# 1988 NEW RESEARCH PROGRAM & ABSTRACTS



# American Psychiatric Association

141ST ANNUAL MEETING MONTREAL, QUEBEC, CANADA MAY 7-12, 1988

Theme: Opportunities & Challenges for Psychiatrists & Psychiatry: 1988-2000

## PROGRAM AND PAPERS ON NEW RESEARCH

## IN SUMMARY FORM

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

## MONTREAL, QUEBEC, CANADA May 7-12, 1988

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.

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## American Psychiatric Association

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

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May 7, 1988

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 1988 New Research Program.

This year's program reflects the increasing importance of basic and clinical neuroscience to psychiatry. For the first time, all New Research Sessions are being held in one location, the fourth floor of the Convention Centre. They are organized by topic and have been expanded to accommodate a bumper crop of excellent submissions.

The program begins Monday, May 9, at 9:00 a.m. with a discussion of Science Policy and Research Priorities in the United States and Canada. It continues at 10:45 a.m. with Research Advances in Psychiatry: An Update for the Clinician, with special emphasis on affective disorders and kindling, anxiety disorders and neurotransmitters, Alzheimer's Disease, and structural brain imaging.

The New Research Oral/Slide Sessions will be held Tuesday, May 10, through Thursday, May 12, 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 and childhood disorders (Thursday). Poster Sessions, also held Tuesday through Thursday from 12 noon to 2:00 p.m., will be devoted to schizophrenic and organic mental disorders (Tuesday); mood disorders, psychoimmunology, psychopharmacology, and other somatic therapies (Wednesday); and personality, substance abuse, and eating disorders, as well as other issues (Thursday).

The 36 Oral/Slide and almost 300 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.

Sincerely,

Charles A. Jaufmann

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

#### New Research 2—Oral/Slide Session—Room 401-A, Fourth Floor, Convention Centre

#### SCHIZOPHRENIC DISORDERS

Chp.: Joe Co-Chp.:	I E. Kleinman, M.D. Llyewellyn B. Bigelow, M.D.	
NR1	Temporal Lobe Pathology in Schizophrenia Richard L. Suddath, M.D., Manuel F. Casanova, M.D., Terry E. Goldberg, Ph.D., David G. Daniel, M.D., Daniel R. Kelsoe, M.D., Daniel R. Weinberger, M.D.	9:00 a.m.
NR2	Progressive Ventricular Changes in Schizophrenia Bryan T. Woods, M.D., Francine M. Benes, M.D., Deborah Yurgelun-Todd, M.D.	9:15 a.m.
NR3	Apomorphine and rCBF in Schizophrenia David G. Daniel, M.D., Karen F. Berman, M.D., Ralph Fawcett, M.D., Daniel R. Weinberger, M.D.	9:30 a.m.
NR4	Adrenergic Receptor Supersensitivity in Schizophrenia David L. Garver, M.D., Paul R. Sanberg, Ph.D., Lawrence Frohman, M.D.	9:45 a.m.
NR5	Biology of Schizotypal and Schizophrenic Patients Larry J. Siever, M.D., Zvi Zemishlany, M.D., Emil F. Coccaro, M.D., Miklos F. Losonczy, M.D., Thomas B. Horvath, M.D., Michael Davidson, M.D., Howard Klar, M.D., Kenneth L. Davis, M.D.	10:00 a.m.
NR6	DSM-III-R Schizophrenia is Too Narrow Wayne S. Fenton, M.D., Thomas H. McGlashan, M.D., Robert K. Heinssen, Ph.D.	10:15 a.m.

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Tuesday, May 10, 1988, 9:00 a.m.-10:30 a.m.

#### New Research 3—Oral/Slide Session—Room 401-B, Fourth Floor, Convention Centre

#### ANXIETY DISORDERS

Chp.: Minna R. Fyer, M.D.

NR7	Cholecystokinin Induces Panic in Panic Disorder Jacques Bradwejn, M.D., Greg B. Meterissian, M.D., Diana Koszycki, B.A.	9:00 a.m.
NR8	Carbon Dioxide Sensitivity in Panic Disorder Laszlo A. Papp, M.D., Jack M. Gorman, M.D., Raymond Goetz, Ph.D., Michael R. Liebowitz, M.D., Abby J. Fyer, M.D., Donald F. Klein, M.D.	9:15 a.m.
NR9	Neuroanatomical Correlates of Lactate-Induced Panic Eric M. Reiman, M.D., Mark A. Mintun, M.D., Marcus E. Raichle, M.D., E. Robins, M.D., J.L. Price, Fusselman Fusselman, M.S., K.A. Hackman, B.S.	9:30 a.m.
NR10	Psychiatric Diagnoses and Luteal Variation in PMS Women Teri B. Pearlstein, M.D., Judith Thoft, Ed.D, Debra Rubinstein, Ed.D, Ellen Frank, Ph.D., Ana Rivera-Tovar, M.S., Tammy A. Mieczkowski, B.S.	9:45 a.m.
NR11	Neuropsychiatric and Biochemical Subgroups in OCD Eric Hollander, M.D., Wilma Rosen, Ph.D., Jim Towey, Ph.D., Gerard Bruder, Ph.D., Erica Schiff- man, M.D., Michael R. Liebowitz, M.D.	10:00 a.m.
NR12	Obsessive-Compulsive Disorder in First Degree Relatives of Obsessive-Compulsive Disorder Children Marge C. Lenane, M.S.W., Susan Swedo, M.D., Henrietta Leonard, M.D., Deborah L. Cheslow, B.S., Judith L. Rapoport, M.D., David L. Pauls, Ph.D.	10:15 a.m.

Tuesday, May 10, 1988, 12 noon-2:00 p.m.

#### New Research 4---Poster Session---Room 407-B, Fourth Floor, Convention Centre

#### SCHIZOPHRENIC AND ORGANIC MENTAL DISORDERS, BIOLOGICAL AND CONSULTATION/ LIAISON PSYCHIATRY

Moderators: Barbara A. Parry, M.D., Stephen I. Deutsch, M.D.

- NR13 A Computerized Database System for Psychiatric and Consultation Records Hoyle Leigh, M.D.
- NR14 American Sexual Experience in the AIDS Era Samuel S. Janus, Ph.D., Cynthia L. Janus, M.D.
- NR15 New Dyskinesia Model: Effect of Metoclopramide Luis A. Marco, M.D., Leonard D. Aldes, Ph.D., Robert B. Chroister, Ph.D., Timothy F. Reed, B.S.
- NR16 Cognitive Sequelae of Tardive Dyskinesia Marion E. Wolf, M.D., Alan S. DeWolfe, Ph.D., Joseph J. Ryan, Ph.D., Aron D. Mosnaim, Ph.D.
- NR17 Rarity of Dystonia in Elderly Patients Gerard Addonizio, M.D., George S. Alexopoulos, M.D.
- NR18 Antimuscarinic Plasma Activity and Cognition Ole J. Thienhaus, M.D., James Thoene, Frank Zemlan, Ph.D.
- NR19 Acceptance of HIV-Antibody Testing by Cocaine Abusers William W. Weddington, M.D., Barry S. Brown, Ph.D.
- NR20 Factorial Validity of the Toronto Alexithymia Scale R. Michael Bagby, Ph.D., Graeme J. Taylor, M.D., James D. Parker, M.A., David P. Ryan, Ph.D., Ken Citron, M.D.
- NR21 Calcium Channel Blockers in Tardive Dyskinesia Erica J. Duncan, M.D., Lenard Adler, M.D., Burt Angrist, M.D., Eric Peselow, M.D., Stewart Reiter, M.D., John Rotrosen, M.D.
- NR22 Beta-Blockers in Akathisia: Mediation by Beta-1 or Beta-2? Lenard Adler, M.D., Erica J. Duncan, M.D., Burt Angrist, M.D., Paula Hemdal, M.D., Tony Kim, M.D., John Rotrosen, M.D.
- NR23 Prospective Study of Tardive Dyskinesia in the Elderly Bruce L. Saltz, M.D., John M. Kane, M.D., Margaret Woerner, Ph.D., Jeffery A. Lieberman, M.D., Jose Alvir, P.H.
- NR24 Behavioral and Physiological Effects of a Beta-Blocker and Relaxation Therapy on Mild Hypertensives C. Alex Adsett, M.D., Anthony Bellissimo, Ph.D., Alba Mitchel, M.Sc., Nancy Wilczynski, B.Sc., Brian Haynes, M.D.
- NR25 Symptom Management Training for Schizophrenics Robert P. Liberman, M.D., Thad A. Eckman, Ph.D., Stephen R. Marder, M.D., W.& Wirshing, M.D., K. Johnston-Cronk, B.S.
- NR26 Cerebral Blood Flow in Post-Stroke Depression Joseph A. Schwartz, M.D., Nancy M. Speed, M.D., James M. Mountz, M.D., M.D. Gross, M.D., D.E. Kuhl, M.D.
- NR27 Nadolol for Chronic Impulsive Aggressive Behavior Paul Sorgi, M.D., Linda S. Cole, M.D., Daniel Knoedler, M.D., William N. Arnold, M.D., John J. Ratey, M.D.
- NR28 Neurochemical Correlates of Deficit Schizophrenia John G. Csernansky, M.D., Roy J. King, Jr., M.D., William O. Faustman, Ph.D., James A. Moses, Jr., Ph.D., Margaret E. Poscher, M.D., Kym F. Faull, Ph.D.
- NR29 Neuroendocrine Effects of 52028 RP in Schizophrenia Luc-Andre Granier, M.D., Fabrice Duval, M.D., M. Antoine Crocq, M.D., Bruno Musch, M.D., Christine Pilate, M.D., Jean-Paul Macher, M.D.
- NR30 Interictal Behavioral Disorder in Epileptics Narayan P. Verma, M.D., Cynthia D. Nichols, M.A., Manfred F. Greiffenstein, Ph.D., Barbara A. Buber, N.P.
- NR31 Neuroleptic Response: Familial Patterns of Illness Frederic J. Sautter, Ph.D., Barbara E. McDermott, M.A., David L. Garver, M.D.

Elaine R. Peskind, M.D., Murray A. Raskind, M.D., Richard C. Veith, M.D., Steven C. Risse, M.D., Thomas H. Lampe, M.D., Daniel M. Dorsa, M.D. NR33 Predictors of Adaptation in Dementia Caregivers William Borden, Ph.D., Rhonda Frankel, M.A., Ben L. Gierl, M.D., Alice Ras, B.A. Schizoaffective Disorder: A Distinct Entity? **NR34** Jean-Pierre Lindenmayer, M.D., Stanley Kay, Ph.D., Herman M. van Pragg, M.D. Dementia with Coexistent Depression **NR35** Blaine S. Greenwald, M.D., Deborah B. Marin, M.D., Elisse Kramer, Ph.D., Leila Laitman, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D. Schizophrenic Drug-Free Relapse: A Peak in Week Three **NR36** George G. Dougherty Jr., M.D., Jeffrey L. Peters, M.D., Daniel P. van & Kammen, M.D., Kenneth L. Goetz, M.D., Eric Thomas, B.A. P300 and Clinical Symptomatology in Psychoses **NR37** Michael W. Torello, Ph.D., Steve B. Schwarzkopf, M.D., Paul M. Vespa, B.S., Stephen C. Olson, M.D., Jeffrey A. Coffman, M.D., Henry A. Nasrallah, M.D. A Time-Sampling Methodology for the Assessment of Negative Symptoms **NR38** John J. Boronow, M.D., Faith Dickerson, Ph.D., Norman B. Ringel, M.D. **NR39** The Neurological Soft Signs Scale John Herrera, Ph.D., Robert Saul, M.D., Felipe Castro, Ph.D., C. Heh, M.D., J. Costa, M.D., J. Sramek, Pharm.D., S. Potkin, M.D., D. Guiasekaram, M.D. Dopamine System Development: The Effect of Prenatal MPTP on Dopamine-Mediated Behavior **NR40** Ellen Weissman, M.D., Andrew B. Norman, Ph.D., Stephen F. Calderon, M.D., Eve M. Zubrycki, B.S., Paul R. Sanberg, Ph.D. Thiothixine Serum Level: Clinical Improvement and Tardive Dyskinesia **NR41** Jerome A. Yesavage, M.D., Javaid I. Sheikah, M.D., Elizabeth D. Tanke, Ph.D., John G. Csernansky, M.D. **NR42** Validity of Sagittal Brain Area Measurement Jeffrey A. Coffman, Steven B. Schwarzkopf, M.D., Stephen C. Olson, M.D., Judy A. McLaughlin, M.S., Idenry A. Nasrallah, M.D., Judith Brandt, R.N. **NR43** Leukoencephalopathy: Clinico-Anatomic Correlates Gary S. Figiel, M.D., C. Edward Coffey, M.D., William T. Djang, M.D., Richard D. Weiner, M.D. **NR44** Antidepressants in Depressed Schizophrenics Mark S. Kramer, M.D., Wolfgang H. Vogel, Ph.D., Celeste DiJohnson, B.S., Patricia Sheves, Ph.D., Stephen Cavicchia, Psy.D., Patrick Litle, Ph.D. Family History of Depression in Alzheimer's Disease **NR45** Brian A. Lawlor, M.D., Trey Sunderland, M.D., Alan M. Mellow, Ph.D., James L. Hill, Ph.D., Paul A. Newhouse, M.D., Dennis L. Murphy, M.D. Proband Phenotype and Familial Risk of Dementia **NR46** Richard C. Mohs, Ph.D., Linda M. Bierer, M.D., Jeremy M. Silverman, Ph.D., Daniel P. Perl, M.D., Elisse Kramer, Ph.D., Daniel S. Lobel, M.A. Reversal of Cholinergic Lesion Deficits by NGF **NR47** Vahram Haroutunian, Ph.D., Philip Kanof, M.D., Kenneth L. Davis, M.D. PET Scans with Verbal Tasks in Alzheimer's Disease **NR48** James B. Brunner, M.D., Marka Moulthrop, Ph.D., John T. Metz, Ph.D., Daniel J. Luchins, M.D., Malcolm D. Cooper, M.D. **NR49** Haloperidol Treatment in Alzheimer's Disease Davangere P. Devanand, M.B., Harold A. Sackeim, M.D., Richard P. Brown, M.D., Richard Mayeux, M.D., John McGuire, B.A. Pallidal Hypermetabolism in Schizophrenics with Tardive Dyskinesia **NR50** Jorg J. Pahl, M.D., George Bartzokis, M.D., John C. Mazziotta, M.D., Jeffrey L. Cummings, M.D., Lori Altschuler, M.D., Steven M. Marder, M.D. **NR51** CSF HVA Associated with Familial Schizophrenia Miklos F. Losonczy, M.D., Michael Davidson, M.D., Jeremy M. Silverman, Ph.D., Richard S. E. Keefe, M.A., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

**NR32** 

Endocrine Response to Physostigmine in Alzheimer's

NR52	Anticholinergic Challenge in Normal Elderly People Zvi Zemishlany, M.D., Richard C. Mohs, Ph.D., Anne B. Thorne, B.A., Michael Davidson, M.D., Kenneth L. Davis, M.D.
NR53	CSF HVA and 5-HIAA in Alzheimer's Disease Daniel S. Lobel, M.A., Linda M. Bierer, M.D., Michael Davidson, M.D., Miklos F. Losonczy, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.
NR54	CSF MHPG and Illness Duration in Alzheimer's Disease Linda M. Bierer, M.D., Michael Davidson, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.
NR55	Psychological Responses to HIV Serological Testing Samuel W. Perry, M.D., Lawrence B. Jacobsberg, M.D., Baruch Fishman, Ph.D., Allen J. Frances, M.D., Pamela Weiler, B.M., Barbara Kaplan, B.S.N.
NR56	Attributional Style and HIV-Antibody Testing Baruch Fishman, Ph.D., Samuel W. Perry, M.D., Lawrence B. Jacobsberg, M.D., Allen J. Frances, M.D., Alan Eisenstat, M.D.
NR57	Post-Translational Processing of Preamyloid Protein William Wallace, Ph.D., John Anderson, Ph.D., Ivan Leiberburg, Ph.D.
NR58	A Novel Alzheimer Amyloid cDNA with Additional Exon Nikolaos Robakis, Ph.D., Larry Refolo, Ph.D., DeBomoy Lahiri, Ph.D., L. Refolo, Ph.D., D.K. Lahiri, Ph.D., G. LaFouci, Ph.D.
NR59	Eye Movement Deficits in HIV Infected Patients Bruce Brew, M.D., John A. Sweeney, Ph.D., John Keilp, M.S., Allen J. Frances, M.D., Virginia Walsh, B.S., Robert Price, M.D.
NR60	Saccades During Visual Fixation in Schizophrenia Margaret Rea, John A. Sweeney, Ph.D., Carla Solomon, Ph.D., Michael Deck, M.D., John J. Mann, M.D., Al- Ien J. Frances, M.D.
NR61	Medical Illness and Depression Mary Ann Knesevich, M.D., William Scheftner, M.D., John Rice, Ph.D.
NR62	Cortisol and Melatonin Rhythms in Alzheimer's Disease N. P. Vasavan Nair, M.D., Mukul Sharma, M.D., Mira Thakur, M.Sc., Remi Quirion, Ph.D.
NR63	High Phenylaceturia Characterizes Schizoaffectives Hector C. Sabelli, M.D., U.N.B. Dura, M.D., Jan A. Fawcett, M.D., Javaid I. Javaid, Ph.D., Joe Wager
NR64	Cerebral Third Ventricle Size in Psychoses Marcia J. Kaplan, M.D., David L. Garver, M.D., Marjorie Lazoff, M.D., Kathleen Kelly, M.S.N.
NR65	Automated Visual CPT in Schizophrenia Paul G. Nestor, Ph.D., Steven F. Faux, Ph.D., Robert W. McCarley, Larry Seidman, Ph.D., Martha E. Shen- ton, Ph.D., Stephen Sands, Ph.D.
NR66	Schizophrenia: Generalizability of P3 Deficit Steven F. Faux, Ph.D., Martha E. Shenton, Ph.D., Robert W. McCarley, M.D., Paul G. Nestor, Ph.D., Brian Marcy, B.A., Amy Ludwig, B.A.
NR67	Heterogeneity of Alzheimer's Disease Vinod Kumar, M.D., Ezio Giacobini, M.D.
NR68	Utah Molecular Genetic Study of Schizophrenia William F. Byerley, M.D., Jean Marc Lalouel, M.D., John J. Holik, B.A., Dora M. Stauffer, B.Sc., Paul H. Wender, M.D., Ray White, Ph.D.
NR69	Familial Versus Sporadic Psychosis: Auditory Evoked Potential Differences Steven B. Schwarzkopf, M.D., Michael W. Torello, Ph.D., Paul M. Vespa, M.S., Stephen C. Olson, M.D., Jeffrey A. Coffman, M.D., Henry A. Nasrallah, M.D.
NR70	Neuroleptic Treatment and EEG Alpha Asymmetry Thomas C. Floyd, M.A., Edward L. Merrin, M.D., George Fein, Ph.D.
NR71	Reference Effects on EEG Alpha Asymmetry Edward L. Merrin, M.D., Thomas C. Floyd, M.A., George Fein, Ph.D.
NR72	Increased HVA Response to Muscarinic Agonist in Alzheimer's Disease Nunzio Pomara, M.D., Michael Stanley, Ph.D., Matthew Galloway, Ph.D., Dennis Deptula, Peter A. LeWitt, M.D., Thomas B. Cooper, M.A.

NR73	Hypofrontality, Neuropsychology and Schizophrenia David L. Braff, M.D., Sidney Zisook, M.D., Monroe Cullum, Ph.D., Robert Heaton, Ph.D.
NR74	Tiospirone in Treatment Refractory Schizophrenics Jeffery N. Wilkins, M.D., Neil Hartman, M.D., Donald Freidenberg, M.D., April Clemens, R.N., Jeffrey L. Cummings, M.D.
NR75	AIDS Risk Behavior in Adolescents Steven E. Keller, Ph.D., Steven J. Schleifer, M.D., Jacqueline Bartlett, M.D., Robert L. Johnson, M.D., Cheryl Thompson, Ph.D.
NR76	Hypercortisolism in Alzheimer's Disease Isabella J. E. Heuser, M.D., Jorge J. Juncos, M.D., Ijaz Khan, M.D., Mark A. Demitrack, M.D., Mitchel A. Kling, M.D., Philip W. Gold, M.D.
NR77	Neuroleptic Reintroduction Following Neuroleptic Malignant Syndrome Thomas Stewart, M.D., Patricia I. Rosebush, M.D.
NR78	Serum Abnormalities in Neuroleptic Malignant Syndrome Patricia I. Rosebush, M.D., Michael F. Mazurek, M.D.
NR79	Clinical Relevance of Mapping EEG in Dementia Trey Sunderland, M.D., Richard Coppola, D.Sc., James L. Hill, Ph.D., Fran Oakley, O.T.R., Robert M. Cohen, M.D., Herbert Weingartner, Ph.D.
∕ NR80	Hospital Utilization in Schizophrenia Lloyd E. Rader, M.D., Daniel E. Rodell, Cornelia M. Beck, Steven C. Buchanan, M.D., T. Michael Kashner, Ph.D., Floyd Westendorp, M.D.
NR81	Premorbid Functioning and Outcome in Schizophrenia Richard S.E. Keefe, M.A., Richard C. Mohs, Ph.D., Miklos F. Losonczy, M.D., Michael Davidson, M.D., Thomas B. Horvath, M.D., Kenneth L. Davis, M.D.
NR82	Plasma Interferon in Schizophrenia Darrell G. Kirch, M.D., Olivia T. Preble, Ph.D., E. Fuller Torrey, M.D.
NR83	Amphetamine and CT Findings in Schizophrenia Llewellyn B. Bigelow, M.D., Terry E. Goldberg, Ph.D., David G. Daniel, M.D., Joel E. Kleinman, M.D.
NR84	Age Disorientation and Schizophrenic Dementia Terry E. Goldberg, Ph.D., Joel E. Kleinman, M.D., David G. Daniel, M.D., Michael S. Myslobodsky, M.D., Daniel R. Weinberger, M.D.
NR85	Medial Prefrontal Cortex Lesions in the Rat George E. Jaskiw, M.D., Farouk Karoum, Ph.D., William J. Freed, Jr., Ph.D., Joel E. Kleinman, M.D., Daniel R. Weinberger, M.D.
NR86	Stage four Sleep and CT Scan Measures in Schizophrenia Jeffrey L. Peters, M.D., Welmoet B. van Kammen, M.D., Thomas C. Neylan, M.D., Kenneth L. Goetz, M.D., Daniel P. van Kammen, M.D.
NR87	Lithium and Growth Hormone Response in Psychoses Surendra Kelwala, M.D., Anil Jain, M.D., Sheena Jenson, B.A., Vijaya Chilakamarri, M.D., Basivi Baddigam, M.D., Samuel Gershon, M.D.
NR88	A Parallel Distributed Processing Model of Attention Deficit in Schizophrenia Jonathan D. Cohen, M.D.
NR89	Negative Symptoms in Schizophrenia and Depression Jacqueline A. Samson, Ph.D., Alexander Young, B.S., Ming T. Tsuang, M.D., John C. Simpson, Ph.D.
NR90	Tardive Dyskinesia: Machine-Measured Characteristics William C. Wirshing, M.D., George Bartzokis, M.D., Jeffrey L. Cummings, M.D.
NR91	CSF Norepinephrine and Relapse in Schizophrenia Kenneth L. Goetz, M.D., Jeffrey L. Peters, M.D., David Shaw, Ph.D., Jeffrey K. Yao, Ph.D., Welmoet B. van Kammen, M.D.
NR92	Biological Markers of the Positive and Negative Syndromes Anand K. Pandurangi, M.D., Solomon C. Goldberg, Ph.D., David Ross, M.D., Alfred L. Ochs, Ph.D., Douglas G. Brink, Pharm.D., Mark H. Hill, M.A.
NR93	MEG Auditory Sources May Differ in Schizophrenia Martin Reite, M.D., Peter Teale, M.S., Leigh Goldstein, M.S., John Whalen, B.A.

