar manic (n=three) and other (n=three). Eighteen pts were assessed weekly using Clinical Global Improvement (CGI) scale. HL Cps were assayed using RIA with minimum sensitivity of 0.5 ng/ml and CV=8.2 percent at 2-10 ng/ml. Mean oral HL Cps=8.43±6.78 ng/ml were greater than those obtained afater consecutive HD injections, however, the transition was smooth. There was a significant different between the HL Cps by ANOVA ($F=4.45$ ng/ml, $p=0.003$, df4, 67). A series of cases will be used to illustrate the therapeutic relationship of dosing to Cp. To illustrate, patient A was successfully switched from 15 mg oral HL (CP=8.0 ng/ml) to 300 mg HD given within the first two weeks, for each of two consectuvei months. HD Cps were 2.0 ng/ml (week 1 on HD), 3 ng/ml (week 2 on HD), and 5.0 ng/ml (week 4 on HD).

NR283 **Wednesday, May 10, 12 noon–2:00 p.m.**

CONTINUATION AND MAINTENANCE ECT-EFFICACY AND SAFETY

Richard Jaffe, M.D., Psychiatry, Phila Psych Center, Ford Rd & Monument Avenue, Philadelphia, PA 19131; William R. Dubin, M.D., Richard Roemer, Ph.D., Louis Lipschutz, M.D., Beth Shoyer, M.G.A.

Summary:

Twenty-nine elderly psychiatric outpatients (mean age 70 years) diagnosed as suffering from major depressive episode, recurrent type, have been followed in an open study for over 24 months, utilizing standardized rating scales to determine frequency of outpatient maintenance electroconvulsive therapy (ECT) treatments. ECT has been utilized in the outpatient service for acute treatment, continuation treatment, and maintenance treatment for the prevention of depressive recurrence. Following the acute treatment of depression, patients were treated in a protocol that involved gradually decreasing frequency of ECT to once monthly. The Hamilton Rating Scale for Depression and the Brief Psychiatric Rating were used to determine efficacy of treatment. Clinical deterioration, relapse, and recurrence were treated with the increased frequency of outpatient ECT to maintain patients in an euthymic range. Patient acceptance has been studied through quantification of dropouts as compared with generally accepted dropout rates in various outpatient medication protocols. Outcomes have been: (1) discharged euthymic-24 percent; (2) continuing in treatment-41 percent; (3) relapsed in first two months-10 percent; (4) suffered a recurrence of depression-10 percent; (5) dropped out-seven percent; (6) other outcome-seven percent. The use of maintenance ECT in recurrent affective disorder will be discussed.

NR284 **Wednesday, May 10, 12 noon–2:00 p.m.**

DEPRESSION AND TINNITUS: NORTRIPTYLINE TREATMENT

Mark Sullivan, M.D., Psychiatry, University of Washington, RP-10, Seattle, WA 98195; Wayne Katon, M.D., Robert Dobie, M.D., Connie Sakai, M.S.P.A.

Summary:

Tinnitus is known to be associated with high frequency sensorineural hearing loss, but the reason for marked differences in severity among sufferers and an effective mode of treatment are not known. Our previous studies have shown a high prevalence of major depression among patients with the chief complaint of tinnitus. To investigate the efficacy of treating depression in the treatment of tinnitus, a single-blind, placebo-washout, non-randomized pilot study of the tricyclic antidepressant, nortriptyline, was undertaken in disabled tinnitus patients who also met diagnostic criteria for major depression. Nineteen patients began the study, two responded to placebo, and two dropped out prior to completion. Fourteen considered their tinnitus improved and 12 chose to continue nortriptyline after the study. Depression severity decreased, on the average, by 65 percent ($p<0.0001$). Tinnitus loudness measured by audiometric matching decreased by a mean of 10dB or 50 percent ($p<0.02$). Significant improvement with treatment was also noted in self-reports in tinnitus loudness ($p<0.05$) and severity ($p<0.01$), in somatic and psychological symptoms as assessed by the SCL-90 (almost all scales $p<0.01$), and in psychosocial dysfunction as assessed by the Chronic Illness Problem Inventory (most scales $p<0.05$). These results suggest that what initially appears to be irreversible otologic disability in these patients may be in large part reversible psychiatric disability.

NR285 **Wednesday, May 10, 12 noon–2:00 p.m.**

CHEST PAIN DYSPHIA AND PSYCHIATRIC DISORDER

Robert G. Harper, Ph.D., Psychiatry, Baylor College Med., 6565 Fannin MS706, Houston, TX 77088; John R. Stroehlein, M.D., Francis Kane, Jr., M.D.

Summary:

We report a restrospective study of all patients examined in the GI motility lab of The Methodist Hospital during the year 1987. *Methodology:* 250 patients were sent 1) a self-report questionnaire regarding current GI symptoms 2) current anxiety symptoms (17 such derived from SADS-LA) and depressive symptoms (ten from SADS-LA) 3) a brief symptom inventory relating to symptomatology in the past month. *Results:* One hundred sixty-three (65 percent) patients responded: males 38.9 percent, female 61.6 percent. 61.3 percent had either six anxiety symptoms more than six months or panic attacks with at least four symptoms or both. Panic attacks were reported by 38.5 percent. Ninety-one percent had attacks three weeks in a row. (usually weekly or oftener). Of the sample 29.4 percent had four or more symptoms of depression for two or more weeks. Forty percent of those with Anxiety Disorder qualified for Major Depressive Disorder. Eighty-eight percent of the sample were still symptomatic—chest pain (54 percent), heartburn (45 percent), and trouble swallowing (35 percent) were the most frequent symptoms. Abdominal pain with constipation and/or diarrhea was also reported frequently and correlated highly with anxiety disorder ($p = .0001$). Elevated BSI Somatizaiton scales at levels seen in psychiatric outpatients were seen in 74 percent of men and 78 percent of women. Forty-nine percent of men and 48 percent of women had at least two scales with significant elevations. Sixty-eight percent were told they suffered from "stress", only 18 percent were referred for consultation. Sixty-eight percent said they would go for psychiatric consultation if told to do so. Those with suicidal thoughts wre referred only 52 percent of the time. No significant differences were found among esophagela spasm, normal, and organic pathology groups for diagnoses mentioned above.

NR286 **Wednesday, May 10, 12 noon–2:00 p.m.**

DRUG FREE SCHIZOPHRENICS SHOW LEFT-SIDED P3 DEFICIT

Steven F. Faux, Ph.D., Harvar-Brocton VA, Dept of Psychiatry, 940 Belmont St. (116A), Brocton, MA 02401; Paul G. Nestor, Ph.D., Robert W. McCarley, M.D., M.E. Shenton, Ph.D., T. Horvath, M.D., K. Davis, M.D.

Summary:

Three previous auditory P300 topographic mapping studies from our group found a voltage deficit maximal at the left temporal electrode, T3, in neuroleptic-medicated chronic schizophrenics (SZ) compared with normal controls (NC). We are now testing a neuroleptic-free group. To date we have run identical P300 protocols on 8 right-handed NC and 8 right-handed DSM III-R/RDC diagnosed SZ free from neuroleptics for a minimum of 14 days; SZ and NC mean ages were not different (40.9 vs. 39.4 years respectively). Previous findings on neuroleptic-medicated SZ were confirmed in that: 1) comparison of integrated voltages over 300-400 ms (at T3, C3, Cz, T4) showed maximal amplitude reductions at T3 in SZ (mean: .60 uV versus NC mean: 3.99 uV, $p<.002$, Mann-Whitney [M-W]) and 2) the 2 uV T3 seperation criterion used in previous studies correctly classified all but one member of each group ($p<.0001$, binomial test). In contrast, group amplitudes at the homotopic right temporal electrode (T4) were not statistically significantly different. These findings persisted when integrated voltages were adjusted for individual latency differences; the mean P300 peak latency in unmedicated SZ was longer than in NC (440 ms vs. 381 ms, $p<.02$, M-W), in contrast to the absence of latency differences between NC and medicated SZ groups. These data provide evidence that neuroleptic medication does not confound P300 topography, and support the hypothesis that the left temporal P300 feature may be a useful biological marker for major psychopathology. Work in progress will increase the N of this study and examine the specificity of the P300 left temporal feature to schizophrenia.

NR287 **Wednesday, May, 10, 12 noon–2:00 p.m.**

PSYCHIATRIC MORBIDITY IN IRRITABLE BOWEL SYNDROME

Mark D. Fossey, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29424; R. Bruce Lydiard, M.D., William H. Marsh, M.D., James C. Ballenger, M.D.

Summary:

Thirty-five outpatients in a gastroenterology clinic were administered the Structured Clinical interview for DSM-III-R. All interviews were administered by one of two psychiatrists. Analysis of the first 21 patients revealed a high prevalence of psychiatric morbidity compared to ECA data. Seventy percent had a lifetime history of major depression and 33 percent were currently depressed. Thirty-eight percent had a lifetime history of panic disorder and 24 percent had the disorder currently. Sixty-two percent had either an anxiety disorder or major depression currently. Thirty-eight percent were found to have somatization disorder. Other psychiatric disorders including substance abuse, did not appear to be more common than in the general population. Sixty-two percent had previously been evaluated by a psychiatrist although only 38 percent received treatment. Seventy-one percent had received psychotropic medications in the past, usually from a primary care physician. Sixty-seven percent had been treated with anxiolytics and 52 percent had received antidepressants, usually in subtherapeutic doses. These early results support previous studies suggesting a high prevalence of psychiatric disorders in patients with Irritable Bowel Syndrome (IBS). This would suggest a need for increased psychiatric intervention in this population, especially in the skilled use of psychopharmacology.

NR288 **Wednesday, May 10, 12 noon–2:00 p.m.**

PSYCHOPATHOLOGY AND ATYPICAL CHEST PAIN IN THE EMERGENCY ROOM

Lawson Wulsin, M.D., Psychiatry, Univ of Cincinnati, 231 Bethesda Ave ML 559, Cincinnati, OH 45267; Lesley Mussio, M.D., James R. Hillard, M.D., Peter Geier, M.D.

Summary:

To evaluate the prevalence and persistence of psychiatric diagnoses in ER Patients with atypical chest pain, we administered the Structured Clinical Interview for DSM-III-R (SCID) to 30 adults recruited within 72 hours of their ER visit who also returned for a second SCID interview six to 12 months later. The sample is typical of large urban public ER's: mean age 49, 63 percent female, 66 percent black, 73 percent unemployed or on disability, mean years of school = ten. All but 2 subjects had pain that was atypical for angina.

We found axis I SCID diagnoses in 17 (57 percent) subjects initially and in 15 (50 percent) at follow-up. Multiple diagnoses appeared in 11/17 (65 percent) initially and in 9/15 (60 percent) at follow-up. Eleven (37 percent) subjects developed one or more new diagnoses by follow-up.

Initially, nine (30 percent) subjects had a current affective disorder (six with major depression) and 14 (46 percent) had a current anxiety disorder (11 with Panic disorder, seven with generalized anxiety). At follow-up ten (33 percent) had a current affective disorder (five with major depression) and ten had a current anxiety disorder (seven with Panic disorder). Three subjects had major depression initially and at follow-up. Five had panic disorder initially and at follow-up.

This study suggests that: 1) the prevalence of psychopathology in this ER population is high, 2) the most common disorders are panic disorder, generalized anxiety, and major depression, 3) multiple diagnoses are the rule, though specific diagnoses may not remain stable over time, and 4) the incidence of new psychiatric disorders is high in this population subsequent to presentation to medical ER.

NR289 **Wednesday, May 10, 12 noon–2:00 p.m.**

NEUROENDOCRINE ASPECTS OF CHRONIC FATIGUE SYNDROME

Mark A. Demitrack, M.D., Clin Endo Branch, NIMH Bldg 10 3S231, 9000 Rockville Pike, Bethesda, MD 20892; Stephen E. Straus, M.D., Janet K. Dale, R.N., Markus J.P. Kruesi, M.D., George P. Chrousos, M.D., Philip W. Gold, M.D.

Summary:

Patients with chronic fatigue syndrome (CFS) show many symptoms reminiscent of major affective disorder (MAD). To explore possible biological similarities in these illnesses, we report here a study of basal ACTH and cortisol (F) and their responses to corticotropin-releasing hormone (CRH) injection in CFS patients. We have previously noted that patients with MAD show high basal F and blunted ACTH responses to CRH, indicating normal glucocorticoid negative feedback upon the pituitary. These data suggest that high basal F in MAD reflects a defect at or above the level of the hypothalamus resulting in the hypersecretion of CRH. Nineteen medication-free patients meeting CDC criteria for CFS, and 17 healthy controls, had basal ACTH and F measured q 15 min from 1800-200 hrs; ovine CRH, 1 ug/kg IV, were then given and ACTH and F monitored for two additional hours. The free cortisol index are calculated from cortisol binding globulin (CBG) and total F levels. Basal total F was lower in patients than in controls (3.2 ± 0.3 vs 5.4 ± 0.7 ug/dl, $p<.02$). Basal CBG, on the other hand, was higher in patients (17.8 ± 0.5 vs 15.2 ± 1.1 ug/dl, $p<.005$), while the free cortisol index was lower (104 ± 11 vs 321 ± 106 ng/dl, $p=.04$). In contrast to F, basal ACTH was higher in patients than controls (12.2 ± 1.7 vs 7.5 ± 0.7 pg/ml, $p=.04$). However, peak ACTH and F responses were similar in both groups.

The presence of basal hypocortisolism and elevated basal ACTH in these patients is in marked contrast to the high basal F seen in MAD patients and suggests the presence of mild adrenal hypofunction and/or inactivation of the central CRH system; this latter system is known to play an important role in arousal. Either of these disturbances may be relevant to the chronic fatigue which is the hallmark symptom of CFS.

NR290 **Wednesday, May 10, 12 noon–2:00 p.m.**

QUALITY OF LIFE WITH A CARDIAC DEFIBRILLATOR: THE AUTOMATIC IMPLANTABLE CARDIAC DEFIBRILLATOR

Milton H. Miller, M.D., Psychiatry, Marbor-UCLA Med Center, 1000 W. Carson N. St. Box 8, Torrance, CA 90509; David Cannom, M.D., Annette Brodsky, Ph.D.

Summary:

Among patients surviving sudden cardiac arrest, 35 percent remain high risk for recurrence of fatal arrhythmia. The Automatic Implantable Cardiac Defibrillator (AICD) has been approved by FDA for treatment and some 4,000 patients worldwide have had surgical implantation of a half-pound machine that shocks the heart when fatal rhythms begin. Treatment is successful—death rate changes from 35 percent to near zero. What about quality of life?

Presenters are a psychiatrist, psychologist, and cardiologist, subjects, an AICD patient group in the practice of cardiologist DC. Patients, 14-75 years in age, have lived with an AICD one to seven, and present diverse medical, psychiatric, and cardiac histories. Patient/spouse questionnaires have been completed, interviews with patient/ spouse conducted, individual consultations arranged, and authors participate in every-three-month "self-help" meetings.

Principle findings: despite difficulty of life-change, patients/spouses are enormously grateful for life; still, not only patients (47 percent) but spouses (37 percent) suffer depression, anxiety, loss of life interest, and substantial drop in sexual activity (50 percent); patients and spouses are often "too grateful" to complain; "self-help" meetings are extraordinarlly valued. Physicians implanting life-saving devices have an obligation to be aware of quality of life issues for patient and spouse.

NR291 **Wednesday, May 10, 12 noon–2:00 p.m.**

MEDICAL COMPLIANCE IN HEART TRANSPLANT RECIPIENTS

Michael E. Swain, M.D., Psychiatry, Loyola Medical, 2160 S. First Avenue, Maywood, IL 60153; Michael Levick, C.S.W., Marge Gier, C.S.W., Kathy Grady, R.N., Bonnie Grusk, R.N., Deborah Couch, M.D.

Summary:

Donor hearts for transplantation are a limited resource; recipients face numerous medical complications and other stresses. Psychiatrists are consulted to evaluate heart transplant candidates for their psychological suitability, and to predict probable compliance with medical regimens and life-style changes. The psychosocial histories of 50 heart transplant recipients were reviewed; cardiac transplant nurses made global assessments of compliance in eight areas: 1. diet, 2. exercise, 3. smoking, 4. immunosuppressant medications, 5. all other medications, 6. vital sign recording, 7. attendance at clinc, and 8. attendance at scheduled tests. Variables not found to be significantly correlated with the degree of compliance include: cardiac diagnosis, sex, ethnicity, length of time with cardiac disease, length of survival, level of stress due to medical complications, or presence of psychiatric history (Axis I, except substance abuse). The authors determined that four factors were significantly correlated with degree of compliance; marital status, alcohol history, previous medical compliance history, and level of education. A proposed prospective study, with a more detailed measure of compliance, is discussed.

NR292 **Wednesday, May, 10, 12 noon–2:00 p.m.**

SLEEP IN CUSHING'S DISEASE

Henry W. Lahmeyer, M.D., Psychiatry, Univ Of Illinois at Chic, 912 South Wood Street, Chicago, IL 60525

Summary:

Depression is the most conmon affective complication of Cushing's Syndrome, affecting over 50 percent of patients with psychiatric symptoms. Primary depression is associated with hypercortisolemia in over 35 percent of patients, particularly in severely depressed melancholic patients. Sleep is usually disturbed in both conditions. Patients with Cushing's Syndrome appear to have reduced sleep efficiency and very little delta sleep. Endogenously depressed patients with high cortisol levels have shortened REM latency. REM sleep abnormalities have not been described in depressed Cushing's Syndrome patients even though it provides a good natural model of organic depression.

Two severely depressed Cushing's Syndrome patients were studied in the Sleep Laboratory while depressed. One patient was re-studied after she had bilaterial adrenalectomy and was stable on replacement hydrocortisone, and the other patient was re-studied after being placed on amitriptyline therapy. Both patients had no delta sleep and both had abnormally elevated REM activity. Adrenalectomy in one patient normalized REM and delta sleep. Amitriptyline normalized REM sleep but not delta sleep in the second patient.

These findings may indicate a linkage between hypercortisolemia and these specific sleep abnormalities seen in depression.

NR293 **Wednesday, May 10, 12 noon–2:00 p.m.**

BIRTH ORDER IN DSM-III-R SOMATIZATION DISORDER

Frank W. Brown, M.D., Psychiatry, UAMS, 4301 West Markham SLOT 554, Little Rock, AR 72205; G. Richard Smith, M.D.

Summary:

Birth order has been reported to be nonrandomly distributed in patients with somatization disorder, therefore implicating environmental factors etiologically. Using a prospective design, we tested this a hypothesis that patients with somatization disorder would have a significantly earlier birth order. A study sample of 143 patients, 76 meeting strict DSM-III-R criteria for somatization disorder and 67 controls, were studied using Slater's index to measure birth order position. Slater's index in a normally distributed population approaches 0.5. Slater's index for all patients meeting DSM-III-R somatization disorder was .5196 ($t = 0.42$, $df = 75$, NS). When birth order was considered separately for the 11 males and the 65 females with somatization disorder, Slater's index showed a nonsignificant difference from a normally distributed population (ma1es:0.6257, $t = 0.98$, $df = 10$; females:0.5013, $t = 0.02$, $df = 64$).

The findings that Slater's index for somatization disorder do not show significant deviations from the theoretical mean of 0.5 provides no support for the notion that environmental influence on somatization disorder occurs through birth order as reported previously. This study showed that birth order position is not associated with the DSM-III-R diagnosis of somatization disorder. Although environmental factors may influence the development of somatization disorder, the expression of environmental influence through birth order is thus unlikely.

NR294 **Wednesday, May, 10, 12 noon–2:00 p.m.**

PSYCHIATRIC DIAGNOSES IN VOLUNTEERS FOR HIV TESTING

Lawrence B. Jacobsberg, M.D., Psychiatry, Cornell Univ Med, 525 East 68th Street, New York, NY 10021; Samuel W. Perry, M.D., Allen J. Frances, M.D., Baruch Fishman, Ph.D., Pamela Weiler, B.M., Karen Fogel, R.N., Joanne Ryan, R.N.

Summary:

Objective: The determine the rates of DSM-III-R diagnoses among individuals volunteering for HIV serological testing. *Significance*: The presence of DSM-III-R disorders may affect seroprevalence risk behaviors, distress, coping, and counseling needs. *Methods*: We administered the Structured Clinical Interview for DSM-III-R (for Axis I) and the Personality Disorders Examination (for Axis II) one week prior to HIV serological testing to a heterogeneous population of 231 physically asymptomatic adults at perceived risk for AIDS who had enrolled in a prospective psychobehavioral study. *Results*: Overall rates for the presence of any Axis I disorder were 25.5 percent current and 64.1 percent lifetime; for Axis II disorders the overall rate was 28.6 percent. Compared to reported community samples, these subjects had high rates of mood disorders, both current (males: 14.4 percent; females: 11.8 percent) and lifetime (males: 41.2 percent; females: 47.1 percent). Even after the 21 subjects with intravenous drug use as a risk factor were eliminated from analysis, lifetime rates of nonalcohol substance dependence were high (males: 30.0 percent; females: 31.6 percent). An Axis II disorder was present in 50.8 percent of subjects with a current Axis I diagnosis and in 35.8 percent of those with a lifetime Axis I diagnosis. Conversely, most subjects (53.6 percent) with an Axis II diagnosis met criteria for a currant Axis I disorder and almost all (94.6 percent) met criteria for a lifetime Axis I disorder. *Conclusion*: A large subgroup of the volunteers for testing had histories of depression and nonalcohol substance dependence. A substantial subpopulation with Axis I psychopathology may have additional treatment needs posed by Axis II disorders.

NR295 **Wednesday, May, 10, 12 noon–2:00 p.m.**

RISK BEHAVIOR AND HIV TESTING

John W. Bobo, Ph.D., Psychiatry, Cornell Medical Center, 525 East 68th Street, New York, NY 10021; Baruch Fishman, Ph.D., Samuel W. Perry, M.D., Lawrence B. Jacobsberg, M.D., Joanne M. Ryan, R.N.

Summary:

Objective. To examine the hypothesized relationships between HIV risk behavior,psychological variables, and effects of HIV testing. *Methods*. One hundred fifty-four physically asymptomatic gay/bisexual men voluntarily sought HIV testing and were evaluated with clinical ratihgs of psychiatric diagnosis (SCID,PDE), and self-report measures of risk behavior, hardiness, social support, attributional style, and distress (Beck Depression, Brief Symptom, and Spielberger Anxiety Inventories). Risk behavior and distress measures were repeated nine weeks after notification and counseling. *Results*. One hundred thirty-two subjects (86 percent) reported no Unprotected Anal Sex (UAS) in the month prior to HIV testing; of 79 subjects seen nine weeks later (25 percent HIV+), 75 continued to abstain from UAS. Twenty-two subjects (14 percent) engaged in UAS in the month prior to testing; of 11 subjects seen nine weeks later (27 percent HIV+), all had abstained from UAS in the past month. Psychological variables and serological status did not distinquish the two behavior groups at either measurement point. *Conclusions*. Most participants ceased high risk behavior at least one month prior to HIV testing . This "floor effect" impeded determining the relation between risk behaviors, psychological variables, and effects of HIV testing and counseling. This study documents the need for prospective studies to determine if risk reduction surrounding HIV testing is sustained over time, and how psychological factors and known HIV status predict possible behavioral relapse.

NR296 **Wednesday, May 10, 12 noon–2:00 p.m.**

FINDINGS ON SCREENING CHECKING IN HIV DEMENTIA

James W. Dilley, M.D., Psychiatry, Univ of Cal. San Fran, Box 0884 San Fran Gen Hospital, San Francisco, CA 94143; Alicia Boccellari, Ph.D., Ann Davis, Andrew Moss, Ph.D., Peter Bacchetti, Ph.D., Bridget Wagner, M.D.

Summary:

Objective: To describe the development of a screening self-report symptom checklist to detect individuals at risk for the development of HIV Related Dementia.

Methods: Seventy-nine subjects (56 HIV+ and 23 HIV− Controls) completed a 55-item checklist of HIV Related CNS symptoms. Subjects were also given a battery of neuropsychological tests (NP) and psychiatric rating scales. Measures of immune functioning were also obtained. The HIV Dementia Symptom Checklist (HDSC) documents the presence and severity of self-report prodromal physical symptoms and neurological/neurobehavioral changes.

Results: Cronbach's alpha ($\infty = 0.96$) was calculated to estimate the internal consistency of the scale. Furthermore, the total score on the HDSC was shown to have a low but significant correlation with numbers of Helper T-Cells (CD_4 $r = -0.20$, $p < .05$). The score also correlated with impairment on NP testing, particularly on measures of verbal memory ($r = -.27$, $p < .01$), visual-spatial memory ($r = -0.31$, $p < .01$), fine motor speed ($r = -0.24$, $p < .05$), speeded mental operations ($r = 0.36$, $p < .001$), and sustained concentration ($r = 0.43$, $p < .001$). While no significant differences between the groups on measures of depression and anxiety were found, the HDSC significantly differentiated the HIV+ group from the HIV− controls ($p = < .001$), on both the prodromal physical symptoms and the neuropsychological/neurobehavioral symptoms.

Conclusions: While cross validation of these results are needed, these preliminary data suggest that the HDSC may be a practical and efficient way to identify those subjects who are at risk for developing HIV-related cognitive impairment. They may also help identify those individuals in need of neurological or NP evaluation.

This work is supported in part by grant # DA04873 from the National Institute of Drug Abuse.

NR297 **Wednesday, May, 10, 12 noon–2:00 p.m.**

PSYCHOLOGICAL RESPONSES TO HIV SEROLOGICAL TESTING

Samuel Perry, M.D., Psychiatry, Cornell Univ Med, 525 East 68th Street, New York, NY 10021; Lawrence B. Jacobsberg, M.D., Baruch Fishman, Ph.D., Allen J. Frances, M.D., Allan B. Novick, M.D., Ronald R. Rein, M.A.

Summary:

A prospective study was conducted to assess the emotional impact of voluntary HIV serolcgical testing on 214 physically asymptomatic adults at risk for AIDS (138 gay/bisexual men, 25 intravenous drug users, 51 heterosexuals with suspected HIV-infected partners. Visual analogue scale (VAS) measures of anxiety and depression of the 174 seronegatives fell ($p < .001$) immediately upon notification compared to scores two weeks and immediately before notification, even though most seronegatives (76 percent) had correctly predicted their results. At ten weeks after notification, their scores on VRS, Spielberger State Anxiety Inventory (SAI), and Beck Depression Inventory (BDI), remained significantly below entry values (all $p < .02$). Immediately after notification, the 40 seropositives (88 percent of whom were gay/bisexual males) had a transient increase in depression, but did *not* show a significant increase in the VRS measure of anxiety. At ten weeks after notification with continuing psychoeducational counseling, reported depression had returned to its initial level and anxiety was significantly *decreased* compared to entry values (all $p < .02$). The findings indicate that in our research subjects HIV testing with adequate counseling was emotionally helpful for both seropositives and seronegatives at two months following notification.

NR298 **Wednesday, May, 10, 12 noon–2:00 p.m.**

STRESS PREVENTION TRAINING AFTER ANTIBODY TESTING

Baruch Fishman, Ph.D., Psychiatry, Cornell Univ Med College, 525 E. 68th St c/o Dr S. Perry, New York, NY 10021; Samuel Perry, M.D., Lawrence B. Jacobsberg, M.D., Allen J. Frances, M.D., Pamela Weiler, M.A., Allan B. Novick, M.A.

Summary:

Aim: To determine the effectiveness of a manualized Stress Prevention Training program (SPT) after HIV testing. *Method:* 164 asymptomatic subjects at risk for AIDS were tested for antibodies to HIV and counseled by a psychiatric nurse; 23 seropositives (HIV+), and 54 seronegatives (HIV–) were then randomly assigned to six weekly sessions of SPT, and 24 HIV+ and 72 HIV– received either additional information through an interactive video program or no additional counseling (NC-SPT). Monitored for adherence by audiotapes, the SPT program is based on cognitive behavioral principles and is designed to enhance sense of personal control and to train coping skills, such as reframing dysfunctional thoughts, problem solving, assertiveness and relaxation. All subjects completed the Beck Depression Inventory (BDI) and State Anxiety Inventory (SAI) one week and ten weeks after notification of test results. *Results:* Mean improvement in depressive and anxiety symptoms (initial BDI or SAI scores minus follow-up scores) was significantly greater for HIV+ subjects who received SPT than for those who did not, but there was no difference for HIV– because their distress scores dropped immediately after notification. Analyses of Covariance (ANCDVA) with initial BDI or SAI scores as covariates supported these significant interactions: Mean BDI change: HIV+/SPT = 4.5; HIV+/NO-SPT = 0.5; $F(1,167) = 8.3$, $p < .005$. Mean SAI change: HIV+/SPT = 9.8; HIV+/NO-SPT = 4.2; $F(1,159) = 5.1$, $p < .05$. *Conclusion:* SPT is an effective method of reducing distress in HIV+ during the first few weeks following notification of HIV test results. Studies are currently being conducted to determine the longer term effectiveness of SPT on various risk groups and on their risk behaviors.

NR299 **Wednesday, May 10, 12 noon–2:00 p.m.**

ANTISOCIAL PERSONALITY: HIGHER AIDS RISK IN INTRAVENOUS DRUG USERS

Robert K. Brooner, Ph.D., Psychiatry, Johns Hopkins, D5 East 4940 Eastern Avenue, Baltimore, MD 21224; George E. Bigelow, Ph.D., Frederick Schaerf, M.D.