- NR94 Illness, Wellness in a Large Schizophrenia Pedigree
   Anne S. Bassett, M.D., Dolores Malaspina, M.D., Barry Jones, M.D., Pamela Forsythe, M.D., Angus Beck, M.D., Charles A. Kaufmann, M.D.
- NR95 Global and Focal Cerebral Atrophy in Schizophrenia William R. Yates, M.D., Victor Swayze, M.D., Nancy C. Andreasen, M.D.
- NR96 Temporal Horn Area Increased on Schizophrenia CTs Jeremy Broadhead, M.D., Godfrey D. Pearlson, M.D., Ashok J. Kumar, M.D., Pricilla Dorsey, B.S., Larry E. Tune, M.D.
- NR97 Plasma Haloperidol: Gas Chromatography Versus Radioreceptor Assay Jack Hirschowitz, M.D., Robert Hitzemann, Ph.D., Barbara Hitzemann, B.S., Beatrice Kovazsnay, M.D., Gail Brogini, B.S.N., Kathy Folkerts, B.S.N.
- NR98 Confounds of Neuroendocrine Challenge Tests Barbara E. McDermott, M.A., Charles Beasley, M.D., Kathleen Kelly, M.S.N., Jack Hirschowitz, M.D., David L. Garver, M.D.
- NR99 Simple Schizophrenia: Then and Now Todd J. Boffeli, B.S., Donald W. Black, M.D., George Winokur, M.D.
- NR100 Inpatient Treatment of Alzheimer's Disease by THA L. Jaime Fitten, M.D., Kent M. Perryman, Ph.D., Patricia Gross, Ph.D., Alan Steinberg, Ph.D., Harriet Fine, Pharm.D., Joseph Cummins, Ph.D.
- NR101 Denial and Patients with Breast Lumps Rima Styra, M.D., Isaac Sakinofsky, M.D., Leo Mahoney, M.D., Nick Colapinto, M.D., Donald Currie, M.D.
- NR102 Plasma Debrisoquin Levels in Studies of HVA in Man Mark A. Riddle, M.D., James F. Leckman, M.D., George M. Anderson, Ph.D., Maureen T. Hardin, M.S.N., Soo C. Cho, M.D., Donald J. Cohen, M.D.
- NR103 Computer-Analyzed EEG and Treatment of Alzheimer's Disease Andrew F. Leuchter, M.D., Stephen Read, M.D., Jill Shapira, M.N.C., Donald Walter, Ph.D., Cheryll Smith, Ph.D.
- NR104 The Effect of Dark-Adaptation on Smooth Pursuit Eye Tracking in Schizophrenia and Lithium-Treated Affective Disorder Pam M. Cooper, Ph.D., R.T. Pivik, Ph.D.
- NR105 Oxiracetam: Treatment in Alzheimer's Dementia Maurice W. Dysken, M.D., Susan Anton-Johnson, R.P.H., Linda Klein, M.A., Michael Kuskowski, Ph.D., Frank Stallone, Ph.D., Richard Katz, Ph.D.
- NR106 Effects of Neuroleptic Reduction in Schizophrenia Gerard Leblanc, M.D., Hugues J. Cormier, M.D., Sylvie Vaillancourt, MPs, Marie-Andree Gagne, Ph.D., Christian Gingras, B.Sc.
- NR107 Schizophrenia: Factor Analysis of Monoamine Indices Ede Frecska, M.D., Mihally Arato, M.D., Csaba M. Banki, M.D., Gyorge Bagdy, Ph.D., Andras Perenyi, M.D., Arpad Bela, M.D.
- NR108 19F MRI and MRS of Fluphenazine in Vivo and Vitro David C. Arndt, M.S., Adam V. Ratner, M.D., Kym F. Faull, Ph.D., Jack D. Barchas, M.D., Stuart W. Young, M.D.
- NR109 Cerebral Function During Cognition in Down Syndrome Karen F. Berman, M.D., Mark Schapiro, M.D., Robert P. Friedland, M.D., Stanley I. Rapoport, M.D., Daniel R. Weinberger, M.D.

#### New Research 5-Oral/Slide Session-Room 401-A, Fourth Floor, Convention Centre

#### **MOOD DISORDERS**

Chp.: Trey Sunderland, M.D.

NR110	Growth Hormone as Trait Disturbance in Depression Samuel C. Risch, M.D., Richard Hauger, M.D.	9:00 a.m.
NR111	Low CSF 5-HIAA Differentiates Suicide Attempters Michael Stanley, Ph.D., Barbara Stanley, Ph.D., J. John Mann, M.D., Allen J. Frances, M.D., Lil Traskman-Bendz, M.D.	9:15 a.m.
NR112	Temporal Lobe Size By MRI in Affective Disorder Peter Hauser, M.D., Lori Altshuler, M.D., Robert M. Post, M.D., Wade Berrettini, Ph.D., I.D. Dauphinais, M.D., Joel Gelernter, M.D.	9:30 a.m.
NR113	MAOI Treatment of Imipramine-Resistant Depression Michael E. Thase, M.D., David J. Kupfer, M.D.	9:45 a.m.
NR114	Clonidine for Mania: Placebo Controlled Trial Philip G. Janicak, M.D., Rajiv P. Sharma, M.D., Edward Altman, Ph.D., Javaid I. Javaid, Ph.D., Puskoor M. Kumar, M.D., John M. Davis, M.D.	10:00 a.m.
NR115	ECT's Effect on Sleep in Major Depression Henry W. Lahmeyer, M.D., Philip G. Janicak, M.D., Michael Easton, M.D., John M. Davis, M.D.	10:15 a.m.

#### New Research 6—Oral/Slide Session—Room 401-B, Fourth Floor, Convention Centre

#### PERSONALITY, SUBSTANCE ABUSE AND EATING DISORDERS

Chp.: George S. Alexopoulos, M.D.

NR116	Serotonergic Correlates of Personality Disorder Emil F. Coccaro, M.D., Larry J. Siever, M.D., Richard Kavoussi, M.D., Robert Trestman, M.D., Luana Howard, R.N., Kenneth L. Davis, M.D.	9:00 a.m.
NR117	Desipramine Facilitation of Cocaine Abstinence Frank H. Gawin, M.D., Herbert D. Kleber, M.D.	9:15 a.m.
NR118	Carbamazepine Treatment of Alcohol Withdrawal Robert J. Malcolm, M.D., James C. Ballenger, M.D., Raymond F. Anton, M.D., Bruce Lydiard, M.D., E. Strugis, Ph.D., Linda Williams, B.S.	9:30 a.m.
NR119	Opioid Detoxification Using Buprenorphine Dennis S. Charney, M.D., Thomas R. Kosten, M.D., John H. Krystal, M.D., Lawrence Price, M.D., Charles I. Morgan, M.D., Herbert D. Kleber, M.D.	9:45 a.m.
NR120	Familial Alcoholism in Opioid Addicts Thomas R. Kosten, M.D., Bruce J. Rounsaville, M.D.	10:00 a.m.
NR121	Evidence for Altered CSF HVA Levels in Bulimia David C. Jimerson, M.D., Walter H. Kaye, M.D., Michael D. Lesem, M.D.	10:15 a.m.

#### Wednesday, May 11, 1988, 12 noon-2:00 p.m.

New Research 7—Poster Session—Room 407-B, Fourth Floor, Convention Centre

#### MOOD DISORDERS, PSYCHOIMMUNOLOGY, PSYCHOPHARMACOLOGY AND OTHER SOMATIC THERAPIES

Moderators: Stephen G. Rayport, M.D., Abby J. Fyer, M.D.

- NR122 Evaluation of Midazolam in Chronic Insomniac Paulo F. Alterwain, M.D., Jaime M. Monti, M.D.
- NR123 Effect of Zolpidem on Sleep in Insomniac Patients Jaime M. Monti, M.D., Paulo F. Alterwain, M.D., Daniel Monti, M.D.
- NR124 Continuation Treatment for the Elderly Depressed Anastasios Georgotas, M.D., Robert E. McCue, M.D., Thomas B. Cooper, M.A., Narmada Nagachandran, M.D., Irene Chang, B.A.
- NR125 Premenstrual Symptoms in the General Population Martine Lalinec-Michaud, M.D., Viviane Kovess, M.D.
- NR126 Thyroid Hormone Potentiation of Antidepressants Russell T. Joffe, M.D., William Singer, M.D.
- NR127 The Diagnosis of Major Depression by Self-Report Scott Wetzler, Ph.D., Rene Kahn, M.D., Alan Dubro, Ph.D.
- NR128 Thyroid Function in Lithium Maintenance Treatment Julie A. Hatterer, M.D., James H. Kocsis, M.D., Peter E. Stokes, M.D.
- NR129 Role of Phospholipase A2 Overactivity Joseph R. Hibbln, B.A., June W. Palmer, Ph.D., John M. Davis, M.D.
- NR130 Efficient ECT: Temporoparietal Placements Differ Helen M. Pettinati, Ph.D., Stephani M. Nilsen, R.N., Kenneth W. Willis, M.D., Richard D. Weiner, M.D.
- NR131 Methysergide Blocks the Postictal Prolactin Surge Athanasios P. Zis, M.D., Ronald A. Remick, M.D., Campbell M. Clark, Ph.D., B.E.K. Grant, R.N., Gregory M. Brown, M.D.
- NR132 A Longitudinal Study of Mood Variations and Immune Dysfunction William J. Lancee, M.Sc., S.J.J. Freeman, M.D., Mary Kay O'Neil, Ph.D.
- NR133 Depression, Cellular Immunity and Suicidality David J. Borrelli, M.D., Elinor Levy, Ph.D., Patricia Salt, Ph.D., Steven M. Mirin, M.D., Paul H. Black, M.D.
- NR134 Psychosocial Factors in Recurrent Suicidality
   Gabor I. Keitner, M.D., Christine Ryan, Ph.D., Ivan W. Miller, Ph.D., Nathan B. Epstein, M.D., Duane S.
   Bishop, M.D., William H. Norman, Ph.D.
- NR135 Desipramine Blood Level and Therapeutic Response Mahmoud N. Musa, M.D., Bahjat Qaqish, M.D.
- NR136 Psychological Modulation of Cell-Mediated Immunity
   G. Richard Smith, M.D., Diane F. O'Rourke, Ph.D., Carolyn Conger, Ph.D., Ronald K. Charlton, Ph.D., Russell W. Steele, M.D., Susan S. Smith, M.S.W.
- NR137 Multiple Hormone Responses to Clonidine Infusion Jay D. Amsterdam, M.D., Brett Skolnick, Ph.D., Greg Maislin, M.S., Jennifer Phillips, B.S., Neil J. Berwish, M.D., Andrew Winokur, M.D.
- NR138 Long-Term Continuation Antidepressant Treatment Thomas A. Aronson, M.D., Sashi Shukla, M.D.
- NR139 Imipramine Binding in Adolescent Suicide Attempters Lee S. Cohen, M.D., Michael Stanley, Ph.D., Paul D. Trautman, M.D., Sarah Mack, B.A., David Shaffer, M.D.
- NR140 A Controlled Trial of Fluvoxamine in Major Depression John P. Feighner, M.D., William F. Boyer, M.D.
- NR141 Cognitive Effects of Corticosteroids in Man Owen M. Wolkowitz, M.D., Victor I. Reus, M.D., Herbert Weingartner, Ph.D., Raymond Deicken, M.D., Karen Thompson, B.S., Alan Breier, M.D., Allen Doran, M.D., David Pickar, M.D.

- NR142 A Pilot Clinical Trial of M-Chlorophenylpiperazine in Depression Alan M. Mellow, M.D., Brian A. Lawlor, M.D., Trey Sunderland, M.D., Edward A. Mueller, M.D., Susan E. Molchan, M.D., Dennis L. Murphy, M.D.
- NR143 Esmolol Infusion Controls Rise of HR and BP in ECT Anthony L. Kovac, M.D., Manuel Pardo, M.D., Hiroshi Goto, M.D., Kasumi Arakawa, M.D.
- NR144 Magnetic Resonance Brain Study in Bipolar Patients Henry A. Nasrallah, M.D., Stephen C. Olson, M.D., Jeffrey A. Coffman, M.D., Steven B. Schwarzkopf, M.D., Judy A. McLaughlin, M.S., Judith Brandt, R.N.
- NR145 Altered Serotonin Binding in Suicide Victims Larry D. Sparks, Ph.D., Karley Little, M.D.
- NR146 Muscarinic/Nicotinic-Evoked Catecholamine Release Marvin A. Oleshansky, M.D., Yoshikazo Nakazato, Ph.D., Peter Chiang, Ph.D.
- NR147 Effect of Naloxone on Prolactin Levels with ECT Trevor R.P. Price, M.D., Michael R. Sperling, M.D., Thomas W. McAllister, M.D., Shlomo Melmed, M.D.
- NR148 Chronobiological Influence in TRH-TSH Challenge Fabrice Duval, M.D., Luc-Andre Granier, M.D., M. Antoine Crocq, M.D., Marie Claude Mokrani, Ph.D., Michel Toussaint, Comp.Eng, Jean-Paul Macher, M.D.
- NR149 Linkage of Bipolar I Disorder to Chromosome 11 John C. Kluznik, M.D., Harry Orr, Ph.D., Stephen Rich, Ph.D., Beverley Koller, Ph.D., Lisa Duvick, M.D.
- NR150 Quantitative EEG Correlates of Depressive Phenomenology Kenneth R. Alper, M.D., A.L. Lieber, M.D., Leslie S. Prichep, Ph.D.
- NR151 Brain MRI Before and After Electroconvulsive Therapy
   Laszlo Gyulai, M.D., Trevor R.P. Price, M.D., Thomas W. McAllister, M.D., Robert I. Grossman, M.D., Bruce
   H. Braffman, M.D., Anish U. Shah
- NR152 EKG Changes with Hydroxynortriptyline Metabolites Lon S. Schneider, M.D., Thomas B. Cooper, M.A., James Severson, Ph.D., Bruce R. Sloane, M.D.
- NR153 Imipramine Binding in Primary and Secondary Major Depression James Severson, Ph.D., Lon S. Schneider, M.D., Bruce R. Sloane, M.D., Eric R. Frederickson, B.S., Ronald Gleason, M.D.
- NR154 Personality Traits in Recovered Depressed Elderly Mary F. Zemansky, Ph.D., Lon S. Schneider, M.D., Vicki E. Pollock, Ph.D., Bruce R. Sloane, M.D., Ronald Gleason, M.D., Michael S. Bender, Ph.D.
- NR155 Topographic EEGs in Recovered Depressed Elderly Vicki E. Pollock, Ph.D., Lon S. Schneider, M.D., Bruce R. Sloane, M.D., Ronald Gleason, M.D.
- NR156 Glycopyrrolate Versus Atropine in Post-ECT Amnesia Barbara R. Sommer, M.D., Andrew Satlin, M.D., Loren M. Friedman, M.S., Jonathan O. Cole, M.D.
- NR157 Bipolarity and High Achievement: A Familial Association William H. Coryell, M.D.
- NR158 Prognosis of Major Depression in the Community J. Kent Sargeant, M.D., Martha L. Bruce, Ph.D., L. Florio, M.S.
- NR159 Brain CT Findings in Late-Onset Depression
   George S. Alexopoulos, M.D., Robert C. Young, M.D., Robert C. Abrams, M.D., Charles A. Shamoian, M.D.
- NR160 Caffeine Augmentation of ECT Edward Coffey, M.D., Gary S. Figiel, M.D., Richard D. Weiner, M.D., Terry Clark, M.D., Martha Cress, R.N.
- NR161 Unilateral Versus Bilateral ECT: Long-Term Memory Follow-Up Richard D. Weiner, M.D., C. Edward Coffey, M.D., Jonathan Farber, Ph.D., Rebekka Arias, B.S., Jonathan Davidson, M.D.
- NR162 Seasonality and Phototherapy in the General Public Siegfried Kasper, M.D., Susan L.B. Rogers, R.N., Thomas A. Wehr, M.D., Pamela A. Madden, M.S., Norman E. Rosenthal, M.D.
- NR163 Familial Association Between ADD and MDD Stephen Faraone, Ph.D., Joseph Biederman, M.D.

NR164 Trytophan Depletion Alters Mood in Depression Pedro L. Delgado, M.D., Lawrence Price, M.D., Dennis S. Charney, M.D., George K. Aghajanian, M.D., Harold Landis, George R. Heninger, M.D. Effects of Thymoleptic Drugs on Serotonin Function NR165 Lawrence H. Price, M.D., Dennis S. Charney, M.D., Pedro L. Delgado, M.D., George R. Heninger, M.D. NR166 SAD: Varied Schedule Phototherapy and Catecholamines Janis L. Anderson, Ph.D., Russell G. Vasile, M.D., Kerry L. Bloomingdale, M.D., Joseph J. Schildkraut, M.D. NR167 Plasma MHPG in Major Depressive Disorder Kim Owen, M.D., Larry J. Siever, M.D., Emil F. Coccaro, M.D., Richard Kavoussi, M.D., Richard C. Mohs, Ph.D., Ren-kuy Yang, M.D., Peter J. Knott, Ph.D., Kenneth L. Davis, M.D. **NR168** Family History of Depressed Personality Disorders Jeremy M. Silverman, Ph.D., Larry J. Siever, M.D., Lynn Pinkham, M.A., Steven Greenwald, M.A., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D. Fenfluramine Challenge in Major Depression NR169 Michael D. De Meo, M.D., P. Anne McBride, M.D., J. John Mann, M.D., John Keilp, M.S. Effect of ECT on Beta-Adrenergic Receptors NR170 John C. Mahler, M.D., James P. Halper, M.D., Richard P. Brown, M.D., Michael De Meo, M.D., John A. Sweeney, Ph.D., J. John Mann, M.D. NR171 Autoradiography of Brain 5-HT2 Binding in Suicide Victoria Arango, Ph.D., Paul Ernsberger, Ph.D., Peter M. Marzuk, M.D., D.J. Reis, M.D., J. John Mann, M.D. NR172 Single Visit Dexamethasone Suppression Test Naveed Igbal, M.D., Gregory M. Asnis, M.D., Jill Friedman, Ph.D., Herman M. van Praag, M.D. Long-Term Follow-Up of Treated Chronic Depressives NR173 Bruce M. Sutton, M.D., James H. Kocsis, M.D., Allen J. Frances, M.D. NR174 Five-to Seven-Year Follow-Up of Late-Life Mania Upma Dhingra, Peter V. Rabins, M.D. NR175 Melatonin Advances Circadian Rhythms in Humans Robert L. Sack, M.D., Alfred J. Lewy, M.D. Risk Factors for DSM-III Defined Depressions in Women NR176 Alan J. Romanoski, M.D., Gerald Nestadt, M.D., Marshal F. Folstein, M.D., Ernest M. Gruenberg, M.D., Paul R. McHugh, M.D. Epidemiology of DSM-III Depressive Disorders in the United States NR177 Raman Chahal, M.D., Alan J. Romanoski, M.D., Gerald Nestadt, M.D., Marshal F. Folstein, M.D., Ernest M. Gruenberg, M.D., Paul R. McHugh, M.D. Antidepressant Response in Autoimmune Thyroiditis NR178 John J. Haggerty Jr., M.D., Jerry Browne, M.S., Robert N. Golden, M.D., Cort Pedersen, M.D., Dwight L. Evans. M.D. Natural Killer Cytotoxicity in Depressive Illness NR179 Ziad Kronfol, M.D., Kavita Goel, M.P.H., Joann Goodson, R.N., Madhavan Nair, Ph.D., Stanley Schwartz, M.D. **NR180** Depressives Nonseasonal Response to Bright Light Daniel F. Kripke, M.D., J.C. Gillin, M.D., Daniel J. Mullaney, M.S. Aggression, Suicide, CSF 5-HIAA and Family Instability NR181 Gerald L. Brown, M.D., Peter F. Goyer, M.D., Danuta M. Lamparski, Ph.D., Markku Linnoila, M.D., Frederick K. Goodwin, M.D. Cognitive Performance and Perception in LLPDD NR182 Peter J. Schmidt, M.D., Birgitta Both-Orthmann, Kari L. Muller, M.D., David R. Rubinow, M.D. NR183 Abnormal Sympathetic Nervous System Responses in MDD Philip J. Wilner, M.D., Richard P. Brown, M.D., James P. Halper, M.D., John A. Sweeney, Ph.D., Katherine Johnson, R.N., J. John Mann, M.D. EEG Sleep and Longitudinal DST Response **NR184** Shashidhar M. Shettar, M.D., James E. Shipley, M.D., Roger F. Haskett, M.D., Leon J. Grunhaus, M.D., Suzanne Bahadosingh, Atul C. Pande, M.D.

NR185 Sleep, Fatigue and Mood in Premenstrual Syndrome Margaret F. Jensvold, M.D., Kari L. Muller, M.D., David R. Rubinow, M.D. **NR186** Melatonin Secretion and Sleep in the Elderly Clifford M. Singer, M.D., Robert L. Sack, M.D., Duane Denney, M.D., Mary L. Blood, B.S., Robert F. Vandiver, M.D., Alfred J. Lewy, M.D. The Timing of Sleep and Bright Light Exposure in Treating Winter Depressives NR187 Alfred J. Lewy, M.D., Clifford M. Singer, M.D., Robert L. Sack, M.D. Carbamazepine Inhibits Signal Transduction Through the Phosphatidylinositol Cycle **NR188** Robert E. Vadnal, M.D., Nicolas G. Bazan, M.D. Circadian Rhythms in Depression and Recovery NR189 Eric Souetre, Edouard Salvati, M.D., Jean-Luc Belugou, M.D., Dominique Prinquey, M.D., Bernard Krebs, M.D., Guy Darcourt, M.D. NR190 Seasonal Changes in Mood at Three Latitudes Norman E. Rosenthal, M.D., Steven D. Targum, M.D., John P. Docherty, M.D., Howard A. Hoffman, M.D., Joel R. Hamovit, M.S.W., Michael J. Bryant, B.A., Siegfried F. Kasper, M.D. NR191 Seizure Threshold During ECT in Manic Patients Sukdeb Mukherjee, M.D., Harold A. Sackeim, M.D. NR192 Personality Traits in Geriatric Depression Robert C. Abrams, M.D., Robert C. Young, M.D., Jonathan H. Holt, M.D., George S. Alexopoulos, M.D. Heat Shock Proteins in Suicide NR193 Joel E. Kleinman, M.D., David Goldman, M.D., Chitra Rajagopal, M.D., Markku Linnoila, M.D. NR194 Hopelessness as a Predictor of Ultimate Suicide Aaron T. Beck, M.D., Gary Brown, M.S., Robert J. Berchick, Ph.D., Robert A. Steer, Ed.D. Optimizing Diagnostic Tests Using ROC Analysis NR195 Douglas Mossman, M.D., Eugene Somoza, M.D. NR196 Cortisol and Epinephrine After ACTH in Depression Peter E. Stokes, M.D., Peter M. Stoll, M.A., Carolyn R. Sikes, M.A., Melissa A. Yu, B.S., Irene Gurvits, B.S. NR197 ECT Phase-Delays Hamster Circadian Activity Rhythms John D. Hallonguist, Ph.D., Jack S. Brandes, M.D. **NR198** Depression, Cortisol Secretion and Leukocyte Traffic Gregory M. Asnis, M.D., Andrew H. Miller, M.D., Christine Lackner, B.S., Allen J. Norin, Ph.D. NR199 An In Vitro Assay for Glucocorticoid Resistance Andrew H. Miller, M.D., Gregory M. Asnis, M.D., Christine Lackner, B.S., Allen J. Norin, Ph.D. NR200 High DA D2 Receptors in Psychotic Bipolars on PET Dean F. Wong, M.D., Godfrey D. Pearlson, M.D., Christopher Ross, M.D., Larry E. Tune, M.D., Mary J. Bas-com, B.A., Henry N. Wagner, Jr., M.D., Robert F. Dannals, M.D., Jonathan Links, Ph.D. NR201 Does Treatment Influence Mortality in Depressives? Donald W. Black, M.D., George Winokur, M.D., Amelia Nasrallah, M.A., Mohandoss Emmanuel, M.S., Robert Woolson, Ph.D. NR202 Aldosterone in Late Luteal Phase Dysphoric Disorder: Effects of Atenolol Jeffrey L. Rausch, M.D., David S. Janowsky, M.D., Shahrokh Golshaan, Ph.D., Karen Kuhn, B.A. NR203 Motility Rhythms in Psychotic Inpatients Martin H. Teicher, M.D., Andrew Sussman, B.A., Ross J. Baldessarini, M.D., Harris Lieberman, Ph.D. Membrane Molecular Studies in Bipolar Depression NR204 Alan G. Mallinger, M.D., Clareann H. Bunker, Ph.D., Jonathan M. Himmelhoch, M.D., Michael E. Thase, M.D., Christine S. Dippold, B.S., Steven Knopf, B.S. NR205 Panic and Childhood Trauma in Depressed Women Gregory Gillette, M.D., James Garbutt, M.D., Kevin Robertson, M.A. NR206 Fluoxetine Versus Doxepin in Depression Eric C. Dessain, Ann P.C. Merzel, B.A., Susan J. Dugan, B.S., Paul W. O'Neil, M.Ed., Loren M. Friedman, M.S., Jonathan O. Cole, M.D.

- NR207 Daytime Amnesia with Triazolam Edward O. Bixler, Ph.D., Rocco L. Manfredi, M.D., Constantin Soldatos, M.D., Caroline Kamper, B.S., Eric Fee, B.S.
- NR208 Benzodiazepine Anxiolytics and Rebound Insomnia Anthony Kales, M.D., Antonio Vela-Bueno, M.D., Alexandros Vgontzas, M.D., Marianne McCormick, B.S., Charles Falcone, B.S.
- NR209 Rebound Anxiety with Short Half-Life Hypnotics Rejean Fontaine, M.D., Paul Beaudry, M.D., Patrick Le Morvan, Ph.D., Linda Beauclair, M.D., Guy Chouinard, M.D.
- NR210 Validity of the Inventory to Diagnose Depression Mark Zimmerman, M.D., William Coryell, M.D.
- NR211 Delayed Sleep Phase Syndrome: Preliminary Effects of Phototherapy Jean R. Joseph-Vanderpool, M.D., Eric Souetre, M.D., Karen Kelly, M.D., Patricia M. Schulz, M.S.W., Richard Allen, Ph.D., Norman E. Rosenthal, M.D.
- NR212 Mood Disorders in Parkinson's Disease Ijaz Khan, M.D., Jorge J. Juncos, M.D., Isabella J. E. Heuser, M.D., Mitchel A. Kling, M.D., Harvey Whitfield, M.D., William Gallucci, B.S., Tom Chase, M.D., Philip W. Gold, M.D.
- NR213 Elevated CSF CRF in Completed Suicides Mihaly Arato, M.D., Csaba M. Banki, M.D., Garth Bissette, Ph.D., Charles B. Nemeroff, M.D., Erzsebet Demeter, Ph.D., Aniko Faluks, Ph.D.
- NR214 Antidepressant Activity of ACE-Inhibitors Angelo Bosio, M.D., Rosangela Rosola, Daniela Canini, M.D., Carlo Abbati, M.D., Lidia Sorlini

### New Research 8---Oral/Slide Session-Room 401-A, Fourth Floor, Convention Centre

#### ORGANIC MENTAL DISORDERS AND AIDS

Chp.: Philip R. Beck, M.D.

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NR215	RCBF Effects of Scopolamine Compared to Dementia William G. Honer, M.D., Isak Prohovnik, Ph.D., Gwenn Smith, M.A., Louis R. Lucas, M.Sc.	9:00 a.m.
NR216	Scopolamine and CNS Metabolism: A Model for SDAT? Michael Gross, M.D., Thomas E. Nordahl, M.D., Trey Sunderland, M.D., William E. Semple, Ph.D., Susan M. Dowling, B.A., Robert M. Cohen, M.D.	9:15 a.m.
NR217	Neuropeptides in Alzheimer's Disease Michael F. Mazurek, M.D., M. Flint Beal, M.D.	9:30 a.m.
NR218	Optic Nerve Head in Alzheimer's Disease Michael Davidson, M.D., Clark Tsai, M.D., Robert Ritch, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.	9:45 a.m.
NR219	SPECT Scan Changes in HIV-Related Dementia Godfrey D. Pearlson, M.D., Frederick Schaerf, M.D., Norman D. LaFrance, M.D., Justin McAr- thur, M.D., Mary J. Bascom, B.A.	10:00 a.m.
NR220	AIDS is Associated with a High Rate of Suicide Peter M. Marzuk, M.D., Helen Tierney, M.D., Kenneth J. Tardiff, M.D., Edward B. Morgan, M.P.H., J. John Mann, M.D.	10:15 a.m.

Thursday, May 12, 1988, 9:00 a.m.-10:30 a.m.

#### New Research 9-Oral/Slide Session-Room 401-B, Fourth Floor, Convention Centre

#### CHILDHOOD DISORDERS

Chp.: Rege S. Stewart, M.D.

NR221	Psychiatric Correlates of Behavioral Inhibition in Clinical and Epidemiologic Samples of Young Children Joseph Biederman, M.D., Jerrold F. Rosenbaum, M.D., Jerome Kagan, Ph.D.	9:00 a.m.
NR222	Depression, Dysphoric Affect and Mother/Child Interaction Grazyna Kochanska, Ph.D., Leon Kuczynski, Ph.D.	9:15 a.m.
NR223	Social Deprivation and Long-Term Vulnerability William T. McKinney, M.D., Gary W. Kraemer, Ph.D., Michael H. Ebert, M.D., Dennis E. Schmidt, Ph.D.	9:30 a.m.
NR224	Psychiatric Sequelae of Childhood Disability Naomi Breslau, Ph.D., Glenn C. Davis, M.D.	9:45 a.m.
NR225	Serotonergic Function in Autistic Young Adults 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.
NR226	Panic Disorder in Children: Does it Exist? Donna Moreau, M.D., Virginia S. Warner, M.P.H., Myrna M. Weissman, Ph.D.	10:15 a.m.

#### New Research 10—Posater Session—Room 407-B, Fourth Floor, Convention Centre

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

Moderators.: Susan J. Fiester, M.D., Charles A. Kaufmann, M.D.

- NR227 PTSD in Vietnam Veterans: Clinical-EEG Findings Afshin Alavi, M.D., Marion E. Wolf, M.D., Aron D. Mosnaim, Ph.D.
- NR228 Further Empirical Research on Defense Styles Michael P. Bond, M.D., J. Christopher Perry, M.D., Maryse Gautier, M.Ed., Marilyn Goldenberg, M.S.W., Joan Oppenheimer, B.A., Joan Simand, M.S.W.
- NR229 Borderline and Anxiety Disorder Coeffect on Outcome
   H. George Nurnberg, M.D., Marjorie Raskin, M.D., Philip E. Levine, M.D., Simcha Pollack, Ph.D., Robert
   Prince, Ph.D., Ozzie Siegel, Ph.D.
- NR230 Caffeine Dependence in Moderate Coffee Drinkers John R. Hughes, Stephen T. Higgins, Ph.D., Suzy Gulliver, M.S., Gina Mireault, B.A.
- NR231 Schizotypal Gender Differences Thomas H. McGlashan, M.D.
- NR232 Defenses and Parental Bonding in Eating Disordered Women Howard Steiger, Ph.D., Julie Vanderfeen, B.Sc., Pierre P. Leichner, M.D.
- NR233 Sleep Encephalograpy of Panic Disorder Patients and Normal Controls Robert B. Lydiard, M.D., Michele T. Laraia, M.S.N., James C. Ballenger, M.D., Elizabeth Howell, M.D., Victor Prockow, John Gross, M.D.
- NR234 Prevalence of Anxiety Disorders Among Alcoholics Elizabeth Howell, M.D., Robert B. Lydiard, M.D., Robert J. Malcolm, M.D., James C. Ballenger, M.D.
- NR235 Gabaminergic Mechanisms in Antipanic Drug Efficacy Michael F. Breslow, M.D., Martha Fankhauser, M.S., Rebecca L. Potter, M.D., John Misiaszek, M.D., Keith M. Meredith, Ph.D., Deane G. Hope, Jr., M.Ed.
- NR236 Arrest History of Hyperactive Boys Grown Up Salvatore Mannuzza, Ph.D., Rachel Klein, Ph.D., Paula Konig, B.A., Noreen Bonagura, M.S.W., Tina Giampino, B.A.
- NR237 Reliability of Anxiety Diagnoses and Symptoms
   Abby J. Fyer, M.D., Salvatore Mannuzza, Ph.D., Lynn Y. Martin, R.N., M.S. Gallops, M.Ph., Jack M. Gorman,
   M.D., Michael R. Liebowitz, M.D., Donald F. Klein, M.D.
- NR238 Strategic Self-Therapy for Personality Disorders John O. Beahrs, M.D., John L. Butler, M.D., Stanley G. Sturges, M.D.
- NR239 Adrenergic Dysfunction in Anxiety Disorders Oliver G. Cameron, M.D., Charles B. Smith, M.D., George C. Curtis, M.D., Myung A. Lee, M.D., Peggie J. Hollingsworth, Ph.D., George N.M. Gurguis, M.D.
- NR240 Depression and Previous Alcoholism in the Elderly Brian L. Cook, D.O., George Winokur, M.D., Vickie Beach, R.N.
- NR241 Season of Birth and Child Temperament: New Findings Michel Maziade, M.D., Robert Cote, Ph.D., Jacques Thivierge, M.D.
- NR242 Extreme Temperament in a Child Psychiatric Sample Chantal Caron, M.D., Michel Maziade, M.D., Robert Cote, Ph.D., Pierrette Boutin, M.Ps., Jacques Thivierge, M.D.
- NR243 DST and TRH Tests in Post-Traumatic Stress Disorder Victor S. Wahby, M.D., Thomas R. Kosten, M.D., Earl Giller, Jr., M.D., John W. Mason, M.D.
- NR244 The Cornell Nurses' Rating Scale: A Nurse's Rating Scale for Psychiatric Patients Susan Evans, R.N., Richard P. Brown, M.D., Marc Glassman, Ph.D., Kenneth H. Larson, R.N.
- NR245 Diagnosis and Predicting Against Medical Advice Discharge Status Robert K. Heinssen, Ph.D., Thomas H. McGlashan, M.D.

- Plasma Catecholamines in Social Phobia NR246 Andrew P. Levin, M.D., Diana Sandberg, M.D., Jon Stein, M.S., Barry Cohen, M.S., Tim Strauman, Ph.D., Michael R. Liebowitz, M.D. NR247 Personality Disorders in Eating Disorder Patients Ronald N. Marcus, M.D., Katherine A. Halmi, M.D., Alison Gartner, Ph.D., Armand Loranger, Ph.D. Eating Disorders in Substance Abuse Patients NR248 Katherine A. Halmi, M.D., Ronald N. Marcus, M.D. NR249 Depression in Adolescents with Conduct Disorder William Martin, M.D., Catherine A. Martin, M.D., Lisa M. White, B.S., William Workman, B.S., Laurie L. Humphries, M.D. NR250 Malpractice: Physician Stress Reaction Catherine A. Martin, M.D., John F. Wilson, Ph.D., N. Donald Feibelman, M.D. The Interaction of Prolonged Total Sleep Deprivation and d-Amphetamine on Arousal, Cognition and Mood NR251 Paul A. Newhouse, M.D., Gregory L. Belenky, M.D., Maria L. Thomas, M.A., David Thorne, Ph.D., Helen Sing, M.S., Joanne Fertig, Ph.D., David Penetar, Ph.D. Magnetic Resonance Imaging in Obsessive Disorder NR252 Jordan Garber, M.D., Jambur V. Ananth, M.D., Lee Chiu, M.D., Armen Djenderedjian, M.D. Nicotine Gum, Tobacco Dependence and Withdrawal NR253 Michael G. Goldstein, M.D., Kenneth Ward, B.S., Raymond Niaura, Ph.D. NR254 Lactate Response in Pure Generalized Anxiety Deborah S. Cowley, M.D., Stephen R. Dager, M.D., Jon McClellan, M.D., Peter P. Roy-Byrne, M.D., David L. Dunner, M.D. Persistent Endocrine Abnormalities in Bulimia NR255 Alan B. Levy, M.D., William B. Malarkey, M.D., Katherine Dixon, M.D. Obsessive Compulsive Disorder with Psychotic Features NR256 Jane L. Eisen, M.D., Steven A. Rasmussen, M.D. Family Function in Obsessive Compulsive Disorder NR257 Barbara Livingston, M.S.W., Jane L. Eisen, M.D., Lois McCartney, M.S.W., Robert L. Lindsey, M.D., Steven A. Rasmussen, M.D. NR258 Do Borderline Patients Regress in the Hospital? Alexis A. Giese, M.D., Ellen Leibenluft, M.D., David L. Gardner, M.D., Richard C. Filson, Ed.D., Elizabeth Zimmerman, B.A. NR259 Follow-Up Study of Inpatients with Anorexia Nervosa David Greenfeld, M.D., Marie Hobart, M.D., Walter R. Anyan, M.D., Margaret Plantes, M.A., Donald M. Quinlan, Ph.D., Elaine Glass, M.S.W. NR260 Substance Use, Suicide and Borderline Personality Disorder Rebecca A. Dulit, M.D., Minna R. Fyer, M.D., Steven W. Hurt, Ph.D., Allen J. Frances, M.D., Timothy Sullivan, M.D., John F. Clarkin, Ph.D. Yale-Brown Obsessive Compulsive Scale: Validity NR261 Wayne K. Goodman, M.D., Lawrence Price, M.D., Steven A. Rasmussen, M.D., Carolyn Mazure, Ph.D., George R. Heninger, M.D., Dennis S. Charney, M.D. Benzodiazepine Receptor Antagonist Effects in Panic Disorder NR262 Scott W. Woods, M.D., Dennis S. Charney, M.D., Jonathan M. Silver, M.D., John H. Krystal, M.D., George R. Heninger, M.D. Characteristics of Self-Defined Panic Attacks NR263 John H. Krystal, M.D., Scott W. Woods, M.D., Candy L. Hill, M.S., Dennis S. Charney, M.D. NR264 Bromocriptine Versus Desipramine in Cocaine Withdrawal Irl L. Extein, M.D., Sharman S. Allen, M.D., Mark S. Gold, M.D., Aldo Morales, Jr., M.D., Paul J. Goodnick, M.D., David A. Gross, M.D. NR265 Discriminant Validity of Schizotypal Personality Elizabeth Squires-Wheeler, Ph.D., Andrew E. Skodol, M.D., L. Erlenmeyer-Kimling, Ph.D. NR266 Behavioral and Prolactin Responses to Fenfluramine in OCD
  - M. Katherine Shear, M.D., Michael D. De Meo, M.D., P. Anne McBride, M.D., James P. Halper, M.D., Jaw-Sy Chen, Ph.D., J. John Mann, M.D.

- NR267 Eye Tracking in Obsessive Compulsive Disorder John A. Sweeney, Ph.D., M. Katherine Shear, M.D., James P. Halper, M.D., Michael De Meo, M.D., Brett Clementz, M.S., Virginia Walsh, B.S.
  NR268 Co-Alcoholism in Psychiatric Outpatients Donna A. Vaughan, M.D., Beryl Silkey, Sc.M., Julie A. Parsons, M.D.
  NR269 PET Study of Bulimic Normal Differences Joseph C. Wu, M.D., Monte S. Buchsbaum, M.D., Barton J. Blinder, M.D., Melissa Derfler, M.D., Jennifer Hagman, M.D.
- NR270 Panic Disorder: Clonezepam Versus Alprazolam and Placebo George E. Tesar, M.D., Jerrold F. Rosenbaum, M.D., Mark H. Pollack, M.D., Gary S. Sachs, M.D., John B. Herman, M.D., Joseph N. Sidari
- NR271 Relationship Between CSF CRH and MHPG in Anorexia Nervosa Michael D. Lesem, M.D., Philip W. Gold, M.D., Arlene P. Hegg, M.D., David C. Jimerson, M.D.
- NR272 Neuropsychological Functioning and Brain Glucose Metabolism in Normal Weight Bulimics Melissa A. Rooney-Chiles, M.A., Barton J. Blinder, M.D., Joseph C. Wu, M.D., Monte S. Buchsbaum, M.D., Robert A. Lear, Ph.D.
- NR273 Elevated Production of Lactate in Panic Disorder Richard Maddock, M.D., Jose Mateo-Bermudez, M.D.
- NR274 Adult Children of Alcoholics: Personal and Transgenerational Patterns Vicki L. C. Weatherford, Ph.D., Edward Kaufman, M.D.
- NR275 Alcoholism and Mental Comorbidity in the Homeless Alan Ross, Ph.D., Alan J. Romanoski, M.D., Gerald Nestadt, M.D., Pamela J. Fischer, Ph.D., William R. Breakey, M.D.
- NR276 Dimensions of Conduct Disorder Among Adolescents Spyros J. Monopolis, M.D., George U. Balis, M.D.
- NR277 Effects of Child Sexual Abuse on Adult Intimacy Sherry Stewart, M.A., Jenny G. Stadler, M.A., Pamela M. Cole, Ph.D.
- NR278 Guilt in Offspring of Depressed Mothers Carolyn Zahn-Waxler, Ph.D., Grazyna Kochanska, Ph.D., Janice Krupnick, L.S.W., Donald McKnew, M.D.
- NR279 Comorbidity of Social Phobia in Panic Disorder Murray B. Stein, M.D., Cheryl A. Shea, M.A., Thomas W. Uhde, M.D.
- NR280 Effects of Opioid Blockade in the Eating Disorders Harry A. Brandt, M.D., Arlene P. Hegg, M.D., David Pickar, M.D., Timothy D. Brewerton, M.D., David C. Jimerson, M.D.
- NR281 Platelet Serotonin Uptake in Bulimia Nervosa David S. Goldbloom, M.D., Lisa Hicks, B.A., Paul E. Garfinkel, M.D.
- NR282 Eating Disorders and Alcoholism: Coprevalence Lisa Hicks, B.A., David S. Goldbloom, M.D.
- NR283 CSF Oxytocin in Anorexia Nervosa Mark A. Demitrack, M.D., Michael D. Lesem, M.D., Harry A. Brandt, M.D., Teresa A. Piggot, M.D., David C. Jimerson, M.D., Philip W. Gold, M.D.
- NR284 Substance Abuse in Schizophrenics at Admission Andrew I. Shaner, M.D., Jeffery N. Wilkins, M.D., David A. Gorelick, M.D.
- NR285 Social Status-Setting Alters PCP Effects in Monkeys James E. Dillon, M.D., Jeffery N. Wilkins, M.D., Michael J. Raleigh, Ph.D.
- NR286 Stress and Depression in Inner City Adolescents Steven J. Schleifer, M.D., Jacqueline Bartlett, M.D., Barbara J. Scott, Robert L. Johnson, M.D., Steven E. Keller, Ph.D.
- NR287 The Tridimensional Personality Questionnaire: A Validity Study with Alcoholics Danuta M. Lamparski, Ph.D., Debra K. Garnett, M.S.W., Markku Linnoila, M.D.
- NR288 Multiple Personality and Partial Complex Seizures Colin A. Ross, M.D., G. Ron Norton, Ph.D., Sharon Heber, R.N., Geri Anderson, R.P.N.

NR289	Pubertal Timing and Diet Practices in Adolescence Adam Drewnowski, Ph.D., Doris K. Yee, M.A., Dean D. Krahn, M.D.
NR290	Children's Exposure to Parental Psychopathology John E. Richters, Ph.D.
NR291	Expressed Emotion and Child Psychopathology Carl E. Schwartz, M.D., William R. Beardslee, M.D., David J. Dorer, Ph.D., Philip W. Lavori, Ph.D., Martin B. Keller, M.D.
NR292	Adult Children of Problem Drinkers in the Community Nady El-Guebaly, M.D., John R. Walker, Ph.D., Colin A. Ross, M.D., Raymond F. Currie, Ph.D.
NR293	Weight Loss, Opiate Function and Eating Behavior Arlene P. Hegg, M.D., Michael D. Lesem, M.D., Harry A. Brandt, M.D., David C. Jimerson, M.D.
NR294	Compulsive Personality Disorder in the Community Marshal F. Folstein, M.D., Gerald Nestadt, M.D., Alan J. Romanoski, M.D., Ernest M. Gruenberg, M.D., Paul R. McHugh, M.D.
NR295	Personality Disorders in Baltimore's Homeless Gerald Nestadt, M.D., William R. Breakey, M.D., Alan J. Romanoski, M.D., Pamela J. Fisher, Ph.D.
NR296	Studies of Basal Metabolism in Bulimia Michael J. Devlin, M.D., B. Timothy Walsh, M.D., Steven B. Heymsfield, M.D., Sondra Dantzic, B.A., Linda Wong, B.A.
NR297	Influence of Perceived Control on Carbon Dioxide Panic William S. Sanderson, Ph.D., Ronald M. Rapee, Ph.D., David H. Barlow, Ph.D.
NR298	Habituation of Startle in PTSD William A. Ball, M.D., Michelle E. Cohen, Ph.D., Steven M. Silver, Ph.D., Adrian R. Morrison, D.V.M., Richard J. Ross, M.D.
NR299	Self-Report Versus DST in Assessing Depressed Children Mary A. Fristad, Ph.D., Elizabeth B. Weller, M.D., Ronald A. Weller, M.D., Marijo Teare, B.S., Sheldon H. Preskorn, M.D.
NR300	WITHDRAWN
NR301	Cortisol Functioning in Bereaved Children Elizabeth B. Weller, M.D., Ronald A. Weller, M.D., Mary A. Fristad, Ph.D., Jennifer M. Bowes, B.A.
NR302	Family Psychopathology in Depressed Children Ronald A. Weller, M.D., Elizabeth B. Weller, M.D., Mary A. Fristad, Ph.D., Loribeth Cohn, B.S., Sheldon H. Preskorn, M.D.
NR303	Personality Profiles in Anorexia at Ten-Year Follow-Up Edward J. Schork, Ph.D., Katherine A. Halmi, M.D., Elke D. Eckert, M.D., Aline L. Bisgaier, B.A.
NR304	Dysregulation of 5-HT Function in Bulimia Nervosa Timothy D. Brewerton, M.D., Edward A. Mueller, M.D., Harry A. Brandt, M.D., Michael D. Lesem, M.D., Dennis L. Murphy, M.D., David C. Jimerson, M.D.
NR305	P300 Augmentation in Post-Traumatic Stress Disorder Ron K. Wolner, M.D., Lawrence C. Kolb, M.D., Venkat Ramani, M.D.
NR306	A Clinical and Demographic Study of Hyperactive Adults Walid O. Shekim, M.D., Robert Asarnow, Ph.D., Esther Hess, M.A., Ruth Chao, M.A., Noel Wheeler, Ph.D.
NR307	Inter-Rater Agreement in Psychotherapy Research Gordon D. Strauss, M.D., Marcia K. Goin, M.D., Robert S. Martin, M.D.
NR308	Clinical Correlates of Brain Metabolism in Bulimia Jennifer Hagman, M.D., Barton J. Blinder, M.D., Joseph C. Wu, M.D., Monte S. Buchsbaum, M.D., Melissa Derfler, M.D.
NR309	Attentional Bias in Panic Disorder Roger L. Cambor, M.D., M. Katherine Shear, M.D., Lisa A. Spielman, B.S., John A. Bargh, Ph.D., John A. Sweeney, Ph.D.
NR310	Depression as an Eating Disorder: Nutrition, Behavior and Neuroendocrinology Manfred M. Fichter, M.D., K.M. Pirke, M.D.

- NR311 Correlates of Axis II Comorbidity in Bulimia Bruce Sieleni, M.D., William R. Yates, M.D.
- NR312 Psychiatric Examinations of Homeless Men and Women William R. Breakey, M.B., Alan J. Romanoski, M.D., Gerald Nestadt, M.D., Pamela J. Fischer, Ph.D., Alan Ross, Ph.D.
- NR313 HPA Axis Function and CSF Peptides in Alcoholics Bryon Adinoff, M.D., Peter R. Martin, M.D., Michael J. Eckardt, Ph.D., George H.A. Bone, M.D., Marku Linnoila, M.D., Philip W. Gold, M.D.
- NR314 Childhood Trauma in Borderline Personality Disorder Judith L. Herman, M.D., J. Christopher Perry, M.D., Bessel van der Kolk, M.D.
- NR315 Personality Disorder in Obsessive Compulsives Russell Noyes, Jr., M.D., Donald W. Black, M.D., William R. Yates, M.D., Bruce Pfohl, M.D., James H. Reich, M.D.
- NR316 Personality Disorder in Morbidly Obese Patients George Winokur, M.D., Donald W. Black, M.D., William R. Yates, M.D., Sue Bell, R.N., Edward E. Mason, M.D., Rise B. Goldstein, M.S.W., James H. Reich, M.D.
- NR317 As Needed Treatment of Panic Disorder with RO 16-6028 Heinz Katschnig, M.D., Walter A. Merz, M.D., Detlev O. Nutzinger, M.D.
- NR318 Antidepressants and Nicotine Withdrawal Symptoms Neil B. Edwards, M.D., Joseph K. Murphy, Ph.D., Anna D. Downs, Ph.D., Bette J. Ackerman, Ph.D.
- NR319 Epidemiologic Analysis of Alcohol and Drug Use as Risk Factors for the Incidence of Self-Reported Delusions and Hallucinations Allen Y. Tien, M.D., James C. Anthony, Ph.D.
- NR320 Methods for Establishing a Focus for Psychotherapy K. Roy Mackenzie, M.D.
- NR321 Family History of Controls Who Panic with Lactate Richard Balon, M.D., Margaret Jordan, Robert Pohl, M.D., Vikram K. Yeragani, M.D., Wendy Jankowski, B.S.
- NR322 An Empirical Classification of Personality Disorder W. John Livesley, M.D.