Summary:

Intravenous drug users (IVDU's) are a primary risk group for HIV-I infection and AIDS. IVDUs with concurrent psychiatric disorder have a poorer treatment prognosis (1). However, little is known about the contribution a of psychiatric comorbidity in IVDUs to HIV-1 risk behaviors. The present study related psychiatric diagnoses with patterns of behavior involved in HIV-1 transmission—specifically, intravenous drug injection and needle sharing. Participants ($N = 66$) were consecutive enrollees in an HIV-1 testing and education program. Diagnoses of psychiatric disorders were made using a structured psychiatric interview (2), and detailed quantitative information on number of injections, number and percent times needle sharing, and number of needle share partners for the preceeding 12 months were collected. Analyses compared rates of these AIDS risk behaviors for subjects with versus without a DSM-III-R diagnosis of Antisocial Personality Disorder (ASPD). The two groups were similar for number of reported drug injections, but differed in indices of needle sharing. IVDUs with ASPD reported a significantly greater number (10.21 versus 2.43/mo) and percentage (37.39 versus 12.7/mo) of needle sharing ($p = .008$ and $p = .002$, respectively), and a greater number (3.27 versus .58/mo) of needle sharing partners ($p = .006$). Thus, these data identified a subgroup of IVDUs at higher risk of HIV-1 infection, and emphasize the importance of careful assessments and interventions for improving the treatment enrollment and performance of ASPD patients.

NR300 **Wednesday, May, 10, 12 noon–2:00 p.m.**

NEUROPSYCHOLOGICAL FUNCTION IN HIV ASYMPTOMATIC MALES

Deborah Belsky-Barr, M.A., Psychiatry, Cornell Univ Med, 525 East 68th Street, New York, NY 10021; Samuel W. Perry, M.D., Rex Swanda, Ph.D., Lawrence B. Jacobsberg, M.D., Richard Shidledecker, M.A., Steven Mattis, Ph.D., William B. Barr, Ph.D.

Summary:

Reports suggest HIV-induced mental changes may occur prior to physical manifestations of immunosuppression. To examine this unresolved issue, medical history and physical exams were obtained on 20 HIV seropositive gay/bisexual men to ensure that they were truly asymptomatic. Additional confounds were reduced by excluding subjects with DS.M-III-R Axis I or II psychopathology, including substance dependence (SCID, PDE), bereavement (PERI), medication during past month, and history of concussion or migraine. A two-hour battery of standardized neuropsychological tests was then administered to assess attention concentration, memory, language, conceptualization, and motor performance. For comparison, 20 HIV seronegative gay/bisexual men were tested after identical screening and matching for age, education, and distress (BDI, Spielberger Anxiety). T-tests and logistical regression did not find significant differences between the two groups. Results indicate the importance of careful screening and tightly-matched seronegative subjects before concluding HIV causes significant mental changes in advance of other indicators of infection.

NR301 **Wednesday, May, 10, 12 noon–2:00 p.m.**

HIV INFECTION: PSYCHIATRIC AND NEUROLOGIC FINDINGS

Robert Kertzner, M.D., NYS Psychiatric Institute, 722 West 168th Street, New York, NY 10032; Jack Gorman, M.D., Janet Williams, D.S.W., Yaakov Stern, Ph.D., Richard Mayeux, M.D., Anke Ehrhardt, Ph.D.

Summary:

To study the interrelationships among Human Immunodeficiency Virus (HIV) infection, neuropathology, psychopathology, and immune dysfunction, we have organized a five-year follow-up study of seropositive and seronegative gay men. Data are now available for the first series of evaluations of 160 gay men (118 seropositive, 42 seronegative). Medically, the HIV positive men were at a relatively asymptomatic stage of illness, but as expected, had lower T helper cells, higher T suppressor cells, and lower T4/T8 lymphocyte ratios than HIV negatives. Seventeen of 117 seropositive men in the cohort were positive for p24 antigenemia. Only six HIV positive men and three HIV negative men met criteria for current major depression and mean Hamilton Depression scores were only 4.38 and 3.67, respectively, for the two groups. Neurological examination revealed little pathology, with mean Kurtze scale scores of 1.16 and 1.19 for HIV positive and negative men, respectively. Neuropsychological testing uncovered few overall differences between positive and negative men. Mean global performance ratings, for example, were 1.30 for HIV positives and 1.00 for HIV negatives. However, there were significant, although subtle, differences between HIV positive and HIV negative men for verbal memory, reaction time, and tests for executive function.

NR302 **Wednesday, May 10, 12 noon–2:00 p.m.**

MEDICAL STUDENT ATTITUDES ABOUT THE AIDS EPIDEMIC

Carol A. Bernstein, M.D., Medical Education, NYS Psych Institute, 722 West 168th Street Box 125, New York 10032; Judith Rabkin, Ph.D., Robert Kertzner, M.D., Ray Goetz, Ph.D.

Summary:

AIMS: As AIDS continues to have a major impact on health care, understanding its effects on education and training is crucial. We conducted an anonymous survey of second-year medical and dental students to examine attitudes about occupational contagion, treating AIDS patients, and ways in which the AIDS epidemic might affect professional careers and anxiety about personal risk factors.

METHODS: A 21-item questionnaire was distributed to students before and after a symposium on AIDS and HIV infection. Because of concerns about confidentiality, responders were only identified by sex and school. *RESULTS:* Eighty percent of dental students and 74 percent of medical students returned the questionnaire. Significant differences were apparent between professions. Forty-one percent of medical students and 64 percent of dental students expressed moderate to marked levels of anxiety about risk due to professional roles ($p = .01$) Sixty-four percent of dental students felt they would not treat HIV + patients if they had a choice, compared to only 12 percent of medical students ($p < .000$). Thirty percent of medical students and 64 percent of dental students said that HIV + physicians (dentists) should not be allowed to provide direct patient care ($p < .000$). Higher levels of anxiety were associated with more restrictive attitudes for all students ($p < .05$). Twenty-nine percent of medical students felt that the AIDS epidemic would influence their choice of specialty and 33 percent felt it would influence choice of training hospital. We found no differences between the sexes on any measures.

SIGNIFICANCE: A substantial minority of medical students and even more dental students do not acknowledge the responsibility to treat all patients within their areas of expertise. Results suggest that AIDS-related anxiety may influence career choices, behavior patterns, and perhaps the quality of care patients receive. Differences in attitudes between professional groups may point to the need for different educational strategies. We will discuss these strategies and directions for future research.

NR303 **Wednesday, May, 10, 12 noon–2:00 p.m.**

MANDATORY HIV TESTING OF INTRAVENOUS DRUG USERS

Mark H. Pollack, M.D., Habit Mang. Inst., Boston; Psychiatry, Mass General Hospital, ACC-715 15 Parkman Street, Boston, MA 02114; Lawrence D. Rosen, B.A., Eileen Coppola, R.N.P.

Summary:

Intravenous drug users (IVDUs), a high risk group for the Acquired Immunodeficiency Syndrome (AIDS), represent a major vector of HIV entry into the general population. Effort to decrease HIV spread in IVDUs include education and increased availability of drug abuse treatment; mandatory testing for exposure to HIV has also been suggested. Consecutive ($n = 183$) IVDU admissions to an outpatient methadone program, annonymously responded to a questionnaire assessing whether mandatory testing on admission would deter their entry into treatment, and about their history of needle sharing (NeS) and unprotected intercourse (UI).

Significantly fewer patients would enter drug treatment if testing were mandatory vs. voluntary (75 percent vs. 97 percent, $p < .001$). Length of addiction, history of needle sharing, sex, age, marital status, children or a history of previous testing were not significantly correlated with willingness to undergo mandatory testing. Men with a history of UI were less likely to enter treatment under mandatory testing ($p < .02$).

No significant recent decrease in risk-taking behavior was reported in this population: Seventy-four percent had a history of NeS, 45 percent in the last year; 56.7 percent stopped NeS in the last year, 51.6 percent started; 71 percent reported a history of UI, 47 percent in the last year; 51.4 percent stopped UI in the last year, 41.4 percent started.

These results have important public health implications: mandatory testing would likely deter entrance into drug abuse treatment. Risk-taking behavior in this population has not been significantly reduced; continued education and innovative approaches are necessary to effect such reduction.

NR304 **Wednesday, May 10, 12 noon–2:00 p.m.**

HIV DEMENTIA IN DRUG USERS: NEUROPSYCHOLOGICAL DATA

Leonard Handelsman, M.D., Psychiatry, Bronx VA Medical Center, 130 W. Kingsbridge Rd 116A, Bronx, NY 10468; Marvin J. Aronson, Ph.D., Gail Maurer, Ph.D., Sanford Herman, M.D., Robert Ness, M.A., Jeffrey Jacobson, M.D.

Summary:

The neuropsychological profile of HIV dementia in gay male cohorts reveals deficits in attention, psychomotor rate visual-spatial performance, and problem solving(2). To characterize the deficit of HIV dementia in drug users, a neuropsychological battery was administered to 30 drug users (11 HIV-; 11 CDC-Stage 2; eight CDC-Stage 4, AIDS) with heroin and/or cocaine dependence but not ETOH dependence (DSM-III-R). Demographic features of the subjects were: age, 37 ± 5 years; education, 12.2 ± 1.2 years; ethnicity: two Caucasian, eight Black, 20 Hispanic. There were no significant differences in neuropsychological performance between the HIV- and HIV $\pm$ Stage 2 subjects (Neuman-Keuls, $P < .05$). Robust differences in neuropsychological test results emerged between the Stage 4 group and the combined HIV- and Stage 2 groups: Mini-mental state exam; Digit Span (WAIS-R); Logical Memory and Visual Reproduction (Wechsler Memory Scale); Trails B, Fingertapping, Category (Halstead-Reitan) (Mann-Whitney U Test, 1-tailed, $p < .05$). Differences could not be explained by age, education, ethnicity, medical debilitation, or substance use history. The results suggest a broad range of neuropsychological deficits in AIDS patients at risk by drug use. Drug user subjects across HIV status performed less well than gay male cohorts. Deficits in attention, visual memory, and abstraction may limit the impact of HIV education to reduce virus transmission.

NR305 **Wednesday, May 10, 12 noon–2:00 p.m.**

HIV DEMENTIA IN DRUG USERS: NEUROLOGICAL EVALUATION

Jill A. Wiener, M.D., Neurology, Bronx VA Medical Center, 130 W. Kingsbridge RD 116A, Bronx, NY 10468; A. James Rowan, M.D., Leonard Handelsman, M.D., Marvin J. Aronson, Ph.D., Gail Maurer, Ph.D., Gladys Velazquez, M.D.

Summary:

A wide range of neurological defecits are attributed to HIV infection. Twenty-four drug users (seven HIV-; nine CDC-Stage 2, eight Stage 4, AIDS) were examined by a neurologist (JW) as part of a multi-modal study. JW was blinded to HIV serostatus. A standard mental status exam (MSE) was used. There were no differences between the HIV- and Stage 2 groups. However, robust differences emerged between the Stage 4 group vs. the combined HIV- and Stage 2 groups for self-reported complaints of cognitive ability (Fisher's exact, $p < .03$), increased severity of abnormalities on MSE (CHi-square, $p < .001$), and on the other domains of the neurological exam (Mann-Whitney U Test, $p < .02$). These findings could not be attributed to differences in age, education, substance use history, medica debility, or behavioral disorders. The external validity of the clinical MSE was demonstrated by the association between MSE findings and performance scores on a wide range of neuropsychological functions: Mini-mental state exam; Digit Span, Vocabulary (WAIS-R), Logical Memory, Visual Reproduction (Wechsler Memory Scale); Trails A and B, Category (Halstead-Reitan) (ANOVA, $df = 2,24$; 1-tailed $p < .05$). These results support the feasibility, sensitivity, and validity of the MSE and neurological exam in the assessment of HIV dementia in patients at risk by drug use.

NR306 **Wednesday, May 10, 12 noon–2:00 p.m.**

CAN MRI ABNORMALITIES PREDICT AIDS DEMENTIA

Miklos Losonczy, M.D., Psychiatry, Bronx VA Medical Center, 130 W. Kingsbridge RD 116A, Bronx, NY 10468; Leonard Handelsman, M.D., In Sook Song, M.D., Sun Park, M.D., Sanford Herman, M.D., Marvin J. Aronson, Ph.D.

Summary:

Aids Dementia Complex (ADC) has been associated with a direct invasion of the brain by human immunodeficiency virus (HIV), resulting in a demyelinating process that is associated with cortical atrophy (GA), ventricular enlargement (VE), and signal abnormalities (SA) on MRI (Post et al, 1988). HIV + asymptomatic homosexuals are reported to show neuropsychological deficits (Grant et al, 1987). In order to examine the predictive value of MRI abnormalities for the development of ADC in a population of veterans with a history of IV drug abuse, we have studied ten men who are HIV + asymptomatic (CDC stage II), and eight men with Stage IV disease and who showed evidence of ADC on neurological exam. These subjects were compared to six men with histories of IV drug abuse who were seronegative for HIV. The subjects were matched for age, severity of drug abuse, and history of alcohol abuse. MRIs were blindly rated by consensus of two neuroradiologists for the presence of CA, VE, and SA. There were no significant differences between these three groups, but CA was definitely present in only 1/6 controls, 6/10 Stage II subjects, and 5/8 Stage IV subjects. Only 1/8 subjects with ADC had a normal MRI. Implications of these data for the predictive role of MRI will be discussed.

NR307 **Wednesday, May 10, 12 noon–2:00 p.m.**

DETECTION OF SPEM ABNORMALITIES IN HIV INFECTED PATIENTS

Robert E. Litman, M.D., NSB, NIMH Bldg 10 RM 4N212, 9000 Rockville Pike, Bethesda, MD 20892; Christine Ollo, Ph.D., Thomas Clem, B.S.E.E., Daniel W. Hommer, M.D., David Rubinow, M.D., David Picker, M.D.

Summary:

We have quantified smooth pursuit eye movements (SPEM) using a high resolution, infra-red oculography system in eight asymptomatic HIV seropositive patients. Compared to 12 normal controls, SPEM gain (eye velocity/target velocity) is significantly decreased (HIV seropositive patients' mean 0.78, SEM = 0.03, control mean 0.87, SEM = 0.03, $p<0.05$). Saccadic frequency (saccades/second of smooth pursuit) is significantly increased among HIV seropositive patients compared to normal controls (HIV mean 1.69 sac/sec, SEM = 0.23, control mean 0.92 sac/sec, SEM = 0.14, $p<0.003$). There were no consistent correlations found between SPEM variables and neuropsychological measures of frontal lobe function, motor function, and attention/concentration in HIV patients. SPEM abnormalities were found in patients with normal neuropsychological test scores, suggesting that SPEM abnormalities in HIV seropositive patients may be an earlier, more sensitive measure of CNS dysfunction than is neuropsychological testing. The high incidence of SPEM abnormalities in otherwise asymptomatic HIV infection may reflect the control of SPEM by multiple different brain sites (parietal, temporal, and frontal lobes). SPEM recording may be a valuable technique for detection of early brain, dysfunction and monitoring treatment in asymptomatic CNS HIV infection.

NR308 **Wednesday, May 10, 12 noon–2:00 p.m.**

DISSOCIATION IN RELATION TO CHILDHOOD ABUSE

James A. Chu, M.D., Psychiatry, Harvard Medical School, McLean Hosp 115 Mill Street, Belmont, MA 02178; Diana L. Dill, Ed.D.

Summary:

Recent reports have emphasized the importance of traumatic etiologies in the development of psychiatric illness among adult female inpatients, as well as overall greater disturbance among patients with abuse histories (e.g. Bryer et al, 1987). This study examined whether dissociative symptoms, in particular, were specific to patients with abuse histories. Ninety-eight (52 percent) out of 188 female patients aged 18-60 consecutively admitted to the adult inpatient programs of a psychiatric teaching hospital agreed to complete the Dissociative Experiences Scale (Bernstein and Putnam, 1986), the Life Experiences Questionnnaire (Bryer et al, 1987), and the SCL-90-R. A prevalence of 51 percent was found for physical abuse before age 16, and 36 percent for sexual abuse before age 16. In addition, a high rate of dissociative symptoms was found, with 23 percent of patients reporting symptoms in excess of the median for patients with PTSD. Patients reporting abuse histories clearly experienced more severe dissociative symptoms than did patients without abuse histories (Mann-Whitney $U = 754$, $p < .001$, for physical abuse; $U = 689$, $p < .01$, for sexual abuse). Results will be discussed in terms of how they may facilitate identifying patients with abuse histories and directing treatment to the underlying etiology of their illness.

NR309 **Wednesday, May 10, 12 noon–2:00 p.m.**

HYPNOTIZABILITY, DISSOCIATION, AND ABSORPTION

David A. Baron, D.O., OCD, NIMH Bldg 10 3N238, 9000 Rockville Pike, Bethesda, MD 20892; Peter J. Schmidt, M.D., Bernard Frankel, M.D., David R. Rubinow, M.D.

Summary:

There is aneodotal evidence that the capacity to experience dissociative phenomena, the capacity to became absorbed by an internal or external stimulus, and hypnotizability may be interrelated and may reflect different aspects of some underlying, more fundamental neuropsychological process. This study examined the relationship between these three traits in 33 normal volunteers, 17 females and 16 males (age range 23-37 years, mean 28 years). Dissociative capacity was assessed by the Dissociative Evaluation Scale (DES), a 28-item self-administered visual analogue questionnaire developed by Carlson and Putnam. Similarly, a selfadministered test derived from Tellegen and Atkinson's personality Inventory, the Absorption Scale (AS), was used to evaluate absorptive capacity. Finally, hypnotizability was determined by an experienced psychiatrist using the Stanford Hypnotic Susceptibility Scale Form C (SHSS-C), a widely used instrument designed to assess the ability of a subject to respond to a yielded series of suggestions. Mean scores and Spearman correlation coefficients were computed. The individual means ($+$ SD) were as follows: SHSS-C 8.17 ± 1.87, DES 19.47 ± 15.31, AS 49.46 ± 5.23. Elevated mean scores on the DES may reflect a sampling bias selecting for normals who wished to participate in a study of hypnosis. DES and AS scores were significantly correlated with each other ($r = .61$, $p < .01$) but were not significantly correlated with SHSS-C scores. Although the ability to predict hypnotizability with a self-administered psychometric instument would be valuable, the reported tendency to dissociate or to become absorbed do not successfully predict hypnotizability.

NR310 **Wednesday, May 10, 12 noon–2:00 p.m.**

RESULTS OF OUTREACH TO HOMELESS MENTALLY ILL VETERANS

Robert A. Rosenheck, M.D., NEPEC 182, West Haven VAMC, West Spring Street, West Haven, CT 06516; Peggy Gallup, M.P.H., Catherine Leda, M.P.H., Dennis Thompson, Paul Errera, M.D.

Summary:

Introduction/Methods: Outreach, followed by active case management, has emerged as a major, although largely unevaluated, approach to providing mental health care to the homeless mentally ill. As part of a comprehensive longitudinal evaluation of a national Veterans Administration outreach program for homeless chronically mentally ill veterans, clinicians at nine of 43 program sites completed a 97-item clinical process summary, covering the first three months of clinical work with 529 homeless veterans.

Results: After three months, 32.5 percent of these homeless veterans were still involved in the program although 20.0 percent had not been seen at all after the first outreach contact. Case management activities most frequently involved making referrals (85.6 percent), developing treatment plans (76.2 percent) and monitoring use of services (51.8 percent). Substantial percentages of these veterans were engaged in rehabilitation (36.2 percent) or in a psychotherapeutic relationship (25.4 percent). Of those who terminated, 40.5 percent had been engaged in the program; 34.0 percent were not interested in the services available, and 20.2 percent terminated because of their psychopathology or low tolerance of constraints required for participation in treatment. There was some variation in outcome by diagnosis and length of time homeless.

Conclusion: Patient specific outcome data from multiple sites indicate that the homeless mentally ill can be meaningfully engaged in treatment, although a significant percentage of them make minimal use of service offered, and only a third stay involved for more than three months.

NR311 **Wednesday, May 10, 12 noon–2:00 p.m.**

ENGAGEMENT OF HOMELESS PSYCHIATRICALLY ILL VETERANS IN VA DOMICILARY TREATMENT

Robert A. Rosenheck, M.D., NEPEC 182, West Haven VAMC, West Spring Street, West Haven, CT 06516; Catherine Leda, M.P.H., Sharon Medak, Dennis Thompson, Richard Olson, M.H.A.

Summary:

Introduction: The Veterans Administration's Domiciliary Care for Homeless Veterans (DCHV) program, was established in 1987, in 20 U.S. cities as a model program to engage homeless veterans, and veterans at risk of homelessness, in residential treatment and rehabilitation.

Methods: Comprehensive, standardized data on social adjustment and health care status were collected at admission and at the at the time of discharge of all veterans treated in this program during the first year. This report presents preliminary outcome data on the first 937 discharges.

Results: On examination, 96.3 percent of those admitted received a DSM-III psychiatric or substance abuse diagnosis; 87.5 percent were homeless and 12.5 percent were at risk for homelessness. At the time of discharge ALOS = 74.6 days) only 32.9 percent had successfully completed the program; 32.1 percent left prematurely; and 24.9 percent were asked to leave because of noncompliance with program requirements (most often for substance abuse). Among the 69.7 percent of those whose post-discharge residential plans were known, 53.2 percent were living in an apartment, room, or house, 35.9 percent were living in a supervised environment (predominantly health care facilities or transitional residences); 8.1 percent had no residence; and 2.8 percent had some other arrangements. Engagement and outcome also vary depending on diagnosis and length of time homeless.

Conclusion: These are among the first empirical outcome data on residential treatment of the homeless. While premature termination is frequent, there is evidence of improvement in residential status.

NR312 **Wednesday, May 10, 12 noon–2:00 p.m.**

ADMITTING A RELATIVE DURING HOSPITALIZATION

Aris D. Liakos, M.D., Psych Univ of Alberta, 1E7.31 Walter C Mackenzie, Health Science Center, Edmonton, Alberta, Canada T6G 2B7

Summary:

For a period of three years we have monitored the results of admissions to an open general hospital psychiatric unit at the University of Ioannina, Greece, where we accommodate a relative to stay in hospital with the patient for the first crucial period of admission. This 20-bed inpatient and 10 day-patient unit is operated under the principles of a therapeutic community, and serves a population of 350,000. It is linked to a 24-hour emergency psychiatric service program, an outpatient clinic and a general teaching hospital. Ninety-two percent of all patients needing admissions are treated in the unit as informal patients. Thirty percent of all admissions are accompanied by the admission of a relative who also stays in hospital during the initial hospitalization period.

This latter practice is important as it reduces compulsory admissions and considerably overcomes the "stigma" of hospitalization since it occurs under the terms and conditions identical to other medical specialties.

It helps the *staff* to feel more at ease with the potentially suicidal patients and facilitates identification of abnormal patient-family interactions. It helps the *relatives* who learn from the staff how to deal with morbid patients' behavior and lessons their fantasies related to psychiatric hospitalization. Finally, it helps the *patients* to accept inpatient treatment and reduces violent behavior to nearly zero.

NR313 **Wednesday, May 10, 12 noon–2:00 p.m.**

RACE AND ETHNICITY IN BIOLOGICAL RESEARCH

William B. Lawson, M.D., Psychiatry, Vanderbilt Med Center, A2215 MCN, Nashville, TN 37232; Mi Talluri, M.D., Charles F. Morgan, B.S.

Summary:

Recent findings of an underrepresentation of Blacks in drug trials led us to review the literature for participation of minorities in research in biological psychiatry. A review of the three most frequently cited psychiatric journals of the past two years showed that of over 520 articles, only 40 (eight percent) described the race or ethnicity of the subjects or patients. Of those, four involved Blacks, six involved Hispanics, and 11 involved Asians. These findings are especially disturbing given recent studies demonstrating racial and ethnic differences in a variety of biological markers, and plasma levels of many psychotropic medications. The policy by some journals to require reporting of the ethnicity of the patient populations appears warranted.

NR314 **Wednesday, May 10, 12 noon–2:00 p.m.**

PSYCHIATRIC MORBIDITY IN URBAN AND RURAL NEW ZEALAND WOMEN

Sarah E. Romans-Clarkson, M.B., Psych Medicine, University of Otago, Sixth Floor Dunedin Hospital, Dunedin, New Zealand; Valerie A. Walton, M.A., G. Peter Herbison, M.Sc., Paul E. Mullen, M.B.

Summary:

A random community survey into psychiatric disorder in urban and rural New Zealand women is described. The measures for psychiatric disorder were the GHQ-28 (n = 1516) and the short PSE (n = 314). The urban sample was drawn from an integrated, well serviced university city with a population of 105,000. A large number of socio-demographic variables were studied.

Certain demographic differences were found between the two samples; urban women were more often at age extremes, not married, better educated, and had better household and child care facilities, had better access to neighbors, shops, and family doctor, but drove a car less often.

There were no overall urban-rural differences in psychiatric morbidity on either measure. Multiple regression found the same three factors accounted for most of the explained variance in both the urban and the rural total PSE scores; these were the quality of social networks, difficulties with alcohol, and the past experience of childhood sexual abuse. Low socio-economic status, poor physical health, and adult experiences of sexual and physical abuse were correlated with increased psychiatric morbidity for both groups. These results suggest that urban-rural residence in and of itself, does not influence the prevalence of anxiety and depressive syndromes.

NR315 **Thursday, May 11, 9 a.m.–10:30 a.m.**

RELATIONSHIP BETWEEN NEUROPSYCHOLOGICAL AND IMMUNE VARIABLES IN HIV POSITIVE ASYMPTOMATIC MEN

James W. Dilley, M.D., Psychiatry, Univ of Cal, San Fran, Box 0884 San Fran Gen Hospital, San Francisco, CA 94143; Alicia Boccellari, Ph.D., Ann Davis, Andrew Moss, Ph.D., Peter Bacchetti, Ph.D., Myla Young, M.D.

Educational Objectives:

Participants will be able to: 1. List four predictors of progression to AIDS in a cohort of HIV seropositive men; and 2. Discuss the relevant literature on neuropsychological impairment in asymptomatic seropositive men.

Summary:

Objective: To describe the interrelationship between neuropsychological (NP) function, immune status, and neuropsychiatric measures in asymptomatic HIV positive gay men.

Methods: Fifty-six asymptomatic gay men (HIV + = 33, HIV – = 23) were given a one time battery of NP tests and psychiatric rating scales. Measures of immune function were also obtained. Group differences between HIV + and HIV – groups were determined by use of multiple T-tests. (Bonferroni correction was applied.) Additionally, the HIV positive group was divided into those with CD_4 cells $\leq$ 400 (N = 14) and $>$ 400 (N = 19). Correlations were calculated between the immune and NP measures.

Results: 1. No significant differences were found between the positive and negative groups on age, education, and occupational levels. 2. No statistically significant differences were found between the HIV + and HIV – groups on any of the NP measures. 3. In the HIV + group, no statistically significant differences were found between those with $CD_4 \leq 400$ and those with $CD_4 \leq 400$ on the NP measures. Additionally, no differences were found on the NP measures between the CD_4 400 group and the HIV negative group.

Conclusions: These results help to confirm a lack of documented neurophychological impairment in otherwise asymptomatic HIV + men. This finding held up even when comparing those HIV + men with CD_4 count of $\leq$ 400 with the seronegative group.

This work has been supported in part by grant # DA04873 from the National Institute on Drug Abuse.

References:

1. Moss AR, Baccetti P, Osmond D, et al Seropositivity for HIV and athe Development of AIDS or AIDS related condition: three year follow-up of the SF Gen Hosp Cohort. *Brit Med Jour*; 296:745-750. 1988

2. Grant I, Atkinson JH, Hesselink JR, et al. Evidence for early CNS involvement in the AIDS & other HIV infections: studies with neuropsychologic testing and magnetic resonance imaging. *Ann Intern Med*; 103:828-36. 1987

NR316 **Wednesday, May 10, 12 noon–2:00 p.m.**

EARLY DETECTION OF HIV EFFECTS ON BRAIN FUNCTION

Andrew Leuchter, M.D., Psychiatry, UCLA, 760 Westwood Plaza, Los Angeles, CA 90024; Thomas F. Newton, M.D., Wilfred Vangorp, Ph.D., Eric Miller, Ph.D., Herbert Weiner, M.D., David Freeman, Ph.D., Gwen Eran, Ph.D., Paul Satz, Ph.D.

Educational Objectives:

To discuss CEEG as a possible tool for early detection of HIV effects on brain function.

Summary:

Computer-analyzed electroencephalography (CEEG) was performed in subjects with AIDS or symptomatic HIV infection (n = 24), asymptomatic HIV infection (n = 6), and normal age-matched controls (n = 13). The group of HIV-infected subjects were cognitively intact, while all subjects with AIDS had cognitive impairment on neuropsychological testing. Using discriminant analysis, CEEG distinguished between HIV-infected subjects and normal controls, and between symptomatic and asymptomatic HIV-infected subjects with greater than 80 percent accuracy. Asymptomatic HIV subjects were distinguished from controls primarily by decreased coherence in high-frequency bands in antero-posterior electrode pairings; there were no significant differences between these groups in spectral power. AIDS subjects also were distinguished from controls by decreased high-frequency coherence, and from both control and asymptomatic HIV groups by decreased spectral power ratios. Detailed neuropsychologic data were available for 19 HIV-infected subjects, and repeated tests were performed on a subset of subjects. CEEG data were highly correlated with results of neuropsychologic testing, and on repeated examination, predicted changes in neuropsychological measures. These preliminary results suggest that CEEG spectra and coherence measures may be useful in the early detection of HIV effects on brain function.

References:

1. Leuchter, A.F., Spar, J.E., Walter, D.O., & Weiner, H. EEG spectra and coherence in the diagnosis of Alzheimer's type and multi-infarct dementia. *Archives of General Psychiatry,* 44: 993-998. 1987

2. Leuchter, A.F., Walter, Donald O. Diagnosis and Assessment of Dementia Using Functional Brain Imaging. *International Psychogeriatrics,* Vol. 1, No. 1, 1989 (in press).

NR317 **Thursday, May 11, 9:00 a.m.-10:30 a.m.**

^{123}IodoQNB SPECT IN ALZEHEIMER'S AND PICK'S DISEASES

Daniel R. Weinberger, M.D., Neuroscience, NIMH Neurosci Ctr St Eliz, 2700 Martin Luther King Ave SE, Washington DC 20032: Raymond E. Gibson, Ph.D., Richard Coppola, D. Sc., Douglass W. Jones, Ph.D., Karen F. Berman, M.D., Allen R. Braun, M.D., Barry R. Zeeberg, Ph.D., Trey Sunderland, Ph.D., Richard C. Reba, M.D.