#### NR1 TEMPORAL LOBE PATHOLOGY IN SCHIZOPHRENIA

Richard L. Suddath, M.D., NIMH WAWRH, St. Elizabeths Hospital, 2700 Martin L. King Jr. Ave SE, Washington, DC 20032; Manuel F. Casanova, M.D., Terry E. Goldberg, Ph.D., David G. Daniel, M.D., John R. Kelsoe, M.D., Daniel R. Weinberger, M.D.

#### **Educational Objectives:**

To increase understanding of structural pathology in brain areas implicated in the pathogenesis of schizophrenia.

#### Summary:

Although numerous neuroimaging studies have confirmed the presence of enlarged cerebral ventricles in schizophrenia, the focus of tissue loss explaining this pathology remains elusive. Recent advances in computerized image analysis (CIA) allow the quantitative examination of multisequence MRI with the capabilities of contrast enhancement, color coding, magnification, and automated edge detection. Since many clinical and postmortem studies have implicated both the prefrontal and temporal regions in schizophrenia, we chose to apply this CIA system to a volumetric determination of both gray and white matter in these structures. MRI films were digitized from a light box and displayed on a monitor which permitted the application of the computerized functions. Our study included 17 schizophrenics and an equal number of age- and sex-matched normal controls. The results indicate a 16% reduction (p<03, MANOVA) of temporal lobe gray matter bilaterally in schizophrenics, with no significant difference in temporal lobe white matter, frontal gray, or frontal white matter volume. In addition we found that lateral ventricular volume was increased by 45% in the schizophrenic group, and that this volume (when referenced to an unaffected brain region) correlated inversely with the volume of the temporal lobes. These findings suggest focal temporal lobe gray matter pathology in schizophrenia.

#### References:

1. Bogerts B, Meertz E, Scholfeldt-Bausch R: Basal ganglia and limbic system pathology in schizophrenia: A morphometric study of brain volume and shrinkage. Arch Gen Psychiatry; 42:784-791, 1985.

2. Brown R, Colter N, Corsellis JAN, Crow TJ, Frith CD, Jagoe R, Johnstone EC, Marsh L: Postmortem evidence of structural brain changes in schizophrenia: Differences in brain weight, temporal horn area, and parahippocampal gyrus compared with ... Arch Gen Psychiatry; 43:36-4, 1986.

#### NR2

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

#### PROGRESSIVE VENTRICULAR CHANGES IN SCHIZOPHRENIA

Bryan T. Woods, M.D., Neurology, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Francine M. Benes, M.D., Deborah Yurgelun-Todd, M.D.

#### **Educational Objectives:**

To make listeners aware of the implications of the observed ventricular changes in schizophrenia for: 1) theories of etiology and mechanism; 2) issues of heterogeneity in schizophrenia; 3) the possibility of prevention or amelioration of chronic deterioration in some schizophrenic patients.

#### Summary:

Excessive ventricular enlargement in some schizophrenic patients is well-documented<sup>1</sup>; there remains a question of whether this enlargement is a static change that precedes onset of overt illness<sup>1</sup> or is progressive over the course of clinical illness<sup>2</sup>. We measured changes in the ventricular-brain ratio (VBR) on CT scans acquired at intervals ranging from 12 to 54 months on nine *DSM-III* schizophrenic patients (mean scan interval 30 months, initial VBR 10.0) and nine *DSM-III* bipolar affective disorder patients (mean scan interval 19 months, initial VBR 6.6). We controlled for between-scan variability due to short-term factors by measuring VBR changes in patients with two separate scans less than six months apart (mean interval two months, initial VBR 5.2). The schizophrenic group showed a mean VBR increase of 2.5 (t=3.73, p<.01 two-tailed), the bipolars a mean increase of 0.7 (n.s.), and the short-term control group of decrease of 0.8 (n.s.). The schizophrenic change was significantly greater than in either bipolars (p<.05) or controls (p<.01); the bipolar increase was also significantly different from controls (p<.05). The ventricular enlargement in the schizophrenics showed a zero correlation with scan interval. Consistent with this nonlinear relationship, patients with more than two scans tended to show sudden step-wise increases in VBR, which appeared to have a delayed temporal relationship to periods of clinical deterioration. Possible etiological mechanisms and treatment implications of these delayed changes are discussed.

#### **References:**

<sup>1</sup>Weinberger DR: Computer tomography (CT) findings in schizophrenia; speculation on the meaning of it all. J Psychol Res 18:477-490, 1984.

<sup>2</sup>Woods BT, Wolf J: A reconsideration of the relation of ventricular enlargement to duration of illness in schizophrenia. Am J Psychiatry 140:1564-1570, 1983.

#### NR3 APOMORPHINE AND RCBF IN SCHIZOPHRENIA

David G. Daniel, M.D., CBDB, NIMH, 2700 Martin L. King Jr. Ave. SE, Washington, DC 20032; Karen F. Berman, M.D., Ralph Fawcett, M.D., Daniel R. Weinberger, M.D.

#### **Educational Objectives:**

To describe the effect of a dopamine agonist on cerebral blood flow in patients with schizophrenia. The implications of these findings for our understanding of the interaction of dopamine activity imbalances with prefrontal cortex dysfunction in schizophrenia will be discussed.

#### Summary:

We have previously observed a direct correlation in schizophrenia between CSF HVA and relative activity of the prefrontal cortex during a prefrontal activation task, suggesting that reduced mesocortical dopaminergic function might be related to hypofrontality. To further explore the role of dopamine on cortical function we conducted a double-blind, placebo-controlled study of the effects of .005 mg/kg of apomorphine, a direct acting dopamine agonist, on regional cerebral blood flow (Xe-133 rCBF) during a prefrontal cortex activation procedure in six drug-free schizophrenic patients. Following a simple Numbers Matching control task, each subject received either placebo or active apomorphine (SQ) and then performed a prefrontal activation task (Wisconsin Card Sort). In each patient with schizophrenia, apomorphine increased relative prefrontal flow (paired t=2.93, n=6, p=.03) during the prefrontal cortex activation procedure. In addition, during the prefrontal activation task patients showed greater increases in relative prefrontal flow compared to the control task with apomorphine than with placebo (paired t=3.31, n=6, p=.02). The results suggest that in schizophrenia enhanced prefrontal dopamine increases relative rCBF in the prefrontal cortex, an area implicated by recent cognitive and physiological studies in the pathophysiology of schizophrenia. **References:** 

<sup>1</sup>Weinberger DR, Berman KF, Zec RF: Physiological dysfunction of dorsolateral prefrontal cortex in schizophrenia, I: Regional cerebral blood flow (rCBF) evidence. Arch Gen Psychiatry; 43:114-125, 1986.

<sup>2</sup>Johns CA, Levy MI, Davis BM et al: Apomorphine and schizophrenia. Psychopharmacology Bulletin; 20:103-107, 1984.

#### NR4 ADRENERGIC RECEPTOR SUPERSENSITIVITY IN SCHIZOPHRENIA

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

David L. Garver, M.D., Psychiatry, Univ of Cincinnati, 231 Bethesda Avenue ML 559, Cincinnati, OH 45267; Paul R. Sanberg, Ph.D., Lawrence Frohman, M.D.

#### **Educational Objectives:**

To explore the Noradrenergic Hypothesis of Schizophrenia in terms of post synaptic  $\alpha$ -receptor sensitivity, and understanding the potential consequence of such sensitivity upon amplification of NE-associated events in schizophrenics.

#### Summary:

Activity of the hypothalamic-pituitary growth hormone (GH) axis is modulated by several neurotransmitters and neuromodulators. Prominent in the facilitation of GH release are a  $\alpha$ -adrenergic and dopaminergic receptors believed to be located on growth hormone releasing factor (GRF) neurons in the arcuate nucleus of the hypothalamus. Both  $\alpha$ -adrenergic agonists (such as clonidine [CL]) and dopamine agonists (such as apomorphine [AP]) trigger GRF release from the median eminance and, secondarily, GH from the pituitary. The relative GH response to CL and to AP can be used to determine the relative functional sensitivity of  $\alpha$ -adrenergic and dopamine receptors associated with the hypothalamic-pituitary GH axis.

The ratio of CL/AP-induced GH release is  $0.02\pm0.17$ (SD) in controls and  $0.98\pm0.23$  in drug-free DSM-III schizophrenics (t=7.10, df10; p<0.00003). The difference in functional receptor sensitivity is not due to a difference in the AP-induced response (155±9.2 ngGH/ml in controls and 14.7±12.5 in schizophrenics), but is a result of an increment in the response to CL (2.4±2.2 in controls and 12.5±9.1 in schizophrenics; t=2.87, df=10; p<0.02). Similarly, though there was no significant difference in the ratio of AP/GRF release of GH between controls and schizophrenics (p=0.34), the ratio of CL/GRF-induced GH release was  $0.10\pm0.07$  in controls and  $1.24\pm0.71$  in schizophrenics (t=3.14, df=7; p<0.02).

Using the GH response to both AP and to GRF as an integral standard, DSM-III schizophrenics appear to have a functional supersensitivity of post-synaptic  $\alpha$ -adrenergic receptor activity as demonstrated by excessive GH responses to CCL. Discussion focuses upon these findings and the Norepinephrine Hypotheses of schizophrenia.

#### **References:**

1. VanKammen VP, Antleman S: Mini-review: Impaired noradrenergic transmission in schizophrenia. *Life Science* 34:1403-1413, 1984.

2. Sternberg DE, Charner DS, Heninger GR, Leckman JF, Hafstad KM, Landis DH: Impaired presynaptic regulation of norepinephrine in schizophrenia. Arch. Gen. Psychiatry 39:285-289, 1982

#### NR5 BIOLOGY OF SCHIZOTYPAL AND SCHIZOPHRENIC PATIENTS

Larry J. Siever, M.D., Psychiatry, Bronx VA Med Ctr, 130 W. Kingsbridge Road, Bronx, NY 10468; Zvi Zemishlany, M.D., Emil F. Coccaro, M.D., Miklos F. Losonczy, M.D., Thomas B. Horvath, M.D., Michael Davidson, M.D., Howard Klar, M.D., Kenneth L. Davis, M.D.

#### **Educational Objectives:**

To educate the psychiatric community about new biologic findings linking schizotypal personality disorder to chronic schizophrenia.

#### Summary:

Ventricular brain ratio (VBR), smooth pursuit eye movement (SPEM) and auditory evoked potentials (EP) were evaluated in subsamples of 24 schizotypal personality disorder patients (SPD), 38 schizophrenics, 24 normal controls (NC) and 17 patients with other personality disorders (PD), excluding paranoid and schizoid PD. Mean VBR in schizophrenia (7.0 + 3.8) and in SPD (6.4 = 3.0) was significantly greater than that of NC (4.7 + 1.7) (p<0.5, t-test). The VBR of other PD (5.9 + 1.7) was not significantly different from NC. The mean qualitative rating of SPEM in all three groups of patients differed significantly (p < 00.5), t-test) from NC. SPEM impairment (1 SD from normal mean), however, was more prevalent only in schizophrenics (63%) and in SPD (58%) when compared to NC (25%) (Fisher exact test, p<.05). Preliminary results of auditory EP suggest that schizophrenics and SPD both have lower N200-P300 amplitude than NC. To date, all of the biologic measures implicated as abnormal in schizophrenia that have also been tested in SPD patients have revealed similar, although milder, abnormalities in SPD. These results suggest that the two disorders may be related as a part of a continuum of schizophrenia-related disorders.

#### **References:**

Siever, L. Biologic correlates of schizotypal personality disorder. Schiz. Bull. 11:538-553, 1985.

<sup>2</sup>Siever, LJ, Coursey RD, Alterman IS, et al. Impaired smooth pursuit eye movements: a vulnerability marker for schizotypal personality disorder. *Am J Psychiatry* 141:1560-1565.

#### NR6

#### DSM-III-R SCHIZOPHRENIA IS TOO NARROW

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

Wayne S. Fenton, M.D., Research Inst, Chestnut Lodge, 500 West Montgomery Avenue, Rockville, MD 20850; Thomas H. McGlashan, M.D., Robert K. Heinssen, Ph.D.

#### Educational Objectives:

Following the presentation, the listener will understand the differencies between *DSM-III* and *DSM-III-R* definitions of schizophrenia, will be able to identify which patients meeting *DSM-III* do not meet *DSM-III-R*, and will be able to consider the pros and cons of changing the criteria.

#### Summary:

Since the American Psychiatric Association's official nomenclature is likely to be widely adopted in clinical research settings, proposed changes bear careful evaluation.<sup>1</sup> The authors compare *DSM-III* and *DSM-III-R* definitions of schizophrenia by applying both to a heterogeneous sample of 532 inpatients treated in a long-term residential setting and reevaluated an average of 15 years later as part of the Chestnut Lodge Follow-up Study.<sup>2</sup> Using a procedure in which data from patients were serially "sifted" through each subcriteria of both systems, we found that patients meeting *DSM-III-R* were a subset of those meeting *DSM-III. DSM-III-R* reduced the total number of patients diagnosed schizophrenic by 10%. The cohort excluded by *DSM-III-R* was largely made up of patients with non-bizarre (somatic, grandiose, religious, or other non-persecutory) delusions without hallucinations. These patients are classified by *DSM-III-R* under the category of "atypical psychosis." The availability of baseline, premorbid, and long-term follow-up data on all patients allowed a statistical comparison (t-test and chi-square) of the cohort of *DSM-III* schizophrenic patients excluded by *DSM-III-R* (N=18) to those still considered schizophrenic (N=164) by *DSM-III-R*. With the exception of sign and symptom variables used to define them, the excluded patients did not differ from the included *DSM-III-R* schizophrenic patients on *any* demographic, premorbid, or long-term outcome dimensions. In the absence of evidence of improved validity the authors argue that research progress will be impeded if new and arbitrary 'standards' for defining the disorder are introduced every several years.

#### **References:**

<sup>1</sup>Fenton WS, Mosher LR, Matthews S: Diagnosis of Schizphrenia: A critical review of current diagnostic systems. *Schiz Bull*: 7(3):452-476, 1981.

<sup>2</sup>McGlashan, TH: The Chestnut Lodge follow-up study: I: Follow-up methodology and study sample. *Arch Gen Psychiatry*: 41:573-585, 1984.

#### NR7 CHOLECYSTOKININ INDUCES PANIC IN PANIC DISORDER

Jacques Bradwejn, M.D., Psychiatry, McGill University, 3830 Lacombe, Montreal, Quebec, Canada H3T1M5; Greg B. Meterissian, M.D., Diana Koszycki, B.A.

#### **Educational Objectives:**

To report the panicogenic effect of cholecystokinin in panic disorder patients and discuss the role of this peptide in the neurobiology and treatment of anxiety disorders.

#### Summary:

Cholecystokinin (CCK) is a peptide found in high concentrations in the mammalian CNS, with highest concentrations in the limbic system. When applied on limbic neurons CCK produces a powerful excitation. It has been shown that benzodiazepines, by activating their receptors, selectively suppress CCK-induced excitation of rat hippocampal pyramidal neurons. The excitatory property of CCK and its selective inhibition by benzodiazepines point to the possibility of CCK being a natural anxiogenic and/or panicogenic. We tested this hypothesis by injecting CCK to panic disorder patients.

Ten untreated patients fulfilling the *DSM-III* criteria for panic disorder received i.v., CCK and saline separately during two consecutive days, in a double-blind fashion. Fifty micrograms of CCK-30-33, a short active form of CCK that crosses the blood brain barrier was administered. All of the ten subjects panicked after the CCK injection, while none panicked after the saline injection. All panics were identical in symptomatology to previously experienced panics; no new symptoms or adverse effects were reported.

This is the first report of a panicogenic action of a naturally occuring CNS molecule, and evidence that CCK might be a mediator of the panic phenomenon.

#### References:

1. Bradwejn, J., deMontigny, C.: Benzodiazepines antagonize cholecystokinin-induced activation of rat hippocampal neurones. Nature 312: 363-364, 1984.

2. Bradwejn, J., deMontigny, C.: Effects of PK 8165, a partial benzodiazepine receptor agonist, on cholecystokinin-induced activation of hippocampal pyramidal neurons. Eur J. Pharmacol 112:415-418, 1985.

#### NR8 CARBON DIOXIDE SENSITIVITY IN PANIC DISORDERS

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

Laszlo A. Papp, M.D., Psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; Jack M. Gorman, M.D., Raymond Goetz, Ph.D., Michael R. Liebowitz, M.D., Abby J. Fyer, M.D., Donald F. Klein, M.D.

#### **Educational Objectives:**

To provide new evidence that CO<sub>2</sub> sensitivity is a crucial factor in the pathophysiology of panic.

#### Summary:

Carbon dioxide (CO<sub>2</sub>) inhalation reliably induces panic in patients with panic disorder (PD). One explanation is that these patients are hypersensitive to CO<sub>2</sub>. According to this hypothesis panic patients chronically hyperventilate and keep their CO<sub>2</sub> level at minimum in order to avoid triggering their possibly hypersensitive CO<sub>2</sub> receptors.

In order to directly test this theory,  $CO_2$  sensitivity was measured with the steady-state canopy method. Minute ventilation (MV) and arterial PCO<sub>2</sub> were determined during room air and ventilation and then while breathing room air mixed with 5%  $CO_2$ . In order to control for the ventilatory effect of panic, only non-panicking subjects were evaluated. They reached steady-state MV within 10 minutes during each period.

 $CO_2$  sensitivity slopes were calculated by dividing change in MV by change in PaCO<sub>2</sub>. Because of the significant sex differences (M;8.07+5.87 vs. F;0.90+0.59) and the small number of female controls, men were analyzed separately. Male PD patients (N=7) had significantly higher  $CO_2$  sensitivity than normal controls (N=5) (8.07+5.87 vs. 2.49+2.14; z=2.03, p 0.043). This finding is one of the first demonstrations of a pathophysiologically significant biological difference between PD patients and controls that is not the direct result of a panic attack.

#### **References:**

1. Rebuck AS, Slutsky AS: Measurement of ventilation responses in hypercapnia and hypoxia, in Hornbein TF (ed) Regulation of breathing Part II. New York Marcel Dekker, 1981.

2. Carr DB, Fishman SM, Systrom D. et al: Carbon dioxide in panic disorder and premenstrually normals. Preceedings, APA annual meeting, Chicago, 1987.

#### NR9 NEUROANATOMICAL CORRELATES OF LACTATE-INDUCED PANIC

Eric M. Reiman, M.D., Psychiatry, Washington Univ Med, 4940 Audubon Avenue, St Louis, MO 63110; Mark A. Mintun, M.D., Marcus E. Raichle, M.D., E. Robins, M.D., J.L. Price, Fusselman Fusselman, M.S., K.A. Hackman, B.S.

#### **Educational Objectives:**

The learner will be shown a new strategy for the analysis of PET data to identify significant CBF changes associated with lactate infusion in panicking and non-panicking patients.

#### Summary:

Positron emission tomography (PET) was employed to measure regional cerebral blood flow (CBF) in patients with panic disorder and in normal control subjects before and during the infusion of sodium lactate. A powerful new strategy for the analysis of PET data<sup>1</sup> was employed to identify significant CBF changes associated with lactate infusion in the panicking patients, non-panicking patients and controls. Lactate-induced panic was associated with CBF increases in bilateral regions corresponding to temporopolar cortex; bilateral regions corresponding to the lateral putamen, claustrum or insular cortex; bilateral regions corresponding to the superior colliculus; and a region corresponding to the left side of the anterior cerebellar lobe. Lactate was not associated with significant CBF changes in non-panicking patients or controls. Thus, the identified regions appear to reflect neuroanatomical correlates of an anxiety attack.<sup>2</sup>

#### **References:**

<sup>1</sup>Fox PT, Mintun MA, Reiman EM, Raichle ME: Enhanced Detection of Focal Brain Responses Using Intersubject Averaging and Distribution Analysis of Subtracted PET Images. (Submitted)

<sup>2</sup>Reiman EM, Mintun MA, Raichle ME, Robins E, Price JL, Fusselman M, Hackman KA: Neuroanatomical Correlates of a Lactate-Induced Anxiety Attack. (Submitted)

#### **NR10**

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

## PSYCHIATRIC DIAGNOSIS AND LUTEAL VARIATION IN PMS WOMEN

Teri B. Pearlstein, M.D., W.P.I.C., 3811 O'Hara Street Room E-821, Pittsburgh, PA 15213; Judith Thoft, Ed.D., Debra Rubinstein, Ed.D., Ellen Frank, Ph.D., Ana Rivera-Tovar, M.S., Tammy A. Mieczkowski, B.S.

#### **Educational Objectives:**

The learner will be shown findings that a majority of women with prospectively confirmed PMS have a history of affective disorder, particularly post-partum depression.

#### Summary:

Fifty-six women with prospectively confirmed Late Luteal Phase Dysphoric Disorder (LLDD) were clinically evaluated at both follicular and premenstrual visits. The Schedule for Affective Disorder and Schizophrenia (SADS) and the Structured Clinical Interview for *DSM-III-R* Personality Disorders (SCID-II) were conducted at the follicular visit. The Hopkins Symptom Checklist (SCL-90), Barratt Impulsivity Scale (BIS), Multi-dimensional Health Locus of Control Scale (MHLC) and Social Adjustment Self-Report Scale (SAS-SR) were administered at both the follicular and luteal visits.

Thirty-one women (55%) had a history of RDC-defined major depression of greater than one month's duration, and 42 women (75%) had a history of major or minor depression. One third of parous subjects had a history of post-partum depression, which is twice the reported 10-15% lifetime prevalence. Nine women (17%) met *DSM-III-R* criteria for Avoidant Personality Disorder.

Paired t-tests of the SCL-90 and SAS-SR yielded significant differences between the follicular and luteal visits, reflecting luteal increases in psychopathology and social maladjustment. Paired t-tests of the MHLC and BIS did not yield significant differences, suggesting that these two scales do not discern luteal changes in perceived locus of control of health or impulsivity.

This study confirms earlier findings that a majority of women with prospectively confirmed PMS have a history of affective disorder, particularly post-partum depression. The SCL-90 and SAS-SR detect significant luteal increases in symptomatology. **References:** 

## <sup>1</sup>Dejong, R., Ribnow, D., Roy Byrne, P, et al. Premenstrual Mood Disorder and Psychiatric Illness. American Journal of Psychiatry, 142:1359-1361, 1985.

<sup>2</sup>O'Hara, M.W. Post-partum "blues", depression, and psychosis: a review. Journal of Psychosomatic Obstetrics and Gynecology, 7:205-227, 1987.

#### NR11 NEUROPSYCHIATRIC AND BIOCHEMICAL SUBGROUPS IN OCD

Eric Hollander, M.D., Psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; Wilma Rosen, Ph.D., Jim Towey, Ph.D., Gerard Bruder, Ph.D., Erica Schiffman, M.D., Michael R. Liebowitz, M.D.

#### **Educational Objectives:**

To report abnormalities in auditory evoked potentials, neuropsychological testing, neurological soft signs, and neuropharmacological challenge studies in obsessive compulsive disorder (OCD). To describe correlations between biochemical and neuropsychiatric markers which have implications for distinct subgroups within OCD, and for treatment outcome.

#### Summary:

We studied 31 adults with obsessive-compulsive disorder (OCD) using a broad battery of neuropsychiatric and neuropharmacological markers prior to treatment with 5HT reuptake blockers, and compared baseline findings with 15 normal controls. We report an exacerbation of OCD symptoms in 61% of OCD patients following M-CPP (0.5 mg/kg po), a selective 5HT agonist, and a reduction in OCD symptoms in 100% of patients following IV clonidine (2ug/kg), a NE alpha-2 agonist. There was a significant reduction in N200 and P300 latency, and an increase in N200 and slow wave amplitude on auditory evoked potentials in OCD patients compared to controls, and these group differences increased on more difficult discrimination tasks. On the matching familiar figures test (MFFT), a neuropsychological test of visual discrimination, there was a bimodal distribution within the OCD patients, with one group having long latencies and a low error rate (slow/accurate), and the other having short latencies and a high error rate (fast/inaccurate). On neurological soft-sign testing, OCD patients had increased abnormalities of total soft-signs, fine motor coordination, and visuospatial function. There were significant interrelationships between neuropsychiatric and biochemical abnormalities, and the relationship between baseline markers and treatment outcome will be described. There appears to be a subgroup of OCD patients who get worse on M-CPP, are slow and accurate on visual discrimination tasks, have less abnormal neurological soft-signs, and a positive response to clomipramine and fluoxetine treatment.

#### **References:**

<sup>1</sup>Zohar J, Meuller EA, Insel TR, et al: Serotonergic responsivity in obsessive compulsive disorder. Arch. Gen. Psychiatry 44:945-951, 1987.

<sup>2</sup>Ciesielski HR, Beech HR, Gordon PK: Some electrophysiological observations in obsessional states. Br. J. Psychiatry 138:479-484, 1981.

#### NR12 OBSESSIVE-COMPULSIVE DISORDER IN FIRST DEGREE RELATIVES OF OBSESSIVE-COMPULSIVE DISORDER CHILDREN

Marge C. Lenane, M.S.W., Child Psychiatry, NIMH Bldg 10 Rm 6N240, 9000 Rockville Pike, Bethesda, MD 20892; Susan Swedo, M.D., Henrietta Leonard, M.D., Deborah L. Cheslow, B.S., Judith L. Rapoport, M.D., David L. Pauls, Ph.D.

#### **Educational Objectives:**

At the end of the program, the attendee should be able to state ways of investigating rates of obsessive compulsive behaviors of relatives of persons with OCD and recognize the value of family study methods over family history methods.

#### Summary:

Clinical experience with obsessive-compulsive disorder (OCD) children and adolescents seen at the NIMH suggested that family members were at increased risk of having OC symptomatology. We now report the results of a systematic prospective investigation utilizing personal interviews with 89 biologic parents (96.7%) of 46 consecutively admitted children, aged 6–19, with severe primary OCD seen by the NIMH Child Psychiatry Branch in our ongoing series of studies of the neurobiology of OCD. A forensic psychiatric diagnosis of one additional father makes the total n=90. Assessment methods included the SADS-L, Leyton Obsessional Inventory, genogram and family history. Parents were assigned to one of three OC categories (lifetime and/or current): OCD (meeting *DSM-III* criteria), subclinical OCD (probable OCD, but not meeting *DSM-III* criteria for COD), and OCP (meeting *DSM-III* criteria for compulsive personality disorder). Subjects could also receive a non-OCD psychiatric diagnosis with 20 fathers (45%) and 30 mothers (65%) having a lifetime Axis I diagnosis, most commonly depression (25%), alcoholism (13%) or generalized anxiety disorder (13%).

	OCD	Subclinical OCD	OCP
Fathers $n = 44$	12 (27%)	8 (18%)	3 (7%)
Mothers $n = 46$	4 ( 9%)	7 (15%)	0 (0%)
Total n = 90	16 (18%)	15 (17%)	3 (3%)

Eighteen percent of parents were found to have clinical OCD and 17% subclinical OCD in contrast to the expected incidence of 2–3% recently reported for the general U.S. population. (Ref). This striking excess supports a familial and/or genetic role in the etiology of childhood onset OCD.

#### References:

1. Journal article: Robins LN, Helaer JI, Weisman MM, et al. Lifetime prevalence of specific psychiatric disorders in three sites. Arch Gen Psychiatry 41:949-958, 1984.

2. Journal article: Andreason NC, Endicott J, Sptizer RL, et al. The Family History Method Using Diagnostic Criteria: reliability and validity. Arch Gen Psychiatry 34:1229-1235, 1977.

#### NR13 A COMPUTERIZED DATABASE SYSTEM FOR PSYCHIATRIC AND CONSULTATION RECORDS

Hoyle Leigh, M.D., Psychiatry, Yale University, 51 Russet Drive, Guilford, CT 06437

#### Summary:

We report the development of a clinical and educational computerized system for generating psychiatric records and consultation notes. Simultaneously, it generates the Patient Evaluation Grid (PEG) developed by Leigh, Feinstein, and Reiser—a biopsychosocial inventory of the patient which serves an educational as well as clinical function. The PEG consists of the nine areas of investigation about patients formed by the intersection of the three dimensions of the patient (biological, personal, environmental) with three time contexts (current, recent, background). In addition, a PEG Management Form is displayed, with three-dimensional diagnoses and managment plans. The IBM program is menu-driven, and the clinician inputs data in traditional format (Chief Complaint, Present Illness, etc). The data base includes demographics, clinical and laboratory data, and administrative/financial data. The menus include programs for printing narrative summary, PEG, printed consultation note, thank-you note for the referring physician, billing, monthly report based on diagnosis or treatment, and customized research programs. This system is being used extensively at Yale in teaching medical students and residents as well as in clinical research.

#### NR14 AMERICAN SEXUAL EXPERIENCE IN THE AIDS ERA

Samuel S. Janus, Ph.D., New York Medical College, 983 Park Avenue, New York, NY 10028; Cynthia L. Janus, M.D.

#### Summary:

Introduction: An explosion of news stories over the past three years has focused attention on the fact that Americans are sharing their sex lives with a dread disease, A.I.D.S. There have been many research studies of patients with A.I.D.S. and of A.I.D.S. itself. There has, however, been no national study of sexual practices and attitudes of Americans in the past decade. This study uncovers and documents sexual reality today including "safe sex," de-rigeur fashionable sex and deviance. *Population:* The population for this study consists of 1,825 Americans, 960 women and 865 men, randomly surveyed dur-

ing 1987–1988. The results are compared with a survey by these authors of 4,010 Americans in 1982–1984.

Method: Respondents were surveyed utilizing a specially developed 228 item questionnaire. In addition, 200 in-depth interviews were conducted. Results were analyzed in all areas of sexual function. The burgeoning role of deviance in daily life, and new concepts of normalcy are examined.

Results: American sexuality has changed radically; there is no universally accepted consensual morality. Sexual practices and sexual identity are personally determined. While A.I.D.S. is a source of anxiety, is has not become a stop sign for frenetic sexual behavior. This study shows, that contrary to popular and media belief, there is greatly increased sexual activity. Sex in the post-middle age population, women, children and in the workplace has grown at an explosive rate. Some respondents reported having 300–400 sex partners. More than any other time, the sexual roles and social roles of Americans have changed dramatically.

#### **NR15**

#### Tuesday, May 10, 12 noon-2:00 p.m.

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

NEW DYSKINESIA MODEL: EFFECT OF METOCLOPRAMIDE

Luis A. Marco, M.D., Psychiatry, USA College of Med., 2451 Fillingim St, Mobile, AL 36617; Leonard D. Aldes, Ph.D., Robert B. Chroister, Ph.D., Timothy F. Reed, B.S.

#### Summary:

We have recently developed<sup>1</sup> and further refined<sup>2</sup> a new rodent model of neuroleptic-induced acute and tardive dyskinesia. It consists of anesthetizing rats with ketamine HCL (100 mg/kg, IM) sufficiently to allow mounting them in a stereotaxic instrument, tying the tip of the tongue to a force displacement transducer (FDT) such that it is in contact with its cantilever to monitor tongue protrusions (P) and retrusions (R) through one channel and inserting a pressure transducer (PT) balloon below the soft palate to monitor swallowing (S) through another polygraph channel. The trachea is cannulated. R are recorded as upward and P as downward deflections in the FDT channel. S appear as upward deflections in both channels and are of a duration (0.5 sec) 2x that of P and R. Thus, all three events can be identified. Neuroleptics suppress P, R, and S for 10–120 minutes depending on dose. Metoclopramide (MCP) a procainamide derivative with dopamine (D<sub>2</sub>) blocking but no antipsychotic activity has been claimed to ameliorate tardive dyskinesia, particularly tongue P (Karp et al. 1981). We have used our model to test this claim. MCP was injected IM at doses of 0.5, 1.0, and 2.5 mg/kg to rats exhibiting a continuous record of P,R, and S. Order of disappearance was: first P, then R, and last S. Suppressive effects were most marked at 30 minutes with gradual recovery in 60–120 minutes. Recovery followed the reverse pattern: S followed by R, then P. Since P also appears to be the first mechanism being released by ketamine, MCP earliest selectivity for P may provide clues to the pathogenesis of both neuroleptic- and ketamine-induced dyskinesia. It remains to be determined whether MCP is a better long-term antidyskinetic agent than neuroleptics. Supported by RO 1 NS24747 Grant to L. Marco.

## References:

<sup>1</sup>Aldes *et al.* 1987. <sup>2</sup>Marco *et al.* 1987 a, b.

#### NR16

### COGNITIVE SEQUELAE OF TARDIVE DYSKINESIA

Marion E. Wolf, M.D., Psychiatry, Veterans Administration, Buckley Road, North Chicago, IL 60064; Alan S. DeWolfe, Ph.D., Joseph J. Ryan, Ph.D., Aron D. Mosnaim, Ph.D.

#### Summary:

Severity and localization of tardive dyskinesia symptoms, and primary psychiatric diagnosis were related to neurocognitive dysfunction, as measured by the Wechsler Adult Intelligence Scale and Wechsler Memory Scale. Total TD symptom severity correlated significantly negatively with 10 of 14 WAIS scores and with four of seven Wechsler Memory scores. The magnitude of the relationships between TD symptom severity and cognitive deficit was strongly affected by the location of the symptoms and the diagnosis of the patient. Severity of facial TD symptoms correlated significantly negatively with 11 of 14 WAIS scores and all memory scores. TD symptoms in the extremities correlated significantly negatively with only two WAIS and two memory scores. Length of institutionalization was found to be related to TD symptoms in schizophrenic but not in affective disorder patients. The clinical implications of these findings will be discussed.

#### NR17 RARITY OF DYSTONIA IN ELDERLY PATIENTS

Gerard Addonizio, M.D., Psychiatry, NY Hospital-CUMC-WD, 21 Bloomingdale Road, White Plains, NY 10605; George S. Alexopoulos, M.D.

#### Summary:

This retrospective study examines the notion that neuroleptic-induced dystonia is less frequent in elderly patients. We examined hospital records of 45 patients aged 18–35 and 45 patients aged 60–80 for dystonia. Type and dosage of neuroleptic, anticholinergic use, and other medicines were noted. Thirty-one percent of young patients developed dystonia compared to 2% of elderly patients (X<sup>2</sup>=11.52, df=1, p<0.001). Dosage of each neuroleptic and CPZ equivalents were compared between both groups. With haloperidol, young patients developed dystonia more frequently than older patients (X<sup>2</sup>=9.40, df=1, p<0.01) and there was a trend in the same direction with fluphenazine (X<sup>2</sup>=1.42, df=1, p<0.30). Young dystonic patients comparison of young dystonic patients and elderly non-dystonic patients revealed no dosage difference (t=.31, df=56, n.s.). Logistic regression analysis demonstrated young age and dystonia had the strongest association (X<sup>2</sup>=13.72, df=1, p<0.001) and no significant effect of anticholinergics (X<sup>2</sup>=0.12, df=1, p<0.72). There was a significant negative association between dosage of neuroleptic and development of dystonia (X<sup>2</sup>=6.83, df=1, p<0.009) suggesting that certain patients are susceptible to this reaction. In summary, the low frequency of dystonia in the elderly is not the result of type of neuroleptic, dosage, or anticholinergic drugs. Potential age related reasons for this effect and the clinical relevance of this finding will be discussed.

#### NR18

#### ANTIMUSCARINIC PLASMA ACTIVITY AND COGNITION

#### Tuesday, May 10, 12 noon-2:00 p.m.

Ole J. Thienhaus, M.D., Psychiatry, Univ of Cincinnati, 231 Bethesda Avenue, Cincinnati, OH 45267; James Thoene, Frank Zemlan, Ph.D.

#### Summary:

The study was aimed at determining whether in response to oral doses of drugs with anticholinergic side effects, nondemented elderly subjects show impairment of cognitive function. We generated preliminary data on the relationship between antimuscarinic plasma activities and cognitive-functional status in a small sample (N=10) of psychiatric inpatients. The patients were older adults, mean age 59±9 years, without clinically measurable cognitive impairment. Radioreceptor binding assay with [3-H]-quinuclidinyl benzilate (QNB) served to analyze plasma samples for antimuscarinic activity. Samples were obtained before initiation of psychopharmacotherapy, and after target dosage had been reached. The QNB-method assays total anticholinergic activity across individual agents which, in our patients, included neuroleptics, cyclic antidepressants, and antiparkinsonian drugs. Measurements are expressed in atropine equivalents. We found that objective measures of concentration, recall, and short-term memory remained stable after psychotropic drug regimens were instituted. Only self-rated memory deteriorated. At the same time, anticholinergic plasma activity, which initially was absent, reached the measurable range. Our data indicate that in standard dosing ranges the anticholinergic effects of psychotropic medications do not cause significant changes of cognitive function in nondemented patients. Our findings support the rational use of psychopharmacologic agents in cognitively intact older patients. They further provide a standard of reference for similar studies in demented individuals.

#### NR19 ACCEPTANCE OF HIV-ANTIBODY TESTING BY COCAINE ABUSERS

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

William W. Weddington, M.D., Addiction Research, P.O. Box 5180, Baltimore, MD 21224; Barry S. Brown, Ph.D.

#### Summary:

One hundred of 101 applicants for outpatient treatment for cocaine abuse consented to voluntary HIV-antibody testing when the testing was offered as an option within the medical assessment at intake. Twelve applicants tested HIV-antibody positive; eight of these had injected drugs parenterally with syringes and needles used by other addicts and four had never taken drugs intravenously. There were no significant differences between HIV-antibody positive and negative applicants regarding the percentages who completed the evaluation, began treatment, and completed four weeks of treatment. A subgroup of 48 patients were interviewed regarding their knowledge of HIV infection, AIDS, and risk factors associated with transmission of HIV. All 48 patients had heard of HIV, AIDS, and recommendations that they use condoms as well as clean syringes and needles. None of the 48 patients reported that they used condoms; 10 reported reduced sexual activity and number of sexual partners, and none of those who shared needles reported that they had discontinued sharing other addicts' drug paraphernalia. The authors conclude that on-site, voluntary HIV-antibody testing for drug-abusing patients entering treatment appears feasible and is not a deterrent to persons entering and continuing in treatment for drug abuse. The finding that persons at risk for HIV infection have knowledge of risk factors and have not changed risk-taking behaviors associated with HIV contagion points out the urgent need for further education and counseling.

#### NR20 FACTORIAL VALIDITY OF THE TORONTO ALEXITHYMIA SCALE

R. Michael Bagby, Ph.D., Psychology, Clarke Inst., 1001 Queen Street West Metfors, Toronto, Ont., Canada M6J1H4; Graeme J. Taylor, M.D., James D. Parker, M.A., David P. Ryan, Ph.D., Ken Citron, M.D.

#### Summary:

The Toronto Alexithymia Scale (TAS) is a recently developed self-report measure of the alexithymia construct. In studies with college students the TAS has proven to have good internal consistency, a replicable factor structure theoretically congruent with the alexithymia construct, excellent discriminant validity with other personality measures, and moderate correlations with measures of somatic complaints. While these results are encouraging, it is essential that the scale also be validated with clinical populations. In this study, the TAS was administered to 214 psychiatric outpatients (88 males, 126 females). Factor analysis (principal factor extraction, varimax rotation) produced four interpretable factors, all with eigenvalues greater than 1.5: (1) ability to identify and distinguish between feelings and bodily sensations; (2) ability to describe feelings to others; (3) daydreaming; (4) externally oriented thinking. These four factors accounted for 43.4% of the variance. Congruence coefficients were calculated to compare the factor structure obtained from our original college sample with the factor structure from the present patient sample. All four factors showed good congruence (>0.90). In addition, the TAS yielded a Cronbach's Alpha of 0.77. These results indicate that the TAS is a reliable and construct-valid measure for the assessment of alexithymic characteristics in clinical settings.

#### NR21

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

#### CALCIUM CHANNEL BLOCKERS IN TARDIVE DYSKINESIA

Erica J. Duncan, M.D., Psychiatry, New York VAMC, 408 First Ave at East 24th St, New York, NY 10010; Lenard Adler, M.D., Burt Angrist, M.D., Eric Peselow, M.D., Stewart Reiter, M.D., John Rotrosen, M.D.

#### Summary:

Case reports have noted improvement in tardive dyskinesia (TD) after treatment with the calcium-channel blocking agents verapamil (1) and diltiazem (2). We now describe data from single-blind (rater blind) investigations with these agents in treating TD. In addition, data from a similar study with nifedipine (now in progress) will be reported.

Verapamil (160-320 mg/day) was administered to nine schizophrenic patients with TD; six of the nine had mild improvement in TD with decreases in AIMS scores of two points or more. Mean AIMS scores on items #1–7 (n=9) were: Baseline =10.1 $\pm$ 3.6 SD; Treated=8.2 $\pm$ 2.8 SD (t=2.74, p<0.05).

Twelve patients with TD (schizophrenia=10; bipolar, manic=2) received diltiazem (120-240 mg/day); mild improvement in TD was seen in six patients (decrease in AIMS scores by two points or more), no change in another four, and mild worsening was seen in two patients. Mean AIMS scores on items #1-7 (n=12) were: Baseline=11.4 $\pm$ 3.4; Treated=10.2 $\pm$ 3.6 (NS).

Hypotension limited the dose of verapamil in five patients and the dose of diltiazem in two patients; decreases in pulse rate limited the dose of diltiazem in another three patients.

Our findings of only minimal to moderate improvement in TD differ from the marked improvement noted in prior reports; however, in some patients the improvement in TD was clinically meaningful.

#### NR22

#### BETA-BLOCKERS IN AKATHISIA: MEDIATION BY $\beta$ -1 OR $\beta$ -2?

Lenard Adler, M.D., New York VAMC, Dept. of Psychiatry, (116A), 408 First Ave. at East 24th St. New York, NY 10010; Erica Duncan, M.D., Burt Angrist, M.D., Paula Hemdal, M.A., Tony Kim, M.D. and John Rotrosen, M.D.

#### Summary:

Beta-blockers are emerging as treatments for neuroleptic-induced akathisia (NIA) (1,2). Propranolol, which blocks both  $\beta$ -1 and  $\beta$ -2 receptors, has been most extensively studied. The relative contribution of  $\beta$ -1 vs.  $\beta$ -2 receptors is unclear. In two studies to date the effects of selective  $\beta$ -1 blockers were inconsistent (3,4). We now describe data from studies of two lipophilic  $\beta$ -blockers: 1) the selective  $\beta$ -2 blocker ICl 118,551 and 2) the selective (at low doses)  $\beta$ -1 blocker metoprolol.

Ten patients were treated in a parallel group, double-blind study of ICI 118,551 (n=6) vs. placebo (n=4). Mean measures of akathisia were lower in the ICI cohort than in those who received placebo. This study was halted prior to completion when ICI 118,551 was withdrawn from clinical evaluation.

However, four patients to date have shown improvement with low dose metoprolol treatment. This improvement was not enhanced by subsequent treatment with propranolol. This study is still in progress.

ICI 118,551 is the only  $\beta$ -2 selective blocker studied in akathisia to date. The improvement seen suggests a role for  $\beta$ -2 receptors in NIA. On the other hand, improvement after putative selective  $\beta$ -1 blockade was also seen. Thus, the role of subsets of  $\beta$  receptors is unclear; it is even possible that there is redundancy of function of these receptors in the CNS.

#### NR23 PROSPECTIVE STUDY OF TARDIVE DYSKINESIA IN THE ELDERLY

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

Bruce L. Saltz, M.D., Psychiatry, Hillside Hospital, PO. Box 38, Glen Oaks, NY 11004; John M. Kane, M.D., Margaret Woerner, Ph.D., Jeffery A. Lieberman, M.D., Jose Alvir, P.H.

#### Summary:

Abnormal involuntary motor activity is a well-known complication of antipsychotic drug (APD) treatment. Increasing age has been the risk factor most consistently associated with the development of tardive dyskinesia (TD), the most serious druginduced, extrapyramidal side-effect syndrome. A prevalence survey at our institution previously demonstrated an increased susceptibility to TD in elderly patients treated with APDs, which was not due to an increased base rate of spontaneous dyskinesia or medical illness. To more fully investigate this increased susceptibility, we initiated a prospective study of 400 geriatric patients beginning APD treatment.

We have examined 98 individuals over age 55 with no prior APD exposure, whose physicians were starting treatment with APDs for clinical indications. For these preliminary data 62 patients were available with at least one month follow-up (mean age, 76). Females comprised 67.7% of this group, and 89% were Caucasian. These patients had been followed for a mean of 3.9 months (range 1–15) with a cumulative APD exposure of 3.4 months (range 1–13). The incidence of abnormal involuntary movements by cumulative APD exposure was 47.2% at eight months (95% confidence interval 18.8–75.5). This exceeds greatly reported incidence figures for nongeriatric adult populations. Additional analyses and the implications of these preliminary findings will be discussed.

#### NR24 BEHAVIORAL AND PHYSIOLOGICAL EFFECTS OF A BETA-BLOCKER AND RELAXATION THERAPY ON MILD HYPERTENSIVES

C. Alex Adsett, M.D., Psychiatry, McMaster Medical, 1200 Main Street West, Hamilton, Ontario, Canada L8N3Z5; Anthony Bellissimo, Ph.D., Alba Mitchel, M.Sc., Nancy Wilczynski, B.Sc., Brian Haynes, M.D.

#### Summary:

A random controlled study compared the BP lowering effectiveness of relaxation therapy, a beta blocker, and the combined use of these in mildly hypertensive blue collar steel workers. 47 male steel workers with mild hypertension and no target organ disease were randomly allocated to a) relaxation and beta blocker, b) relaxation and placebo drug, c) education and beta blocker, or d) education and placebo drug. Each subject had 8 sessions of small group relaxation training or education, a stress test preintervention and 3 months post intervention and 6 months follow-up. Compliance was assessed by self-report and pill count. The stress test consisted of HR & BP response to a) mental arithmetic, b) steady state exercise, and c) reaction time. The JAS, Hassles and Uplifts, State Trait Anxiety and Anger Expression self report measures were obtained pre- and post-intervention. BP measurement was standardized and blind. Results: beta blocker was more effective than placebo in lowering BP (p=.00) but relaxation practice was not. Beta blocker produced less increase in HR than control during mental stress (p=.01) and reduced mean trait anxiety score (p=.03). A significant interaction effect of B blocker and relaxation was found for Type A behavior (p=.01) and factor S subscale (p=.04). However, there was no correlation between drop in JAS score and BP lowering. An interaction effect was found for mean number of hassles (p=.04) and for anger—in (p=.04). Conclusion: Relaxation is not more effective than placebo, and combined relaxation/beta blocker treatment is not superior to beta blocker alone in treating mildly hypertensive steel workers. A possible variable is the unique type of stress in this population.

#### NR25

#### SYMPTOM MANAGEMENT TRAINING FOR SCHIZOPHRENICS

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

Robert P. Liberman, M.D., Psychiatry, UCLA, 760 Westwood Plaza, Los Angeles, CA 90024; Thad A. Eckman, Ph.D., Stephen R. Marder, M.D., W. Wirshing, M.D., K. Johnston-Cronk, B.S.

#### Summary:

A behaviorally oriented program for teaching schizophrenic outpatients to manage their psychiatric symptoms is being evaluated within the context of a controlled study investigating the use of low-dose neuroleptic therapy together with highly structured skills training interventions based upon principles of learning. This presentation focuses on data collected from the first two cohorts of patients to be entered in the study protocol. Carefully diagnosed schizophrenic patients were randomly assigned to treatment and control conditions in a two-group before-after design. Patients in the experimental condition received skills training in a modular program designed to teach them to (1) identify warning signals of relapse; (2) cope with prodromes; (3) cope with persistent symptoms; and (4) promote a healthy lifestyle (including drug and alcohol refusal). Patients in the control condition were provided with similar information in an unstructured, group discussion format. Patients in both conditions met for  $1\frac{1}{2}$  hours, twice weekly, for five months. The impact of treatment was evaluated with respect to both knowledge acquisition and skill attainment. Results clearly indicated the superiority of the behavioral training procedure. Patients who received module training increased their knowledge of symptom management from 75% to 86% (t=2.47, P<.05), while patients in the control condition failed to demonstrate any gain in knowledge (pre=77%; post=74%). Results on behavior performance tests measuring skill attainment followed a similar pattern. Patients who underwent behavioral training made significant gains in percent skill attainment in each of the four skill areas taught (pre=54%; post=84%; P<.01) while those participating in the control condition did not improve (pre=55%; post=55%).
## NR26 CEREBRAL BLOOD FLOW IN POST-STROKE DEPRESSION

NADOLOL FOR CHRONIC IMPULSIVE AGGRESSIVE BEHAVIOR

NEUROCHEMICAL CORRELATES OF DEFICIT SCHIZOPHRENIA

Joseph A. Schwartz, M.D., Psychiatry, University of Michigan, 1500 Medical Center Dr. B1204, Ann Arbor, MI 48109; Nancy M. Speed, M.D., James M. Mountz, M.D., M.D. Gross, M.D., D.E. Kuhl, M.D.

#### Summary:

Depression affects 50% of stroke patients. We hypothesized that severity of depression is related to the lesion's size and its proximity to the frontal pole. To test these hypotheses, we used <sup>99M</sup>Tc-HM-PAO SPECT (single photon emission computer tomography) to define regional blood flow impairment in 15 patients (13 male; age 65±10) undergoing stroke rehabilitation.