Educational Objectives:

To inform about a new methodology for studying *in vivo* brain.

Summary:

^{123}IodoQNB is a high affinity mixed muscarinic receptor ligand that can be used with SPECT to image the distribution of muscarinic receptor sites in the human brain. To study the distribution of this receptor in patients with primary degenerative dementia (PDD), ten patients with Alzheimer's Disease (AD), two patients with a clinical diagnosis of Pick's Disease (PK), and 11 normal controls received approximately 4mCi ^{123}IodoQNB and were scanned with a multicrystal head SPECT system approximately 20 hours after injection. High resolution images were achieved with virtually no counts from the cerebellum, suggesting that nospecific binding was negligible. Ten of the patients had obvious discrete areas of reduced ligand uptake. An ROI analysis normalized to visual cortex revealed that both PK patients had left perfrontal and anterior temporal uptake below the control range and that the pariental cortex uptake was significantly lower in the AD patients compared with controls (MANOVA $p<.001$) and in a discriminant analysis correctly classified all but two subjects, while also discriminating AD from PK patients. These results indicate the muscarinic receptor imaging with SPECT is practicable and that in contrast to postmortem studies, muscarinic boning *in vivo* may be consistently abnormal in patients with PDD.

References:

(1) Eckelman WC, et al: External imaging of cerebral muscarinic acetylcholine receptors. *Science* 223:291-292, 1984.

NR318 **Thursday, May 11, 9:00 a.m.–10:30 p.m.**

DEMENTIA AND TANGLE FORMATION IN ALZHEIMER'S DISEASE

Linda M. Bierer, M.D., Psychiatry, Bronx VA Medical Center, 130 West Kingsbridge RD 116A, Bronx, NY 10468; Daniel P. Perl, M.D., Vahram Haroutunian, Ph.D., Philip Kanof, M.D., Daniel Lobel, M.A., Kenneth L. Davis, M.D.

Educational Objectives:

To review clinico-pathologic correlates to dementia in AD; to review the potential contribution of age at death to these findings; to present new data utilizing the Clinical Dementia Scale (Modified) to assess end-stage AD.

Summary:

Previous studies have indicated an inverse relation between neurofibrillary tangle (NFT) formation and age at death among AD subjects, but have failed to show an association between cortical tangles and preterminal dementia severity analogous to that demonstrated for plaque counts. We have had the opportunity to study 40 cases of definite AD defined by a progressive dementing course and CERAD neuropathologic criteria. Plaques and tangles were rated blindly according to CERAD specifications and the Modified Clinical Dementia Rating scale (CDR-M) was scored on the basis of chart review. Dementia ratings were significantly correlated with the extent of neurofibrillary tangle formation in the mid-frontal ($Sr = .492$, $p = .005$) and superior temporal cortices ($Sr = .537$, $p = .001$), and with plaque scores in the hippocampus ($Sr = .537$, $p = .001$) and superior temporal cortex ($Sr = .323$, $p = .041$). Although inverse correlations between regional tangle scores and age at death were apparent in this series, the relations of NFT scores to dementia ratings remained significant when age at death and estimated duration of dementia were taken into account. Regional choline acetyltransferase measurements for a sub-sample of 19 subjects revealed significant positive correlations with age at death ($r = .505$ to $.759$) and negative correlations with CDR-M ratings ($r = .657$ to $.852$) in nine of ten cortical areas studied. These results extend the range of clinico-pathologic correlates in AD and suggest that the CDR-M may usefully be applied to chart review material

References:

1. Terry, RD, Hansen, LA, DeTeresa, R, et al.: Senile dementia of hte Alzheimer type without neocortical neurofibrillary tangles. *J. Neuropathology and Exp. Neurol.,* 46:262-268, 1987.

2. Heyman, A, Wilkinson, WE, Hurwitz, BJ, et al.: Early-onset Alzheimer's disease: Clinical predictors of institutionalization and death. *Neurology,* 37:980-984, 1987.

NR319 **Thursday, May11, 12 noon–2:00 p.m.**

AN INHIBITOR OF THE CHOLINERGIC RECEPTOR IN ALZHEIMER'S

Gary D. Tollefson, M.D., Psychiatry, St. Paul Ramsey, 640 Jackson Street, St. Paul MN 55101; Marlyse Wiebanga, B.S., William H. Frey, II, Ph.D.

Educational Objectives:

Those attending will be encourage to better understand (1) The evidence interfacing Alzheimer's dementia (AD) with the muscarinic cholinergic nervous system and. (2) Preliminary evidence for a naturally occurring human receptor inhibitor that (3) appears to mainifest greater activity in AD (than matched controls) resulting in (4) an alteration of the receptor density (Bmax).

Summary:

Alzheimer's desease (AD) is a progressive dementing disorder and a major public health concern. Memory loss, cardinal to the AD symptom complex, is mediated by acetylcholine (ACh). Pharmacologic manipulation of brain ACh induces amnestic deficits similar to AD. While the etiology of AD is unknown, one consistent finding has been the depletion of choline acetyltransferase and related cell death within the nucleus basalis of Meynert. Recent investigation demonstrate 1) presynpatic cortical muscarinic cholinoceptors (M2) are down-regulated ($\leq$60 percent and 2) via perfusion imagery (^{123}I-QNB), a decrease in posterior temporal and parietal ACh binding occurs in AD. Our study hypothesis was premised on an endogenous factor that interacts at the muscarinic ACh receptor and mediates cognitve loss seen in AD.

We now report evidence of an endogenous inhibitor of the muscarinic ACh receptor, found withing the 140,000xg soluble fraction, from post-mortem human frontal cortex. Premilinary studies of nine AD subjects and matched non-demented controls revealed a greater activity ($p = 0.035$) of this inhibitor in AD brain, as seen by a decrease in ^{3}H-QNB binding. The inbition of the muscarinic ACh receptor is concentration dependent, and diminished, but not abolished in the presence of EDTA or following heat treatment. Preliminary gel filtration studies have indicated the inhibitor has a molecular weight less than 10,000 daltons.

Reference:

(1) Perry EK, Perry RH, Smith CJ, et al: Nicotinic Receptor Abnormalities in Alzheimer's and Parkinson's Disease. *Journal of Neurology, Neurosurgery and Psychiatry*, 50:806-809, 1987.

(2) Holman BL, Givson RE, Hill TC, et al: Muscarinic Acetylcholine Receptors in Alzheimer's Disease. *JAMA,* Vol. 254, 3063-3066, 1985.

NR320 **Thursday, May 11, 9:00 a.m.–10:30 p.m.**

TOURETTE'S SYNDROME IS NOT LINKED TO D2 RECEPTOR

Joel Gelernter, M.D., Psychiatry, Yale Medical School, 1309 SHM 333 Cedar Street, New Have, CT 06511; Andrew J. Pakstis, Ph.D., Phillip Chappell, M.D., R. Kurlan, M.D., D.K. Grandy, Ph.D., J. Bunzow, Ph.D., A.E. Retief, Ph.D., M. Litt, Ph.D., O. Civelli, Ph.D., K.K. Kidd, Ph.D.

Educational Objectives:

To extend what is known of pathophysiology of Tourette's syndrome using the method of a linkage study with candidate genes. An additional objective is to demonstrate the benefits of adopting a multilocus approach to candidate gene investigations.

Summary:

Tourette's syndrome (TS) may have a dopaminergic mechanism such as hypersensitivity of dopamine receptors. The recent cloning of a D_2 receptor (Bunzow J et al. Nature 336:783-787, 1988) made it possible to test involvement of a D_2 receptor gene in this disorder using restriction fragment length polymorphisms (RFLPs). We established genetic linkage between the D_2 receptor locus (using probe hD_2G1), and another locus on chromosome 11, D11S29 (using probe L7). We have not yet observed any obligate recombinants between these loci. Both of these probes recognize Taq I polymorphisms. We studied these markers in a large Mennonite TS kindred (Kurlan et al, Neurology 36:772-776, 1986). We used two disease models: only individuals with the full TS syndrome considered as affected or also including as affected individuals with only chronic multiple tics (CMT). The most efficient way to test for linkage is with a multipoint strategy; therefore, the LINKMAP program of the LINKAGE package (Lathrop GM et al. Am J Human Genet 37:482-498, 1985) was used for the multipoint linkage analyses.

With the first model (TS only), complete ($0 = 0.0$) linkage of TS with these markers was ruled out (LOD score -11). The area of exclusion (LOD score between -2 and -11) extends more than 15 centimorgans from D_2 and D11S29 in each direction. Using the broader illness definition (TS or CMT), which is supported by segregation analysis (Pauls DL and Leckman JF, NEJM 315:993-997, 1986), the region of exclusion from linkage is even more extensive.

This result provides strong evidence against linkage of the D_2 receptor locus identified by hD_2GI with Tourette's syndrome. Use of multipoint analysis allowed exclusion of a broader genomic area amounting to about one percent of the human genome. This exclusion narrows the range of acceptable theories for TS pathophysiology.

References:

1. Bunzow J et al., Nature 336:783-787
2. Pauls and Leckman, *N Engl J Medicine* 315:993 997

NR321 **Thursday, May11, 12 noon–2:00 p.m.**

FOLLOW-UP OF EXTREME TEMPERAMENT FROM AGE 7 TO 16

Michel Maziade, M.D., Laval Robert-Giffard, Centre De Recherche, 2601 De La Canardiere, Beauport QC, Canada G1 J 2G3; Jacques Thivierge, M.D., Robert Cote, Ph.D., Burno Laplante, M.D.

Educational Objectives:

Review of cross-sectional and longitudinal epidemiological studies of the risk associated to adverse temperament in children. Report on a nine year longitudinal study of two extreme subgroups of different temperament selected from a large random sample of the general population of Quebec.

Summary:

Two extreme subgroups of children, (N = 38) one of easy and one of difficult temperament, were selected from a large random sample (N = 900) of the general population at age seven. The two groups were matched for sex and SES. Temperament was defined as extreme scores on a composite derived from a first factor (principal component analysis) that was closely similar to the NYLS "easy-difficult" cluster. Children were reassessed double-blind at the age of 12 (Maziade et al, 1985)[2] and recently at the age of 16 in terms of their clinical status (DISC-P) interview reviewed by two independent psychiatrists), family functioning (McMaster model semi-structed interview), IQ, and acedemic performance. New findings are that extreme temperament at seven predicts psychiatric status in adolescence ($X^2 = 4.82$, $df = 1$, $p = .03$) only when family functioning is also taken into account. A logistic regression analysis was applied and concluded to a statistically significant second order interaction between temperament and family behavior control (discipline). Almost all the extremely difficult children living in families with a dysfunctional discipline displayed clinical disorders in adolescence. Conversely, extreme temperament had little effect on longitudinal academic performance. Also, this nine-year follow-up provides evidence that the continuity of the temperament phenomenology over the years can be distinguishable from that of clinical symptomatology.

Reference:

(1) Maziade M. et al: Significance of extreme temperament in infancy for clinical status in preschool yearc: I. Value of extreme temperament at 4-8 months or predicting diagnosis at 4.7 years. Br J Psychiatry, in press. (2) Maziade M. et al: Value of difficult temperament among 7-year-olds in the general population of predicting pyschiatric diagnosis at age 12. Am J Pyschiatry 142, 943-946, 1985.

NR322 **Thursday, May11, 12 noon–2:00 p.m.**

YOUNG ADULT MENTAL STATUS OF HYPERACTIVE BOYS

Salvatore Mannuzza, Ph.D., Hillside Research, Long Island Jewish, 270-05 76th Ave. Staff House, New Hyde Park NY 11042; Rachel G. Klein, Ph.D., Noreen Bonagura, M.S.W., Patricia Malloy, B.S.W., Tina L. Giampino, B.A.,

Educational Objectives:

At the end of the program, the learner should have a better understanding of the risks that hyperactive children have for the development of mental disorders in young adulthood. This study represents a replication of a previous study done on a independent sample.

Summary:

We previously reported a prospective follow-up study of 101 young adult males (ages 16-23 years) who had been diagnosed as hyperactive in childhood (ages six to 12 years), compared with 100 normal controls (Gittelman, Mannuzza, Shenker, & Bonagura, 1985). Compared to controls probands had significantly higher rates of attention deficit disorder (ADD, 40 percent vs. 3 percent), antisocial disorder (27 percent vs. 8 percent), drug use disorder (16 percent vs. 3 percent), and any diagnosis (48 percent vs. 20 percent) at follow-up. The present study was an attempt to replicate these findings on an independent sample of 94 hyperactive boys who were seen at the same child clinic, chosen by the same selection criteria, and administered the same interview at follow-up (ages 16-25 years), compared with 86 normal controls. Assessments were made by psychologists who were blind to group membership. Information was obtained for 90 percent of the original cohort. Replicating previous results, we found that significantly more probands than controls were given ongoing diagnoses of ADD (43 percent vs. 3 percent), antisocial disorder (32 percent vs. 9 percent), and any diagnosis (56 percent vs. 19 percent). There was also a tendency for more probands than controls to have a drug use disorder at follow-up (10 percent vs. 3 percent $p = .10$).

Reference:

(1) Gittelman, R., Mannuzza, S., Shenker, R., & Bonagura, N. Hyperactive boys almost grown up: 1. Psychiatric status. *Arch. Gen. Psychiatry,* 42, 937-947, 1985.

(2) Weiss, G., & Hechtman, L.T. *Hyperactive Children Grown Up.* New York: Guilford Press, 1986.

NR323 **Thursday, May 11, 9:00 a.m.–10:30 a.m.**

HOMELESS ADOLESCENTS: LIFE STYLE AND SEXUAL BEHAVIOR

Milton Greenblatt, M.D., Psychiatry, Olive View Medical Center, 14445 Olive View Drive, Sylmar CA 91342; Marjorie J. Robertson, Ph.D.

Educational Objectives:

Present data on life style, survival strategies, and risky sex behaviors of homeless adolescents in Hollywood, Los Angeles.

Summary:

Face-to-face field interviews with 93 hcmeless adolescents, ages 13 to 17, in Hollywood, Los Angeles, reflect a population in severe crisis, but in large measure hidden from public view. They are aliens in their own land; work is restricted by child labor laws; they shun or often are excluded from schools, social services, medical care, and even shelters; and generally fear authority.

Many of these youths have left home "of their cwn choice" after life became intolerable. Most have been cast out. Their life styles are characterized by a "feral-urban" type of existence. Sexual behaviors of this population are particularly distressing, strongly supporting a high risk of ALDS or other sexually transmitted diseases. Prostitution is common, particularly as a survival mode; and unwanted pregnancies are a risk.

Yet, these street children are sophisticated about risky sex behaviors; and nearly all say they would accept HIV testing.

References:

1. *Runaways—Illegal Aliens in Their Own Land,* by Dorothy Miller, Donald Miller, Fred Hoffman, Robert Duggan. Praeger Publishers, 1980.

2. *Homeless Adolescents.* Studies of 93 Adolescents in Hollywood, Los Angeles. By Olive View Medical Center Adolescent Research Group. Submitted for publication.

NR324 **Thursday, May 11, 9:00 a.m.–10:30 a.m.**

COPING OF JAPANESE CHILDREN IN THE USA: ONE-YEAR LATER

Hisako M. Koizumi, M.D., Psychiatry, Ohio State University, 473 West 12th Avenue, Columbus, OH 43210; Jennifer Farkas, Ph.D., Tetsunori Koizumi, Ph.D.

Educational Objectives:

(1) To become familiar with the process, stress, and coping of cross-cultural adjustment of children and mothers in the globalization of the world. (2) To become familiar with factors facilitating the adjustment.

Summary:

Thirty Japanese children and mothers are followed through interviews, rating scales, and school reports prospectively for one year as the initial phase of a five-year study of their cross-cultural adjustment in America. Over a one-year period, children (trend) and mothers ($p<0.05$) steadily increased positive feelings about staying in America. Making friends, and mastering English, are cited positively by children, and comfortable living and gaining new perspectives by mothers. Learning English is cited by both as the most difficult experience followed by mothers' worries about children's education upon their eventual return to Japan. Child Depression Inventory (CDI) scores decreased (not significant), as did mother's Zung Depression Inventory scores ($p<0.05$) and mothers' UCLA Loneliness Scale scores (trend). Children's steady adjustment is also reflected by their preference of American schools to Japanese Saturday school (67 percent) and their responses to three wish questions which reflected a growing comfort with the English language. There is a trend of older children mastering English faster than the younger ones. Children who scored initially above normal range in CDI (37 percent) continue to score high at one-year ($r = 0.62$). Personality structure and prior adjustment are emerging as important factors in predicting cross-cultural adjustment and continuous follow-up is needed.

References:

(1) Garmezy, N., and Rutter M. (Editors): *Stress, coping and development in children.* New York, McGraw Hill, 1983.

(2) Hsu, J., Tseng, W-S, et al.: Family Interaction Patterns Among Japanese Americans and Caucasian Families in Hawaii. *Am. J. Psychiatry,* 142:5, 577-580. 1985.

NR325 **Thursday, May 11 9:00 a.m.-10:30 a.m.**

SEROTONIN MEDIATED RESPONSES IN AUTISTIC DISORDER

P. Anne McBride, M.D., Psychiatry, Cornell Medical College, 525 East 68th Street, New York NY 10021; George M. Anderson, Ph.D., Margaret E. Hertzig, M.D., John A. Sweeney, Ph.D., Donald J. Cohen, M.D., J. John Mann, M.D.

Educational Objectives:

To present results from an ongoing research project.

Summary:

Introduction: Altered serotonergic function has been postulated in autism. We have previously reported evidence of altered serotonin-mediated responses in a small group of autistic young adults, which included: blunted prolactin release following challenge with the indirect serotonin agonist fenfluramine; and decrease serotonin-amplified platelet aggregation, a response mediated by the platelet 5;HT2 receptor complex. We now report further results of our ongoing study, which support and extend the above findings. *Results:* While we continue to observe reduced fenfluramine-induce prolactin release in an expanded group of autistic subjects, the cortisol response to fenfluramine is not significantly different in autistic subjects versus normal controls. Autistic subjects exhibit decreased platelet 5-HT2 receptor number as well as blunted serontonin-amplified platelet aggregation responses. Among autistic subjects, fenfluramin-induces prolactin release is positively correlated with the serontonin-amplified platelet aggregation response and negatively correlated with whole blood serotonin content. *Conclusions:* The finding of decreased fenfluramine-induced prolactin release is consistent with the hypothesis that the responsivitiy of CNS serotonergic pathways is reduced in autistic young adults. The apparent dissociation of prolactin and cortisol responses to fenfluramine challenge may reflect the fact that serotonin appears to promote release of the two hormones by different mechanisms or effects of nonserotonergic influences at the level of the hormone secreting cell. Correlations between central and peripheral measures suggest system alteration in serotonergic function in autism, which may include changes in the responsivity of 5-HT2 receptor populations.

References:

(1) McBride, P.A., Mann, J.J., Plley, J.J., Wiley, A.J., Sweeney,J.A.: Assessment of Binding Indices and Physiological Responsiveness of the 5-TH2 Receptor on Human Platelets. *Life Sce,*40: 1799-1809, 1987.

(2) McBride, P.A., Anderson, G.M., Herzig, M.E., Sweeney, J.A., Kream, J., Mann, J.J.: Serotonergic Responsivity in Male Young Adults with Autistic Disorer: Results of a Pilot Study, *Arch Gen Psychiatry,* in press.

NR326 **Thursday, May 11, 9:00 a.m.–10:30 a.m.**

IMIPRAMINE AND CHILDHOOD MDD: LVELS AND RESPONSE

Sheldon H. Preskorn, M.D., Psych. Research Inst., 929 North St Francis, Wichita KS 67214; Elizabeth Weller, M.D., Carroll W. Hughes, Ph.D., Ronald Weller, M.D., Mary A Fristad, M.A.

Educational Objectives:

The objective is to demonstrate that imipramine is superior to pacebo for treating childhood MDD at plasma levels of 125-250 ng/ml.

Summary:

This paper reports on efficacy data from two sequential studies of imipramine (IMI) for the treatment of childhood major depressive disorder (MDD): a fixed dose and a placebo controlled, double-blind study. All subjects were hospitalized for MDD and were six to 12 years old. In the first study ($n = 35$), all received 75 mg of IMI with the treatment team blind to the plasma drug levels achieved. In the second study ($n = 30$), the laboratory was able to adjust the dose without the treatment team's knowledge so the IMI-treated patients achieved a combined plasma level of IMI + DMI of 125-250 ng/ml. The acute treatment phase of both studies lasted six weeks preceeded by a drug-free observation period. In the first study, antidepressant response was correlated with plasma levels of IMI and DMI separetely and combined ($r = 0.42, p < 0.02; r = 0.55$, $p < 0.001$; and $r = 0.68$, $p < 00.01$ respectively). Optimum response occured within a combined range of 125-250 ng/ml. In the second study, IMI was superior to placebo ($p < 0.05$). Without breaking the blind, the treatment. In conclusion, IMI is superior to placebo for treating their prepubertal MDD at combined plasma levels of 125-250 ng/ml while levels above this range have been associated with undesired cardiac and central nervous system (CNS) effects.

References:

(1) Huges C, Perskorn S, Weller E, Weller R, Hassanein R: Imipramine vs placebo studies of childhood depression: Baseline predictors of response to treatment and factor analysis of presenting symptoms. *Psychopharm Bull* 24:275-279, 1988.

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NR327 **Thursday, May 11, 12 noon–2:00 p.m.**

PSYCHOLOGICAL PREDICTORS OF RESPONSE TO CO_2

Ronald M. Rapee, Ph.D., CSAD, 1535 Western Avenue, Albany, NY 12203; Michelle Q. Craske, Ph.D., David H. Barlow, Ph.D.

Summary:

Eighty-four subjects diagnosed as suffering from a DSM-III-R anxiety disorder underwent 15-minute inhalations of 5.5 percent CO_2 in air. There were 51 subjects with panic disorder and 33 with another anxiety disorder. Panic attacks were experienced by 34 subjects (40.5 percent). All subjects completed a number of questionnaires immediately prior to beginning the inhalations to examine potential predictors of their response. Subjects who experienced a panic attack differed from those who did not on state anxiety, subjective units of discomfort, predicted ability to cope with a panic attack, and predicted ability to tolerate anxiety. Level of experienced fear was significantly correlated with (in descending order) state anxiety, subject units of discomfort, pre-pCO_2 level, predicted ability to cope with a panic attack, predicted likelihood of experiencing relaxation, and predicted probability of experiencing a panic attack. Finally, state anxiety was significantly correlated with (in descending order) predicted ability to cope, subjective units of discomfort, probability of experiencing a panic attack, probability of experiencing relaxation, anxiety sensitivity, and pre-pCO_2 levels. The results suggest that the main predictor of response to CO_2 is state anxiety and that this state anxiety may be contributed to by subjects' predictions that they will experience a panic attack and how well they can cope with a panic attack should it occur.

NR328 **Thursday, May 11, 12 noon–2:00 p.m.**

ANXIETY DISORDERS AND ADHD, RS

Walid O. Shekim, M.D., Psychiatry, UCLA NPI, 760 Westwood Plaza RM C8-871, Los Angeles CA 90024; Sacha Bystrisky, M.D., Esther B. Hess, M.A.

Summary:

A substantial number of adults with attention deficit -hyperactivity disorder, residual state, meet DSM-III-R criteria for generalized anxiety disorder. We compared two groups of patients, one group who met criteria a for ADHD, RS and another group who met criteria for anxiety disorders. Both groups were matched for age, sex, socioeconomic, and marital status. Diagnoses were made using structured interviews, SADS-L, and SCID, and packet including SCL-90R were given to both groups. Up to the time of this submission, a total number of 17 patients with anxiety disorders are included. Seven met criteria for ADHD, RS, and one met criteria for undifferentiated ADHD. When we excluded those with major affective disorder and borderline personality disorder (two diagnoses ordinarily excluded from ADHD, RS groups) only three met ADHD criteria. The ADHD, RS, group differed from the anxiety group in the number of diagnoses present (3.9 ± 1.2 vs 1.9 ± 0.8, $p<0.0002$). On the SCL-90R factor scores the ADHD, RS, group tended to be more stressed (1.3 ± 1.6 vs 0.3 ± 0.3, $p<0.07$). However, the anxiety group scored higher on somatization (1.4 ± 0.9 vs 0.8 ± 0.6, p 0.06); paranoid ideation (1.5 ± 0.8 vs 0.9 ± 0.7, $p<0.04$), psychoticism factor (1.3 ± 0.9 vs 0.7 ± 0.7, $p<0.07$. As expected, the anxiety group made a total of 17 different anxiety diagnoses while the ADHD, RS made only eight diagnoses. The implications of these findings from a larger sample will be presented and discussed in terms of phenomenology and co-morbidity of ADHD, RS.

NR329 **Thursday, May 11, 12 noon-2:00 p.m.**

LONG-TERM EFFICACY OF IMPRAMINE IN PANIC DISORDER

Linda M. Nagy, M.D., Psychiatry, Yale University, 34 Park Street, New Haven CT 06508; John H. Krystal, M.D., Dennis S. Charney, M.D., Kathleen R. Merikangas, M.D., Scott W. Woods, M.D.,

Summary:

Imipramine (IMI) is well known as a effective short-term treatment of Panic Disorder (PD) and Agoraphobia with panic attacks (APA). Less is known abou the long-term outcome of IMI treatment or how long-term outcome compares to patients treated with other anti-panic medications. *METHODS:* Twenty-five of 33 patients (76 percent) with DSM-III diagnosis of APA or PD treated in a placebo-controlled efficacy study of IMI betweeen 8/82 and 2/85 were located and reinterviewed 15 to 52 months (mean 33 ± 7 months) following discharge (DC) from the study. During the initial study of all patients also received behavioral group therapy. Following DC they received available treatment in their communities. Course of illness were evaluated by two research psychiatrists using a semi-structured psychiatric interview and by repeating ratings used during the initial study. *RESULTS:* At follow-up (FU) approximately half (13/25) the patients were able to discontinue medication. Nine continued IMI: six on a lower dose, two on the same does, and one on a higher dose as compared to DC. Mean dose of IMI at DC was 124 ± 33 mh/d and at FU was 80 ± 47 mg/d. The remaining three patients were taking other antipanic medications at FU. Improvement in panic attack frequency, all anxienty, and all impairment ratings observed at DC was maintained at FU in the sample as a whole. Maintenance of improvement was similar between patients who continued and discountinued IMI. Compared with alprazolam-treated patients drawn from the same cohort (Nagy et al. APA NR43, 19987), there was a trend for a greater proportion of IMI-treated patients to be off medications at FU (13/25 vs 18/60, $X2 = 3,67$, 1 df, $p = .052$). *IMPLICATION:* Preliminary data analysis suggests favorable long-term outcome in patients treated with IMI and behavioral group therapy. Additional comparisons with alprazolam-treated patients will be discussed.

NR330 **Thursday, May 11, 12 noon–2:00 p.m.**

CLINICAL CHARACTERISTICS OF HOUSEBOUND AGORPHOBICS

Alan L. Gordon, M.D., Butler Hospital, 345 Blackstone Blvd, Providence, RI 02906; Cynthia A. Berry, M.D., John W. Norton, M.D., Steven A. Rasmussen, M.D.

Summary:

There has been little systematic study of patients with agoraphobia and panic disorder who are housebound or severely limited in their access to treatment due to their anxiety. Because of their inaccessibility, these patients carry a high risk for increased morbidity and are usually not included in research studies. We undertook a pilot study to clinically characterize housebound agoraphobic patients. A newspaper article that solicited responses from individuals that considered themselves housebound due to anxiety identified 52 probands Thirty-two returned a self-report anxiety questionnaire on anxiety and were interviewed by one of us using a semistructured diagnostic interview. Thirteen were independently rated as severely limited or totally house-bound by the investigators. Twenty-eight (81 percent) of the sample were women. The mean age was 45.6 $\pm$ 16.1. Twenty eight (88 percent) reported spontaneous panic attacks, while 15 (47 percent) reported having been awoken from sleep by their panic attacks. There were no significant differences in the frequency or severity of 43 symptoms characteristic of panic attacks between these patients and a group of panic patients presenting to our Anxiety Disorders Clinic Considerable comorbidity with affective, other anxiety, and personality disorders as well as schizphrenia was present. Our results indicate that most housebound patients with anxiety meet diagnostic criteria for agoraphobia and panic and are similar to clinic patients with regard to frequency and severity of panic attacks. The interaction of personality variables, psychosocial factors as well as the number and type of coexisting Axis I disorders appear to play a key role in how agoraphobic patients actually become housebound. Further epidemiologic and clinical studies of housebound agoraphobics are indicated.

NR331 **Thursday, May 11, 12 noon–2:00 p.m.**

LACTATE-INDUCED PANIC IN ALCOHOLICS

Deborah S. Cowley, M.D., Psychiatry, Univ of Washington, 1959 NE Pacific RP-10, Seattle, WA 98195; Carl F. Jensen, M.D., Donald J. Johanessen, M.D., Lorne Parker, M.D., Stephen R. Dager, M.D., R. Dale Walker, M.D.

Summary:

The reason for the observed increased prevalence of panic and anxiety disorders in alcoholics remains undetermined. Alcoholism has been suggested to represent a form of self-medication of panic symptoms, but chronic ethanol use and withdrawal may itself be anxiogenic. The diagnosis of panic in alcoholics is difficult since panic and withdrawal symptoms are similar. To determine the biological similarity of panic states in alcoholics and nonalcoholics and to investigate lactate infusion as a possible diagnostic test in alcoholics, we performed lactate infusions in abstinent alcoholics with (ALCp; $n = 12$) and without (ALC; $n = 10$) panic attacks and in nonalcoholics with panic disorder (PD; $n = 16$). Subjects received 10 cc/kg. 0.5 molar sodium lactate intravenously over 20 minutes and panic symptoms, subjective anxiety, heart rate, and blood pressure were measured. PD and ALCP subjects had similar rates of lactate-induced panic (eight of 16 versus five of 12; $x^2 = 0.2$, $df = 1$, $p =$ n.s.) while ALC subjects had a lower panic rate than either of the other two groups (0 of 10; $x^2 = 7.3$, $df = 2$, $p < 0.03$). Both groups with panic attacks had significantly higher panic symptom scores and anxiety self-ratings with lactate than did alcoholics without panic attacks. These findings suggest that panic states in alcoholics resemble those in patients with panic disorder, at least in sensitivity to sodium lactate infusion. The possible usefulness of lactate infusion in the diagnosis of panic in alcoholics will be discussed.