We measured lesion volume by summing the areas with a 25% reduction in blood flow compared to the contralateral side. Impairment in frontal lobe blood flow was determined by the ratio of average counts per pixel in the damaged frontal lobe over the normal frontal lobe. Depression was rated blindly using the Hamilton Depression Scale.

We found that depression scores correlated with lesion volume (r=.49, p=.07, df=14). Patients with SPECT lesions were significantly more depressed than patients without SPECT lesions fulfilling our 25% criteria (t=2.53, p<.05, df=13). Depression scores tended to rise with blood flow deficits in either frontal lobe (r=.44), p=.10, df=14). There was no difference in severity of depression between patients with right and left frontal deficits (t=.94), p>.2, df=13). This pilot study suggests that regional blood flow imaging by SPECT is a valuable tool for investigating the pathophysiology of post-stroke depression.

## NR27

## Tuesday, May 10, 12 noon-2:00 p.m.

Paul Sorgi, M.D., Psychiatry, Wright State University, School of Medicine Box 927, Dayton, OH 45401; Linda S. Cole, M.D., Daniel Knoedler, M.D., William N. Arnold, M.D., John J. Ratey, M.D.

#### Summary:

Eleven inpatients with chronic mental illness and chronic impulsive aggressive behavior were entered into a double blind, placebo controlled study. Criteria for entry into the study included a two-month history of four episodes per month of impulsive aggressive behavior as described in the Overt Aggression Scale. Subjects also met the first two criteria of the diagnosis of Intermittent Explosive Disorder as described in *DSM-III*. Subjects were maintained on concurrent psychotropic medication, with all dosages frozen at pre-study levels. One patient was dropped due to a hypotensive episode while taking placebo; one patient was dropped due to worsening aggressive behavior. Initial analysis shows consistent trends toward greater improvement in the treatment group as measured by BPRS, CGI, irritability subscale of the Nosie 30, and by modified OAS. CGI severity scale showed a pre-treatment mean of 4.6 for the placebo group, and 5.0 for treatment group with post treatment means being 4.6 and 3.67, respectively. CGI improvement score consistently favored the treatment group with post treatment means of 3.4 for placebo and 2.3 for treatment group.

## NR28

#### Tuesday, May 10, 12 noon-2:00 p.m.

John G. Csernansky, M.D., Psychiatry, Stanford University, TD114, Stanford, CA 94305; Roy J. King, Jr., M.D., William O. Faustman, Ph.D., James A. Moses, Jr., Ph.D., Margaret E. Poscher, M.D., Kym F. Faull, Ph.D.

#### Summary:

Biological correlates of deficit characteristics in schizophrenia are being increasingly sought. In the literature, higher cerebrospinal fluid (CSF) 5-hydroxyindoleacetic acid (5-HIAA) concentrations, and lower CSF homovanillic acid (HVA) concentrations have been associated with slowed motor behavior and communication in schizophrenic patients. To derive a single, reliable measure of deficit characteristics in schizophrenic patients, we entered three items of the Brief Psychiatric Rating Scale (BPRS) reflecting negative symptoms, a work-history measure derived from the Strauss-Carpenter Scale, and three subscale scores of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) into a principal components analysis to derive a single factor score. CSF HVA concentrations were not associated with this deficit factor score in schizophrenic patients. However, CSF 5-HIAA concentrations directly correlated with this factor score, and post-hoc bivariate correlation estimates between each of the measures comprising the factor and CSF 5-HIAA suggested that all measures contributed to the correlation between the factor score and CSF 5-HIAA concentrations. These findings add support to the hypothesis that brain serotonin function is linked to deficit schizophrenic characteristics.

#### NR29 NEUROENDOCRINE EFFECTS OF 52028 RP IN SCHIZOPHRENIA

Fabrice Duval, M.D., Specialise, Centre Hospitalier, Service Du Dr Macher, Rouffach, France 68250; Luc-Andre Granier, M.D., M. Antoine Crocq, M.D., Bruno Musch, M.D., Christine Pilate, M.D., Jean-Paul Macher, M.D.

## Summary:

52028 RP is an antagonist of peripheral benzodiazepine receptors (PBR) (1). Mammalian studies have shown that in depolarisation conditions 52028 RP decreases synthesis and/or release of dopamine from caudate nucleus dopaminergic neurons. In order to evaluate 52028 RP activity we investigated neuroendocrine and chronobiological effects before and after treatment in 11 patients (6 males and 5 females; age=30.1 yrs±13) who met *DSM-III* criteria for schizophrenia. Analyses of circadian secretions of ACTH, cortisol, TSH, and prolactin were performed as well as neuroendocrine investigations using several challenges (including dexamethasone, TRH, clonidine, apomorphine, and 5 hydroxytryptophane) both sets of investigations were performed after a minimum 10 day washout and after three weeks of 52028 RP treatment (24.7 days±5.7). The data analyses showed: 1) A significant increase in plasma cortisol (p=0.001) and ACTH (p=0.002) after DST. 2) A significant increase in growth hormone differential ( $\Delta$ GH) after Apomorphine challenge (p=0.04). 3) A significant decrease of free thyroxine (p<0.03) compared to baseline and a tendency toward an increase in  $\Delta$ TSH (p=0.08) after TRH stimulation. 4) A tendency toward an increasing amplitude of 24 hour cortisol secretion (p=0.07). 5) A significant improvement in 24 hour ACTH percent of rhythm. Clinical evaluation performed during biological investigation showed a significant improvement on both the Hamilton Depression (p=0.01) and Hamilton Anxiety scales (p<0.03) and a trend to decrease BPRS (p=0.07) and SANS (p<0.08). Our results suggest, that 52028 RP has an atypical psychotropic drug profile including chronobiologic, anxiolytic, and stimulant activity.

## NR30

## INTERICTAL BEHAVIORAL DISORDER IN EPILEPTICS

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

Narayan P. Verma, M.D., Neurology 127, VAMC, Southfield and Outer Drive, Allen Park, MI 48101; Cynthia D. Nichols, M.A., Manfred F. Greiffenstein, Ph.D., Barbara A. Buber, N.P.

## Summary:

Interictal behavioral disorder (IBD) is defined as a dispositional metamorphosis in personality leading to maladaptive behavior. It eludes explanation with regards to its severity, nature, and precise pathogenesis. In general, irritative temporal lobe discharges are considered to increase the risk of IBD. However, recent data indicate that IBD occurs in primary generalized epilepsy as well, though not as frequently.

We have prospectively studied the IBD in over 150 patients with epilepsy utilizing a neuropsychological test battery (Bear-Fedio Inventory, trails A and B, Warrington recognition memory test, Boston naming test, and tapping). An initial analysis of 25 patients with Idiopathic Epilepsy (IE; age  $52.44\pm8$  yrs) and 32 patients with Symptomatic Epilepsy (SE; age  $45.56\pm10.24$  yrs) revealed higher Bear-Fedio Scores in SE both on self-reported survey ( $38.83\pm16.36$  vs.  $33.86\pm17.97$ ) and reliable-informant survey ( $35.22\pm14.53$  vs.  $30.00\pm15.63$ ). The differences appeared to be accounted for by a higher prevalence of partial complex seizures in the SE group (9/32 vs. 3/25) and a higher average impairment ratings (AIR) in that group ( $1.9175\pm0.7265$  vs.  $1.5089\pm0.5532$ ) on neuropsychological tasks. In addition, a correlational analysis of the compiled Bear-Fedio Score and the AIR revealed a r=0.56.

Such data are in keeping with our previous report of a lack of influence of the etiology (Idiopathic vs. Symptomatic) on the severity of IBD. In addition, they suggest a correlation between IBD and AIR.

## NR31 NEUROLEPTIC RESPONSE: FAMILIAL PATTERNS OF ILLNESS

Frederic J. Sautter, Ph.D., Psychiatry, Univ of Cincinnati 231 Bethesda Avenue ML 559, Cincinnati, OH 45267; Barbara E. McDermott, M.A., David L. Garver, M.D.

## Summary:

The speed with which antipsychotic response occurs following the initiation of neuroleptic drug differs markedly among psychotic patients. Data from our laboratory indicate that latency of antipsychotic response may be used to separate distinct subtypes of mood-incongruent psychotics. Rapid Neuroleptic Responders (RNRs) show a latency to response of  $5.5\pm1.0$  (SD) days; Delayed Neuroleptic Responders (DNRs) show a latency to response of  $16.0\pm6.2$  (SD) days. These two subtypes were compared for differences along familial parameters.

First-degree relatives of 16 RNR and 16 DNR probands were compared for differences in lifetime risk for mood-incongruent psychotic disorder. Comparison for differences in schizophrenic-spectrum disorder indicated differences between the groups that approached significance (p<.08). The morbid risk for schizophrenic-spectrum disorder in relatives of RNRs was 5.7%; relatives of DNRs showed a morbid risk of 16.0%. Because we have obtained follow-up data that suggest that these two subtypes show a different course of illness, all first-degree relatives who had suffered a psychotic episode were evaluated on the basis of residual impairment using the Global Assessment Scale (GAS) from the SADS. Relatives of DNRs showed significantly more residual impairment than relatives of RNRs (p<.02). These data indicate that rapid and delayed neuroleptic response identifies a poor disease outcome.

## **NR32**

## Tuesday, May 10, 12 noon-2:00 p.m.

# ENDOCRINE RESPONSE TO PHYSOSTIGMINE IN ALZHEIMER'S

Elaine R. Peskind, M.D., Psychiatry, Univ of Washington, School of Medicine RP-10, Seattle, WA 98195; Murray A. Raskind, M.D., Richard C. Veith, M.D., Steven C. Risse, M.D., Thomas H. Lampe, M.D., Daniel M. Dorsa, M.D.

## Summary:

Cholinergic neurons in the nucleus basalis of Meynert degenerate in Alzheimer's Disease (AD). Both vasopressin and corticotropin releasing factor containing neurosecretory cells are innervated by cholinergic neurons, some of which probably originate in the basal forebrain cholinergic system. Epinephrine release from the adrenal medulla is also mediated by a central cholinergic mechanism. To assess CNS cholinergic neuroendocrine regulation in AD, we measured plasma vasopressin,  $\beta$  -endorphin, and epinephrine responses to a cholinergic challenge elicited by I.V. administration of the acetylcholinesterase inhibitor physostigmine (0.0125 mg/kg) in male patients with AD (n=12) and compared their responses to those of age-matched normal control subjects (n=12).

Physostigmine administration resulted in a prompt increase in plasma vasopressin (10 fold),  $\beta$ -endorphin (2-3 fold) and epinephrine (3 fold) levels in elderly control subjects. In contrast, AD patients showed attenuated responses to physostigmine. These differences were most pronounced when control and AD patients who experienced nausea (n=2 and 6, respectively) were excluded. When expressed as area under response curves, AD patient vasopressin (2±1.2 pg/ml/min) and  $\beta$ -endorphin (5±1.5 pg/ml/min) responses were significantly (p<.02) less than those of control subjects (14±5 and 28±4 pg/ml/min, respectively). AD epinephrine response (10±3 pg/ml/min) tended to be lower than that of control subjects (60±27 pg/ml/min; p<.01).

We conclude that the cholinergic deterioration of AD also influences central nervous system regulation of neuroendocrine systems.

#### NR33 PREDICTORS OF ADAPTATION IN DEMENTIA CAREGIVERS

## Tuesday, May 10, 12 noon-2:00 p.m.

William Borden, Ph.D., Geriatrics, III State Psych Inst, 1601 W. Taylor 9W, Chicago, IL 60612; Rhonda Frankel, M.A., Ben L. Gierl, M.D., Alice Ras, B.A.

## Summary:

This study examined the effects of a series of psychological and social characteristics on subjective well-being in spousal caregivers of older adults with chronic dementia. Flfty-one spouses completed questionnaires and interviews assessing dementia severity, distress in appraisal of dementia characteristics, perceived support from family and peers, reliance on specific coping strategies, and psychological well-being. The results of path analysis (recursive multiple regression) show that gender, distress in perception of dementia symptoms, perception of peer support, and three coping strategies (problem-solving, positive focus, and wishful thinking) are significant predictors of well-being. Overall, the predictor variables accounted for 60.3 percent of the total variance in psychological well-being.

The results of this study document the salience of these characteristics in further study of caregiver functioning. More generally, findings provide support for multidimensional, relational models of stress, coping, and adaptation. The implications of the study are discussed in the contexts of clinical practice, social policy, and future research.

#### NR34 SCHIZOAFFECTIVE DISORDER: A DISTINCT ENTITY?

Jean-Pierre Lindenmayer, M.D., Psychiatry, Albert Einstein Col Med, 60 Remsen Street, Brooklyn, NY 11201; Stanley Kay, Ph.D., Herman M. van Pragg, M.D.

## Summary:

Whether schizoaffective disorder is a distinct nosological entity, differing fundamentally from schizophrenia, remains uncertain. We explored the diagnostic boundaries using a multidimensional comparative paradigm. Based on SADS and RDC, we identified 21 hospitalized schizoaffective patients and 21 schizophrenics, matched for age and length of illness. The groups were contrasted on psychopathological, affective, cognitive, and historical variables using standardized clinical and psychometric batteries. Symptomatically, the two groups were similar in overall severity of illness and positive syndrome, but schizoaffectives were distinguished by less negative syndrome (p<.02) and less social avoidance (p<.025). Although there were no differences in manifest affect, schizoaffectives rated significantly higher on subjective experiences of depression (p<.05) and guilt (p<.02). The cognitive examination revealed comparable IQ's, education, and organic integrity, yet schizophrenics showed consistently greater cognitive abnormality. This was evidenced on separate measures of abstract thinking, thought disorganization, stereotyped thinking, cognitive development, and information processing. Finally, schizoaffectives had more substance abuse in their families and shorter duration of inpatient stay during the past 18 months, reflecting basic differences in genealogy and treatment response. The results support the validity of schizoaffective disorder as separate from schizophrenia, distinguishable by cognitive and negative profiles, family history, and course of illness.

## NR35

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

## DEMENTIA WITH COEXISTENT DEPRESSION

Blaine S. Greenwald, M.D., Psychiatry, Mt. Sinai Medical Center, Box 1229 1 Gustave Place, New York, NY 10029; Elisse Kramer, Ph.D., Deborah B. Marin, M.D., Leila Laitman, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

## Summary:

Depressive features frequently accompany dementia. Less commonly encountered in demented patients is a major depressive syndrome meriting treatment. When this occurs, cognitive impairment may worsen. Prevalence of major depression complicating dementia and its rate of treatment response were examined. Dementia/depression inpatients (n=10) were prospectively compared with nondepressed demented (n=10) and nondemented elderly depressed (n=33) inpatients. All were psychoactive drug-free and met their respective *DSM-III* criteria. Scales administered at admission and discharge included ratings of cognition/memory (MIT, DRS, MMSE) and depression (HDRS, SADS-PSE inventory, CGI). Nine percent of dementia patients seen on an inpatient and outpatient geropsychiatry service met criteria for superimposed major depression. Seventy percent of the dementia/depression group and 72 percent of the depressed group responded to somatic antidepressant treatment. Signs and symptoms of depression complicating dementia are mostly similar to affective phenomena occuring in non-demented geriatric depressives. Clinical features that distinguished groups will be reported. Within the dementia/depression group: severity of dementia and depression were inversely related; and depression interacted with dementia to lower performance on memory/orientation tests. Following treatment, although cognitive impairment remained, performance improved. This study is unique in that it examines *syndromal* depression complicating dementia, wherein diagnosis is validated by treatment response.

## NR36 SCHIZOPHRENIC DRUG-FREE RELAPSE: A PEAK IN WEEK THREE

**P300 AND CLINICAL SYMPTOMATOLOGY IN PSYCHOSES** 

George G. Dougherty Jr., M.D., Psychiatry, Univ of Pittsburgh, VA Medical Center Highland Dr, Pittsburgh, PA 15206; Jeffrey L. Peters, M.D., Daniel P. van Kammen, M.D., Kenneth L. Goetz, M.D., Eric Thomas, B.A.

## Summary:

The withdrawal of schizophrenic patients from neuroleptic is currently the only way to identify patients with long times to relapse. However, early after drug withdrawal, relapse rate may depend not only on individual and environmental factors (1,2), but also on periods of altered vulnerability in absolute time. In a study at our facility, 24 stable and remitted, hospitalized adult male schizophrenics (*DSM-III* & RDC) had their neuroleptic changed to haloperidol for at least 2 weeks, then were blindly withdrawn from drug for 6 weeks or until relapse, whichever came first. Relapse was defined as a 3 point rise in the daily Bunney-Hamburg Psychosis score above baseline, for 3 successive days. Ten patients relapsed during the 6 week period: 1 (wk 1), 2 (wk 2), 6 (wk 3), 1 (wk 4), 0 (wks 5 & 6). If we expect an exponential distribution of relapse times for all 24 patients, the x<sup>2</sup> goodness-of-fit test (with 14 nonrelapsers censored) rejects this null hypothesis (X<sup>2</sup>(5)=15..79, p<.01). Or, assuming 10 patients relapse over 6 weeks, the null hypothesis of a uniform distribution is rejected also (X<sup>2</sup>(5)=15.20, p<.01). Study of the nonrelapsers found the earliest significant reduction in the Simpson-Angus scale at 2 weeks (repeated measures ANOVA, F(1,13)=8.32, p<.01). Blink rates unobtrusively measured for 3 minutes during weekly interviews rose in non-relapsers, when a few patients with very high blink rates on haloperidol were excluded (r.m.ANOVA, F(6,54)=7.92, p<.001): the earliest elevation was at 3 weeks (f(1,54)=6.59, p<.05). Nonrelapser drug-free improvement occurred, with the earliest total BPRS reduction at 3 weeks (r.m.ANOVA, F(1,12)=13.29, p<.01). A biological event in the dopamine system following haloperidol dissociation may account for the week 3 changes and, in part, for the relapses.

## NR37

## Tuesday, May 10, 12 noon-2:00 p.m.

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

## Summary:

Abnormalities of the P300 component of the auditory event-related brain potential have been described in a number of psychiatric groups. However, these electrophysiological changes have not systematically been correlated to clinical symptomatology.

We have tested 22 medicated psychotic subjects, diagnosed as schizoaffective or schizophrenic (paranoid or nonparanoid) on *DSM-III-R* criteria using a standardized interview (SCID). Positive and negative symptoms were assessed using the SAPS and SANS, respectively. An auditory "oddball" P300 task was used in which each subject counted the number of high frequency tone pips occurring in a series of high and low pitched tones. Approximately 40 artifact-free trials to the high pitched tone were averaged. Counting accuracy and P300 amplitudes and latencies at CZ were scored by individuals blind to the diagnosis. Results indicated that counting performance was similar between groups. An ANOVA and post-hoc Tukey test revealed that the P300 amplitude but not latency was significantly greater in the paranoid schizophrenic group (T=3.11, p<02). Moreover, striking correlations were seen between P300 latency and positive symptoms in the schizoaffective and nonparanoid schizophrenic groups (r=-.80, p<.02; r=-.87, p<.02, respectively). This was not the case in the paranoid schizophrenic group. No such correlations were found with negative symptoms in any group.

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

## A TIME-SAMPLING METHODOLOGY FOR THE ASSESSMENT OF NEGATIVE SYMPTOMS

John J. Boronow, M.D., Sheppard-Pratt Hospital, 6501 N. Charles St PO Box 6815, Baltimore, MD 21285; Faith Dickerson, Ph.D., Norman B. Ringel, M.A.

#### Summary:

We present data using a new time-sampling instrument (ROUNDS) which records patient sleep, withdrawal, socialization, posture, and location. Thirty-seven chronically psychotic inpatients were rated hourly with ROUNDS during 1987, as well as weekly with the BPRS and behavioral performance measures in a token economy. Preliminary analysis suggests that ROUNDS is highly correlated with the BPRS in areas of predicted overlap (e.g., BPRS ITEM 3 with PASSIVE ISOLATION, r=.647, p<.000). More importantly, ROUNDS permits a refinement of concepts such as "withdrawal." Patients who are autistically withdrawn not only are more blunted and motorically retarded, but also more suspicious, hallucinated, uncooperative, delusional, and likely to fail in the token economy (R=.71, p<.000). Conversely, patients who are withdrawn but engaged in some activity are not associated with any specific pahtology and, in fact, are more likely to succeed in the token economy (R=.485, p<.000). ROUNDS also quantifies negative symptom behavior. For example, the 13 "pure" RDC schizophrenics in this sample averaged 7.7 waking hours a day withdrawn from others. Such quantitative measures will be assessed for their usefulness in distinguishing subgroups. In addition, we will demonstrate how the ROUNDS methodology can be applied to the examination of dynamic fluctuations in symptomatology and as a dependent measure to assess the efficacy of a discrete intervention on the course of negative symptoms in a patient or group of patients.

#### **NR39**

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

# THE NEUROLOGICAL SOFT SIGNS SCALE

John Herrera, Ph.D., Clin Research, Metro State Hospital, 11400 Norwalk Blvd, Norwalk, CA 90250; Robert Saul, M.D., Felipe Castro, Ph.D., C. Heh, M.D., J. Costa, M.D., J. Sramek, Pharm. D., S. Potkin, M.D., D. Guiasekaram, M.D.

## Summary:

Research in schizophrenia in the last decade has led to increasing speculation (Weinberger, 1987) that this illness is a primary brain disease associated with structural and physiological pathology. In this preliminary study, a 48-item neurological examination was developed in consultation with experts and administered by a neurologist to 25 medication-free (1-2 week placebo washout) schizophrenic patients. A principal component exploratory factor analysis with varimax rotation yielded two clinically interpretable factors, and two subscales were identified and summed to provide a Neurological Soft Signs total score. Sensation (6 items, alpha=.95) and Body Movement (5 items, alpha=.68). On the basis of the Neurological Soft Signs total score, patients were then assigned to high (n=10) or low (n=15) neuro soft signs groups and their clinical and biodemographic variables were examined. Examination of the BPRS subscales revealed that high neuro soft signs patients were rated higher on negative symptoms (p<.01), and low neuro soft signs patients presented more paranoid (p.05) clinical pictures. Results with the Negative Symptom Rating Scale (Lagar, et al., 1985) yielded similar findings; high neuro soft signs patients were rated higher on total negative symptoms (p<.01) and on the following subscales: thought (p<.05) and affect (p<.01). High neuro soft signs schizophrenic patients were also found to have had more psychiatric hospitalizations (p.<.01), a longer duration of illness (p.<.01), younger age at the onset of their illness (p.<.01), and concurrently older age than low neuro soft signs patients (p.<.01). The authors will discuss the clinical implications of their findings.

Tuesday, May 10, 12 noon-2:00 p.m. DOPAMINE SYSTEM DEVELOPMENT: THE EFFECT OF PRENATAL MPTP ON DOPAMINE-MEDIATED BEHAVIOR

# Ellen Weissman, M.D., Psychiatry, Univ of Cincinnati, 231 Bethesda Ave, Cincinnati, OH 45267; Andrew B. Norman, Ph.D., Stephen F. Calderon, M.D., Eve M. Zubrycki, B.S., Paul R. Sanberg, Ph.D.

# Summary:

Systemic exposure to the neurotoxin MPTP produces a Parkinsonian syndrome in humans and primates, but not in rats. However, in cell culture, MPTP interferes with embryonic rat dopamine (DA) neuronal function, and its active metabolite, MPP+, selectively destroys the neurons. This study examined whether similar effects occur in vivo. Pregnant rats were injected daily from E13 until birth with vehicle. MPTP, or MPP+ 10mg/kg ip. Offspring were tested for behavioral sequelae at postnatal days 21 and 50. MPTP treated pups were hypoactive on both test days. Behavioral responses to amphetamine are mediated by release of endogenous DA from striatal DA terminals. The destruction of DA terminals would abolish the behavioral effects of amphetamine. The prenatal MPTP group was hyporesponsive to d-amphetamine (Img/kg ip) on both test days. Prenatal MPP+ pups were hyporesponsive to d-amphetamine on day 21 but had recovered to control responses on day 50. Apomorphine (0.2mg/kg sc) produced increased stereotypy following MPTP/MPP+ prenatal treatment on both days 21 and 50. These results suggested persistent postsynaptic supersensitivity to dopaminergic agonists following prenatal MPTP/MPP+ treatment. Presence of a behavioral response to d-amphetamine indicated that striatal DA neurons were intact. This contrasts to the sensitivity of immature rat DA neurons in cell culture. Functional recovery occurred in the MPP+ group. Further investigation into the resistance of fetal rat striatal DA neurons to MPTP and the mechanisms of recovery in MPP+ prenatally treated pups may provide a clue to the prevention of Parkinson's disease and related syndromes, such as the movement disorders associated with neuroleptic drug use.