NR332 **Thursday, May 11, 12 noon-2:00 p.m.**

CO_2 SYMPTOM PROFILE: PANIC DISORDER AND AGORAPHOBIA

Diana Kosyzchi, M.A., Psychiatry, ST. Mary's Hospital, 3830 Lacombe Avenue, Montreal PQ, Canada H3T 1M5; Jacques Bradwejn, M.D., James F. Campbell, Ph. D.,

Summary:

CO_2 induces panic attacks in patients with panic disorders; however its differential cognitive, affective, and somatic profile has not been defined in different diagnostic groups. The present study compared response profiles to a single inhalation of 35 percent CO_2 in 15 patients with panic disorder (PD), 15 patients with panic disorder with agoraphobia (AG), and 15 healthy volunteers (HV). Responses were evaluated with a DSM-III-R derived panic inventory, a modified Agorphobics Cognitions Questionnaire (Chambless et al) and a Fear of Symptoms Inventory. Preinhalation anxiety was measured with the State Anxiety Questionarie (Speilberger et at), and the somatic subscale of the Hamilton Anxiety Scale. Panic attacks occured in ten of 15 AG, nine of 15 PD, and three of 15 HV. Subjects showed differences in frequency and intensity of somatic symptoms, fear of these symptoms, and on affective symptoms, with increased severity form HV to PD to AG. AG showed more depresonalization and derealization than PD and HV, and differed in catastrophic cognitions from HV only. AG showed greater preinhalation anxiety than PD and HV. The study suggest different sensitivities to CO_2 among panic disorder subtypes. Further studies on panic attacks should take into account diagnostic differences.

NR333 **Thursday, May 11, 12 noon–2:00 p.m.**

INCREASED INSPIRATORY RESISTANCE IN CO_2 INDUCED PANIC

Laszlo A. Papp, M.D., Psychiatry, Columbia Univ LIJMC, 722 West 168th Street, New York, NY 10032; Jack M. Gorman, M.D., Robert Gully, B.A., Eric Hollander, M.D., Julie Hatterer, M.D., Donald F. Klein, M.D.

Summary:

While the phenomenon is well documented, the pathophysiology of carbon dioxide (CO_2) induced panic in patients with panic disorder is still unclear. One research strategy is to "dismantle" the complex physiological changes induced by CO_2 and examine the components separately. Simply reducing the diameter of the airway, for instance, causes the patient to experience dyspnea similar to that during CO_2 inhalation but without the CO_2 induced acid-base changes.

Seventeen panic patients, 19 social phobics, and 72 normal controls inhaled a mixture of 35 percent CO_2/65 percent O_2 for 30 sec. via facemask and also breathed through a valve reducing the diameter of the airway for 30 sec. in a double-blind, counterbalanced, randomized design.

Ten of the 17 panic patients panicked to CO_2 and 4 of the 17 to the increased inspiratory resistance (IIR) (McNemar's $x^2 = 4.5$; $df = 1$; $p < 0.03$). Six of the 19 social phobics panicked to CO_2 and one of the 19 to IIR (McNemar's $x^2 = 5.0$; $df = 1$; $p < 0.02$). None of the controls panicked to either procedure.

CO_2 was significantly more potent than IIR in provoking panic in patients with anxiety disorders. The implications of these findings in the context of the theorized pathophysiology of panic disorder will be presented.

NR334 **Thusday, May 11, 12 noon-2:00 p.m.**

RELATIONSHIP OF CSF-PGE TO MHPG, HVA, 5HIAA IN PANIC

Raymond F. Anton, M.D., Psychiatry, Med Univ of So. Carolina, 171 Ashley Avenue, Charleston SC 29425; James L. Ballenger, M.D., Bruce Lydiard, M.D., William Z. Potter, M.D.

Summary:

It has been suggested that neurotransmitter recepter regulatory mechanisms, especially those of the noradrenergic alpha2 receptors, may be abnormal in patients with panic disorder. Prostaglandins of the E series (PGE) have been shown to be important in the regulation or "coupling" of alpha2 receptor agonist to their effector mechanisms. The study of these processes is difficult in the clinical situation. Nevertheless, we have attempted to begin to evlauate the linkage of PGE with transmitter production by exmaing the level of PGE in the same CSF sample in which MHPH, HVA, and 5HIAA is also measured.

Twenty drug free patients who met DSM-III criteria for panic disorder and ten healthy contols, after a four day low monoamine diet, and overnight fast, and bed rest, has CSF removed by lumbar puncture. PGE was measired by RIA from a 1 ml aliquor (33- 35th cc). MHPG, HVA, and 5HIAA were measured by HPLC with Electrochemical Detector from a pooled aliquot (1-12th cc) of CSF.

There was a significant positive relationship ($R = 0.7$, p 0.05) between PGE and MHPG in the control group but not ($R = 0.09$) in the panic group. No other relationship reached significance except for a trend for PGE to be correlated with 5HIAA ($R = 0.61$, $p < .1$) in the control group only.

These data suggest a possible "coupling" of PGE and noradrenergic, and perhaps serotonin, output in the control population which doesn't exit in panic disorder patients. This would support a hypothetical dysregulation of neuro-modulation in the panic disorder patients.

NR335 **Thursday, May 11, 12 noon-2:00 p.m.**

CHOLECYSTOKININ PANIC: PATIENT CONTROL DIFFERENCES

Jacques Bradwejn, M.D., Psychiatry, McGill University, 3830 Lacombe Avenue, Montreal PQ, Canada H3T 1M5; Diana Koszycki, M.A., Greg B. Meterissian, M.D., Christian Shriqui, M.D.

Summary:

Cholecystokinin (CCK), a peptide found in high concentration in mammalian cortex and limbic structures, fulfills the criteria for a neurotransmitter. It excites cortical and hippocampal neurons, an effect which is antagonzied by benzodiazepines. We reported that CCK-tetrapeptide induced panic attact identical to natural panic attacks in panic disorder patients. The objective of the present study was to compare the action of 50 micrograms IV of CCK-tetrapeptide in panic disorder patients and healthy controls. A double-blind placebo (saline) control design with randomized sequence of injection was used. Eleven patients (six males, five females) and 15 healthy volunteers (ten males, five females) participated. DSM-II-R criteria with moderated to severe affective symptoms were used as criteria for panic attacks in controls. All patients experienced a panic attack with CCK and none with placebo; six of 15 controls experienced a panic attack with CCK and none with placebo. The mean time of onset and mean duration ($\pm$ SEM) of panic attacks were: 20 ± 3 seconds and 20.7 ± 7.6 minutes for patients, 21.3 ± 2 seconds and 9.1 ± 1.9 minutes for volunteers. These results suggest a threshold specificity for response to CCK-tetrapetide in patients. A dose response study in both groups is warranted.

NR336 **Thursday, May 11, 12 noon-2:00 p.m.**

SUBTYPES OF PANIC DISORDER AND DRUG RESPONSE

Wolfgang Maier, Psychiatry, University of Mainz, Untere Zahlbacher Str. 8, Mainz FRG 6500, West Germany; Nicolas Argyle, M.B., Raben Rosenberg, M.D., David Shera, M.A., Philip W. Lavori, Ph.D., Otta Benkert, M.D.

Summary:

The validity of subtyping panic disorder by current avoidance behavior and current (secondary) major depression (MDE) as proposed by DSM-III-R (APA, 1987) was tested using the data from the Cross-National-Collaborative-Panic-Study, Second Phase (CNCPS, 1989) (n = 1,180 intent-to-treat-patients); avoidance behavior as well as MDE were associated with an increased severity of psychopathology and a higher frequency of the DSM-III disorder at baseline; the influences of both diagnostic variables were additive or superadditive. Avoidance behavior, expecially the discrimination between agorphobic and nonagoraphobic patients, but not MDE predicted an unfavorable response in the eight week drug trial, independent of the particular treatment (imipramine, alprozolam, placebo). The early response (within the first three weeks) to placebo of agoraphobic patients was less favorable (significant interaction effect). There was an indication, of the need of active treatment for panic disorder with agoraphobia. Neither avoidance behavior, MDE, or psychosocial variables are useful for choosing between imipramine and alprazolam in order to optimized the treatment response.

NR337 **Thursday, May 11, 12 noon-2:00 p.m.**

LONG-TERM OUTCOME OF PANIC DISORDER

Mark H. Pollack, M.D., Psychiatry, Mass General Hospital, 15 Parkman Street Acc 715, Boston MA 02114; Jerrold F. Rosenbaum, M.D., George E. Tesar, M.D., Gary S. Sachs, M.D., Lee S. Cohen, M.D., Lawerence D. Rosen, B.A.

Summary:

Although the acute response to pharmacotherapy of panic disorder has been well studied, there is little systematic data addressing the more critical issue of the longitudinal course and outcome of these patients. We report data at mean of 17.6 months for 59 of 72 (81.9 percent patients initially randomized into a six week double = blind, placebo = controlled trial alprazolam and clonazepam for panic disorder, including measures of panic attacks, phobic avoidance, anticipatory anxiety, clinician global impression (CGi), and current treatment.

A positive outcome at follow-up (CGI$\leq$2, not at all to borderline ill) was significantly associated with panic disorder subtype (i.e. none, limited, extensive phobic avoidance), and global phobic distress at baseline assessment of the acute trial, and total panic attacks, anticipatory anxiety, fear, avoidance, global distress, and CGI at trial endpoint ($p<.05$). In contrast to other reports, current or past major depression were not significantly correlated with outcome at follow-up. However, concomitant dysthymic disorder and social phobia did correlate with negative outcome.

Mean overall CGI at baseline was 4.5 ($\pm$0.9) (moderately to markedly ill) and 2.9 $\pm$ 1.7 at follow-up (borderline to mildly ill); 47.5 percent of patients at follow-up had CGI$\leq$2, 22 percent were medication-free. Information will be presented on outcome of treatment with individual medication regimes and on course of treatment including changes in pharmacotherapy and addition of behavioral and psychotherapy.

This study suggest that panic disorder may have a chronic course with most patients requiring ongoing treatment, findings that should be considered in clinical practice and the design of future treatment studies.

NR338 **Thursday, May 11, 12 noon–2:00 p.m.**

PERIODICITY IN PANIC DISORDER

Michael Kahan, M.D., Phobia Clinic, Hillside Hospital, P.O. Box 38, Glen Oaks, NY 11004; Charlotte Zitrin,, M.D., Martin H. Blum, M.D., James C. Ballenger, M.D., Richard Swinson, M.D., Lawrence McDonald, M.D.

Summary:

Infradian rhythms have been shown in affective disorders but to date there have been no studies finding periodicity in panic disorder. If infradian rhythms were to exist in panic disorder it would add to our understanding of this common condition.

Ninety patients with panic disorder were seen at three centers and were followed for an average of 50 days, with daily diaries of spontaneous, anticipatory, and situational attacks. Spectral analysis was performed on the time series, and comparisons were made between the three types of attacks, and between patients on placebo versus those on alprazolam. All patients exhibited at least one significant periodicity, and the most significant periodicities measured as cycles with the greatest amplitude, were in the one to two week range. The findings and implications will be discussed.

NR339 **Thursday, May 11, 12 noon–2:00 p.m.**

PUBLIC SPEAKING IN SOCIAL PHOBIC SUBTYPES

Andrew P. Levin, M.D., Holliswood Hospital, 87-37 Palmero Street, Holliswood, NY 11423; Diana Sandberg, M.D., John Stein, M.A., Michael R. Liebowitz, M.D.

Summary:

Thirty-seven patients meeting DSM-III-R social phobia criteria (28 generalized, nine discrete) and 14 controls were monitored during a ten minute simulated speech. Generalized patients demonstrated significantly more behavioral symptoms and subjective complaints than either the discrete group or the controls. Heart rate results showed greater increases in normals and discrete social phobics compared with generalized patients. The groups did not differ in plasma levels of cortisol, epinephrine, or norepinephrine. The heart rate results predict greater efficacy of beta-blockade in normals and discrete patients compared with generalized patients. In addition, these data reveal that while generalized social phobics are distinguishable from controls on subjective, behavioral, and physiologic measures, the features that distinguish discrete social phobics from normals are elusive.

NR340 **Thursday, May 11, 12 noon-2:00 p.m.**

PANIC DISORDER PREVALENCE IN CARDIOLOGY PATIENTS

Richard J. Goldberg, M.D., Psychiatry, Rhode Island Hospital, 593 Eddy Street, Providence RI 02903; Philip Morris, M.D., Frederic Christian, M.D., James Badger, R.N., Stephen Chabot, M.D., Matthew Edlund, M.D.

Summary:

This study was designed to assess the prevalence of panic disorder in cardiology patients. All active patients, in a cardiology practice (n = 414) were mailed a panic symptom screening questionnaire. Three hundred and ten questionnaires (75 percent) were returned. Of these, 104 (25 percent) were classified as having possible panic disorder. Of these 104 patients, 52 were contacted and complete a semistructured diagnostic psychiatric interview (Scid-Up) to evaluate DSM-III = R diagnoses of depressive illness or anxiety disorder. Sixty = nine percent of the patients were male with an average age of 61.5 years. Nineteen patients had panic disorder, and 17 had other psychiatric disorders. The estimated prevalence of panic disorder in the ambulatory cardiology practice was 6.3 percent. Of interest, the panic disorder patients could be divided into two groups on the basis of the duration of the panic symptoms. Approximately half the patients had short duration panic disorder (an anverage duration of 5.03 years) emerging after the onset of significant cardiac disease. The other half had long duration panic disorder (an average duration of 33.2 years) which continued through the emergence of cardiac disease in later life.

NR341 **Thursday, May 11, 12 noon-2:00 p.m.**

COURSE OF PANIC DISORDER IN PREGNANCY

Lee S. Cohen, M.D., Psychiatry, Mass General Hospital, 15 Parkman Street, Boston MA 02114; Jerrold F. Rosenbaum, M.D., Vicki L. Heller, M.D.

Summary:

Once characterized as a time of emotional well-being for women, pregnancy is a period during which psychiatric symptoms emerge, persist, or worsen. We report on 21 pregnant women who met SM = III-R criteria for panic disorder and who were followed during pregnancy through the obstetric-psychiatric consultation service at an ambulatory psychopharmacology unit. Demograph data were collected from the sample as was information regarding duration of illness, comorbidity, history of panic symptoms in previous pregnancies, and levels of antipanic somatotherapy prior to pregnancy (and during pregnancy if drugs were continued). Severity of panic disorder was assessed for the three months prior to pregnancy and at least once per trimester including a Clinical Global Impression score (CGI, 1 = not all ill - 7 = markedly ill).

Despite case reports suggesting that women with anxiety disorders have fewer symptoms during pregnancy, none of the pregnant women in our sample experienced a marked improvement in symptoms (Δ CGI of a least two units) though some women were able to reduce slightly previous levels of antipanic medication. No women, on the other hand, suffered clinically meaningful worsening of their disorder. In the case of multiparous women, intensity of panic symptoms in a previous pregnancy (if any) did not predict comparable levels of distree in a subsequent pregnancy. That women with panic disorder may not be "protected" against anxiety symptoms during pregnancy has implications for pre-pregnancy counseling and planning for treatment during pregnancy; clinicians must weight the risk of drug exposure against possible risks of the underlying disorder.

NR342 **Thursday, May 11, 12 noon–2:00 p.m.**

TRAZODONE FOR CLOMIPRAMINE AND LITHIUM RESISTANT OBSESSIVE COMPULSIVE DISORDER

Haggai Hermesh, M.D., Ward A, GEHA Psychiatric Hospital, P.O. Box 72, Petah Tikva 49100, Israel; Dov Aizenberg, M.D., Hanan Munitz, M.B.

Summary:

Trazodone (TZ) up to 250mg/b.i.d. was administered to nine patients suffering from obsessive-compulsive disorder (OCD) in a prospective non-blind study. These patients had previously failed to respond to clomipramine (CMI) up to 300mg/d, as well as to CMI augumentation with lithium carbonate (serum levels 0.6-1.1 m''Eq.1). Clinical evaluation included: five measures of obsession and compulsions (OC), two of depression, and one of daily functioning. In the whole group, all five measures of OC showed a significant improvement by ANOVA with repeated measures. Three particular patients markedly benefited from TZ. The drugs efficacy for them was substantiated by follow-ups, in which the original OC symptoms re-emerged five times, following TZ withdrawal. The five exacerbations were ameliorated after TZ readministration. A possible aggravation of OCD due to TZ was not observed. Severity of initial OC symptoms and depression did not correlate with clinical outcome due to TZ, nor did any change in OC symptoms correlate with changes in depression measures. In the three patients in whom OC improved the most, depression was alleviated only mildly. Our findings support the few previous reports of TZ anti-OC efficacy and may suggest the involvement of hetergeneous CNS seortonin dysfunction in OCD.

NR343 **Thursday, May 11, 12 noon-2:00 p.m.**

FLUVOXAMINE VERSUS DESIPRAMINE IN OCD

Wayne K. Goodman, M.D., Psychiatry, Yale University, 34 Park Street, New Haven CT 06508; Pedro L. Delgado, M.D., Lawrence H. Price, M.D., Joseph Palumbo, M.D., Steven A. Rasmussen, M.D., Dennis S. Charney, M.D.

Summary:

The hypothese that obsessive = complusive disorder (OCD) involves altered serotonin (5-HT) function is supported by recent evidence that the potent and selective 5—HT reuptake inhibitor fluvoxamine (FVX) is efficacious in OCD. To further evaluate whether the 5-HT reuptake properties of the drug are relevant to its antiobessional action, a double-blind trial was conducted in OCD outpatients comparing the efficacy of FVX with the relatively selective norephinephrine reuptake blocker desipramine (DMI). Preliminary results are presented here. *METHODS:* 38 patients (M = 18 F = 20) with a principal diagnosis of OCD (DSM-III-R) were randomly assigned after one-week, single-blind placebo to eight weeks of either FVX or DMI. More than 50 percent of the patients had concurent depression. Severity of OCD and of depression were rated weekly with the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and the Hamilton Rating Scale for Depression (HAM-D), respectively. ''Responder'' = ''much'' or ''very much improved'' on the CGI. *RESULTS:* Baseline Y-BOCS and HAM-D ratings did not differ significantly between the treatment groups. In the DMI group, there were no significant changes from baseline in either the Y-BOCS or HAM-D. In contrast in the FVX group, there were significant decreases from baseline on both the Y-BOCS (mean decrease = 28 percent) and HAM-D (mean decrease = 22 percent). Furthermore, student t-tests revealted that FVX was significantly superior to DMI in reducing severity of OCD as measured by the Y-BOCS. In the DMI group, two of 19 (11 percent) patients were responders, whereas in the FVX group, ten of 19 (53 percent) patients were responders ($p < .02$, Fischer's Exact). In the FVX group, reduction in Y-BOCS scores was not significantly correlated with baseline HAM-D scores. *CONCLUSION:* The preliminary analysis of these data suggest that FVX was significantly more effective than desipramine DMI in reducing severity of OCD symptoms. This study provides additional evidence that the 5-HT reuptake properties of a drug are relevant to its antiobessional efficacy.

NR344 **Thursday, May 11, 12 noon–2:00 p.m.**

NEUROENDOCRINE SENSITIVITY IN OBSESSIVE COMPULSIVE DISORDER

Eric Hollander, M.D., Psychiatry, Columbia University, 722 West 168th Street Box 13, New York, NY 10032; Concetta Decaria, M.S., Franklin Schneier, M.D., Julie Hatterer, M.D., Laszlo Papp, M.D., Michael R. Liebowitz, M.D.

Summary:

Twenty adult, drug-free obsessive-compulsive disorder (GCD) patients (15 male, five female) and ten normal healthy controls (seven male, three female) underwent acute biological challenges with serotonergic (m-CPP, fenfluramine), noradrenergic (clonidine), and placebo challenges. Neuroendocrine responsivity to these challenges was assessed with measures of peak delta prolactin, cortisol, and growth hormone.

There was substantial blunting of peak delta prolactin in the GCD patients (4.6 ng/ml) compared to normal controls (9.0 ng/ml) following the oral m-CPP challenge (0.5 mg/kg). The peak delta prolactin rise following fenfluramine (60 mg po) was also blunted in the GCD patients (8.2 ng/ml) compared to normals (13.4 ng/ml). There was also blunting of cortisol response to both m-CPP and fenfluramine in the GCD group compared to normal controls. The effects of sex on cortisol and prolactin response to m-CPP and fenfluramine will be discussed.

Contrary to other reports, there was no blunting in peak delta growth hormone response to clonidine in the GCD patients (7.1 ng/ml) compared to normal controls. The effects of sex on cortisol and response to clonidine was robust compared to placebo (0.2 ng/ml).

This suggests desensitization of serotonergic but not noradrenergic hypothalamic receptors in obsessive-compulsive disorder.

NR345 **Thursday, May 11, 12 noon-2:00 p.m.**

TRITIATED IMIPRAMINE BINDING IN OCD

Donald Black, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City IA 52242; Michael Kelly, Pharm. D., Carol Myers, Pharm. D., Russell Noyes, Jr., M.D.

Summary:

The authors evaluated platelet tritiated imipramine binding in 22 outpatients with obsessive-compulsive disorder)OCD) and 22 psychiatrically normal controls matched for age and sex. Mean maximal binding site density (Bmax) and equilibrium dissociation affinity (Kd) values were not significantly different. In OCD patients, Bmax was positively associated with age but was not associated with age of onset, sex, personality disorder, or five measures of illness severity. Eight patients with OCD were subsequently treated with clomipramine up to 300/day for ten weeks. Among these eight patients, Bmax values has a 65 percent mean decrease from baseline, but Bmax values did not change among seven OCD patients receiving placebo. The results suggest that a reduced density of tritiated imipramine binding sites may not be associated with OCD, but that these sites may play a role in its treatment.

NR346 **Thursday, May 11, 12 noon–2:00 p.m.**

OBSESSIONAL PARANOIA: RESPONSE TO 5HT ANTIDEPRESSANTS

Jane L. Eisen, M.D., Butler Hospital, 345 Blackstone Blvd, Providence, RI 02906; Steven A. Rasmussen, M.D.

Summary:

There are several phenomenologic similarities between patients with paranoid delusional disorder and severe OCD. Hyperarousal, a cognitive set that something bad is about to happen, and a relative intolerance for ambiguity and uncertainty, are found in both OCD and paranoia. We have identified ten patients with a primary DSM-III-R diagnosis of OCD who also met criteria for DSM-III-R delusional disorder. These probands were systematically studied with regard to their clinical features and treatment response to serotonin uptake inhibitors. With the exception of their paranoid delusions, there were no significant differences between this group and the 300 other OCD patients in our clinic in terms of demographics, clinical features, and course of illness. Unlike other OCD patients with psychotic features these delusional probands were quite high functioning (mean GAS scores 64.2 $\pm$ 14.3). Both the paranoid delusions and the OC symptoms of these patients responded to serotonin reuptake antagonists without necessitating the use of neuroleptic agents. This supports a previous study showing that paranoid patients with anxiety respond to antidepressants alone (1). The positive response to serotonin uptake inhibitors alone raises the question of whether there is an underlying neurobiological defect that is similar in these two kinds of abnormal fears, both of which involve abnormal risk assessment. Systematic trials of specific serotonin uptake antagonists in delusional disorder are indicated.

NR347 **Thursday, May 11, 12 noon–2:00 p.m.**

RELIGION AND GUILT IN OCD PATIENTS

Kerrin L. White, M.D., Wyman 211, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Sara E. Quay, B.A., Gail Steketee, Ph.D.

Summary:

Prominent features of many patients suffering from obsessive-compulsive disorder (OCD) are high levels of guilt, obsessions concerning sin and hell, and compulsive confession and prayer. The current study examined the relationship between guilt, types of religious upbringing, degree of religiosity, and obsessive-compulsive symptoms.

Participants in this study were 25 obsessive-compulsive and 34 depressed outpatients. Subjects completed the Maudsley Obsessive Compulsive Inventory (MOCI), the Compulsive Activity Checklist (CAC), the Hamilton Depression Scale (HAMD), the State Trait Anxiety Inventory (STAI), and the Problematic Situations Questionnaire (PSQ). Information regarding religion of origin, current practicing religion and religiosity were also collected.

Results indicated that Catholicism was not significantly more prevalent among OCD patients than depressed patients. Obsessive-compulsive scores, however, were significantly and positively correlated with degree of religiosity, while other measures of pathology were not. Highly religious subjects were more likely to experiience higher levels of guilt, and religion currently practiced appeared more closely associated with guilt than did religion of origin.

Results are discussed in light of the relationship of OCD symptom profiles, guilt, and religiosity. Implications for treatment outcome are noted.

NR348 **Thursday, May 11, 12 noon–2:00 p.m.**

CLOMIPRAMINE IN OBSESSIVE-COMPULSIVE DISORDER

Matig R. Mavissakalian, M.D., Psychiatry, Ohio State University, 473 West 12th Avenue, Columbus, OH 43210; Bruce Jones, M.D., Steve Olson, M.D.

Summary:

Twenty-five patients with DSM-III criteria for obsessive-compulsive disorder (DCD) of at least two years duration, moderate to marked severity, and no evidence of depression, complete a a double-blind placebo (12) controlled ten-week study with clomipramine (273.1 ± 43.9 mg/day). Improvement was significantly superior with clomipramine on a number of self and clinician rated scales. There was no improvement in the placebo group. Six of them were treated in an open ten week trial with clomipramine (241.7 ± 49.2 mg/day) immediately following double-blind placebo with significant improvement noted on all measures. The clinical significance of clomipramine treatment was then assessed in an expanded sample of 37 patients, 33 of whom completed ten weeks of clomipramine treatment (239.4 ± 57.0 mg/day) in either the double-blind study (13) or an open protocol (20) which otherwise followed a similar protocol. Four (10 percent) dropped out. At the end of treatment, symptoms had decreased to a subclinical level in 15 (47 percent) patients and nearly one-third of the sample was virtually symptom free. However, one out of four patients failed to improve. Analysis of steady state plasma tricyclic levels (clomipramine (CMI): 169.9 ± 102.1 ng/ml; N-desmethylclomipramine (DCMI): 379.0 ± 160.6 ng/ml) revealed that responders had significantly higher CMI levels and lower DCMI/CMI ratios. A significant degree of correlations were also obtained between-plasma levels of CMI, but not DCMI, and post treatment outcome measures.

NR349 **Thursday, May 11, 12 noon–2:00 p.m.**

REPEAT M-CPP CHALLENGE DURING FLUOXETINE TREATMENT IN OBSESSIVE COMPULSIVE DISORDER

Eric Hollander, M.D., Psychiatry, Columbia University, 722 West 168th Street Box 13, New York, NY 10032; Concetta Decaria, M.S., Raphael Campeas, M.D., Gregory Dalack, M.D., Laszlo Papp, M.D., Michael Liebowitz, M.D.

Summary:

The serotonin aganist m-CPP has been shown to provoke obsessions in a subgroup of OCD Patients. Chronic clomipramine treatment successfully treats obsessive-compulsive disorder, and was reported to blunt behavioral and hyperthermic responses to m-CPP in obsessive-compulsive disorder (2). Six OCD patients who previously had marked exacerbations of OCD symptoms during a baseline m-CPP challenge were treated with the serotonin reuptake blocker fluoxetine (80 mg/day) for 12 weeks. Repeat m-CPP challenge (0.5 mg/kg po) was conducted during chronic fluoxetine treatment, and behavioral and neuroendocrine responses were measured. These were compared to baseline findings.

None of the six OCD patients who had previously had a behavioral exacerbation at baseline had an exacerbation of OCD symptoms with m-CPP challenge during chronic fluoxetine treatment. There was an 18-fold greater GCD exacerbation with m-CPP at baseline compared to repeat challenge. Prior to treatment, GCD patients had a blunted prolactin rise in response to m-CPP compared to normal controls (N = 10). On repeat m-CPP challenge during chronic fluoxetine treatment, GCD patients had a 230 percent prolactin rise, compared to a 58 percent prolactin rise with m-CPP at baseline.

Chronic fluoxetine treatment appears to downregulate behavioral sensitivity and upregulate neuroendocrine sensitivity to selective serotonin agonists in obsessive-compulsive disorder patients.

NR350 **Thursday, May 11 12 noon-2:00 p.m.**

NEUROLEPTIC ADDITION IN FLUVOXAMINE-REFRACTORY OCD

Christopher J. McDougle, M.D., Psychiatry, Yale University, 34 Park Street, New Haven CT 06508; Wayne K. Goodman, M.D., Lawrence H. Price, M.D., Pedro L. Delgado, M.D., John H. Krystal, M.D., Dennis S. Charney, M.D., George R. Heninger, M.D.,

Summary:

Despite the efficacy of 5HT reuptake inhibitors, e.g. fluvoxamine (FVX), in obessive = compulsive disorder (OCD), many patients are unimporved with these agents. This study examined the efficacy of adding a neuroleptic to the regimens of OCD patients who were unresponsibe to an adequate trial of FVX ± lithium. *METHODS:* 17 patients (nine inpatients, eight outpatients) with OCD (DSM-III-R) had neuroleptic treatment ranged between two and eight weeks (duration = 4.7 ± weeks). Outcome was assessed with Yale-Brown Obsessive Compulsive Scale (Y-BOCS) scores before and after neuroleptic addition to FVX ± lithium. Similary, clinical response was assesed on the CGI. Thse cases were then reviewed to determine whether specific target features (comorbid occurence of tic-spectrum disorders or schizotypal personality disorder) predicted a positive neuroleptic response. *RESULTS:* Nine of 17 (56 percent) patients were "responders" (CGI = "much" or "very much improved") at the conclusion of combined neuroleptic/FVX(± lithium) treatment. In the 15 patients for whom complete Y-BOCS scores were available, addition of neuroleptic was associated with a decrease of 9.1 ± 8 (36 percent) from baseline ($p < .001$, paired t-test, two-tailed). Based CGI ratings, 7/8 (88 percent) patients with target features were responders, whereas only 2/9 (22 percent) of patients without target features were responders ($p < .02$, Fisher Exact Test, two-tailed). *CONCLUSION:* The addition of neuroleptic may be an effective treatment strategy in OCD resistant to FVC ± lithium. Comorbid occurrence of the specific target features of tic-spectrum disorders or schizotypal personality disorder was more frequently associated with a positive neuroleptic response.

NR351 **Thursday, May 11, 12 noon–2:00 p.m.**

TRYPTOPHAN DEPLETION ALTERS MOOD IN OCD PATIENTS

Pedro L. Delgado, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06508; Wayne K. Goodman, M.D., Lawrence H. Price, M.D., Dennis S. Charney, M.D., George K. Aghajanian, M.D., George R. Heninger, M.D.

Summary:

Reduction of dietary tryptophan (TRP) decreases plasma TRP, brain TRP, and brain serotonin (5HT) in laboratory animals. Rapid depletion of plasma TRP temporarily reverses antidepressant response in 72 percent of patients with major depression (I). This study investigates the effects of acute TRP depletion (ATD) in obsessive-compulsive disorder (OCD). *METHOD*: 12 DSM-III-R OCD patients (seven drug free symptomatic, 4/7 currently depressed; five in clinical remission of OCD symptoms on fluvoxamine, 3/5 previously depressed) received a 24-hr., 160 mg/day, low-TRP diet followed the next morning by a 16-amino acid drink, in a double-blind, placebo-controlled (ATD and control testing), crossover fashion. On one test the diet and drink were supplemented with L-TRP (control) and on the other test neither the diet nor drink were supplemented (ATD). Behavioral ratings (Hamilton Depression Scale (HDRS) and Yale-Brown OCD Scale (YBOCS)) and plasma (for TRP levels) were obtained prior to the diet and drink, five and seven hrs. after the drink, and 12:00 pm the next day. *RESULTS*: Total and free TRP decreased 85 to 90 percent five hrs. after the TRP-free drink (TFD). Drug-free, symptomatic OCD patients were behaviorally unchanged by ATD or control testing. In remitted OCD patients on fluvoxamine YBOCS scores were unchanged by ATD but the three patients with previous depression became more depressed (mean 95 percent increase in HDRS score; 19 $\pm$ 7 pre-diet, 34 $\pm$ 4 7 hours after TFD). *Implications*: Preliminary results indicate that ATD may reverse antidepressant but not anti-OCD response in remitted OCD patients suggesting that the antidepressant effects of fluvoxamine may be more dependent on 5HT availability than its anti-OCD effects. These findings suggest that OCD may be biologically distinct from depression.

NR352 **Thursday, May 11, 12 noon-2:00 p.m.**

POST TRAUMATIC STRESS IN NYC EMERGENCY SERVICES

Michael Blumenfield, M.D., Psychiatry, NY Medical College, RM B006 Psychiatric Inst WCMC, Valhalla NY 15095; Todd Hertzberg, Michael Riley, John Keating, Ph.D.

Summary:

In order to determine the existence of post = traumatic stress disorder (PTSD) in emergency personnel in New York City, a random sample of 139 police, 101 fire, and 88 emergency medical services (EMS) personnel were given a questionnaire to determine if they have symptoms meeting the DSM = II-R criteria for their diagnosis. They were also given the SCL-90 questionnarie to examine for the presence of other psychological symptoms.

Assuming the exposure to a traumatic event, 5.6 percent of police, 2.0 percent of fire, and 20.0 percent of EMS met DSM = III-R criteria for PTSD. The EMS also clearly exceeded the scores of the normative cohort for the SCL-90 on each of the symptom categories and on the General Severity Index.

Four EMS categories were then studied: 1) 49 student studying to be emergency medical technicians (EMT) for the first time, 2) 48 EMTs from New York State studying to be a New York City EMT, 3) 26 New York City EMTs taking refresher course and, 4) 39 New York City EMTs upgrading to paramedic.

The first group did not have any students meeting diagnostic criteria for PTSD. The overall percentage of the other EMS personnel meeting criteria for PTSD was the same as the pilot study. The linear trend was statistically significant as one moved from the least experienced to the most experienced. The results become more dramatic if the one month time criteria in each symptom category was not required. The data from this study strongly suggest that experience in EMS increase the incidence of PTSD.

NR353 **Thursday, May 11, 12 noon–2:00 p.m.**

RELAPSE IMAGERY WITH PTSD ALCOHOLICS

Francis R. Abueg, Ph.D., Psychology, Palo Alto VAMC, 3801 Miranda Avenue, Palo Alto, CA 94304; Julie Kriegler, Ph.D., Hsiao-Ti Falcone, M.A., Harvey Dondershine, M.D., Fred Gusman, M.S.W.

Summary:

Post-traumatic stress disorder (PTSD) and substance abuse have strongly interactive properties which maintain and exacerbate the respective conditions. Little controlled intervention research has been reported which directly addresses patients suffering from this dual diagnosis. This two-group treatment outcome study incorporates the conceptual model of relapse prevention while taking full advantage of the high suggestibility and imagery skill of PTSD patients.

Forty-two inpatients with Vietnam related PTSD at the Palo Alto VAMC were treated in a 12-session group aimed at 1) increasing their behavioral coping to high-risk for relapse (return to drinking) situations; and 2) developing skills at imagining the relapse "scene" as well as practicing alternatives to drinking. A quasicontrol group of well diagnosed PTSD-alcoholics ($N = 42$) were matched for combat level, PTSD severity, and years of alcohol dependence.

Results confirmed that the intervention did indeed significantly increase self-efficacy to resist drinking in a variety of situations compared with the control group ($p<.01$). Most striking, however, are follow-up data—three and six months post-discharge—which show significantly fewer relapses (P .05), lower rehospitalization rates, and in the case of relapse, lower amount of alcohol consumed.

NR354 **Thursday, May 11, 12 noon–2:00 p.m.**

HEART RATE CORRELATES OF PTSD

Graham M. Reid, M.D., Psychiatry, VA Hospital, 4300 7th Street, Little Rock, AR 72205; Stephen R. Paige, Ph.D., Joseph E.O. Newton, M.D.

Summary:

Our purpose was to examine the reactivity of the autonomic system in patients with post-traumatic stress disorder (PTSD). We measured heart rate and heart rate responses to four intensities (74-104 dB SPL) of (500 msec, 780 Hz) randomly presented neutral tones in 12 Vietnam veterans diagnosed with PTSD, and six matched normal Vietnam veterans. Subjects were evaluated with structured diagnostic interviews, and anxiety and depression rating scales prior to testing. Eighty tones were presented with an average of 15 sec between stimuli. By the third and fourth second following tone onset, the mean HR of the PTSD subjects ($p<.01$) increased more than twice that of the normal group. HR change scores were sensitive to the manipulation of stimulus intensity ($p<.05$) and the the difference between our two groups of subjects. These data suggest that subjects with PTSD are more autonomically hyperreactive than their non-PTSD combat peers and that HR changes to increasing intensity of pure tones provide a measure of "physiological reactivity."

NR355 **Thursday, May 11, 12 noon–2:00 p.m.**

24h URINARY CORTISOL AND CATECHOLAMINES IN PTSD

Roger K. Pitman, M.D., Research SVC, VA Medical Center, 718 Smyth Road, Manchester, NH 03104; Scott Orr, Ph.D.

Summary:

Twenty Vietnam combat veterans meeting DSM-III-R criteria for PTSD and 15 Vietnam combat veterans with no mental disorder (healthy controls), matched for age and severity of combat exposure and free of psychotropic or other potentally confounding medications for at least two weeks, provided single ambulatory baseline 24h urine collections. Immediately after an interview dealing with combat experiences, a second "post-stress" 24h collection was obtained from 13 of the PTSD and ten of the healthy subjects. There were no significant baseline group differences for norepinephrine (PTSD $M = 60.8$, healthy $M = 58.0$) epinephrine (PTSD $M = 10.7$, healthy $M = 10.7$) or MHPG (PTSD M-2942, healthy $M = 2901$) (all units g/24h). However, baseline 24h urinary free cortisol (UFC) excretion was significantly higher in the PTSD subjects: (PTSD $M = 107.3$, healthy $M = 80.5$, $t = 2.4$, $p = .02$). While NE and MHPG went up slightly after the interview in both subject groups, there were no significant baseline-to-post-stress main effects or interactions for the 24h catecholamine data. ANOVA for the UFC data revealed a significant Time main effect (increase across groups): (PTSD $M = +11.7$, healthy $M- +25.8$, $F = 7.2$, $p = .01$), but not a significant Group × Time interaction.

Utilizing a nonpsychiatric combat control group, this study failed to replicate a previously reported finding of decreased 24h urinary cortisol excretion, increased catecholamine excretion, and increased catecholamine/cortisol excretion ratio in combat-related PTSD.

NR356 **Thursday, May 11, 12 noon–2:00 p.m.**

PREDICTING EMOTIONAL RESPONSES TO DISASTERS

Bruno Lima, M.D., Psychiatry, Johns Hopkins Univ, 600 North Wolfe Street, Baltimore, MD 21205; Shaila Pai, Ph.D., Hernan Chavez, M.D., Nelson Samaniego, M.D., Herman Santacruz, M.D., Julio Lozano, M.D.

Summary:

This study reports on a multi-site collaborative effort to investigate the emotional responses to major disasters utilizing the same research design and instruments. The Self-Reporting Questionnaire was used to survey adult victims of different disasters in community settings (n = 200) and in primary care clinics (n = 250), and at a two-year follow-up (n = 40). The data indicate that (i) the prevalence of emotional distress was directly related to the magnitude of the disaster, the level of traumatic exposure, and the continuing stress of inadequate living arrangements, unemployment, and community disorganization; (ii) the symptom profiles were essentially the same for all distressed subjects; and (iii) the strongest predictors of emotional distress were very similar. These findings indicate a consistent pattern of emotional responsiveness to disaster experience: more or fewer victims may become distressed in the aftermath of different disasters, but the level and type of symptoms are similar among the distressed, irrespective of the particular disaster. These findings also support the development of a core curriculum for the training of health workers in those selected mental problems that are regularly present among victims.

NR357 **Thursday, May 11, 12 noon–2:00 p.m.**

PSYCHIATRIC SEQUELAE OF ABUSE IN NONPSYCHIATRIC PATIENTS

Nicholas G. Ward, M.D., Psychiatry, Univ Washington, RP-10, Seattle, WA 98195; Garth G. Gulick, B.S., Albert S. Carlin, Ph.D., Joanne Beaubien, B.S.

Summary:

This study examined the association of sexual, physical, and emotional abuse, with adult depression, history of suicide attempt, somatization, and marital status. Women (N = 200) presenting to a family practice clinic completed structured sexual, physical, and emotional abuse questionnaires as well as the IDDL depression inventory, Beck Depression Inventory (BDI), and SCL-90-R somatization subscale. Using self-defined sexual abuse as a criteria, sexual abuse rates were 78 percent in subjects who had attempted suicide versus 15 percent in nonattempters ($p<.0001$). When compared to nonabused subjects, sexually abused subjects had significantly more lifetime major depression (49 percent vs. 24 percent, $p<.004$), present depression (21 percent vs. 4 percent, $p<.0001$), less frequent first marriage status (22 percent vs. 44 percent, $p<.005$), higher mean somatization scores (12.2 vs. 6.5, $p<.003$) and BDI scores (7.2 vs. 3.0, $p<.001$). Age of onset of sexual abuse did not significantly affect these results. Several different objective criteria for sexual abuse yielded nearly identical outcomes. Self-perceived nonsexual abuse (physical and/or emotional) as well as physical or emotional abuse by objective criteria also yielded very similar outcomes.

NR358 **Thursday, May 11, 12 noon–2:00 p.m.**

FLUOXETINE TRIAL IN BORDERLINE PERSONALITY

Jack R. Cornelius, M.D., Psychiatry, WPIC, 3811 O'Hara Street Room 874, Pittsburgh, PA 15213; Paul H. Soloff, M.D., James M. Perel, Ph.D., Richard F. Ulrich, M.S.

Summary:

Serotonergic mechanisms have been implicated in the etiology of depressive disorders associated with violent suicide attempts and in a number of impulse control disorders. Selective serotonergic medications have recently become available which have shown effectiveness in treating these disorders. However, no trials with these medications have been reported in patients with borderline personality disorder (BPD), a disorder characterized by prominent depressive symptoms and impulsivity. In this study, five inpatients with BPD were treated openly for eight weeks with fluoxetine, a serotonergic medication, with doses ranging from 20 mg. to 40 mg. po qAM. All patients had multiple prior hospitalizations and had failed multiple trials of other medications. Prominent baseline symptom severity in affect and impulse was demonstrated on the Beck Depression Inventory (Mean = 33.8), the Hamilton Depression Scale (Mean = 29.6), and the Ward Scale of Impulse Action (Mean = 12.6). Weekly ratings of symptoms were performed for eight weeks following a one week washout period. Large, statistically significant improvements (on paired Student T test) were observed on the Beck ($\Delta = 15.0$ points, $p = 0.032$), the Hamilton ($\Delta = 18.0$ points, $p = 0.021$), and the Ward Scale ($\Delta = 10.2$, $p = 0.002$). Other scales showing significant improvement include the SCL-90 and the Global Assessment Scale. Fluoxetine plasma levels were also obtained. These promising findings suggest efficacy for fluoxetine in treating the depressive and impulsive symptoms of patients with BPD. Large, double-blind, placebo-controlled studies with serotonergic medications are warranted in patients with BPD.

NR359 **Thursday, May 11, 12 noon-2:00 p.m.**

NEUROPSYCHOLOGICAL TESTING IN BORDERLINE DISORDER

Kathleen M. O'Leary, M.S.W., WAW Bldg, NIMH, 2700 Martin Lurther King Avenue, Washington DC 20032; Pim Brouwers, Ph.D., David L. Gardner, M.D., Rex W. Cowdry, M.D.

Summary:

Sixteen research outpatients with borderline personality disorder (BPD) and 16 normal controls completed a battery of neuropsychological test. No reports of the performance of patients with BPD on an extensive neuropsychological test battery have appeared in the literature to date. Compared with the normals, the BPD performace was significantly impaired on the WASI-R Performance IQ and it subtest, the Digit Symbol, on Money's Road Map Test, and on a series of memory test requiring uncued recall of learned material (the Logical Memory subtest of the Wechsler Memory Scale or WMS, the Rey-Osterrieth Complex Figure Test Recall, The Embedded Figures Test, and the Corsi Blocks). Performance was normal to memory test with cued recall (WMS Associate Learning, The Incidental Facial Memory Test), and performance rose to normal on the WMS Logical Memory when cues were given. BPD performance was also normal on a variety of other tests sensitive to performace anxiety, attention, and visuospatial perception. Concurrent depression was not a significant factor influencing the scores of the BPD group. A history of drug and alcohol use has no significant effect on performance. These results suggest that patients with BPD experience specific difficulties distinguishing field from ground and recalling learned materials without cues.

NR360 **Thursday, May 11, 12 noon–2:00 p.m.**

ESTIMATING THE COMMUNITY PREVALENCE OF BPD

Marvin Swartz, M.D., Psychiatry, Duke Medical Center, Box 3173, Durham, NC 27710; Dan G. Blazer, M.D., Linda K. George, Ph.D., Idee Winfield, Ph.D., Dana Hughes, Ph.D.

Summary:

The authors use a new diagnostic algorithm derived from the Diagnostic Interview Schedule (the DIS/Borderline index) to identify borderline personality disorder among 19 to 55 year olds at the Duke site of the Epidemiologic Catchment Area (ECA) project. A criterion score of 11 or more symptoms from the 24-item DIS/Borderline index identifies 1.8 percent of the sample. The borderline diagnosis is significantly higher among females, the widowed, and unmarried, and there is a trend toward the diagnosis in younger, non-white, urban, and poorer respondents. Extensive psychiatric comorbidity and high use of mental health services are found in the borderline group. Estimates are also made at two other ECA sites, Washington University and UCLA. At these sites the prevalence is approximately 2.2 percent. Differences in demographic characteristics of borderline respondents across sites are discussed.

NR361 **Thursday, May 11, 12 noon-2:00 p.m.**

ASSESSING CHANGE IN PSYCHODYNAMIC PSYCHOTHERAPY

Marcia Goin, M.D., Psychiatry, USC, 1245 Wilshire Blvd #403, Los Angeles CA 90017; Gordon Strauss, M.D., Robert Martin, M.D.

Summary:

Clinicians who treat patients in psychodynamic psychotherapy are frequently skeptical of the applicability of psychotherapy research based on short-term modalities, especially when the outcome measures are largely instruments to assess changes in symptoms and behaviors. An obstacle to studying long = term psychotherapy is the absence of a change measurement for what therapists believe matters as much as symptoms: intrapsychic change. The McGlashan Semi-structured Interview (MSI) was developed for the Chestnut Lodge Follow-up Study. The 32 variables which are scored on a five = point scale are grouped into object relatedness, intergrative capacity, and fullness of experience. Different raters can reliably agree when independently scoring taped MSI interviews. To assess the utility of the MSI as a measure of change in psychotherapy it was administered to five patients before and after a year of weekly psychodynamic psychotherapy. Symptom severity and change were assessed with the Hopkins SCL-90. The MSI detected interesting areas of change in four of the five patients (improvement in three and worsening in one). In three cases the SCL-90 showed the same direction of change. One patient who did not have an elevated SCL-90 at the beginning of treatment showed improvement on the MSI but no change in the SCL-90. A fifth patient showed symptomatic improvement but no change in the MSI. The MSI appears promising as a change measure in psychodynamic psychotherapy reasearch.

NR362 **Thursday, May 11, 12 noon–2:00 p.m.**

INDICATIONS FOR AMBULATORY ALCOHOL DETOXICATION

Motoi Hayashida, M.D., Psychiatry, VA Med Ctr and Univ Penn, Univ and Woodland Avenues, Philadelphia, PA 19104; Arthur Alterman, M.D., Charles O'Brien, M.D., A. Thomas McLellan, Ph.D., Marian Droba, M.D., Karen Sweeney, P.A.

Summary:

Unnecessary use of the inpatient setting for alcohol detoxification is still done too often in the United States. This paper reexamines indications for ambulatory alcohol detoxification, based on the reported available data. In so doing, we will review the literature, beginning with the classic paper on the topic by Feldman A, et al (*Am J Psychiat,* 132:407-12, 1975). Not only the rationale for this procedure with its efficacy and safety, but also its costs will be reviewed. The National Association of Addiction Treatment Providers reports "Highest per diem charges (for inpatient treatment) are for admissions in which the patient receives detoxification treatment only." (p. 3, Analysis of Treatment for Alcoholism and Drug Dependency, 1987). Of a total of 9,915 admissions, 4,196, the largest group, received both detoxification and rehabilitation services, while less than five percent of the reported total outpatient treatment records of 611 received outpatient-detoxification. This paper will explore myths and misguided information surrounding ambulatory alcohol detoxification and proposes an urgent need for the standardization of the ambulatory detoxification procedures to maximize its utilization. There does not seem to be any good excuse now for us not to tap this effective, safe, cost-saving procedure when it is applicable.

NR363 **Thursday, May 11, 12 noon-2:00 p.m.**

SUBSTANCE USE BY PSYCHIATRY RESIDENTS

Patrick H. Hughes, M.D., Psychiatry, Univ of South Florida, 3500 E. Fletcher Ave Ste 424, Tampa FL 33613; Scott E. Conrad, M.D., Dewitt C. Baldwin, Jr., M.D., David V. Sheehan, M.D., Carla L. Storr, M.P.H.

Summary:

Recent studies have identified anesthesiolgists and psychiastrist as being at greater risk than other specialties for substance abuse. Data available neither pinpoint the career stage at which specialty specific drug use begins, nor adequately clarify the presence of specialty specific risk variables.

The authors addressed these questions in an anonymous mailed survey of 3,000 physicians in the Spring of 1987. Third = year residents were randomly drawn from the AMA masterfile to reflect their relative proportions in 13 specialties for 1987 training programs. The response rate was 60 percent (n = 1785). Psychiatry residents accounted for 5 percent of respondents (n = 89).

Compared to other specilties, psychiatry residents had the highest percentage reporting benzodiazepine use in the past year (27.3 percent) and past month (15.9 percent). They were most likely to report use of marijuana in the past year (34.1 percent) and past month (19.3 percent). They reported the highest percentage of daily use of 1/2 pack or more of cigarettes in the past year (9.1 percent). Daily drug use or heavy use patterns were not reported at this early stage in their careers.

Additional data on attitudes, drugs use history, and occupational stress will be compared for the 13 specialties to help explain the trends observed.

NR364 **Thursday, May 11, 12 noon–2:00 p.m.**

TRANSDERMAL CLONIDINE VERSUS CHLORDIAZEPOXIDE IN ACUTE ETOH WITHDRAWAL

Gregory R. Baumgartner, M.D., Psychiatry, University of SC, P.O. Box 202, Columbia, SC 29202; Randall C. Rowen, Pharm.D.

Summary:

A recent report in the literature suggested that oral clonidine may represent a new alternative agent for the management of acute alcohol withdrawal syndrome. However, no study has yet investigated the transdermal form of clonidine for this indication. In a double-blind trial, 50 male patients were randomly assigned to either transdermal clonidine or chlordiazepoxide. On study entry both groups were similar regarding demographics, alcohol withdrawal symptoms (AWS), histories of prior alcohol use, physical findings, and abnormal lab results associated with alcohol dependence. Once in significant withdrawal as measured by the AWS scale, the patients started on their respective medications and then had observations made every 12 hours. Study scales administered were the AWS, the Cognitive Capacity Screening Exam, the Brief Psychiatric Rating Scale, the Hamilton Depression Rating Scale, the Hamilton Anxiety Rating Scale,and subjective rating scales. Clonidine was well tolerated with no patient experiencing major adverse drug reactions or progressed to delirium tremens. Analysis of the study data demonstrated more favorable AWS scores, Cognitive Capacity Screening Exam scores, blood pressure, pulse, restlessness scores, and quality of sleep for clonidine over chlordiazepoxide. In all remaining dependent variables both groups scored equally well.

NR365 **Thursday, May11, 12 noon–2:00 p.m.**

INTENSIVE CASE MANAGEMENT FOR THE CHRONIC PUBLIC INEBRIATE I: IMPLEMENTATION

Mark L. Willenbring, M.D., Psychiatry, MPLS VA Medical Center, 1 Veterans Drive, Minneapolis, MN 55417; Joseph P. Whelan, Michael E. O'Neil, M.A., James O. Dahlquist, J.D.

Summary:

Intensive case management (ICM) has been shown to be an effective treatment for persons with severe and persistent mental illness (PMI). ICM is characterized by a small caseload (11-24), active outreach, and "street" orientation, and is driven by the needs of the client. Chronic public inebriates (CPI) share many characteristics of PMIs (persistent dysfunction, poor treatment response, stigmatization). Many of them have PMI as well. Therefore, ICM may be an effective community treatment for the CPI.

We are currently implementing a demonstration project, in which ICM is being compared with traditional case management and non-case management methods in three groups of CPIs randomly assigned. During the first six months, we have hired and trained staff, recruited 175 clients (half of whom are Native American), and begun community treatment. Alcoholism counselors hired for the project have needed intensive training and support. Project staff have encountered marked resistance among traditional alcoholism treatment staff within the agency, requiring clear administrative support for the project. In contrast, community response has been overwhelmingly positive.

In spite of these problems, preliminary outcome comparisons indicate a 15 percent reduction in detox utilization with ICM within the first three months. Our experience suggests that ICM for the CPI can be effectively implemented within an existing county service agency.

NR366 **Thursday, May 11, 12 noon–2:00 p.m.**

THE EFFECT OF ALCOHOLISM ON DEPRESSION IN MENTAL ILLNESSES

John Louks, Ph.D., Psychology, VA Domiciliary, White City, OR 97503; James Talone, Ph.D., James Smith, Ph.D., Carole Hayne, Ph.D.

Summary:

One hundred forty consecutive admissions to the Veterans Administration Domiciliary at White City, Oregon, were studied to establish the effect of alcoholism on depression in patients with various emotional disorders. Most patients were homeless prior to admission. Diagnosis was based on current formal mental status examinations, psychiatric hospital discharge summaries, and review of the medical record. Depressive severity was estimated by the Beck Depression Inventory. Twenty-four percent of the patients indexed suffered from a major mental illness, and 70 percent were alcoholic. Half of the patients seeking domiciliary care reported significant depressive symptoms when admitted, and 25 percent of the total reported severe depression using standard levels on the Beck Depression Inventory as the criterion. Depressive severity was independent of age, intelligence, cognitive impairment, education, and income. Alcoholism exacerbated depressive severity in patients with major mental illnesses to a much greater degree than it did in other diagnoses, and it should be considered a significant complicating factor in the treatment of the primary mental illness. Since these patients are often not appropriate for existing alcohol treatment programs, alternative approaches to sobriety maintenance must be considered in order to optimally stabilize their primary mental illness.

NR367 **Thursday, May 11, 12 noon–2:00 p.m.**

AN INNOVATIVE TREATMENT FOR COCAINE ADDICTION

James A. Halikas, M.D., Psychiatry, Univ Of Minnesota, Box 393 UMHC, 420 Delaware SE, Minneapolis, MN 55455; Kenneth D. Kemp, M.D.,Kenneth L. Kuhn, M.D., Gregory A. Carlson, Fred S. Crea

Summary:

As many as 60-100 percent of cocaine dependent patients relapse within the first 12 months no matter how high their motivation, because of overwhelming craving. We have developed a new pharmacologic approach, using carbamazepine as an adjunct to other standard rehabilitation efforts, in an attempt to maintain cocaine abstinence, in an open clinical trial. All patients offered carbamazepine to date had long histories of substance abuse (17.7 years), 6.1 mean years of cocaine use, and an average of 3.1 past drug treatment attempts. Eight patients refused it or took it only while inpatient. All eight are still active cocaine users. Seven patients reduced their frequency of cocaine use by two-thirds. Six other patients were clear successes with abstinence ranging from two to nine months (six total days of use in 546 days at risk of use). All of the subjects who took carbamazepine, whether intermittently or regularly, agreed that cocaine craving was significantly reduced, even while in high risk situations. Carbamazepine reverses cocaine-induced-kindling, the facilitation of focal neuronal firing induced by repeated pharmacologic exposure, in the animal research model. Data from this clinical trial through May will be summarized at the time of the presentation, including demographics, dosage, treatment issues, euphoria-blocking effects, and side effects.

NR368 **Thursday, May 11, 12 noon-2:00 p.m.**

SEROTONERGIC FUNCTION IN SUBGROUPS OF ALCOHOLICS

Laure B. Buydens-Branchey, M.D., Psychiatry, Bronx VA Medical Center, 130 West Kingsbridge Road, Bronx NY 10468; Marc Branchey, M.D.

Summary:

Recent studies have shown the existence of two forms of inherited alcoholism. One form, classified as type 2, was found to be highly heritable and to be characterized by alcohol seeking behavior early in life and by impulsive, risk-taking, and criminal behavior. Because alcohol seeking behavior and impulsive and aggressive tendencies are believed to be lined to a low central serotonin (5-HT), we wondered whether type 2 patients would also have an increased frequency and depressive and suicidal tendencies (which are also believed to be influenced by (5-HT) and whether a 5-HT deficit could be demonstrated in these patients. In a first study of 218 alcoholics, were observed that patients with type 2 characteristics (high incidence of paternal alcoholism, alcoholism onset before age 20, and high incidence of criminality) were also three times more likely to have a depressive episode and four times more likely to have attemped suicide than patients without these characterstics. We subsequently studied the tryptophan (TRY) ratio of a population of 112 alcoholics two weeks after their admission to a hospital. The TRY ratio is that of TRY over other amino acids competing with TRY for brain entry and has been shown to influence brain 5-HT. Significant associations between a low TRY ratio and depressive and aggressive tendencies were observed in type 2 patients only and not in the rest of the population. *In conclusion:* We observed that type 2 alcoholics who have been described as having problems in aggression control have more depressive episodes and attempt suicide more often. They appear to to be more susceptible to a decrease in the availablity of 5-HT precursor, TRY. The existence of a preexisting 5-HT deficit is hypothesized in these patients.

NR369 **Thursday, May11, 12 noon–2:00 p.m.**

BUPRENORPHINE TREATMENT OF COCAINE ABUSE

Thomas R. Kosten, M.D., Psychiatry, Yale University, 27 Sylvan Avenue, New Haven, CT 06519; Charles J. Morgan, M.D., Herbert D. Kleber, M.D.

Summary:

Intravenous cocaine abuse among opioid addicts has become a major public health problem that may be reduced by buprenorphine, an opioid mixed agonist antagonist. This open study compared cocaine abuse in buprenorphine (BUP) to methadone (METH) maintained patients using two designs: 1. cross-over and 2. case control. 1. In the cross-over, 12 METH patients at a mean METH dose of 47 (+/−8 mg PO) were switched over to BUP at a mean BUP dose of 3.8 (+/−0.6) mg SL for one month. On METH they had cocaine in 20 percent of their urines over the previous six months, but on BUP their cocaine positive urines dropped tenfold to two percent ($t = 2.8$, $P < 0.02$). 2. In the case control, 41 BUP (3.2 +/− 1.6 mg SL) were compared to 61 METH (43 +/− 8 mg PO) and 36 naltrexone (NLX) patients for the first month in treatment. The groups were comparable in age, sex, race, and number of urines per patient (mean = 8.4). Urines were positive for cocaine in 24 percent of the METH and in 3 percent of the BUP group ($t = 5.8$, $df = 71$, $P < 0.0001$), but overall illicit urines did not differ (33 percent METH vs. 37 percent BUP). The NLX patients showed no-difference from the BUP patients, but a significant difference from the METH patients in cocaine abuse (5 percent positive urines) ($F = 17.95$; $df = 2,137$; $P < 0.0001$). Thus, BUP and opioid antagonists in general may be a more effective treatment than METH for cocaine abusing opioid addicts.