## **NR41**

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

## THIOTHIXINE SERUM LEVEL: CLINICAL IMPROVEMENT AND TARDIVE DYSKINESIA

Jerome A. Yesavage, M.D., Psychiatry, Stanford University, Stanford Univ Sch of Medicine, Stanford, CA 94305; Javaid D. Sheikah, M.D., Elizabeth I. Tanke, Ph.D., John G. Csernansky, M.D.

## Summary:

The purpose of this investigation was to determine the interrelationships of thiothixine serum levels, clinical improvement. and tardive dyskinesia (TD) in schizophrenics of a wide age-range. After a drug-free period of one week, 40 male schizophrenic subjects, 20 with TD and 20 without it, were treated with a fixed dose of thiothixine (10 mg p.o. q.i.d.) for five days, and steadystate serum levels of thiothixine were obtained using a flourescence spectrophotometry. Clinical improvement was measured by comparing ratings on the Brief Psychiatric Rating Scale (BPRS) before the administration of the neuroleptic and at the end of one week after initiation of treatment. The combination of TD, clinical improvement, and their interaction significantly predicted serum levels on a multiple-regression equation; R=0.61, F(3,36)=7.22, p<0.01). Both TD and clinical improvement were significantly related to serum level when the other predictor variables were taken into account; t=3.33, p<0.01 and t=2.71, p<0.05 respectively. The relationship between TD and clinical improvement was in a negative direction but not statistically significant; r(38) = -.21, p < .15. The results suggest that both TD and clinical improvement are associated with higher steadystate serum levels of thiothixine, but they are not related to each other.

## **NR42**

# VALIDITY OF SAGITTAL BRAIN AREA MEASUREMENT

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

Jeffrey A. Coffman, Psychiatry, Ohio State Univ, 473 West 12th Avenue, Columbus, OH 43210; Steven B. Schwarzkopf, M.D., Stephen C. Olson, M.D., Judy A. McLaughlin, M.S., Henry A. Nasrallah, M.D., Judith Brandt, R.N.

## Summary:

Several recent investigations<sup>1,2</sup> used magnetic resonance imaging (MRI) scans to compare midsagittal anatomical structures in schizophrenics and controls, based on a single presumed midsagittal slice chosen by external cranial features. Due to the variability of anatomical conformations in the midsagittal plane, we studied comparative anatomy in mid- and parasagittal regions in 30 prospectively recruited psychotic patients.

MRI parameters included a set of eight sagittal slices surrounding the midline, 3mm thick and offset from each other by 1mm in an inversion-recovery paradigm (TI=800msec, TR=1500msec) using 1.5 scanner. Images were reviewed (blind to diagnosis) and the best midsagittal image was selected for showing the smallest corpus callosum and cerebellar vermian areas and the least inclusion of cerebral white matter. Analysis included the immediate left and right parasagittal slices. For each slice, area measurements were made of cranial area, cerebral area, cerebellar area, frontal lobe area, ventricular area, and callosal area by computerized planimetry.

Intermeasure correlations were (>0.800) between slice measures of cranial area, cerebral area, and callosal area and (<0.700) for frontal and ventricular area. A repeated measures analysis of variance by slice positron showed a high degree of variance (F≥5.0, p≤.02) for ventricular area, cerebral area, and cerebellar area; and low variance only for the corpus callosum (F=0.7, p≈0.50). These suggest that some sagittal measures, while relatively highly correlated and allowing trends between groups to be reasonably measured, might be subject to effects of random and systematic positioning error.

## NR43 LEUKOENCEPHALOPATHY: CLINICO-ANATOMIC CORRELATES

C. Edward Coffey, M.D., Psychiatry, Duke Medical Center, Box 3920, Durham, NC 27710; Gary S. Figiel, M.D., William T. Djang, M.D., Richard D. Weiner, M.D.

## Summary:

In a previous retrospective study of brain magnetic resonance imaging (MRI) and CT, we found that lesions of the subcortical white matter (leukoencephalopathy) were surprisingly common in elderly patients referred for ECT, and that most of these patients had late-age-onset depressive illness. We now describe the results of an ongoing prospective MRI study designed to investigate more formally the clinical and neuroanatomic correlates of these lesions.

Baseline brain MRI (1.5 Tesla) was obtained on 52 of the 61 elderly (60 years or older) patients who received ECT during 1987 at Duke University Medical Center. Using formal rating instruments, the MRI scans were analyzed by a neuroradiologist and a neurologist/psychiatrist both of whom were blind to the clinical interpretation of each study. Leukoencephalopathy was observed in 92% (48) of patients and was frequently associated with cortical atrophy, ventriculomegaly, and lacunae of the brainstem and subcortical gray matter. The severity of the leukoencephalopathy was significantly correlated with the severity of the cortical atrophy. Clinically, these patients had late-age-onset, drug-refractory depressions that responded well to ECT; patients with lacunae of the subcortical gray matter appeared to be at increased risk of post-ECT confusion. Despite extensive lesions in some patients, dementia was uncommon.

We will discuss the potential implications of these findings for the clinical phenomenology, treatment, prognosis, and pathophysiology of depressive illness in the elderly.

#### **NR44**

## ANTIDEPRESSANTS IN DEPRESSED SCHIZOPHRENICS

FAMILY HISTORY OF DEPRESSION IN ALZHEIMER'S DISEASE

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

Mark S. Kramer, M.D., Psychiatry, Jefferson Med Coll, 1040 Walnut Street, Philadelphia, PA 19107; Wolfgang H. Vogel, Ph.D., Celeste DiJohnson, B.S., Patricia Sheves, Ph.D., Stephen Cavicchia, Psy.D., Patrick Litle, Ph.D.

#### Summary:

Fifty-six patients meeting *DSM-III* criteria for long-standing schizophrenia, and also research diagnostic criteria for a current episode of schizoaffective disorder, mainly schizophrenic with a depressive syndrome, scoring at least 30 (mean=55, SEM=1.6) on the Brief Psychiatric Rating Scale (BPRS) and 17 on the Hamilton Scale for Rating Depression (HSRD), were treated for four weeks with haloperidol and benztropine. Haloperidol/benztropine was then continued, while patients, those continuing to score greater than 17 on the HSRD, were randomly treated in a double-blind fashion to either adjunctive amitriptyline, desmethylimipramine, or placebo for an additional four weeks. Patients demonstrated decrements in HSRD and BPRS scores during treatment with haloperidol alone and showed continuing improvements with adjunctive amitriptyline, desmethylimipramine, or placebo treatments. Active antidepressant treatments offered no therapeutic advantage over placebo. However, assessment of the thinking disturbance factor of the Brief Psychiatric Rating Scale revealed that patients receiving antidepressants appeared to improve less than those who received placebo by the end of the four weeks of neuroleptic/antidepressant (or placebo) combined treatment phase. These results suggest that adjunctive antidepressants are not indicated for the treatment of depressive symptoms in actively psychotic hospitalized schizophrenic patients. Adjunctive antidepressants appear to retard the resolution of conceptual disorganization, hallucinatory behavior, or unusual thought content disorder in this population.

#### NR45

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

Brian A. Lawlor, M.D., SCN LCS, NIMH Bldg 10 Room 3D41, 9000 Rockville Pike, Bethesda, MD 20892; Trey Sunderland, M.D., Alan M. Mellow, Ph.D., James L. Hill, Ph.D., Paul A. Newhouse, M.D., Dennis L, Murphy, M.D.

#### Summary:

Although it is estimated that 15%-57% of patients with Alzheimer's disease (AD) suffer from depression, the association between depression and AD is poorly understood. To characterize more fully this complex and multifaceted relationship, we examined the family history of depression and alcoholism in first-degree relatives of both AD patients and controls. Using the retrospective chart review and structured telephone interview methods, we evaluated the first-degree relatives of 44 carefully diagnosed patients with probable AD and 38 age-matched controls.

Our results indicate that 2.9% of 350 AD relatives had a history of depression compared to 1.9% of 259 control relatives (p=NS). Only 2% of AD relatives had a history of alcoholism compared to 4.6% of control relatives (p=.05), the lower incidence of alcoholism being particularly evident in the male relatives of AD probands (p<.04).

It would appear from this preliminary study that familial predisposition to depression and depressive-spectrum disorders may not fully account for the high prevalence of affective illness in this population. Biological factors, such as neuropathological and neurotransmitter changes, may also play an important role. Future biochemical and longitudinal follow-up studies are necessary to understand more clearly the genetic and psychobiological contributions to the expression of depression in AD.

#### NR46 PROBAND PHENOTYPE AND FAMILIAL RISK OF DEMENTIA

Richard C. Mohs, Ph.D., Psychiatry, VA Medical Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Linda M. Bierer, M.D., Jeremy M. Silverman, Ph.D., Daniel P. Perl, M.D., Elisse Kramer, Ph.D., Daniel S. Lobel, M.A.

#### Summary:

We have previously reported that the cumulative risk for Alzheimer's-like dementia (AD) in 1° relatives of probands meeting NINCDS criteria for probable AD approaches 50% by age 90. We have now calculated cumulative risks for relatives of neuropathologically confirmed AD cases and for relatives of clinical cases with rapid vs. moderate cognitive worsening over 2 years follow-up. Of 13 autopsied cases, the clinical diagnosis of AD was confirmed in 10. For these 10 lifetime risk to 1° relatives was 47.1% by age 82; for the relatives of all 13, risks were 38.4% by age 82. Two year follow-up with yearly testing on the Alzheimer's Disease Assessment Scale (ADAS) is available for 28 probands. A median split on the change scores over 2 years will be used to define rapid and moderate rates of progression. Differences in cumulative risk to relatives and age of disease onset will be evaluated.

#### **NR47**

# REVERSAL OF CHOLINERGIC LESION DEFICITS BY NGF

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

Vahram Haroutunian, Ph.D., Psychiatry, MT Sinai School Med, One Gustave Levy Place, New York, NY 10029; Philip Kanof, M.D., Kenneth L. Davis, M.D.

## Summary:

A prominent feature of Alzheimer's disease (AD) is the degeneration of cortically projecting cholinergic cells in the basal forebrain. It has been hypothesized that diminished neurotrophic activity may contribute to this degenerative process. In three experiments rats (Ns=14–16) received ibotenic acid-induced lesions of either the medial septum or the n.basalis of Meynert (nbM). Different groups of rats then received infusions of either 5ug NGF or cytochrome C control solution into the lateral ventricle on days 2, 4, 8, and 12 following the lesion procedure. Cortical or hippocampal levels of choline acetyltransferase (CAT) and acetylcholinesterase (ACHE) were assessed either 2 or 6 weeks post lesion. Six weeks following the lesion cortical or hippocampal cholinergic marker deficits were reduced by approximately 50% (ps<0.05) in lesioned rats receiving NGF. The third experiment assessed the effects of 4 weeks of constant NGF administration in nbM lesioned rats. NGF or cytochrome C was infused into either the lateral ventricle or directly into the lesioned nbM for 4 weeks. The infusion of NGF into the lateral ventricle or the nbM diminished lesion-induced cholinergic marker deficits by 46% (ps<0.01). These results demonstrate that NGF can have a potent cholinergic deficit reducing effect in lesioned rats.

#### **NR48**

## PET SCANS WITH VERBAL TASKS IN ALZHEIMER'S DISEASE

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

James B. Brunner, M.D., Psychiatry, Univ of Chicago, 5841 S. Maryland Avenue, Chicago, IL 60637; Marka Moulthrop, Ph.D., John T. Metz, Ph.D., Daniel J. Luchins, M.D., Malcolm D. Cooper, M.D.

#### Summary:

Three elderly control subjects and two probable Alzheimer's disease (AD) patients underwent four serial Positron Emission Tomography (PET) scans while performing different behavioral tasks during 45-minute uptake periods. Regional cerebral metabolism was determined in 14 brain regions by the 18-F-fluoro-2-deoxyglucose method. The four tasks were sentence repetition, sentence comprehension, paragraph recall, and resting. The first three conditions were auditory verbal tasks matched for auditory input and verbal output. Performance scores on each verbal task were recorded.

Absolute left temporal (LT) lobe metabolism was positively correlated with performance on paragraph recall in all subjects. In controls, normalized LT lobe metabolism was reduced during the resting condition compared to any verbal task. Normalized LT lobe metabolism was consistently lower in AD patients than controls during each condition, with a greater difference found in the verbal task conditions than while at rest. Normalized right temperal lobe metabolism showed a weaker, but similar trend. Other brain areas did not show comparable differences between controls and patients.

Our data show that AD patients fail to show increased metabolism in the LT lobe during a verbal task. Thus, PET scans performed during a verbal task accentuate deficits of LT lobe function in AD patients.

## **NR49** HALOPERIDOL TREATMENT IN ALZHEIMER'S DISEASE

Davangere P. Devanand, M.B., Biol Psychiatry, New York St Psych Inst. 722 West 168th Street Box 72, New York, NY 10032; Harold A. Sackeim, M.D., Richard P. Brown, M.D., Richard Mayeux, M.D., John McGuire, B.A.

## Summary:

An ABA (A=placebo for four weeks, B=haloperidol for eight weeks) single-blind pilot study was conducted in nine outpatients with Alzheimer's disease (NINCDS-ADRDA criteria) who presented with symptoms of psychosis or behavioral disturbance. There was no significant change in target psychopathology during the initial placebo period. Eight weeks of treatment with haloperidol (1 to 5 mg per day) produced significant improvement on several measures: BPRS total scores and psychosis and hostile-suspiciousness factor scores, target symptoms from the SADS-PD, catastrophic reactions and disinhibition syndrome. There was non-significant reversal of these changes in the final placebo period. These findings were confirmed by double-blind ratings of videotapes of the interviews that were conducted with patients and family members.

Doses of 1 to 5 mg per day of haloperidol resulted in extrapyramidal side effects that required lowering of dosage in many instances, and no patient could be maintained on more than 3 mg daily. Cognitive status, as measured by the modified Mini Mental State exam (mMMS), changed over the course of treatment (F=3.03, p<.10). Total mMMS scores did not change during the initial placebo period but declined during the eight week haloperidol phase (mean 23.3 to 18.1, t=2.08, p<.10). There was only partial recovery in mMMS scores during the final four week placebo period (mean 18.1 to 20.1). These initial data suggest that while neuroleptics may have marked efficacy, they produce severe side effects even in moderate doses and may result in further cognitive decline in patients with Alzheimer's disease.

## **NR50**

#### Tuesday, May 10, 12 noon-2:00 p.m. PALLIDAL HYPERMETABOLISM IN SCHIZOPHRENICS WITH TARDIVE DYSKINESIA

Jorg J. Pahl, M.D., Nuclear Med, UCLA School of Med, UCLA School of Medicine, Los Angeles, CA 90024; George Bartzokis, M.D., John C. Mazziotta, M.D., Jeffrey L. Cummings, M.D., Lori Altschuler, M.D., Steven M. Mader, M.D.

## Summary:

18-FDG PET studies were performed on 40 subjects to determine normalized (region/hemisphere; ROI/HEM) glucose (LCMRGIc) metabolic ratios for the precentral gyrus, caudate, putamen, globus pallidus, and cerebellum. Subjects consisted of 26 normal, unmedicated controls (NC; age=[mean+SD] 45.1+15.9 years) and 14 DSM-III-diagnosed chronic schizophrenics who met Schooler and Kane criteria for tardive dyskinesia (TD: age=44.3+11.0 years). Twelve schizophrenics were medicated and two were drug free at the time of the PET scan: nine were on neuroleptics and anticholinergics and three solely on neuroleptics. Choreiform movements were quantified using the AIMS scale. Eight of the 14 TD patients had moderate to severe chorea (AIMS score≥4) in at least two body regions. X-ray CT's were obtained in 12 patients. All showed a normal striatal appearance. Nine out of 14 (65%) TD subjects had basal ganglia hypermetabolism with increases seen in the intensity and the size of the lenticular nuclei on the qualitative PET scan. The globus pallidus, which represents the major outflow tract of the striatum, showed significant hypermetabolism in the TD schizophrenic group (NC=1.19+0.10; TD=1.40+0.10; p<0.001, two-tailed t-test corrected for multiple comparisons). The patient group demonstrated normal caudate and putamen LCMRGIc values despite the use of neuroleptics and the presence of chorea. The increase in mean LCMRGIc values for the hemisphere, precentral gyri, thalamic and cerebellum did not reach statistical significance. Globus pallidus hypermetabolism is not restricted to tardive dyskinesia. Unilateral lesions of the substantia nigra in rats(1) and PET studies in humans suffering from idiopathic Parkinson's disease(2) also demonstrate hypermetabolism of the globus pallidus.

## NR51 CSF HVA ASSOCIATED WITH FAMILIAL SCHIZOPHRENIA

Miklos F. Losonczy, M.D., Psychiatry, Bronx VA Med Ctr, 130 W. Kingsbridge Road, Bronx, NY 10468; Michael Davidson, M.D., Jeremy M. Silverman, Ph.D., Richard S. E. Keefe, M.A., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

## Summary:

Inconsistent findings in prior studies of catecholamine metabolites in the spinal fluid of schizophrenic subjects may reflect differences in samples studied. This presentation addresses these issues by an extensive characterization of schizophrenic subjects, evaluating the relationship of clinical characteristics to CSF levels of HVA, 5-HIAA, and MPHG. The subjects were 72 drug-free RDC+ male veteran schizophrenics (mean age 38.4 yrs) and 18 age- and sex-matched normal controls (mean age 35.4 yrs), who underwent lumbar punctures following 100 mg/kg of probenecid. The levels of HVA and 5-HIAA were highly correlated (r=.73, df=61. p<.0001), but did not correlate with MHPG. Positive family history for schizophrenia spectrum disorders (SSD) was associated with elevated CSF HVA (F(2, 49)=10.6, p<.002), covarying for probenecid). Using morbid risk analysis, the nine subjects 1 SD above the mean HVA level showed a 12.8% risk for SSD in their first-degree relatives compared to zero for the nine subjects 1 SD below the mean (p<.01). There were no differences in normals and schizophrenic subjects as a whole for any of the neurotransmitter levels studied. CSF HVA was unrelated to clinical state, positive and negative symptoms, neuroleptic responsivity, the presence of TD, or SPEM abnormalities. As previously reported in a smaller series, ventricle-brain ratio was associated with decreasing HVA (r=-.42, df=45, p<.005).

# NR52

## Tuesday, May 10, 12 noon-2:00 p.m.

# ANTICHOLINERGIC CHALLENGE IN NORMAL ELDERLY PEOPLE

Zvi Zemishlany, M.D., Psychiatry, Bronx VA, 130 W. Kingbridge Road, New York, NY 10468; Richard C. Mohs, Ph.D., Anne B. Thorne, B.A., Michael Davidson, M.D., Kenneth L. Davis, M.D.

# Summary:

Interference with central cholinergic function by anticholinergic agents has been shown to produce disruption of cognitive performance. The present study was designed to identify the minimum dose of the anticholinergic scopolamine that reliably produces transient cognitive changes in elderly people, to determine which cognitive functions are most sensitive to disruption by anticholinergics and to compare effects in young and elderly subjects. Scopolamine (0.1, 0.2, 0.3 mg) and placebo were given to 12 normal elderly subjects (mean age 64.1 years). Fourteen young people (mean age 26.7 years) received placebo and 0.2 mg only. Scopolamine significantly impaired new learning in the elderly as measured by Selective Reminding Test (SRT) (p<.001) and SRT delayed recall (p<.005), but had no effect on praxis and language functions. When compared to the young group, the elderly showed poorer memory on placebo and a greater impairment on 0.2 mg of scopolamine. Results indicate that memory is more susceptible to disruption by anticholinergics than other cognitive functions, that elderly people are more sensitive to the effects of low doses of anticholinergics than are young people, and that 0.2 and 0.3 mg of scopolamine are effective doses for future anticholinergic challenge studies in subjects at high risk for Alzheimer's disease who might be even more sensitive to anticholinergics than the normal elderly.

## NR53

## CSF HVA AND 5-HIAA IN ALZHEIMER'S DISEASE

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

Linda M. Bierer, M.D., Psychiatry, MT. Sinai Sch of Med, 130 W. Kingsbridge Road, Bronx, NY 10468; Daniel S. Lobel, M.A., Michael Davidson, M.D., Miklos F. Losonczy, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

## Summary:

Reduced CSF HVA has been variably correlated with severity of illness in Alzheimer's disease, and a similar finding has been suggested for CSF 5-HIAA, but not previously confirmed. In this study, 28 drug-free patients with probable Alzheimer's disease by NINCDS criteria underwent AM lumbar puncture and baseline cognitive/behavioral evaluation with the Alzheimer's Disease Assessment Scale (ADAS), Blessed, and Dementia Rating Scale (DRS). CSF HVA, 5-HIAA, and MHPG were measured by HPLC. Mean ( $\pm$ SD) age for this sample was 66.4 $\pm$ 8.8 years (range 50–85), age of onset was 62.3 $\pm$ 9.1 years, and duration of illness was 4.1 $\pm$ 2.5 years. Results showed a significant negative correlation for both CSF HVA and 5-HIAA with cognitive/behavioral dysfunction measured as total ADAS score (r=-.49, p=.008 for HVA; r=-.50, p=.006 for 5-HIAA). In addition, CSF HVA correlated negatively with DRS scores (r=-.44, p=.21), and CSF 5-HIAA with scores on the Blessed (r=-.45, p=.015). Similar relations were not evident for CSF MHPG and measures of cognitive performance. Neither CSF HVA nor 5-HIAA showed a significant relation to age, age of onset, or duration of illness. However, the apparent associations between these indices and those of illness severity disappeared when metabolite data were expressed per mg CSF protein. These data confirm, but underscore the potential contribution of dilutional effects to the repeated finding of reduced CSF HVA in association with severity of illness in Alzheimer's disease.

Linda M. Bierer, M.D., Psychiatry, Bronx VA Med Ctr, 130 West Kingsbridge Road, Bronx, NY 10468; Michael Davidson, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

## Summary:

The antemortem identification of Alzheimer's disease patients with significant noradrenergic involvement may impact upon future pharmacologic approaches to this illness. Because of recent neuropathologic evidence that noradrenergic cell loss may be associated with long illness duration in AD, and neurochemical findings of elevated cortical MHPG in tissue samples from AD patients with particularly diminished NE content, we undertook the evaluation of CSF MHPG in relation to age of onset, duration and severity of illness in a sample of AD subjects. Twenty-eight drug-free patients with probable AD by NINCDS criteria underwent AM lumbar puncture and evaluation with the ADAS, Blessed, and DRS. Mean (±SD) age for this sample was 66.4±8.8 years, age of onset was 62.3±9.1 years, and duration of illness was 4.1±2.5 years (range 1–10). Results showed a significant positive correlation between CSF MHPG and duration of illness (r=.53, p=.004), but no relation between CSF MHPG and age, age of onset, or scores for the ADAS, Blessed, or DRS. Stepwise regression analysis with CSF MHPG as the dependent variable indicated a significant contribution of duration of illness (F=9.95, p=.004), but not of age of onset of ADAS score to the model. These data are consistent with the demonstration of elevated CSF MHPG in "advanced" but not "moderate" AD cases. To the extent that CSF MHPG increases as locus cereuleus neurons degenerate, this measure may provide an antemortem indication of noradrenergic cell loss in AD patients.

#### NR55 PSYCHOLOGICAL RESPONSES TO HIV SEROLOGICAL TESTING

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

Samuel W. Perry, M.D., Psychiatry, Cornell Med College, 525 East 68th Street, New York, NY 10021; Lawrence B. Jacobsberg, M.D., Baruch Fishman, Ph.D., Allen J. Frances, M.D., Pamela Weiler, B.M., Barbara Kaplan, B.S.N.

## Summary:

Goal: To assess psychobehavioral impact over time of receiving HIV antibody results in subjects at risk for AIDS. Method: Pre- and post-test counseling supplemented by six weekly individual cognitive/behavioral sessions, an interactive video program, or educational pamphlets. Results: Of a pilot group of 106 subjects, 81 were males (60 gay/bisexual, 13 with heterosexual partners at risk, one intravenous (IV) drug user, and seven with combinations of the other categories); 25 were females (22 with a known or suspected heterosexual partner at risk for infection, three with IV drug use and a heterosexual partner at risk). Of the males, 17 (21%) were seropositive (all gay/bisexual); of the females, three (12%) were seropositive. Drop-out was 15% prior to supplemental counseling and 15% prior to assessment at two months. Among seronegatives, Beck Depression Inventory scores diminished significantly between assessment one week prior to notification compared by paired analyses with scores two months later (8.4+/--8.1 to 5.8+/--7.0, p=.03). A visual analog scale of depression, rated from 0 to 100, showed a similar decrease (28.4+/-28.8 to 20.0+/-22.5, p=.02). Overall psychiatric symptoms as measured by the Brief Symptom Inventory (BSI) also diminished (26.6+/-24.0 to 20.2+/-21.0, p=.02). In particular there was a significant decrease on both anxiety subscale of the BSI (4.5+/-5.0 to 2.8+/-3.5, p<.01) and on a 100-point visual analog scale (43.3+/-27.6 to 21.0+/-22.1, p < .01). Among seropositives no significant increase was found in depression, psychiatric symptoms, or anxiety at two months. Data regarding risk behaviors and differential response to supplemental counseling will also be presented. Significance: Pilot data indicate that at-risk subjects voluntarily seeking HIV testing and receiving extensive pre- and post-test counseling have a decrease in psychiatric morbidity at two months if seronegative and, if seropositive, have no increase in psychiatric morbidity.