NR370 **Thursday, May 11, 12 noon–2:00 p.m.**

NICOTINE WITHDRAWAL CESSATION BY FLUOXETINE

William E. Hapworth, M.D., Hapworth Centers, 250 West 57th Street, New York, NY 10019; Mada Hapworth, Ph.D.

Summary:

Nicotine addiction is a major public health problem. It is responsible for 325,000 deaths annually and affects 50,000,000 Americans. It has recently been compared to severity of addictions caused by heroin and cocaine by the Surgeon General's office. This addictive component is not fully understood but postulated to be the result of alterations in the brain's neurochemistry, specifically in the seronergic system. As such, abrupt discontinuation of nicotine exposure can leave profound physiological effects, "withdrawal," making abstinence difficult if not impossible. A full 80-85 percent of people relapse after stopping smoking. Our group studied the neurochemistry of nicotine addiction and its amelioration by fluoxetine, a potent serotonin re-uptake blocker. A cohort of chronic nicotine addicts had baseline rating scales, TRH, DST, Beta Endorphins, nicotine levels, as well as general chemistries collected while smoking, during withdrawal and eight weeks into recovery. Fluoxetine remarkably decreased effects almost immediately allowing abstinence in patients without which it would have been very difficult if not impossible. These clinical observations and laboratory data will be presented, suggesting that fluoxetine is an effective antismoking treatment and the biochemical profile of responders.

NR371 **Thursday, May 11, 12 noon-2:00 p.m.**

COGNITIVE DEFICITS ASSOCIATED WITH COCAINE ABUSE

Stephanie O'Malley, Ph.D., Psychiatry, Yale University, 285 Orchard Street, New Haven CT 06511; Frank H. Gawin, M.D., Robert Heaton, Ph.D., Herbert D. Kleber, M.D.

Summary:

Although case reports exists of cocaine-associated cerebral vasculitis and intercranial hemmorhage, the hypothesis that cocain may have less dramatic but more prevalent effects on neuropsychological functioning has not been adequately examined. To address this question, 25 cocaine abusers were compared with normals matched on age, education, sex, and race using the Halstead-Reitan battery and other tests. Potential cocain subjects were excluded if they met DSM-II-R criteria for abuse of any substance other than cocaine or marijuana, had significant neuro-medical risks, or a history of IV use. The cocaine abusers had used an average of 593 grams of cocaine over 48.3 months and had been abstinent 138 days. Multivariate analyses of variance revealed that the cocain abusers performed more poorly on measures of attenion ($p < .01$), learning and incidental memory ($p < .05$), simple motor skills ($p < .001$), and summary scores ($p < .05$). Severity of cocaine abuse correlated significantly with performance on serveral tests that discriminated cocaine abusers from normals. These findings suggest that chronic cocaine abuse is associated with cognitive impairment. Hypothesized mechanisms for these deficits include direct neurotoxin effect or multiple brain microinfarctions secondary to cocain induced hemodynamic changes.

NR372 **Thursday, May 11, 12 noon2:00 p.m.**

OPIATE WITHDRAWAL EFFECTS ON REGIONAL CEREBRAL BLOOD FLOW

John H. Krystal, M.D., Psychiatry, Yale University, CNRU 34 Park Street, New Haven CY 06508; Thomas R. Kosten, M.D., Scott W. Woods, M.D., John Seibyl, M.D., Lawrence H. Price, M.D., George Zubal, Paul Hoffer, M.D., Herbert D. Kleber, M.D., Dennis S. Charney, M.D.

Summary:

This study assessed regional cerebral blood flow (rCBF) alterations suggestive of changes in regional brain activity using Single Photon Emission Computerized Tomography (SPECT) imaging in opiate-dependent patients and opiate-naive healthy subjects at rest and during naloxone-precipated withdrawal. *METHODS:* Patients maintained on methadone (20-30mg./day) and opiate-naive healthy sujects participated in two SPECT scans separated by one day. On scan days patients received either placebo or naloxone O.8 mg., s.c. under randomized double-blind conditions. After symptoms emerged or within 15 min., withdrawl severity was rated and patients were administered 20 mCi or Tc-99m HM-PAO as an rCBF agent. Patients remained at rest in a light-and sound-attenuated room for an additonal five min., after which, oral clonidine was administered to suppress withdrawal. Approximately 45 minutes later, patients were imaged using a Strichman neuro-dedicated multicrystal camera. *RESULTS:* To date, data are only availabe on the first six opiate-dependent patients and reported findings must be considered preliminary. In these subject, naloxone elicited moderate to severe withdrawal. Most patients showed a decrease in frontal and parietal cortical rCBF and an increase in brainstem (pontine) and cingulate rCBF during opiate withdrawal. *COMMENTS:* Pontine activation and frontal inhibition are consistent with the effects of locus coeruleus stimulationon rCBF in animals. These preliminary data are consistent with neuroendocrine data implicating central noradrenergic systems in the human opiate withdrawal syndrome.

NR373 **Thursday, May 11, 12 noon–2:00 p.m.**

PSYCHOPATHOLOGICAL PROFILES IN EARLY SUBSTANCE USE

Welmoet B. van Kammen, Ph.D., Psychiatry, University of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213; Rolf Loeber, Ph.D., Magda Stouthamer, Ph.D.

Summary:

Little is known about the psychopathology of pre-adolescent children who engage in the use of "licit" and illicit drugs. In a randomly selected sample of first and fourth grade boys, who attended public school in an urban school district, self-reported substance use (alcohol, cigarettes, and marijuana) was compared with psychopathological profiles as reported by their mothers on the Child Behavioral Checklist. Non-users differed on these profiles from boys who had used a single substance and those who had reported the use of multiple substances. High scores on substance use was positively associated with delinquency, aggression, and school problems scales for both grades. For the first graders, the withdrawal scale was significantly elevated in the multiple users compared to the non-users. In the fourth graders, an increase in reporting of depression, obsessive behavior, and hyperactivity items by the mother was also related to increased levels of substance use. The results are be discussed in a developmental context of personality traits and other factors usually associated with substance use in adolescents.

NR374 **Thursday, May11, 12 noon–2:00 p.m.**

QUANTITATIVE DRUG DETOXIFICATION UTILIZING LOWER TOTAL DRUG DOSAGES

Steven L. Altchuler, M.D., Mayo Clinic, Dept. of Psychiatry, 200 First St., S.W., Rochester, MN 55905; Michael A. Palmen, M.D., S.C. Lin, M.D.

Summary:

Although the literature uniformly agrees upon the need to withdraw patients carefully from addictive medications, few authors provide any details beyond advising to do it slowly. We have developed a quantitative method that will provide a clinician with specific dosages. We have performed initial trials to see if this approach provided tapers that were clinically useful. Ten patients clinically dependent upon barbiturates, benzodiazepines, sedatives, or opiates were followed. Standard drug withdrawal regimens were calculated, as utilized in our inpatient chemical dependency unit, and then quantitative regimens of equal durations were calculated. The patients were then withdrawn using the quantitative taper. Of the ten patients, nine were successfully withdrawn without modification of the taper. One patient required readjustment of the regimen. The nine patients successfully withdrawn all used less total drugs than would a standard regimen (p 0.01, Sign Test). This approach provides a reproducible, quantitative mechanism for withdrawing patients from medication and uses less total drug than does standard technique. Further controlled studies will assess if this is consistently reproducible, and if a potentially shorter regimen can be utilized.

NR375 **Thursday, May11, 12 noon–2:00 p.m.**

PROLACTIN, COCAINE DEPENDENCE AND TREATMENT

Henry R. Kranzler, M.D., Psychiatry, Univ of CT Hlth Center, Farmington Avenue, Farmington, CT 06032; Dale J. Wallington, B.S.

Summary:

Discrepant findings concerning the association of hyperprolactinemia and chronic cocaine use led us to investigate the presence and clinical significance of elevated prolactin levels among 33 (20 male) cocaine-dependent inpatients. Thirty-nine percent of those tested had prolactin levels that exceeded the upper limit of the reference interval (0.5-13.5ng/m1), consistent with the results from a recent study by Mendelson and colleagues. Current craving for cocaine (measured using a 100mm analog scale) and average use during the month prior to admission ($\bar{X} = 35 \pm 27.2$g) were not correlated with prolactin levels ($\bar{X} = 12.8 \pm 6.28$ng/m1). However, a significantly greater proportion of patients with hyperprolactinemia (nine of 13) left treatment prematurely ($X2 = 7.81$, 1d.f, $p < .01$). An ANOVA with prolactin level (normal-elevated) as the group factor, and days of treatment completed as the dependent measure, approached significance ($p < .09$). One possible explanation for these findings is that the presence of a co-existent impulse-control disorder predisposes to prolactin elevation in response to chronic cocaine use. We will relate these findings to the role of serotonin both in the control of prolactin secretion and in impulse-control disorders.

NR376 **Thursday, May 11, 12 noon–2:00 p.m.**

ACUTE COCAINE REDUCES BRAIN GLUCOSE METABOLISM IN DRUG USERS

Nicola G. Cascella, M.D., Neuropharm. Addiction Res. Center, 4940 Eastern Avenue, Baltimore, MD 21224; Edythe D. London, Ph.D., Motoki Sano, M.D., Dean F. Wong, M.D., Ronald I. Herning, Ph.D., Jonathan M. Links, Ph.D.

Summary:

Cocaine (C) produces a variety of behavioral effects, including euphoria. However, an elucidation of which brain areas mediate its various effects is lacking. By using positron emission tomography (PET) and the radiotracer 2-[^{18}F]fluoro-2-deoxy-D-glucose (FDG), it is possible to map the *in vivo* cerebral metabolic responses and simultaneous drug effects on mood and feeling state in humans. The present study was initiated to identify brain areas which show altered rCMRglu associated with C-induced euphoria, and might thereby be implicated in this effect of C. The study used a double-blind, placebo-controlled, crossover design, and the effects of C on rCMRglu were assessed by the PET FDG method. Subjects for the study were men, 23-40 years of age, with a history of polydrug abuse. Administration of 40 mg C or placebo (P), i.v., on four separate days before and simultaneous to the PET study, indicated that C increased EEG beta activity and produced euphoria, as measured by standard questionnaires. The subjects underwent two FDG scans, with either C or P given simultaneously with FDG. In the first five subjects, C reduced global cerebral glucose utilization by 13 percent. Values of rCMRglu were reduced by up to 26 percent of P values. Decrements in most affected regions were 10-19 percent of P. Decrements in rCMRglu were seen whether metabolic rates were calculated by a single scan or full kinetic model. Some areas showed no statistically significant changes (hippocampus, parahippocampal gyrus, medial halmus, midbrain, pons, cerebellum). No C-induced induced increases were observed. The observed decreases in rCMRglu suggested that 40 mg C, i.v., a dose which induces euphoria, reduces cerebral oxidative metabolism and that this C-induced euphoria is associated with a reduction in telencephalic activity.

NR377 **Thursday, May 11, 12 noon-2:00 p.m.**

BUPRENORPHINE RESPONDERS: A DIAGNOSTIC SUBGROUP?

Richard B. Resnick, M.D., Psychiatry, New York University, 43 West 94th Street, New York NY 10025; Elaine Resnick, M.S.W., Marc Galanter, M.D.

Summary:

A two = year follow-up of heroin dependent subjects (N = 16) who entered a pilot trial of treatment with buprenorphine (a mixed agonist/antagonist) suggest that response to treatment may identify a subgroup of undertreated addicts whose levels of psychosocial functioning are intermediate between those for whom methadone (a pure agonist) or naltrexone (a pure antagonist) would be indicated. Buprenorphine's pharmacologic profile provides a missing link in opiate dependence treatment and makes it acceptable for many addicts who would not accept methadone maintenance or enter a therapeutic community and, consequently, are outside the current healthcare system. Eight of the 16 have been abstinent from heroin fo 26 to 32 months while receiving .03-3.6 mg/day buprenorphine and psychotherapy. Levels of psychosocial functioning (work, home, leisure) and global assessments of functioning are significantly higher for responders than for nonresponders ($p < .01$). Responders (mean age 34 yrs) had been heroin dependent for a mean of 9.5 years (range six to 17 yrs), all are self-supporting, four live with a nonaddicted spouse, five had no prior treatment and three had prior naltrexone treatment but discountinued it and relapsed. Nonresponders (mean age 30 yrs) had been herion dependent for a mean of 7.5 yrs (range two to 19 yrs.), six had no regular employment/income, all were single, and seven had no prior treatment. Dysthymia and personality disorders are prevalent in both groups, but antisocial personality was found in nonresponders only. A new formulation of buprenorphine needs to be developed for use in clinical trials to assess safety and efficacy, consisting 0.5 and 2.0 mg sublingual tablets. If this tablet were combined with naloxone, it would prevent diversion and unathorized i.v. use by opiate dependent individuals.

NR378 **Thursday, May11, 12 noon–2:00 p.m.**

THE ALCOHOLIC'S SENSITIVITY TO INTRAVENOUS DIAZEPAM

Bryon H. Adinoff, M.D., Psychiatry, Medical Univ of SC, VA Med Ctr, 109 Bee Street, Charleston, SC 29403; Daniel W. Hommer, M.D., Thomas Clem, Ph.D., Jeff Moran, Ph.D., Steven M. Paul, M.D., Markku Linnoila, M.D.

Summary:

A number of ethanol's neuropharmacological and behavioral properties appear to occur through an interaction at the GABA-benzodiazepine-chloride receptor complex (BZ receptor). It has been suggested than an altered sensitivity of the BZ receptor may be an etiologic factor in the development or progression of alcohol dependence. In order to explore alterations of the BZ receptor in alcoholics, we measured the effects of diazepam upon saccadic eye velocity in alcoholics. BZs have previously been demonstrated to reduce the peak velocity of horizontal saccades in a dose-dependent manner, and this effect is blocked by BZ receptor antagonists. Eight abstinent alcoholics (>four wks) and eight age-related controls were studied. Diazepam was given at serial doses of 4.4, 4.4, 8.8, 17, 35, and 70 ug/kg iv at 20 minute intervals. Subjects performed a saccadic tracking task within two to five minutes of receiving each dose. Saccadic eye velocity was determined for saccades of amplitudes ($\pm 3.5°$) of 7.5°, 15°, 22.5°, and 30°. Diazepam plasma levels and semantic and episodic memory tasks were obtained following each tracking task. There were no baseline differences between the two groups. Following infusion of diazepam, both groups demonstrated a similar dose-dependent decrease in saccadic eye velocity for all four saccade amplitudes ($p < 0.0001$). There was a dose-dependent impairment in episodic memory tasks and attention ($p < 0.001$), although there were no changes in semantic memory functioning. Memory tasks did not differ between alcoholics and controls in response to diazepam. Diazepam levels between groups did not differ. These results suggest that BZ receptor sensitivity is not altered in abstinent alcoholics.

NR379 **Thursday, May 11, 12 noon–2:00 p.m.**

ALCOHOL ABUSE IN A SCHIZOPHRENIC POPULATION

Cynthia Pristach, M.D., Psychiatry, SUNY at Buffalo, 462 Grider Street, Buffalo, NY 14215; Cedric M. Smith, M.D.

Summary:

Many schizophrenic patients are known to consume alcohol to excess, yet few systematic studies of alcohol abuse in this population have been done. Stable schizophrenia inpatients (n = 21) were given a detailed a interview focusing on changes in drinking behaviors and clinical course of the schizophrenic illness, a Beverage Survey, and a Self-Administered Alcoholism Screening Test (SAAST). SAAST scores ranged from two to 26 (mean = 11) and nearly half (ten, 48 percent) of these patients had a SAAST 10, indicating "probable alcoholism." All ten of these met DSM-III-R criteria for alcohol abuse or dependence determined independently by interview or chart review.

Analysis of data obtained from this initial sample revealed that alcohol abusing schizophrenics tended to have their first psychiatric admissions at an older age compared to nonalcohol abusing cohorts, yet they reported having first symptoms indicative of schizophrenia at a younger age. Alcohol abusers began drinking at a younger age, 14 years or less ($p = .02$), but they were not more likely to admit to polysubstance abuse. Alcohol abuse/dependence was more readily identified by the SAAST and by highly specific discriminating items than by the skilled interview. Analysis of SAAST items exhibited high internal reliability and consistency of responses. Alcohol abuse and dependence may be more common among schizophrenic patients than previously estimated; most of these patients probably can be identified with the SAAST.

NR380 **Thursday, May 11, 12 noon–2:00 p.m.**

TREATMENT GIVEN TO DUAL DIAGNOSED MEN ALCOHOLICS

Elizabeth J. Nickel, M.A., Psychiatry, Kansas Univ Med Center, 39th & Rainbow Blvd, Kansas City, KS 66103; Elizabeth Penick, Ph.D., Barbara J. Powell, Ph.D., Jan Campbell, M.D., Barry I. Liskow, M.D., Marsha R. Read, Ph.D.

Summary:

This "naturalistic," one-year follow-up study of 316, formerly hospitalized, male alcoholics examined the extent and kind of psychiatric/psychosocial treatments received by four groups of patients subtyped according to the presence of co-occurring psychiatric disorders as determined by the structured, DSM-III-compatible, Psychiatric Diagnostic Interview (PDI). The subtypes were: 1) alcoholism only, 2) alcoholism plus affective and/or anxiety disorder, 3) alcoholism plus drug abuse and/or antisocial personality, and 4) a mixed group with alcoholism plus affective/anxiety disorder as well as drug abuse/antisocial personality. Treatment histories differed significantly across the four groups, both before the intake hospitalization and during the 12-month follow up. Men in the alcohol-only subgroup were least likely to receive psychotropic medications, ECT or mental health treatments not exclusively related to their drinking. Men assigned to the mixed affective/anxiety disorder and drug/ASP subtype were most likely to have received these types of treatment. Drinking outcomes after one year appeared only slightly related to the kind or amount of treatment received during follow up, whereas improved psychosocial functioning was more strongly associated with non-alcohol-specific treatment effects, especially for those men with a co-occurring affective or anxiety disorder.

NR381 **Thursday, May 11, 12 noon–2:00 p.m.**

APOMORPHINE CHALLENGE IN COCAINE ABUSERS

Eric Hollander, M.D., Psychiatry, Columbia University, 722 West 168th Street, Box 13, New York, NY 10032; Edward Nunes, M.D., Concetta DeCaria, M.S., Steven Wager, M.D., Donald F. Klein, M.D., Frederic Quitken, M.D.

Summary:

There is indirect evidence that craving for cocaine is mediated by dopaminergic mechanisms. Acute pharmacological challenge with the dopamine agonist apomorphine was used to investigate behavioral and neuroendocrine indices of dopamine function in the "crash" and "craving" phases of the cocaine abuse cycle. Eight chronic cocaine abusing men received a single dose of apomorphine (0.75 mg SQ). Five subjects had last used cocaine three days or less prior to study and low baseline ratings of cocaine craving (crash phase). Three had last cocaine use greater than one week prior to study and high baseline cocaine craving (craving phase). There was no significant change in measures of continuous attention following apomorphine. There were substantial decreases in ratings of cocaine craving (−75 percent), anxiety (−66 percent), and depression (−63 percent) following apomorphine. Patients also felt tired.

There was a 403 percent rise in growth hormone (GH), and a 26 percent decrease in prolactin following apomorphine. This is consistent with a central dopaminergic effect. Correlations between behavioral changes and extent of neuroendocrine alterations reflective of central dopaminergic effect will be discussed. The dopamine model of cocaine abuse will be discussed in light of these findings.

NR382 **Thursday, May 11, 12 noon–2:00 p.m.**

FAMILY FUNCTION IN GIRLS WITH EATING DISORDERS

Regina C. Casper, M.D., Psychiatry, Michael Reese Hospital, Lake Shore Drive at 31st St., Chicago, IL 60616; Maryann V. Troiani, Psy.D.

Summary:

The current study compared family functioning in 17 adolescent patients (mean age 16.7 ± 1.5 years) treated for anorexia nervosa and bulimia nervosa to family functioning in 34 age- and sex-matched normal a adolescents (mean age 15.8 ± 1.0 years). Parents and their children completed the Family Assessment Measure (Skinner, 1983) which consists of an overall family functioning general scale, a dyadic relationship scale, a self-rating scale that assesses individual functioning, as well as an eating disorder screening scale. Results indicate that patients with the bulimic type of anorexia nervosa and their family members reported greater dissatisfaction in their family life and less satisfaction with their relationships than families of patients who had restricting anorexia nervosa or normal families. Families of restricting anorexia nervosa patients and normal families functioned equally well; anorectic restricting patients actually reported a higher level of positive family relationships than normal adolescents. Discrepancies among family members' ratings revealed bulimic anorexia nervosa or bulimia nervosa patients tend to view themselves and their families as more disturbed and dissatisfied than restricting anorectic patients or normal adolescents. The findings suggest type-specific patterns of family functioning for families who have children with restricting anorexia nervosa as opposed to those who have children with bulimic anorexia nervosa or bulimia nervosa. It is also conceivable that denial of conflict contributes to smoother functioning in families of restricting anorexia nervosa patients.

NR383 **Thursday, May 11, 12 noon-2:00 p.m.**

STEALING IN EATING DIORDERED PATIENTS

Dean D. Krahn, M.D., Psychiatry, University of Michigan, 1500 E. Med Ctr Dr 8D8806, Box 0116, Ann Arbor, MI 48109; Pamela Flegel, B.S., Karen K. Canum, R.N., Kenneth R. Castagna, M.S.W.

Summary:

Previous studies have documented a high incidence of stealing among patients with eating disorders. Stealing is especially frequent among patients with bulimic behavior. We reviewed the records of 181 consective patients evaluated at the University of Michigan Eating Disorders Program. The responses of patients with a history of stealing were compared to the responses of patients without a history of stealing on several instruments including the Diagnostic Survey for Eating Disorder (DSED), Eating Disorders Inventory (EDI). SCL-90, and Michigan Alcohol Screening Test (MAST). Fifty-one of 181 patients reported a history of stealing; 31 of 95 bulimia nervosa patients; 4 of 13 anorexia nervosa plus bulimia nervosa patients; 15 of 57 eating disorder not otherwise specified; and 1 of 16 restricting anorexia nervosa patients reported stealing. Patients with a history of stealing (even if not currently stealing) showed significantly elevated scores compared to nonstealers' scales of the SCL-90; significant increases in frequency of binges, laxative use, vomiting, and enema use ($p < .05$). Stealers were significantly more likely than nonstealers to binge in cars, at parties, and with others ($p < .05$), perhaps indicating a general lowering of social constraints in behavior. When only the bulimic patients' responses were analyzed, the bulimic patients with a history of stealing showed significantly more pathologic scores on many SCL-90 subscales including somatization, obsessive-compulsive, depression, anxiety, hostility, phobia, and psychopathy; increased scores on the interpersonal distrust scales; and increase frequency of binges and decreased frequency of normal meals. These results indicate that any history of stealing behavior in an eating disordered patients is an important marker for increased severity of overall psychopathology.

NR384 **Thursday, May 11, 12 noon–2:00 p.m.**

AXIS-II PERSONALITY DISORDERS IN WEIGHT CONTROL

William H. Berman, Ph.D., Psychiatry, Cornell Univ Med Center, 21 Bloomingdale Road, White Plains, NY 10605; Ellen Raynes, Ph.D., Steven Heymsfield, M.D., Margaret Fauci, R.N., Sigurd Ackerman, M.D.

Summary:

Early conceptualizations of obesity viewed the disorder as caused by a variety of neurotic disorders. Subsequent research using more appropriate control groups contradicted these findings, suggesting that obese people are no different from those with other chronic medical problems. However, the absence of a causal link between obesity and psychopathology has obscured the potentially significant role of psychopathology in weight control. Furthermore, only a few diagnostic studies used structured diagnostic interviews, and none have examined the prevalence of DSM-III-R personality disorders.

In the present study, a consecutive sample of 46 patients presenting to a major metropolitan weight control unit were given structured diagnostic interviews (SCID I and II). Twenty-two percent had a current and 18 percent had a past affective disorder, and 47 percent had mild to moderate personality disorders. Comorbidity was high, with 70 percent of those with an Axis I disorder having Axis II disorders. After eight weeks of diet, those patients with a personality disorder lost significantly more weight on a behavioral diet, but significantly less weight on a formula diet, compared to those with no personality disorder ($p<.001$). Axis I disorders were unrelated to weight loss.

These data suggest that there are differential responses to formula and behavioral diets depending on the personality structure of the patient. This has significant implications for intervention with these patients.

NR385 **Thursday, May 11, 12 noon-2:00 p.m.**

SEX ABUSE: ROLE IN EATING DISORDER

Vivian L. Folsom, M.S.S., Psychiatry, University of Michigan, 1500 E. Med Ctr Dr 8D8806, Box 0116, Ann Arbor, MI 48109; Dean D. Krahn, M.D., Karen K Canum, R.N., Laura Gold, Ph.D., Ken R. Silk, M.D.

Summary:

High rates of sexual abuse have been reported in eating disordered patients. Hypotheses linking sex abuse with the dissatisfaction with the adult female body displayed by these patients have been generated. However, no comparison of sexual abuse experiences in age-matched samples of female inpatients on an eating disorder unit (ED), female inpatients on a general psychiatry unit)GP), and females drawn from a normal population (NC) has been reported. We have begun a study comparing the responses of these three groups on the Finkelhor Sexual Life Events Questionnaire, the Eating Disorders Inventory, and the SCL-90. Subject anonymity was maintained. Preliminary data analysis showed that 24 of the first 32 (75%) ED subjects entered in the study reported sexual abuse experiences (defined as sex with someone at least six years older than subject when subject was less than 12 years old or nonconcensual sex after age 12). Ten of 16 (62.5%) GP subjects and six of 16 (37.5%) NC subjects reported sex abuse. Force or threat of force was used by the perpetrator of sexual abuse in 66% of ED's, 50% of GP's, and 19% of NC's. 47% of ED's, 44% of GP's, and 12.5% of NC's experienced intercourse as part of sexual abuse. Chi square analysis revealed significant ($p<.05$) departures observed from expected frequencies, probably due to the high frequencies of abuse in the patient groups. Body dissatisfaction as measured on the EDI was not different in abuse and nonabused ED patients. Thus, ED's experienced far more sexual abuse and sexual abuse of greater severity than did NC's; however, their experiences were similar to those of GP's. Data colection is continuing and analysis of a larger data base and comprehensive analysis of the psychometric data will be presented.

NR386 **Thursday, May 11, 12 noon-2:00 p.m.**

FLUOXETINE IN BULIMIA NERVOSA: DOUBLE BLIND STUDY

Gregory G. Enas, Ph. D., Eli Lilly and Company, Lilly Corporate Center 22/3, Indianapolis IN 46142; Harrison G. Pope, M.D., Louise R. Vevine, M.D., Fluoxentine Bulimic Collaborative Study Group

Summary:

Bulimia nervosa is a major public health problem in the United States. Although this disorder may respond to standard antidepressant medications, the efficacy of thse drugs is frequently limited by side effects. The novel antidepressant fluxetine represents a potentially effective, well-tolerated medication in bulimic patients.

We performed a double-blind trial of fluoxetine in 382 outpatient bulimic women, lasting eight weeks, comparing does of 60 mg daily, 20 mg daily, and placebo. At 60 mg per day, fluoxetine was significantly superior to placebo in decreasing the frequency of binge-eating and vomiting episodes ($p<.001$ for both measures at endpoint). Fluoxetine 20 mg per day proved intermediate between the 60 mg dose and placebo in efficacy. Many symptoms associated with bulimia nervosa, such as depression, pathological eating attitudes and behaviors, and carbohydrate craving, also improved significantly with fluoxetine. Adverse events were generally mild; the dropout rate due to adverse events in the fluoxetine groups (8.5% in the 60mg group and 3.5% in the 20 mg group) was not significantly different from that in the placebo group (6.2%).

In summary, fluoxetine appears to represent a useful addtion to the armamentarium of medications for bulimia nervosa.

NR387 **Thursday, May11, 12 noon–2:00 p.m.**

ZINC DEFICIENCY AND EATING DISORDERS

Laurie L. Humphries, M.D., Psychiatry, Univ of KY Medical Center, 820 South Limestone Annex 2, Lexington, KY 40536; Beverly S. Vivian, R.D., Mary A. Stuart, Ph.D., Craig J. McClain, M.D.

Summary:

Zinc (Zn) plays an integral role in appetite regulation, with Zn deficiency causing severe anorexia. Eating disorders and Zn deficiency have many of the same signs and symptoms. The purpose of this study was to evaluate the effects of Zn supplementation on Zn status in patients hospitalized with eating disorders. Thirteen patients with anorexia nervosa and 14 with bulimia were studied. Zn deficiency was defined as a serum Zn concentration of ≤ 70 μg/dl and/or a urine Zn excretion of ≤ 200 μg/24 h. Ten of 13 patients with anorexia and 8 of 14 patients with bulimia were Zn deficient on admission. Patients then were randomized to receive either 25 mg. of Zn acetate PO TID or placebo for the one-month study period. Serum and urine Zn increased in all patients randomized to Zn supplementation. In the bulimics receiving placebo, there was no major trend in either serum or urine Zn. However, in patients with anorexia nervosa receiving placebo, five out of seven patients had a further decrease in their 24-hour urinary Zn excretion, with all excreting <250 μg 24 h. These data strongly suggest that patients with anorexia nervosa undergoing vigorous refeeding should receive Zn supplementation because of the high risk of developing Zn deficiency during this period of anabolism and presumed increased Zn demands.

NR388 **Thursday, May11, 12 noon–2:00 p.m.**

TREATMENT COMPLIANCE OF OLDER PROBLEM DRINKERS

Roland M. Atkinson, M.D., Psychiatry, VA Medical Center, Portland, OR 97201; Robert L. Tolson, M.S.W.

Summary:

This is a five-year study of variables affecting retention of older problem drinkers in a VA outpatient alcoholism group counseling program designed exclusively to reduce stigma and improve compliance in this group. *Method*: 190 men age 55 years (mean = 62.4), with DSM-III alcohol use disorders but no coexisting mental disorders, agreed to abstain from alcohol and attend weekly groups for 12 months. Referral source (court, self, family, medical), selectively used additional treatments (initial residential treatment, spouse counseling), and 27 pretreatment patient characteristics (demographics, alcoholism history, MMPI scores) were assessed statistically for association with completion of the one-year outpatient program. *Results*: Referral and treatment variables were more strongly associated with outpatient program completion than patient characteristics, especially referral source (X^2 $p = .0003$) and spouse counseling (X^2 $p = .0012$). Court referrals (after drunk driving offenses) had a higher completion rate than others. Spouse counseling substantially increased completion rates in court, family and medical referral groups. Initial residential treatment was associated with increased outpatient completion only for self and family referrals (X^2 $p = .0132$). The patient characteristic most strongly associated with completion (ANOVA $p = .0105$) was age at onset of the first alcohol-related problem (the later the better). *Comment*: This study is the first to report data on multiple factors influencing alcoholism treatment compliance in this age group. Implications of the findings for program design are discussed.

NR389 **Thursday, May 11, 12 noon-2:00 p.m.**

EATING BEHAVIORS DURING THE MENSTRUAL CYCLE

Martha Fankhauser, M.S., Psychiatry, College of Medicine, University of Arizona, Tucson AZ 85724; Rebecca Potter, M.D., Catherine Shisslak, Ph.D., Pamela Fox, Pharm. D.

Summary:

Several studies have reported premenstrual changes in eating behavior and attitudes in women with premenstrual syndrome (PMS). This study compared premenstrual and postmenstrual scores of four scales (Eating attitude Test (EAT), Bulimic Investigatory Test-Edinburg (BITE), Eating Disorders Inventory (EDI), and Daily Rating Form (DRF)), in 28 subjects with a dignosis of PMS and in 24 normal controls for three menstrual cycles. At t-test of pre-and post-menstrual scores for the PMS and non-PMS group was used for data analysis. A p value of < 0.05 was considered significant. The PMS and non-PMS groups did not score significantly different from normal controls on the EAT and BITE scales. The total EDI score and two of the subscales were significantly higher in the PMS group, but the subscales reflecting anorexia and bulimia were not significantly different from normal controls. The PMS group has significantly higher DRF premenstrual ratings for increase in appetite in comparison to the non-PMS group. Our results indicate that women with PMS may have a significant increase in their appetite premenstrually (i.e., eat more and crave certain foods) but do not demonstrate anorexic or bulimic behaviors or attitudes that are found in eating disorder patients.

NR390 **Thursday, May 11, 12 noon–2:00 p.m.**

EATING DISORDERS IN THE PSYCHIATRIC EMERGENCY ROOM

Aimee S. Johnson, M.D., Psychiatry, Univ of Cincinnati, M. 539 UC Medical Center, Cincinnati, OH 45267; James R. Hillard, M.D.

Summary:

The purpose of this study was to assess the prevalence of eating disorders in an urban psychiatric emergency service (PES). Eating disorders, which are seldom diagnosed in the psychiatric emergency service setting have most commonly been diagnosed and treated in white, middle to upper socioecomomic class individuals a group not representative of the typical PES population. A random sample of 143 patients from a centralized PES with a catchment area of 1,000,000 was studied. A two-stage interview was conducted; first, a two-item screening questionaire, with those qualifying receiving a structured interview for diagnosis of DSM-III-R eating disorders. Active bingeing was reported by 14.5 percent of males and 22.4 percent of females. No cases of current anorexia nervosa were discovered. Three percent of females and 9.2 percent of males were diagnosed as having atypical eating disorder. Race and marital status were unrelated to bingeing or to any eating disorder diagnosis. In many cases, the abnormal eating behavior reported had never before been discussed with a mental health professional. This study implies that evaluation for eating disorders should routinely be included in PES evaluations so that these individuals can be diagnosed and referred for appropriate treatment.

NR391 **Thursday, May 11, 12 noon–2:00 p.m.**

SEROTONIN: A TRAIT DISTURBANCE IN ANOREXIA NERVOSA?

Walter H. Kaye, M.D., Psychiatry, Univ Of Pittsburgh, 3811 O'Hara Street RM E 725, Pittsburgh, PA 15213; Harry E. Gwirtsman, M.D., Michael H. Ebert, M.D.

Summary:

Anorexia nervosa is characterized by the marked diminution of food intake in the obsessive pursuit of thinness, a stereotypic rigidity and perfectionism, and frequent mood and euroendocrine disturbances. The possibility of a serotonergic disturbance is of interest since central nervous system serotonin pathways contribute to the modulation of appetite, anxious and obsessive traits, mood, and neuroendocrine function. The study of acutely ill anorexics is confounded by the probability that serotonin activity is altered by malnutrition. Thus, we studied anorexic subjects who were once underweight with anorexia nervosa ($<$75 percent average body weight in the past), but had been refed and had maintained a stable *normal* weight for a mean of 30 months.

Compared to controls ($n = 15$), anorexics that were long-term weight normalized ($n = 17$) had significantly ($p<.05$) elevated levels of CSF 5-HIAA, the major serotonin metabolite suggestive of an increase of serotonin activity. Increased serotonin activity decreases food consumption. Thus, increased serotonin activity may contribute to food refusal and weight loss. It is of much interest that considerable data suggest that altered serotonin activity contributes to the pathogenesis of obsessive-compulsive disorder since anorexics frequently have obsessive behavior. This study raises the possibility that increased sertonergic activity contributes to the characteristic symptom complex of anorexia nervosa.

NR392 **Thursday, May 11, 12 noon-2:00 p.m.**

DIETING AND BULIMIA: A CONTINUUM OF BEHAVIORS

Adam Drewnoski, Ph.D., Psychiatry, Univ Michigan, 1420 Washington Heights M5170, Ann Arbor MI 48109; Doris K. Yee, M.A., Dean D. Krahn, M.D.

Summary:

The prevalence of bulimia nervosa among female students has been estimated at between 1%, and 3%. However, the dichotomous DSM-III-R diagnostic criteria can provide no indication of how many additional women engage in bulimic behaviors, or can be considered at risk for developing an eating disorder. A continuous scale might better assess the extent of pathological efforts at weight control and their changes over time. Our longitudinal study analyzed diet strategies of 908 freshman women for the presence and frequency of binge eating and such dieting strategies as skipping meals, avoiding sugars and fats, use of diet pills, laxatives or diuretics, fasting, and vomiting. Application of criteria based on the frequency of bingeing and increasing severity of dieting produced a continuum of five mutually exclusive categories. Respondents were difined as no-dieters (14% of total sample), casual dieters (41%), intense dieters (32%), dieters at risk (10%) and pathological dieters, i.e. cases of bulimia nervosa (3%). The severity of dieting increased with body weight, body mass index and the magnitude of desired weight loss. In a follow-up survey conducted six months later (n = 708), the categories were; non-dieters (18%), casual dieters (44%), intense dieters (26%), dieters at risk (9%) and bulimics (3%). Analyses of changes in dieting behaviors over time were based on 599 women who responded to both phases of the survey: shifts in status occurred mostly between adjoining categories. New cases of bulimia were drawn exclusively from the intense and at-risk dieters. A category scale of dieting pathology provides an estimate of subclinical or "atypical" eating disorders in the population, and can provide an improved means of tracking the time course of the disease.

NR393 **Thursday, May 11, 12 noon-2:00 p.m.**

ENDOCRINE EFFECTS OF CORTISOL BLOCKADE IN ANOREXIA

Harry A. Brandt, M.D., DIRP/CNE, NIMH Bldg 10 3S231, 9000 Rockville Pike, Bethesda MD 20892; Mitchel A. Kling, M.D., Mark A. Demitrack, M.D., Harvey J. Whitfield, Jr. M.D., Margaret Altemus, M.D., Philip W. Gold, M.D.

Summary:

We previously advanced data suggesting that hypercortisolism in anorexia nervosa (AN) reflects hypersecretion of corticotropin releasing hormone (CRH). Specifically, we have noted the CSF CRH levels are elevated in underweight anorexic subjects show a significant attenuation in ACTH responses to exogenous CRH, indicative of a pituitary corticotroph cell normally responsive to glucocorticoid negative feedback. Surprisingly, these blunted ACTH responses to CRH persist despite resolution of hypercortisolism in patients studied after the short-term correction of the weight loss. To further elucidate the mechanism involved in the hypercotisolism of AN, we report here a study of the plasma ACTH responses to the administration of the competitive glucocorticoid antagonist RU 486.

An oral dose of RU 486 (10mg/kg) or placebo was administered at 0800 h on separate days to seven patients meeting DSM-III-R criteria for anorexia nervosa and nine healthy volunteers. Six anorexic patients were restudied following short-term correction of weight. Blood samples were collected at 10 min intervals between 0400-0800 h (20-24) following dosing. Plasma ACTH was measured by radioimmunoassay.

In underweight anorexics the increment in plasma ACTH responses to RU 486 is higher than controls. When underweight patients were restudied during the short-term recovered phase, they not only lost this exaggerated responsiveness, but in fact failed to show any ACTH increments following RU 486 administration.

These data support the hypothesis that hypercortisolism in underweight anorexics reflects hypersecretion of hypothalamic CRH in that previous data have shown that RU 486 disinhibits the pituitary-adrenal axis only during periods of active functioning of the hypothalamic CRH neruon. The failure of the short-term recovered patients to respond with an ACTH rise following drug administration suggests that the CRH receptor on the pituitary corticotroph cell may be down regulated as a consequence of longstanding hypersecretion of endogenous CRH. Finally, these data indicate that glucocorticoid resistance is not likely to be of significant magnitude in underweight patients, in light of their responsivity to a glucocorticoid receptor antagonist.

NR394 **Thursday, May 11, 12 noon-2:00 p.m.**

LINKAGE STUDIES OF PANIC DISORDER

Raymond R. Crowe, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City IA 52242; Russell Noyes, M.D., Robert Wesner, M.D., Stephen Samuelson, M.D., Rickey Wilson, M.D.

Summary:

We examined linkage between panic disorder and the alpha-haptoglobin (HP) locus in 10 multiplex families of panic disorder in order to test a preliminary finding suggesting linkage between the two. Linkage could be excluded up to six centimorgans (recombination fraction 0.06) from the HP locus. Both the previous set of 26 pedigrees and the present set of 10 were tested for within-group heterogeneity, and no evidence of this was found. However, statistically significant heterogeneity was present between the first and second set of pedigrees ($p<.05$). No clinical evidence of heterogeneity was found between the probands of the two groups of pedigrees. Since linkage analyses are dependent upon assumptions about the genetic model at the disease locus, the data were analyzed under a variety of genetic models and close linkage was excluded by all but one. Taken as a whole, the present evidence does not provide strong support for a disease gene for panic disorder linked to the alpha-haptoglobin locus on chromosome 16q22.

NR395 **Thursday, May 11, 12 noon–2:00 p.m.**

BONE DENSITY IN ANOREXIA AND BULIMIA NERVOSA

Michael Newman, M.D., Psychiatry, Fair Oaks Hospital, 19 Prospect Street, Summit, NJ 07901; Katherine Halmi, M.D.

Summary:

The goals of this study were to assess bone density in patients with anorexia nervosa (AN) normal weight bulimia (B) and in controls, and to examine the relationship between bone mineral density and cortisol and estrogen levels in eating disorder patients. Dual photon absorptiometry was used to determine bone mineral density in 18 anorectics, 12 normal weight bulimics and 12 control subjects. Twenty-four hour urinary free cortisol (UFC) and serum estroadiol were measured in the two patient groups. Results showed that vertebral bone mineral density of the anorectics was significantly diminished compared with controls ($.96 \pm .04 gm/cm^2$ vs $1.13 \pm .03$ gm/cm^2;$p<02$) and narrowly missed being significantly less than that of bulimics (bulimics $1.07 \pm .06$ gm/cm^2; $p<.07$). No significant difference in serum estradiol was found between the two patient populations (AN $11.8 \pm 16.5 ng/d1$ vs B $18.1 \pm 24.9 ng/d1$; $t = 1.73$, $p<.23$). Anorectics had significantly higher values of UFC ($127.4 \pm 53.$&mcg/24h vs $78.9 mcg \pm 43.6 mcg/24h$). Patients of both groups who had elevated UFC were significantly more likely to have bone mineral density values that placed them at risk for a pathological fracture than those with normal UFC values. In summary, elevated UFC in eating disorder patients is likely to be an additional. independent factor contributing to osteoporosis. Normal weight amenorrheic bulimic patients do not have diminished bone mineral density.

NR396 **Thursday, May 11, 12 noon-2:00 p.m.**

OPIOIDS AFFECT TASTE PREFERENCES FOR SUGAR AND FAT

Adam Drewnowski, Ph.D., Psychiatry, Univ of Michigan, 1420 Washington HTS, M-5170, Ann Arbor MI 48109; Blake Gosnell, Ph.D., Dean D. Krahn, M.D., Karen Canum, R.N.

Summary:

Eating binges involving sweet desserts are sometimes thought to be caused by "carbohydrate craving" and a deficiency of a central neurotransmitter, serotonin. However, sweet such as chocolate or ice cream are in reality mixtures of sugar and fat nutrients whose intake has been linked in some animal studies to the endogenous opioid peptide system. To test the hypothesis that human appetite for sweet, high-fat foods is influenced by opiods, we infused nine normal-weight female volunteers (mean age 31.4 yrs; weight 140.7 lbs) with the opioid agonist butorphanol tartrate (1 ug/kg bolus); opioid antagonist naloxone (6 mg bolus followed by 0.1 mg/kg/hr IV drip for 2.5 hrs), or saline placebo. The study followed a double-blind, within-subjects design with drugs presented at least one day apart and in a random order. Taste stimuli presented for sensory and hedonic evaluations were 20 different mixtures of milk (3% fat), half and half (10% fat), light cream (20% fat) and heavy cream (37% fat), each sweetened with 0, 5, 10, 20, 0r 40% sucrose wt/wt. The stimuli, presented chilled to 5 C were offered twice: during pretreatment baseline and one hour following drug infusions. Preference ratings were elevated following butorphanol and reduced following naloxone infusions relative to baseline and relative to saline control. Repeated measures ANOVA showed no effect of drug on baseline score but a main drugs effect posttreatment, $F(2,16) = 6.18$; p 0.01. Perception of sweetness intensity was not affected by drugs. Total intake of chocolate or cookies was not affected by butorphanol, but was reduced by naloxone: the drop in fat calories (59%) was significant. Endogenous opoid peptides may be involved in reported uncontrollable cravings for highly palatable foods. [Supported by NIDA Grant DA05471.]

NR397 **Thursday, May 11, 12 noon–2:00 p.m.**

FAMILY INTERACTIONS IN BULIMIA NERVOSA

D. Blake Woodside, M.D., EDC CW1-311, Toronto General Hospital, 200 Elizabeth Street, Toronto, ON, Canada, M5G 2C4; Lorie F. Shekter-Wolfson, M.S.W., Marion P. Olmsted, M.A.

Summary:

Families have been held to be important precipitating and perpetuating factors in Bulimia Nervosa (BN). Most studies of family interactions in BN have been based on reports from patients only, and have often also been uncontrolled. The effect of chaotic eating on family functioning has not been assessed. The present study reports on family functioning of 95 families of patients with BN (n = 41) and BN with a history of Anorexia Nervosa (AN) (BNhAN, n = 54) using the Family Assessment Measure (FAM) before and after day hospital treatment(DHP) for BN. The FAM was administered to the patient and both parents both before and after DHP. FAM results are reported in terms of transformed scores derived from comparison to a control group of 470 normal families. Patients initially rated their families as distressed while parents did not. Patients also rated themselves within the family as problematic, whereas parents did not rate themselves as problematic. BNhAN patients rated their relationships with their mothers worse than BN patients on the dimension of Communication ($p < .05$). Parents of BNhAN patients rated their relationships with their daughters as more problematic than parents of BN patients on all dimensions ($p < .05$). Post DHP, patient ratings of family functioning as a whole and of themselves had significantly improved on all dimensions ($p < .05$), as had parental ratings of BNhAN children ($p < .05$). No ratings of family functioning were worse post DHP. These results point to a very significant effect of chaotic eating on family functioning, more pronounced for families of BNhAN patients, which largely returns to normal upon restoration of normal eating. We have undertaken a long-term follow-up study to determine whether these changes persist.

NR398 **Thursday, May 11, 12 noon–2:00 p.m.**

CONCOMITANT DISORDERS IN CHILDHOOD DEPRESSION

Carroll W. Hughes, Ph.D., Psychiatry, Univ Of Kansas Sch Med, 1010 N. Kansas Avenue, Wichita, KS 67214; Sheldon H. Preskorn, M.D., Elizabeth Weller, M.D., Ronald Weller, M.D., Ruth Hassanein, Ph.D.

Summary:

In our original inpatient double-blind study of imipramine vs. placebo response in children with major depression, the majority of the children met criteria for concomitant disorders. These included: conduct, oppositional, anxiety, and elimination disorders. Although all of these children met DSM-III-R criteria for major depression based on inpatient structured diagnostic assessment, the question remained, did the depression of these children with different concomitant diagnoses somehow differ and could these differences be measured? *Subjects and Method*: To test for differences in presenting symptomatology the data from the structured assessments (e.g., DICA, CDRS, CDI) of the children from the above study (n = 31) were divided into three groups and then analyzed: 1) depression, 2) depression plus conduct and oppositional disorder, 3) depression plus anxiety and/or elimination disorder. *Results*: Our preliminary findings indicate that there are differences in presenting depression symptomatology among the groups: depressed children without concomitant disorders are more hypoactive (indicated by three independent measures), more likely to have vegetative symptoms, and score higher on overall ratings of depression (CDRS). The parental psychiatric history for each of these groups is differentially loaded. Likewise, the drug response was significantly better in the depressed without concomitant disorder group (by contrast this group had the lowest placebo response rate).

NR399 **Thursday, May 11, 12 noon-2:00 p.m.**

SEPARATION ANXIETY DISORDER IN PEDIATRIC PRIMARY CARE

Jose L. Ayuso-Gutierrez, M.D., Psychiatry, San Carlos Hospital, Isaac Peral SN, Madrid 28040, Spain; Jose L. Ayuso-Mateos, M.D., Maria T. Alonso, M.D., Nuria Perez de Lucas, M.D., Olvido Latorre, M.D.

Summary:

The study of the presence of DSM-III-R Axis I disorders in pediatric primary care practice has recently been the subject of several publications. It seems that doctors who treat these patients detect only a very small percentage of the cases of childhood psychiatric problems identified by child psychiatrists. Childhood separation anxiety has been linked to the development of anxiety disorders in adults, particulary panic disorder. To evaluate the significance of this relationship, we consider the study of the true prevalence of this disorder in the general population to be fundamental. We carried out a study to detect it in patients of a walk-in pediatric clinic at a suburban Madrid primary care center. We developed a semi-structured interview according to DSM-III-R diagnostic criteria. The attending physician carried out the interview with the patients and their parents, and later noted sociodemographic data, the reason for the visit, the number of visits during the previous six months, record of scholastic failure, enuresis and previous psychiatric or psychological treatments. Inter-rater reliability was assessed with test-retest procedures. All patients under 18 years old who visited the clinic during the period of the study were eligible. We presented the preliminary results of the work with data on 100 patients. Separation anxiety was detected in 14% of the sample. We also anlyze the relationship between the presence of separation anxiety and the other variables studied.

NR400 **Thursday, May 11, 12 noon–2:00 p.m.**

DESIGNING A CHILDREN'S PSYCHIATRIC FACILITY

Mardelle M. Shepley, D.Arch., Design Partnership, 375 Freemont Street Ste 200, San Francisco, CA 94105; John Boerger, B.Arch.

Summary:

A pilot study was done at a California hospital in which the relationship between behavioral incidents and environmental locale was examined. Hospital "special incident" reports (373) were reviewed for types of reported behavior and locations of incidents over a one-year period. Behaviors covered included AWOL's, aggressive acts toward staff and peers, alleged client abuse, self abuse, sexual abuse, sexual incidents and suicide attempts. Locations correlated with these behaviors included bathrooms, bedrooms, dormitories, lounges, corridors, courtyards, entry ways and other spaces contained within the existing facility. It was found that areas where "ownership" is ambiguous (corridors, entries and dormitories) are the principal sites of behavioral incidents such as accidents, aggression and suicide. Designs for new facilities should avoid areas of unspecified ownership. The conclusions of the study were combined with other data gathered during the programming/research process (including interviews with staff and patients as well as graphic designs by patients) and a new facility was designed. A post-occupancy evaluation of the facility (due to be completed in early 1990) will evaluate the new design's effectiveness. Further research will also include other facilities and an expansion of the data base over a longer period of time.

NR401 **Thursday, May 11, 12 noon–2:00 p.m.**

CHILDREN'S INTERVIEW FOR PSYCHIATRIC SYNDROMES: A VALIDITY STUDY

Marijo Teare, M.A., Psychiatry, Ohio State University, 473 W 12th Ave 245 Upham Hall, Columbus, OH 43210; Elizabeth Weller, M.D., Ronald A. Weller, M.D., Mary A. Fristad, Ph.D.

Summary:

Children's Interview for Psychiatric Syndromes (ChIPS) is a newly developed structured interview with numerous potential advantages over previously available interviews (e.g., brief to administer [30-45 min]; easily scored; adheres to DSM-III criteria; simple, concise terminology). The current study: 1) compared level of agreement for syndrome and symptom endorsement between ChIPS and Diagnostic Interview for Children & Adolescents (DICA); 2) assessed level of agreement on syndromes between the two interviews and the psychiatrist's diagnosis; 3) investigated whether response bias (i.e., one instrument elicits more "yes" responses than the other) was present. Forty-two consecutive admissions to a child psychiatry unit aged 6-14 were administered the two instruments according to a Latin square design to account for potential interviewer and order effects. All subjects were independently diagnosed using DSM-III criteria by a board certified child psychiatrist blind to interview data. Phi coefficients were calculated for 13 of 17 syndromes compared between ChIPS and DICA (in four cases phi could not be computed because no daignoses were made on one or both instruments). For 10 of 13 syndromes, agreement was significant ($p<.05$; phi coefficient range = .33-.69). Agreement on presence/absence for all 17 diagnoses ranged from 62 percent to 100 percent. Agreement with the psychiatrist's diagnosis was 75 percent for ChIPS and 53 percent for DICA. Item agreement ($p<.05$) occurred for 45 percent of 126 questions compared. No overall response bias was detected; however, ChIPS was significantly more likely to diagnose Attention Deficit Disorder (ADD) and Overanxious Disorder. In conclusion, ChIPS and the DICA provide comparable data, with ChIPS being more likely to agree with the clinician's diagnosis. Studies are underway on a revised ChIPS meeting DSM-III-R criteria.

NR402 **Thursday, May 11, 12 noon-2:00 p.m.**

A FAMILY STUDY OF SOCIAL PHOBIA: PRELIMINARY REPORT

Abby J. Fyer, M.D., Psychiatry, NY State Psych Inst., 722 West 168th Street Box 82, New York NY 10032; Salvatore Mannuzza, Ph.D., Lynn Y. Martin, M.S., Mark Gallops, M. Phil., Donald F. Klein, M.D.

Summary:

Social phobia is a common and chronic illness of unknow etiology. Currently considered a separate disorder, it has historically been clasified with both agoraphobia and/or other specific phobias. Family studies can provide information about both the contribution of intergenerational transmission to psychiatric disorders as well as their distinctness and overlap. In this report we present preliminary data from a blind, direct-interview family study contrasting psychopathology among first-degree relatives of patients with DSM-III-R (1985) social phobia (N = 70) to that among relatives of normal (never mentally ill, N = 145) and psychiatric (agorphobia with panic, N = 79) controls. Two questions are addressed: 1) Is social phobia familial? and 2) To what extend is it distinct from agoraphobia?

Results: Significant between group differences for risk for DSM-III-R (1985) anxiety and affective disorders were not found. However the risk for social phobia among relatives of social phobia (SP) probands was twice as high as the among relatives of normal (NC) and agoraphobia (AGP) probands (13% vs 5% vs 6%). In contrast, the risk for panic disorder, agoraphobia with panic and generalized anxiety disorder were increased among relatives of AGP probands compared to the relatives of the remaining two groups. Significantly higher risk for RDC alcohol abuse was found among relatives of both patient groups compared to normal controls.

NR403 **Thursday, May 11, 12 noon–2:00 p.m.**

CLONAZEPAM IN PANIC DISORDER

Linda Beauclair, M.D., Psychiatry, Allan Memorial, 1025 Pine Avenue West, Montreal, Quebec, Canada H3A 1A1; Rejean Fontaine, M.D., Lawrence Annable, B.Sc., Guy Chouinard, M.D., Naomi Holobow, Ph.D.

Summary:

Recent studies have suggested that benzodiazepines, such as clonazepam and alprazolam, are effective in the treatment of panic disorder. Clonazepam has the advantage over alprazolam that, upon cessation, there is less risk of withdrawal symptoms. We carried out a double-blind, controlled clinical trial to assess the efficacy of clonazepam against placebo in the treatment of patients with recurrent panic attacks. *Method.* Following a one-week washout period, 22 patients with a DSM-III diagnosis of panic disorder or agoraphobia with panic attacks were randomly assigned to four weeks of treatment with clonazepam or placebo under double-blind conditions. The patients were assessed by the psychiatrist at weekly intervals on a Panic Attack Index, a Clinical Global Impression of Panic Scale, and the Hamilton Anxiety Rating Scale, and the patients completed the SCL-90. Plasma levels of clonazepam were measured weekly. *Results.* The endpoint total and factor scores of the rating scales were submitted to analysis of covariance with baseline scores as covariate. Clonazepam was found to be superior ($p<.05$) to placebo on each of the rating scales, and there was a significant correlation ($r = .64$) between plasma concentration and reduction in panic attacks. *Discussion.* Clonazepam appears to be an effective treatment for panic disorder and could be an alternative to alprazolam and imipramine. The most likely mechanism of action of clonazepam is enhancement of GABAergic transmission through its effect on benzodiazepine receptors.

NR404 **Thursday, May 11, 12 noon–2:00 p.m.**

CROSS CULTURAL DIFFERENCES IN PANIC DISORDER

Heinz Katschnig, M.D., Psychiatry, University of Vienna, Waehringer Guertel 18-20, Vienna A 01090, Austria; Gerald L. Klerman, M.D., Raimund Buller, M.D., Joseph A. Deltito, M.D., Philip W. Lavori, Ph.D., Michaela Amering, M.D.

Summary:

Recent epidemiological surveys of English, Spanish, Italian and German speaking populations report that panic attacks and panic disorder occur in different cultural settings. Little, however, is known about possible cross-cultural variations in psychopathological presentation. Clinical data from 1,168 DSM-III-R panic disorder patients from 14 countries (USA, Canada, Mexico, Colombia, Brazil, Sweden, Denmark, UK, Germany, Austria, Belgium, Italy, Spain, France) were analyzed with respect to cross-cultural differences. Symptoms such as "choking or smothering sensations," "fear of dying" and "paresthesias" were more frequent in southern (75 percent) than in northern (52 percent) countries ($P<.001$). These north/south differences are especially marked for North/Latin America. In contrast, agoraphobia was significantly ($P<.001$) more common in northern (84 percent) than in southern countries (69 percent), even more so when North America (90 percent) and Latin America (65 percent) were compared. European/American differences were less pronounced, with the notable exception that "fear of going crazy" and "derealization/depersonalization" were more common in America than in Europe, especially when comparing North America (73 percent) with northern Europe (49 percent; $P<.001$). These and similar results suggest that, while panic disorder is a universal phenomenon, cultural influences, including help-seeking behavior, determine its specific phenomenology in individual clinical and cultural settings. This phenomenon should be considered when comparing results from panic disorder studies in different countries.

NR405 **Thursday, May 11, 12 noon-2:00 p.m.**

CHILDHOOD ABUSE AND LIMBIC SYSTEM DYSFUNCTION

Martin H. Teicher, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont MA 02178; Carol Glod, M.S., Chester Swett, Jr., M.D., Janet Surrey, Ph.D., Catherine Brasher, B.S.

Summary:

Physical and sexual abuse may be significant factors in determining the severity of psychiatric illness. We hypothesized that abuse during early development may alter adrenocorticoid levels, affecting limbic system maturation, resulting in significant neuropsychiatric sequelae. A self-report questionnaire (LSCL-33) was developed to determine the frequency with which 250 outpatients experienced 33 symptoms suggestive of limbic dysfunction (e.g., depersonalization, derealization, memory lapses, deja vu, olfactory hallucinations). This was compared with data on the prior sexual and physical abuse history of the subjects. patients with a history of early abuse had significantly higher limbic system dysfunction ratings in all categories (somatic, senory, behavioral, and mnemenic). Those with both physical and sexual abuse histories had scores 113% greater than those of nonabused patients ($t=6.45$ $p<.0001$). Computerized EEG studies on four patients with early abuse demonstrated fronto-temporal spike waves that radiate into right frontal cortex. These findings may help explain the link between early abuse and neuropsychiatric symptoms, such as dissociation, and may thus serve as a model for the integration of psychosocial and biological theories of psychopathology.

NR406 **Thursday, May 11, 12 noon-2:00 p.m.**

THERAPEUTIC PARAMETERS: STRATEGIC VERSUS EXPLORATORY

John O. Beahrs, M.D., Oregon Health Sci Univ, VA Med Ctr/Outpatient Cli, P.O. Box 1036, Portland OR 97207; John L. Butler, M.D., David J. Drummond, Ph.D., Stanley G. Sturges, M.D., Claudette H. Beahrs, M.S.S.W.

Summary:

Thirty-three patients treated with a limited intensity "strategic self-therapy" paradigm (1988 APA,NR-238) were compared with 32, patients in long-term exploratory psychotherapy, to assess several clinical parameters: patients; regressive potential (RPRS), actual regressive dependency in treatment (RDL), degree of patient's self-therapeutic activity (STAL), and therapeutic progress (TPRS). Measures are mean thereapist estimates of several component variables rated 0-4 + , with inter-rater rtt = +0.89, +0.71, and +0.77 (n = 23). Therapeutic progress was satisfactory for both strategic and exploratory modalities (TPRS:x = 2.26, SD = 0.75 & 2.49, 0.80, ns). While the strategic caseload had higher initial regressive potential (RPRS:x = 2.38, SD*D*0.92 v 2.00, 1.06), regressive dependency was less in this group (RDL: x = 1.00, SD = 0.77 v 1.41, 0.80,p = 0.05). RDL correlated with RPRS within the exploratory caseload (r = +0.74, p<0.001), much less so within the strategic group (+0.45). STAL and TPRS strongly intercorrelated within both (strategic, +0.75; exploratory, +0.78). Dropout rate was 35% in the strategic group (ni = 51) and less than 10% in the exploratory. These data suggest several hypotheses: both modalities are comparably effective; strategic therapy is cost-efficient and minimizes regressive behavior, but at relative cost to therapeutic engagement. Finally, therapeutic progress may depend most highly on patients actively helping themselves, which suggests a shared therapeutic target.

NR407 **Thursday, May11, 12 noon–2:00 p.m.**

URINARY MARKERS AND DRUG COGNITIVE THERAPY COMPARISON

Gary D. Tollefson, M.D., Psychiatry, St. Paul Ramsey, 640 Jackson Street, St. Paul, MN 55101; Michael J. Garvey, M.D., Mark D. Evans, Ph.D., Christopher S. Vye, Ph.D., Steven D. Hollon, Ph.D., Vincente B. Tuason, M.D.

Summary:

Introduction: Recent interest in putative biological markers of depression has been intense. However, their interdigitation with treatment outcome has been principally limited to pharmacotherapy. While cognitive behavioral psychotherapy (CBT) is of comparable efficacy with tricyclic pharmacotherapy, such studies fail to elucidate important questions regarding the role of psychotherapy/environment upon biological parameters. *Methods*: We investigated 45 ambulatory patients screened with the SADS-L and fulfilling RDC criteria for definite unipolar (nonpsychotic) major depression. Subjects entered a 12-week double-blind outcome study with random assignment to imipramine, CBT, a combined strategy, or placebo-supportive contact. We obtained two consecutive 24-hour urine samples at study entrance and again at the 12-week treatment conclusion. Urine was analyzed for melatonin, DHEA-S, cortisol, and MHPG. Outcome analyses of each cell, relative to individual and group depression change scores, were performed. *Results*: The majority of patients in active treatment improved in contrast to placebo. (1) Urinary melatonin served as a measure of treatment response in all three active cells, but not placebo. (2) Change in MHPG was directly and significantly related to changes in cortisol with pharmacotherapy only consistent with theories of adrenergic modulation of the HPA axis; data suggested this was *less* influenced by CBT, independent of depresion response. (3) CBT recipients demonstrated a greater correlation between changes in MHPG and several rating scales, particularly those reflecting anxiety. (4) Changes in MHPG and DHEA-S were significantly related to treatment outcome (depression) in males only.

NR408 **Thursday, May11, 12 noon–2:00 p.m.**

SUICIDAL BEHAVIORS IN AIDS AND HIV POSITIVE PATIENTS

F. Patrick McKegney, M.D., Psychiatry, Montefiore, 111 E. 210 Street, Bronx, NY 10467; Mary A. Odowd, M.D., Carmen Natali, M.D., Jill M. Harkavy, Ph.D., Gregory M. Asnis, M.D.

Summary:

A higher risk of suicide has been postulated for individuals diagnosed with AIDS or HIV positivity. The incidence of suicidal ideation or attempts in a predominantly minority group population of AIDS and HIV+ patients with a high incidence of intravenous drug abuse and heterosexual transmission was assessed in two clinical settings and compared to control populations. Suicidal behaviors of 69 patients attending a psychiatric OPD for HIV-related problems were compared to a demographically similar population in a general psychiatric OPD. There were no significant differences in the incidence of suicidal ideation (±50 percent) or attempts (±28 percent) between the two populations. Within the HIV clinic population, there were no significant differences in the incidence of suicidal behaviors among the diagnostic groups of AIDS, ARC, asymptomatic HIV+ or HLV−. For each of the AIDS diagnosis groups, the mean patient age at the first suicide attempt antedated enrollment in the clinic program by 7-14 years, preceding diagnosis of AIDS or HIV positivity for the majority of patients. Data from 93 psychiatric consultations on AIDS medical inpatients under age 55 were compared with consultations on age-matched inpatients. Again, there were no differences in the assessment of suicidality between these groups. (15-12 percent). In contrast with other published reports, this study of predominantly minority group patients in an area of high substance abuse and heterosexual transmission did not demonstrate a higher incidence of suicidal behavior associated with AIDS or HIV status.

NR409 **Thursday, May11, 12 noon–2:00 p.m.**

COMPARING METHODS TO ASSESS PATIENTS FOR THERAPY

K. Roy Mackenzie, M.D., Psychiatry, University of Texas, P.O. Box 20708, Houston, TX 77225

Summary:

The development of an interpersonal focus is a central technical component of brief psychotherapy. This process has theoretical similarity to making a classical psychodynamic formulation. The brief psychotherapy literature has emphasized the importance of using interpersonal behavioral dimensions. This presentation demonstrates and compares several methods being used for the assessment of patients in this study of brief psychotherapy: (1) Inventory of Interpersonal Problems (IIP)-L. Horowitz: a new self-report questionnaire developed as a complementary instrument to the SCL-90. (2) Relationship Anecdotes Paradigm (RAP) Test-L. Luborsky: a semistructured interview to elicit relationship dimensions with significant others. (3) Structural Analysis of Social Behavior (SASB)-L. Benjamin: a method to organize interpersonal descriptors in a modified circumplex system. (4) Repertory Grid Analysis-G. Kelly: a factor analytic method for determining a personal construct system and locating significant others within it.

Assessment data from 12 subjects are compared and contrasted by translating the results from each instrument in a common interpersonal terminology based on SASB. Each method employs a unique perspective, with some areas of replication between instruments.

NR410 **Thursday, May 11, 12 noon-2:00 p.m.**

RELIABILITY OF THERAPISTS PROCESS ESTIMATES

John O. Beahrs, M.D., Oregon Health Sci Univ, VA Med Ctr/Outpatient Cli, P.O. Box 1036, Portland OR97207; John L. Butler, M.D., David J. Drummond, Ph. D., Claudette H. Beahrs, M.S.S.W.

Summary:

Operationalized measures and experimental controls improve precision and reliability of psychotheraphy research, but often at sacrificed relevance to what actually occurs in clinical practice, where so many causal elements converge that the whole picture is necessarily excluded. Yet all factors contribute to intiuitive assessments made by experienced clinicians; if these can be quantified while preserving reliability, clinical relevance will be retained. This study defines four measures based on this principle, and addesses the inter-rater reliability on which their utility will depend. All are 0-4+. Only the second is opertionalized; the others are a composite (mean) of therapist estimates of several theortically based component parts. Twenty-three patients were independently rated by two therapists (three clinical settings, 10 therapist pairs). The measures, with Pearson reliability coefficient and mean percentage inter-rater differential, are: (1) regressive potential (RPRS): +0.80, 11.0%; (2) regressive dependency (RDL): +0.89, 10.9%; (3) patients' self-therapeutic activity (STAL): +0.71, 14.7%; and (4) therapeutic progress (TPRS): +0.77, 14.3% ($p<0.001$ for all). They may help identify relevant patterns in uncontrolled clinical settings; e.g. STAL and TPRS intercorrelated within both exploratory and strategic psycholtherapy caseload (5 = +0.78; +0.75, n = 32, 33): RPRS correlates with RDL more highly in the former (+0.74, +0.45). Reliability approaches that of many operationalized measures in current use.

NR411 **Thursday, May 11, 12 noon–2:00 p.m.**

INPATIENT GROUP PROCESSES PARALLEL UNIT DYNAMICS

E. Michael Kahn, M.D., Brookside Hospital, 11 Northwest Blvd, Nashua, NH 03063; I. Terry Sturke, M.S.

Summary:

Authorities on inpatient group psychotherapy have often described correspondence between ward dynamics and events within therapeutic groups on the ward. They cite understanding of these "parallel processes" as on key in leadership of inpatient groups. Also, they suggest that dynamics of the inpatient group serve as a "milieu biopsy," guiding staff in management of the ward. The authors sought empirical documentation of this interaction.

The study was conducted on a 14-bed, short-stay, voluntary unit in a public general hospital. Once each week, patients and staff attending the daily community meeting completed Moos's "Ward Atmosphere Scale" (WAS). On the same day, patients and staff participating in the key therapy group completed MacKenzie's "Group Climate Questionnaire-S" (GCQS). For each week, the 10 subscales for the WAS, and the four subscales for the GCQS were computed. Patient and staff scores for most of these scales differed (ANOVA), and independent analyses were undertaken for the two classes of respondents. Aggregate GCQS scale scores, by week, were modeled as functions of aggregate WAS scale scores using stepwise linear regression.

Support, Order, Involvement, and Clarity were the WAS scales that were the most influential in prediction of GCQS scales. These scales address (respectively) staff "presence," planning and organization, energy and cohesion, and explicitness of the treatment process. These influences on group process are quite similar to those which have been attributed to leaders in group therapy (Lieberman, et al.), and those common to individual therapy (e.g., Frank). These data support the hypothesis that unit environment is reflected in the process of the therapeutic groups.

NR412 **Thursday, May 11, 12 noon-2:00 p.m.**

A STATE HOSPITAL FAMILY PSYCHOEDUCATIONAL PROGRAM

Shirley M. Glynn, Ph.D., UCLA Research, Camarillo St. Hospital, Box A., Camarillo CA 93011; Robert Pugh, M.A., Gordon Rose, Ph.D.

Summary:

Educational programs for families of state hospital patients are rare. We have modified the "Survival Skills Workshop" for these families. Modifications included discussing treatment resistance, alternative drugs, potentially positive long-term prognosis. hospital administrative structure, and ways of organizing patients visits. Relatives of schizophrenics under 35 living within 300 miles of the hospital and having made a least one visit in four months were invited. To determine whether attendance increased knowledge among the 53 participants, pre post assessments were conducted on an information quiz and statements indicating understanding about mental illness and support from mental health professionals. All increased significantly ($p < .01$). The second research question involved identifying predictors of attendance from chart reviews and structured telephone interviews with members of all potential families. T-test comparing attending families ($n = 27$) with non-attender ($n = 32$) on many variables (e.g., demographics, patients clinical status and history, family attitudes and knowledge about mental illness) revealed attenders were significantly more likely to be aware of the National Alliance for the Mentally Ill, to have read at least one book on schizophrenia, to know more about schizophrenia, to visit more, and to live closer to the hospital. In a stepwise discriminant analysis, distance from the hospital and knowledge predicted attendance. The relatively high percentage of attending families (44%), and the lack of attitudinal, clinical, or demographic predictors suggests that, even at a state hospital, many relatives, regardless of sex, education, race, or attitudes, desire information. Logistical difficulties presented by distant, centralized facilities are problematic.

NR413 **Thursday, May 11, 12 noon–2:00 p.m.**

TRACKING THE PATHOGENESIS OF MARITAL DISTRESS

Frederick S. Wamboldt, M.D., Psychiatry, George Washington Univ, Ross Hall, RM 613, 2300 Eye St NW, Washington, DC 20037, David Reiss, M.D.

Summary:

Marital distress is the most freguent complaint presented to mental health practitioners. Moreover, severe marital distress can exacerbate major psychiatric disorders and can confound their treatment. However, the treatment of marital disorder has been hindered by our poor understanding of its pathogenesis. This poster will report findings from three separate samples of 16, 70 and 155 couples. Two major hypotheses guide this ongoing research program: first, the inception of marital disorder often can be identified very early in the new relationship; and second, disorders of early marriage stem from impaired relationships between the new couple and their origin families. Our studies capitalize on recent advances in the objective measurement of family process including the direct observation of family relationships.

Three important findings have emerged across studies: (1) Specific characteristics of the origin families directly relate to the development of distress in the new couple. (2) The couple can modify the impact of their family heritage by reaching consensus concerning these origin family characteristics. (3) The origin family of the female partner plays a particularly central role in determining the success or failure of the new relationship. A developmental, gender-sensitive model of early marriage will be presented that integrates the above results in a clinically relevant fashion.

NR414 **Thursday, May 11, 12 noon-2:00 p.m.**

PSYCHIATRIC COMORBIDITY IN SOMATIZATION DISORDER

Frank W. Brown, M.D., Psychiatry, UAMS, 4301 West Markham SLOT 554, Little Rock, AR 72205; G. Richard Smith, M.D.

Summary:

A sample of 196 patients referred from primary care physicians for multiple unexplained somatic complaints was studied to evaluate psychiatric comorbidity. The Diagnostic Interview Schedule was used in 119 patients meeting strict criteria for DSM-III-R somatization disorder and in 100 patients meeting strict criteria for the Feighner Definite criteria. Lifetime prevalence rates were calculated for somatization disorder patients who had other psychiatric comorbid disorders. Comparisons were made with the general population norms from the ECA studies.

With patients meeting the Feighner Definite criteria for somatization disorder, lifetime prevalence rates of all 11 comorbid conditions considered were significantly higher than the general populations (p 0.001, Z test, 2 tailed). With patients meeting the DSM-III-R criteria for somatization disorder, seven comorbid conditions (major depression, alcohol abuse/dependence, schizophrenia, obsessive-compulsive disorder phobic disorders, panic disorder, and antisocial personality disorder) were significantly higher than the general population ($p \leq 0.001$, Z test, 2 tailed).

The highest lifetime prevelence rates for somatization disorder patients (DSM-III-R criteria) were for major depression (54.6%), generalized anixety disorder (33.6%), phobic disorder (31.1%), panic disorder (26.0%), alcohol abuse/dependence)21.0%), obsessive-compulsive disorder (17.6%), antisocial personality disorder (10.8%), and schizophrenia (10.1%). Substance abuse was 4.9% which is not significantly different from the general population lifetime prevalence of 5.9%.

NR415 **Thursday, May 11, 12 noon–2:00 p.m.**

ON THE ABNORMALITY OF NORMAL CONTROL GROUPS

Robert W. Butler, Ph.D., Psychiatry, UCSD Medical Center, 225 Dickinson Street, San Diego, CA 92103; Melissa Jenkins, B.A., David L. Braff, M.D.

Summary:

Most commonly control subjects representative of the normal population are necessary in research in psychopathology. This need has led researchers to institute novel approaches, such as newspaper advertisement, in obtaining putatively normal controls. Ensuring that these normals are free of significant psychopathology and substance abuse, however, is typically accomplished by cursory self-report. We collected extensive psychological, psychiatric, neuropsychological, and information processing data on a group (N = 49) of putatively normal controls obtained by placing advertisements in a local newspaper and posting notices in various agencies and workplaces. We then separated these subjects into three categories: normal (N = 21), abnormal (N = 10), and substance abuse (N = 9) based on an algorithm consisting of Minnesota Multiphasic Personality Inventory (MMPI) variables. Nine of the subjects remained unclassified by this algorithm. The three groups were not significantly different on self-report of alcohol and other substance abuse, in addition to other control variables. The groups were significantly different on a number of measures of psychopathology, neuropsychological functioning, and information processing. The probability of Type II errors increases without accurate screening of control subjects, and there is preliminary support for a MMPI-derived algorithm. Accurate screening of "normal" controls may allow for greater detection of unmediated schizophrenic, schizotypal, and other important potential research subjects. This type of screening is also essential so that researchers can avoid "tainting" putatively normal control groups with abnormal subjects.

NR416 **Thursday, May 11, 12 noon–2:00 p.m.**

UTILITY OF COMPUTER-ASSISTED DSM-III-R DIAGNOSIS

Michael B. First, M.D., Biometrics, NYS Psychiatric Inst., 722 W. 168th Street Box 74, New York, NY 10032; Lewis A. Opler, M.D., Robin M. Hamilton, M.D., Jill Linder, M.D., Louis S. Linfield, M.D., Jonathan M. Silver, M.D., Nina L. Toshav, M.D., David Kahn, M.D., Janet B.W. Kahn, D.S.W., Robert L. Spitzer, M.D.

Summary:

DTREE is a microcomputer-based expert system that guides the user through the diagnosis logic of DSM-III-R. This study examines the utility of DTREE for making diagnoses in an inpatient setting. For each of 20 patients selected from an adult inpatient psychiatric unit, a DTREE-guided DSM-III-R diagnosis (made by the treating clinician) was compared to a consensus "criterion" diagnosis made as follows: A weekly two-hour case conference was conducted, consisting of a presentation by the treating clinician and other staff a chart summary, and the administration of the Structured Clinical Interview for DSM-III-R (SCID), resulting in a consensus conference diagnosis. The final "criterion" diagnosis was then determined by group consensus after pooling all information utilized in deriving the DTREE and conference diagnoses.

The kappa agreements between DTREE and the final "criterion" diagnoses were .80 for schizophrenia (N = 10), .83 for major depression (N = 3), -.08 to 1.00 for all other disorders (N = 7), with an overall pooled kappa of .68. The mean time spent using DTREE was only 13.0 minutes as compared to 2 hours for the SCID plus case conference This rate of agreement suggests that in certain situations DTREE may be a reasonably valid time-efficient alternative to more lengthy structured interviews.

NR417 **Thursday, May 11, 12 noon–2:00 p.m.**

A BRIEF DSM-III BASED PATIENT CLASSIFICATION SYSTEM

John W. Goethe, M.D., Research, Institute of Living, 400 Washington Street, Hartford, CT 06106; Hal Mark, Ph.D.

Summary:

The use of diagnostic data in the analysis of small, hospital-level data sets is confounded by the large number of DSM-III categories. When only a small number of patients are available for analysis, even the 13 DRG designations are too numerous, and the number of observations in each category are too few to sustain any meaningful statistical conclusions. In an effort to address this problem the authors have developed and tested a diagnostic classification system consisting of five categories based upon clusters of Axes I and II DSM-III codes. The five categories identified are: psychotic, affective, substance abuse, dual diagnoses and other. (The "other" cateqory is residual, containing less than 8 percent of the total.) This classification system has been tested using four patient samples to demonstrate its utility in describing patients by length of stay and clinical outcome (N = 87), nursing acuity (N = 180), payor source (N = 181) and the impact of third-party concurrent review (N = 168). The assignment algorithm is clinically derived and has validity. The range of variation between categories suggests that valid diagnostic information is retained and data for case mix analyses are captured with this method.

NR418 **Thursday, May 11, 12 noon–2:00 p.m.**

THE MEANING AND MEASUREMENT OF APATHY

Robert S. Marin, M.D., Psychiatry, Univ of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213; Ruth C. Biedrzycki, M.Ed., Sekip Firincioqullari, M.S.

Summary:

This paper describes the development, reliability and validity of an Apathy Evaluation Scale (AES), which conceptualizes apathy as loss of motivation not attributable to cognitive impairment or emotional disturbance. This definition is discussed in terms of the differential diagnosis of apathy which includes schizophrenia, post-psychotic depression, major depression, frontal lobe syndromes, right hemisphere stroke, Alzheimer's disease, the "subcortical dementias," demoralization, abulia, akinesia, and institutionalism. Clinician, informant, and self-rated versions of the AES were developed. The scale was administered to 68 subjects, (32M, 36F, mean age 69) who met research criteria for left (LH) or right hemisphere (RH) stroke, probable Alzheimer's disease (AD), depressive disorders (DP) and normal (NL). Measures of reliability (internal consistency; test-retest and inter-rater reliability) for each version of the scale were between 0.78 and 0.92. We used the multitrait-multimethod matrix procedure to demonstrate that apathy can be discriminated from depression and that there is convergent validity for the three versions of the AES. For each version of the scale we also found: significant F's ($p = .019$ to $< .001$) in one way ANOVA's for effect of diagnosis; significant t tests ($p = .017$ to $< .001$) for linear contrasts indicating, as hypothesized, significantly elevated AES scores in RH, AD and DP compared to HL and NL. Sheffe's test for multiple pairwise comparisons also indicated significant elevations of AD compared with NL for each version of the AES. Potential applications of the AES to clinical and research problems are discussed.

NR419 **Thursday, May 11, 12 noon-2:00 p.m.**

IMPORTANCE OF AXIS II DIAGNOSES IN AXIS I RESEARCH

Kenneth R. Silk, M.D., Psychiatry, Univ of Michigan, UH 9C 9150/0120 1500 Med C Dr, Ann Arbor MI 48109; Drew Westen, Ph.D., Naomi E. Lohr, Ph.D., Laura Gold, Ph.D., Edna Pressler, M.A.

Summary:

Recent research in personality disorders has repeatedly emphasized the confounding effects of either Axis I or Axis II comorbidity upon diagnostic criteria as it pertains to a particular personality disorder. For example, in patients with borderline personality disorder (BPD), concurrent diagnoses such as affective disorder, anxiety disorder, substance abuse disorder, and schizotypal personality disorder, have all been found to effect clinical symptom presentation. There is also evidence to support the idea that comorbidity in BPD may efffect treatment and long-term outcome as well. However, little attention has been paid to controlling for Axis II comorbidity when doing Axis I research. This is noteworthy since it has been shown that patients defined as treatment-resistant, particularly those with affective or anxiety disorder, have a high incidence of concurrent personality disorder. Our own reasearch reveal that major depresive disorder (MDD) patients who have a concurrent diagnosis of BPD appear different for MDD patients without BD in the following ways: (1) Interpersonally they are more withdrawn, anxious and rejection sensitive. (2) Biologically they show greater variability in biological test results that are related to affective disorder. (3) Psychologically they manifest a different quality of depression, and they utilize different cognitive and emotional processes to mediate their interpersonal functioning. Our findings suggest, then, that Axis I research, particularly in affective and anxiety disorders, must thoroughly consider concurrent Axis II diagnoses in order to diminish heterogeneity withing operationally defined Axis I populations. This attention to Axis II comorbidity could provide more consistent definition of clinical propulations and less contradictory results from different research centers that allegedly are studying similar Axis I subjects.

NR420 **Thursday, May 11, 12 noon–2:00 p.m.**

OPTIMIZING REM STUDIES WITH THE INFO-ROC TECHNIQUE

Eugene Somoza, M.D., Psychiatry, Cincinnati VA Med Center, 3200 Vine Street, Cincinnati, OH 45220; Douglas Mossman, M.D.

Summary:

Diagnostic tests must be evaluated for their intrinsic accuracy and for their applicability to particular patient groups in specific clinical settings. The INFO-ROC technique uses receiver operating characteristic (ROC) analysis and information theory to yield a mathematical and graphic method with which one can evaluate, compare, and optimize the performance of diagnostic tests for any value of disorder prevalence. This technique is appropriate for any test that sorts disordered from nondisordered subjects using a continuous diagnostic variable.

We demonstrate the INFO-ROC technique through an evaluation of REM latency data from five previously published studies which used sleep architecture as a biological marker for depression. The analyses show that REM latency is comparable to the dexamethasone suppression test in its ability to discriminate depressed from control subjects. For each of the five studies, we show how optimal REM latency cutoff times may be selected so that diagnostic information yield is maximized, and we compare the ability of each study to detect depressed subjects in populations where the prevalence of affective disorder can be specified. When the trade-off between risks and benefits can be accurately estimated, we show how ROC methods can provide appropriate REM latency cutoff times to optimize utility at specific prevalences.

NR421 **Thursday, May 11, 12 noon-2:00 p.m.**

SEXUAL HARRASSMENT OF MEDICAL STUDENTS

Andrea Jacobson, M.D., Psychiatry, Univ of Washington, RP-10, Seattle WA 98195; Gwenyth K. McConnell, B.A.

Summary:

At the end of their fourth year of medical school 183 medical students were surveyed about any experiences of sexual harassment in medical school classes or rotation. Response rate was 73%. A detailed, structured self-report instrument, modified from an instrument previously used in a large national survey, was used.

Sexual harassment (including unwelcome sexual remarks, pressure for dates, letters or phone calls of a sexual nature, sexually suggestive looks or gestures, deliberate touching or cornering, or pressure for sexual favors) was reported by 71% of the women and 26% of the men. 33% of women reported deliberate touch, 10% reported pressure for sexual favors, and 58% reported unwelcome sexual remarks. All categories of harassment reported by female medical students were also reported by male medical students, but prevalences were signficantly lower.

Identity of the harassers and gender differences will be reviewed. The consequences of the harassment as perceived by the students will be discussed as well as what, if any action students took to end the harassment or report it to medical school authorities.

NR422 **Thursday, May 11, 12 noon–2:00 p.m.**

RESIDENT'S ATTITUDES TOWARDS PREGNANCY

Devra Braun, M.D., Psychiatry, NY Hospital—Cornell, 21 Bloomingdale Road, White Plains, NY; Virginia L. Susman, M.D.

Summary:

The pregnant resident, once uncommon or ignored, is appearing more frequently in psychiatric training programs. We are conducting a three-year prospective study of psychiatric residents' attitudes toward pregnancy, including attitudes about such issues as the impact of pregnancy on trainees' work performance; the need for special scheduling and consideration; and actual experiences residents have had with pregnant peers. Residents were questioned not only about their own attitudes, but were asked to estimate what the majority of residents of the opposite sex would be likely to feel.

To date, 58 residents from the two major training centers at Cornell University Medical College have completed our 67-item questionnaire. Results in the first year of our study are notable for disparate attitudes between men and women on several items: 1) pregnancy's interference with work, 2) the need for special scheduling and 3) the notion that pregnancy has a humanizing effect on the residency program. Men were more likely to perceive pregnancy as interfering with work performance (chi square $p = .027$); women were more likely to agree with the need for special scheduling (chi square $p = .038$) and the notion that pregnancy has a humanizing effect (chi square $p = .038$). Interesting findings included the projective questions surveying residents' expectations of the opposite sex: In general, male residents assess likely female responses with a higher degree of accuracy than women residents assess male attitudes. Women tended to expect more negative attitudes from their male colleagues than the men actually professed. Theoretical and practical implications will be reviewed.

NR423 **Thursday, May 11, 12 noon-2:00 p.m.**

THE CONTINUING STIGMA (1938-1988) OF VIENNESE PSYCHIATRY

Norbert Loimer, M.D., Psychiatry, Unviersity of Vienna, Wahringergurtel 18/20, Vienna A 01090; Rainer Schmid, Ph.D.,

Summary:

The question of an analysis of the Nazi ideology at the psychiatric clinic of the University of Vienna and its relationship to the following decades demands an answer. The biological traditon of the Viennese "school" of psychiatry (Wagner-Jauregg) and the influence of Freud's school during the First Republic (1918-1938), are described.

The Nazi occupation in 1938 brought a sudden and dramatic change in all aspects of science, research and university administration. Science was replaced by racial ideology; the humane tradition of the university, by intolerance; and the staff by SS members. At the university clinic the programs to eliminate the mentally ill were not carried out directly; patients were sent to institutions where Nazi doctors (f.ex. Gleny) killed them.

After the liberation of Austria in 1945, the humane tradition of the university clinic was re-established by Kavders, Hoff and Berner. All the SS psychiatrists continued their work as psychiatrists but outside of the university — some until today.

Can we overcome stigma torwards the mentally ill if individual former Nazi psychiatrists continue to be "caregivers"?

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GRAPHIC DISPLAY OF PSYCHIATRIC HISTORY AND TREATMENT

Mark D. Rego, M.D., Psychiatry, Yale University, 20 York St. RM 2046 CB, New Haven CT 06504; Seth M. Powsner, M.D., Robert S. Byck, M.D.

Summary:

We have devised a simple computer interface to plot the course of a psychiatric patient's illness. A sample display form a Macintosh™ computer of this HyperCard™ program or "stack" is shown to the right. By including markers for major life events and psychosocial stressors, the more toxic stressors and more effective treatments become evident. The time consuming nature of the task of the charting and the difficulty updating the picture as more information became available, discourage the use of graphic charting in the past. This program simplifies the work involved. The time sequence of up to seven different treatments can be graphed directly above a plot of up to four different behaviors or symptoms. The time scale can be adjusted to suit the particular patient. Up to nine life events can be noted below the time scale and tied to it. A case can be graphed in less than 15 minutes.

NR425 **Thursday, May 11, 12 noon-2:00 p.m.**

SEXUAL TRAUMA: THE CAUSE OF MULTIPLE PATHOLOGY?

Ingunn Skre, Ph.D., University of Oslo, Center for Research in Clinical Psychology, P.O. Box, 1039, Blindern, N-0315, Oslo, 3, Norway; Sidsel Onstad, M.D., Svenn Torgersen, Ph.D., Einar Kringlen, M.D.

Summary:

Twin-family data from Norway indicate that being a victim of sexual assult has impact on the development of panic disorder (PD), major depressive episodes (MDE) and psychoactive substance use disorders (PSUD). Subjects were personally interviewed with SCID-I, supplemented by a checklist registering history of sexual and physical assault.

Sixty-four females had a history of DSM-III-R Axis I disorder. Of these 13 were victims of sexual assault, 14 were victims of physical violence (without sexual assault) and 37 reported no violence.

PD, MDE and PSUD were most common among sexual victims. A big part (38%) of these had all the three disorders. Comorbidity rates were lower in the remaining group (14% and 0%, respectively) (chi-square=14.816, $p<0.001$). Pure MDE (without PD or PSUD) was most common among victims of physical violence (43%, versus 8% and 16%) (chi-square=6.054, $p<0.05$). For pure PD and pure PSUD no significant differences were found between the three groups.

The findings indicate that sexual trauma has far-reaching impact on mental health. In this study sexual trauma may be the major cause of the comorbidity between panic disorder, major depression and substance abuse.

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