## NR56 ATTRIBUTIONAL STYLE AND HIV-ANTIBODY TESTING

Baruch Fishman, Ph.D., Psychiatry CL, Cornell Med College, 525 East 68th Street, New York, NY 10021; Samuel W. Perry, M.D., Lawrence B. Jacobsberg, M.D., Allen J. Frances, M.D., Alan Eisenstat, M.D.

## Summary:

*Goal:* Dysfunctional causal explanations for occurrence of life events (Attributional Style) (AS) have been associated with depressive and psychosomatic symptoms, maladaptive health and illness behaviors. After HIV-antibody test, immediate reaction and long term adjustment may be affected by poor AS. Since AS may be modified with Cognitive-Behavioral methods in post-HIV test counseling, it is important to determine the relationships between AS and distress symptoms in AIDS-risk population. *Method:* We administered the Revised Attributional Style Questionnaire (ASQR), Spielberger State and Trait Anxiety Inventory (SAI, TAI), and Beck Depression Inventory (BDI) to 115 at-risk subjects who presented for HIV testing and counseling in response to newspaper advertising. Most subjects were gay/bisexual men. A few were female sexual partners of bisexual or IV drug men. Distribution of AS scores was compared to random sample of 95 people with no known AIDS risk (from separate ASQR validation study). *Results:* Means/S.D. Attributional Style Total Index (ASTX) were similar for the two samples (12.3/4.3; 13.6/4.2). Correlations between ASTX and emotional distress were very strong (P's<-0001): ASTX & BDI=.59; ASTX & TAI = .57; ASTX & SAI = .41. *Significance:* 1) Based on AS, AIDS-risk sample does not seem more vulnerable to poor adjustment to illness than the general population. 2) Dysfunctional AS is strongly associated with chronic anxiety and reactive depression and anxiety in the AIDS-risk sample. 3) Early detection of individuals with poor AS and effective post HIV-test attitude modification may reduce long-term psychiatric and physical morbidity and risk-increasing behaviors. Research efforts in this direction are indicated.

## NR57

## POST-TRANSLATIONAL PROCESSING OF PREAMYLOID PROTEIN

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

William Wallace, Ph.D., Psychiatry, Mt. Sinai Medical Ctr, One Gustave Levy Place, New York, NY 10029; John Anderson, Ph.D., Ivan Leiberburg, Ph.D.

#### Summary:

Amyloid protein is a small (4 kD) polypeptide that is greatly enriched in the senile plaques of Alzheimer's disease brains. Recent studies have shown that the gene coding for this protein transcribes a mRNA (3.2 kb) which has been proposed to synthesize a larger amyloid precursor polypeptide. We have used antibodies made to synthetic peptides of the proposed precursor to investigate the expression of the precursor and its relationship to the amyloid protein in developing rat brains and in various human brain regions. Analysis on Western blots showed that the relative amount of the primary reacting protein (160 kD) decreased during aging, while other proteins of approximately 280, 60, and 25 kD either increased or remained invariable. However, no additional mRNA species were detected by Northern analysis and the primary translation product synthesized from polysomes, a single polypeptide (95(kD), did not vary with age. In human postmortem brain tissue, while the primary reacting polypeptide was 140 kD in Western analysis, additional larger polypeptides were observed. These were most prominent in cerebral cortex and hippocampus compared with either thalamus or cerebellum, a regional distribution consistent with that of the senile plaques. Translation of either mRNA or polysomes resulted in a similar 95 kD product which did not exhibit any such regional varibility. Thus, three observations argue for post-translational processing of the preamyloid protein: 1. the translation product is larger than the amyloid protein; 2. the mature precursor proteins identified by Western analysis are larger than the translation product; and 3. the preamyloid protein exhibits variable sizes with either age or brain region in the absence of differences in the translation product.

## NR58 A NOVEL ALZHEIMER AMYLOID CDNA WITH ADDITIONAL EXON

EYE MOVEMENT DEFICITS IN HIV INFECTED PATIENTS

Nikolaos Robakis, Ph.D., Psychiatry, Mount Sinai Med Ctr, One Gustave L. Levy Place, New York, NY 10029; Larry Refolo, Ph.D., DeBomoy Lahiri, Ph.D., L. Refolo, Ph.D., D.K. Lahiri, Ph.D., G. LaFouci, Ph.D.

# Summary:

The amyloid peptide (beta-protein) accumulates in the vessels and neuritic plaques in the brain of the Alzheimer's disease and Down Syndrome patients. This peptide is thought to derive from the proteolytic cleavage of a larger precursor 695 residues long encoded by a unique cDNA species. Screening of a human retina cDNA library results in the isolation of an alternative cDNA encoding the amyloid peptide. This cDNA species contains an additional 168 base pairs encoding 56 amino acids inserted in frame, so that the entire encoded polypeptide is 751 resides long. These 56 amino acids show considerable homology with a number of protease inhibitors and may protect this form of the amyloid precursor from degradation. Northern blot analysis using oligonucleotides specific to the additional sequence revealed that the corresponding mRNA is expressed in many different tissues and cell lines including frontal and occipital cortex, retina, neuroblastoma, and He-La cells. In order to study the splicing mechanism responsible for the synthesis of this mRNA we have isolated a genomic clone which hybridizes to the additional sequence. This clone contains an 8kb insert and failed to hybridize to cDNA sequences located immediately upstream or downstream from the 168 bp insert suggesting that this insert constitutes a separate exon unit. Antisera against synthetic peptides specific to this insert and against peptides common to both precursor proteins are being used to study the expression and post-translational modifications of the two different amyloid precursor polypeptides.

# NR59

## Tuesday, May 10, 12 noon-2:00 p.m.

John A. Sweeney, Ph.D., Psychiatry, Cornell Med College, 525 East 68th Street, New York, NY 10021; Bruce Brew, M.D., John Keilp, M.S., Allen J. Frances, N.D., Virginia Walsh, B.S., Robert Price, M.D.

## Summary:

Clinically observed eye movement abnormalities have been described in patients with HIV infection. In this study, we attempted to document and quantify the abnormality, and to relate the finding to the degree of clinically manifest neurological involvement. *Method:* 16 neurologically normal controls and 15 HIV-infected patients performed smooth-pursuit eye tracking tasks. Infra-red (IR) recordings of eye movements were digitized at 250 Hz. and computerized analysis was conducted offline. *Results:* The frequency of corrective saccades during pursuit tracking was elevated significantly in the HIV-infected group. A neurologist's clinical rating of the stage of AIDS dementia complex was significantly correlated with pursuit accuracy (RMS error; r = .56) and saccade frequency (r = .66). Clinical ratings of eye movement abnormalities correlated significantly (r = .49) with saccade rate. *Conclusions:* Eye movement abnormalities occur in HIV seropositive patients and are often detectable upon clinical examination. It seems likely that these oculomotor abnormalities are related to the presence of HIV infection, and as such they may serve as early markers of HIV-related neurological disease. The prognostic implications and the CNS basis of the oculomotor dysfunction remain to be established.

## **NR60**

## SACCADES DURING VISUAL FIXATION IN SCHIZOPHRENIA

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

Margaret Rea, Psychiatry, Payne Whitney, 525 East 68th Street, New York, NY 10021; John A. Sweeney, Ph.D., Carla Solomon, Ph.D., Michael Deck, M.D., John J. Mann, M.D., Allen J. Frances, M.D.

## Summary:

*Goal:* The inability to visually track a slowly moving target is one of the most promising psychobiologic markers for schizophrenia. The present study employed another task, the fixation of a stable rather than moving target, in an effort to more fully understand oculomotor disturbances in schizophrenia. *Method:* Eye movements during fixation of a stable target was monitored (EOG) in 35 schizophrenics and 20 normal controls. *Results:* Seven of 35 schizophrenic patients exhibited more saccades (typically square wave jerks) during fixation than normal controls. For nine schizophrenics tested weekly for four weeks, test-retest reliability of fixation saccade frequency was high (ICC=.75). The frequency of saccades during fixation was significantly associated with attention disturbances, clinical state (BPRS), reduced psychomotor speed, cognitive impairment, frontal horn but not lateral ventricle enlargement on CT scans, and there was a trend (p<.06) toward a relationship with CPZ-equivalent dose. *Implications:* The results indicate that some schizophrenics exhibit difficulty maintaining stable fixation of a stationary target. A disinhibition of subcortical saccade generating burst neurons might underlie this abnormality.

## NR61 MEDICAL ILLNESS AND DEPRESSION

Mary Ann Knesevich, M.D., Psychiatry, Washington University, Jewish Hosp 216 S. KingsHighway, St. Louis, MO 63110; William Scheftner, M.D., John Rice, Ph.D.

## Summary:

The question of whether depressed individuals are more likely to have associated medical illness is one that is of particular interest to psychiatry, because it is a medical discipline. We examined rates of common medical illnesses in 1427 first-degree relatives of depressed probands from five centers in the National Institute of Mental Health Collaborative Study of the Psychobiology of Depression: Boston, Chicago, Iowa City, New York, and St. Louis. A logistic regression model was used to predict the relative risk of having a particular medical illness in individuals carrying the diagnosis of depression when controlling for such factors as age, sex, and alcoholism. Our results suggest that a depressed individual would have a significantly higher risk of having the presence of certain accompanying medical illnesses, namely, myocardial infarction, migraine headaches, frequent respiratory illnesses, frequent staph infections of the skin, and a hyperactive thyroid. Individuals with depression were not found to have a significantly higher risk of having diabetes, hypertension, malignant tumors, or allergies. Further research to elucidate the exact nature of any relationship between various medical illnesses and depression might provide leads into the etiologies of these disorders and aid in their clinical management as well.

## NR62

## Tuesday, May 10, 12 noon-2:00 p.m.

N.P. Vasavan Nair, M.D., Research, Douglas Hospital, 6875 LaSalle Blvd, Verdun, PQ, Canada H4H1R3; Mukul Sharma, M.D., Mira Thakur, M.Sc., Remi Quirion, Ph.D.

## Summary:

The circadian rhythms of melatonin and cortisol were investigated in eight patients with Alzheimer's disease (AD) (57–76 years) and 20 age-matched healthy controls (56–79 years). Patients included in the study were clinically diagnosed as "probable" or "definite" AD (stage 4 or 5 on the Global Deterioration Scale of Reisberg) and further supported by a neuropsychological test battery. After appropriate consent, subjects were admitted to an investigation unit where hourly blood samples were drawn from 8 a.m. until 8 a.m. the next day. The indoor illumination was restricted to 300 Lux during the day and 50 Lux during the night. Serum melatonin and cortisol were estimated by radioimmunoassay. The data were analyzed both for quantitative (24-hour secretion, peak level) and time-related functions (cosinor analysis for acrophase, mesor and amplitude) of hormonal secretions. Preliminary results show significantly higher (p $\sim$ 0.0001) secretion of cortisol (mean $\pm$ S.D.) in AD patients (264=55.9 ug/dL) as compared to controls (162.6 $\pm$ 54.1 ug/dL). No difference in the cortisol rhythm acrophase was seen in the two groups. The data on melatonin are under analysis. Melatonin and cortisol results will be discussed in light of our earlier findings in normal brain aging.

## **NR63**

## HIGH PHENYLACETURIA CHARACTERIZES SCHIZOAFFECTIVES

CORTISOL AND MELATONIN RHYTHMS IN ALZHEIMER'S DISEASE

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

Hector C. Sabelli, M.D., Psychiatry, Rush University, 1725 W. Harrison Suite 1074, Chicago, IL 60612; U.N.B. Dura, M.D., Jan A. Fawcett, M.D., Javaid I. Javaid, Ph.D., Joe Wager

## Summary:

Symptomatology does not suffice for the differential diagnosis of acute psychoses. This study indicates that the 24 hour excretion of phenylacetic acid (PAA) differentiates two types of psychoses. PAA is the main metabolite of phenylethylamine (PEA). An increase in PEA metabolism has been postulated to contribute to schizophrenia (Fischer et al., 1972; Wyatt et al., 1979) and atypical bipolar psychoses (Karoum et al., 1982); a reduction in brain PEA has been proposed to explain depressive symptoms in affective disorders (Fischer et al., 1967; Sabelli et al., 1983) and in schizophrenia (Fawcett et al., 1984). Twentyfour hour urinary PAA was measured using the method of Gusovsky et al. (1984) in 28 acutely psychotic patients (16 schizophrenics according to DSM-///; 12 patients diagnosed as schizoaffective because they presented with affective symptomatology, mood-incongruent psychotic symptoms, and partial response to lithium and carbamazepine). Whereas normals excrete 141.0  $\pm$  10.2mg/24hrs of PAA, schizoaffectives excreted 240.3  $\pm$  51.9mg/day of PAA, and schizophrenics excreted 53.6  $\pm$  15.1. Fourteen schizophrenics and 3 schizoaffectives excreted less than 70 mg/day and 10 schizoaffectives and 1 schizophrenic excreted more than 200mg/day. These results support the notion of a distinct type of acute psychosis characterized by high PEA metabolism and different from schizophrenia in which low PEA metabolism may explain its depressive-like symptomatology.

## NR64 CEREBRAL THIRD VENTRICLE SIZE IN PSYCHOSES

Marcia J. Kaplan, M.D., Psychiatry, Univ of Cincinnati, 231 Bethesda Ave ML 559, Cincinnati, OH 45267; David L. Garver, M.D., Marjorie Lazoff, M.D., Kathleen Kelly, M.S.N.

## Summary:

Enlargement of the third cerebral ventricle in schizophrenics appears to be limited to a unique subgroup of psychotics identifiable by delayed response to drug treatment. Third ventricle area and width were measured from CT scans in 24 mood-incongruent psychotic patients (14 schizophrenic, two schizophreniform disorder, two schizoaffective disorder and six affective disorder with mood-incongruent psychotic features) and 14 controls age- and sex-matched to schizophrenic patients. Patients not responsive to therapeutic levels of lithium within 14 days, as indicated by a 35% symptom reduction on the New Haven Schizophrenic Index (NHSI), were treated with a fixed dose of haloperidol and classified as rapid responders (55% symptom reduction on NHSI within 45.  $\pm$  1.3 days) or delayed responders (55% symptom reduction on NHSI within 18.6  $\pm$  10.5 days). The significant enlargement of third ventricle area was isolated to the delayed neuroleptic responders (19.3  $\pm$  9.0mm<sup>2</sup>) compared with controls (11.7  $\pm$  4.8mm<sup>2</sup>, p = 0.01), lithium responders (11.5  $\pm$  6.3mm<sup>2</sup>) and neuroleptic rapid responders (12.2  $\pm$  5.7mm<sup>2</sup>). Third ventricle width showed a trend towards larger width in the delayed responders. There was a clear positive correlation found between ventricular size and age in the delayed responders (r = 0.08). A comparable relationship between ventricular size and age was not present in controls, in lithium responders or in neuroleptic rapid responders. This finding is consistent with an age-related progressive degenerative process of periventricular structures in the CNS of the neuroleptic-delayed responsive psychotics.

## **NR65**

# AUTOMATED VISUAL CPT IN SCHIZOPHRENIA

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

Paul G. Nestor, Ph.D., Psychiatry, Harvard-Brockton VA, 940 Belmont Street 116A, Brockton, MA 02401; Steven F. Faux, Ph.D., Robert W. McCarley, Larry Seidman, Ph.D., Martha E. Shenton, Ph.D., Stephen Sands, Ph.D.

## Summary:

Since the time of Kraepelin, an impairment in various aspects of attention has been described in schizophrenics (SZ), and often studied by the continuous performance test (CPT). The present study used a modified CPT, which has been demonstrated to be sensitive to changes in attentional processes in healthy subjects (Nuechterlein et al., 1983) and in children at risk for schizophrenia (Nuechterlein, 1983), although heretofore not used directly with SZ. We now report preliminary findings using a newly-developed, computer-based, automated version of this CPT with 11 neuroleptic-mediated SZ, diagnosed by *DSM-III-R* and RDC criteria, and 10 controls. Subjects monitored a series of digits presented singly at a rate of one/sec on a computer display under two levels of perceptual degradation (undegraded and degraded), and pressed a button in response to infrequent (p = 0.25) target digits. Signal detection analysis of performance was used to examine two aspects of visual attention: detection efficiency, and sustained attention. To control for a generalized performance deficit, we included only subjects who achieved a performance criterion (75% accuracy) for each level of degradation following several training sessions. SZ showed a greater decline in detection performance (A'= .906) as a function of stimulus level of degradation, even though their performance in the undegraded condition was generally preserved (A'= .965). However, there were no significant differences between SZ and normals in visual sustained attention, as measured by a decline in performance detection over time on task. The results suggest that schizophrenia has a more pronounced effect on the overall level of attentional resources than on the allocation of resources over time.

## NR66 SCHIZOPHRENIA: GENERALIZABILITY OF P3 DEFICIT

Steven F. Faux, Ph.D., Psychiatry, Harvard-Brockton VA, 940 Belmont Street 116A, Brockton, MA 02401; Martha E. Shenton, Ph.D., Robert W. McCarley, M.D., Paul G. Nestor, Ph.D., Brian Marcy, B.A., Amy Ludwig, B.A.

## Summary:

Two previous auditory P300 topography studies from our group have found a voltage deficit maximal at T3 electrode (left temporal) in *DSM-III* and RDC-diagnosed, medicated chronic schizophrenics (SZ), median ages 28–30, recorded with the full 10–20 electrode system with linked ears reference (LER). We examined the generalizability of these findings by using the same P300 protocol in similarly diagnosed and medicated SZ, but who were a decade older (median age = 40, N = 13), were from a different hospital, were recorded with a different imager and with additional electrodes (10–20 system + 8 interpolated), and who, to test the theoretical possibility (Nunez) of voltage distortions from LER, were recorded with both LER and nose reference (NR). Compared with an age and verbal-IQ-matched control group (N = 14), SZ showed a left P300 deficit for both LER and NR. Integrated voltages over 300–400 ms were significantly reduced at T3 in SZ compared with NL (p<.001 Mann-Whitney), and the deficit area for both reference electrodes included F7 (p's<011, MW); combining T3 and F7 gave the best SZ-NL group separation (p<.001) with one member having overlapping voltage values. Hotelling's T<sup>2</sup> tests verified group x scalp region interactions (p<.05) for both LER and NR. These SZ-NL differences were present on both the simple P300 (waveform following target stimuli) and the P300 derived from the Goodin subtraction procedure. We conclude the P300 deficit appears robust with respect to LER and NR, subject age within the range tested, variation in patient source, and recording/imaging equipment. This P300 deficit is compatible with other evidence suggesting the presence of temporal lobe pathology in SZ.

# NR67 HETEROGENEITY OF ALZHEIMER'S DISEASE

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

Vinod Kumar, M.D., Psychiatry, SIU Sch of Medicine, P.O. Box 19230, Springfield, IL 62794; Ezio Giacobini, M.D.

## Summary:

Recently there has been growing interest in subtyping of Alzheimer's disease. Early onset Alzheimer's disease patients have been reported to be clinically (Seltzer and Sherwin 1983) and biologically (Roth, M. & Wischik, C.M. 1985) different from the late onset patients. We studied the CSF choline, Acetylcholinesterase (AChE) and protein of 52 Alzheimer's disease patients (Early Onset (EO), <65 yr.) N = 18, (Late Onset (LO) >65 yr.) N = 34, and 20 normal age matched controls. We also studied the duration and severity of the illness. We compared the CSF measures between various groups and found that there was no difference in choline and AChE in EO vs. LO patients, but the CSF proteins were significantly (P = 0.045) higher in LO patients than EO patients. Choline was significantly higher in EO and LO patients (P = 0.013 and P = 0.040, respectively) compared to their age matched controls. AChE activity level in EO patients was significantly decreased compared to their age matched controls, but there was no difference between LO patients and their age matched control. There was no relationship between the biological measures (choline, AChE), and the severity or the duration of the illness. The consistently higher choline in Alzheimer's disease patients reflects changes in brain phospholipid metabolism and possibly a change in uptake of choline through the high affinity Na + dependent mechanism. These results suggest that the CSF choline may be used as a putative market of the cholinergic disturbance in Alzheimer's disease patients.

# NR68

# UTAH MOLECULAR GENETIC STUDY OF SCHIZOPHRENIA

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

William F. Byerley, M.D., Psychiatry, Univ of Utah Med Ctr, 50 N. Medical Drive, Salt Lake City, UT 84132; Jean Marc Lalouel, M.D., John J. Holik, B.A., Dora M. Stauffer, B.Sc., Paul H. Wender, M.D., Ray White, Ph.D.

## Summary:

As part of the Utah Molecular Genetic Study of Manic-depression and Schizophrenia, we have identified three multigenerational pedigrees afflicted with schizophrenia. Each family has multiple persons affected by either chronic schizophrenia, chronic schizoaffective disorder, or schizotypal personality, illnesses considered to represent phenotypes of the schizophrenic gene. At least one affected individual is present in each generation, and in all families the schizophrenic phenotypes appear to be assorting on one side of the pedigree. Diagnoses are made according to modified Research Diagnostic Criteria. Aware of Bassett's et al (1987) report of an association between schizophrenia and partial trisomy (q11.2–13.3) of the 5th chromosome, we tested for linkage between the Utah families and five DNA probes (p105–153Ra, pJ0110HC, p105–798, p105–599Ha, pc11p11) localized to the long arm of the chromosome #5. In addition, we undertook an analysis using four polymorphic DNA markers (pINS-310, H-ras, pT142, pADJ762) on the short arm of the 11th chromosome, an area in which tyrosine hydroxylase, the rate-limiting enzyme for dopamine and norephinephrine, is know to reside. Utilizing the computer program LINKAGE we did not find evidence of linkage between schizophrenia and these chromosome regions. Close linkage with a probe (p105–599Ha) mapping the region of the reported trisomy was excluded (p105–599Ha lod score -1.5 at 0 = 0.10;). We will discuss ongoing work using the preliminary map of the human genome to better define the genetics of schizophrenia.

Steven B. Schwarzkopf, M.D., Psychiatry, Ohio State Univ, 473 West 12th Avenue, Columbus, OH 43210; Michael W. Torello, Ph.D., Paul M. Vespa, M.S., Stephen C. Olson, M.D., Jeffrey A. Coffman, M.D., Henry A. Nasrallah, M.D.

## Summary:

In a previous visual evoked potential study, familial schizophrenic patients (FH POS) showed significantly prolonged P200 latencies compared to negative family history patients (FH NEG). In the present study, we attempted to replicate this neurophysiological difference in the auditory system.

Methods: Twenty-six schizophrenic/schizoaffective patients agreed to participate. Auditory evoked potentials were collected using a P300 "oddball" paradigm. P200 latencies were examined at the CZ electrode. Waveforms were visualized and latencies recorded by a technician blind to the family history status of the patient. Family history data were gathered by standardized interview (FH RDC).

Results: Analysis involved a repeated measures ANOVA with P200 latency measured for the frequent and infrequent conditions. As was previously seen in the visual system, the FH POS (first-degree relative hospitalized for psychosis) group showed significantly prolonged latencies of the P200 waveform compared to the FH NEG group (frequent condition, P = .018). There was a significant interaction between condition (frequent vs. infrequent) and family history status (P = .034).

Results suggest neurophysiological differences between the FH POS and FH NEG groups. More specifically, this may indicate a difference in central nervous system reactance between these two groups that generalizes over the auditory and visual systems.

## **NR70**

# NEUROLEPTIC TREATMENT AND EEG ALPHA ASYMMETRY

Edward L. Merrin, M.D., Psychiatry, VA Medical Center, 4150 Clement Street 116N, San Francisco, CA 94121; Thomas C. Floyd, M.A., George Fein, Ph.D.

## Summary:

Lateralized shifts in EEG alpha power have been described in association with neuroleptic treatment of schizophrenic patients. Because topographic localization is difficult with traditional common reference recording techniques in which activity at recording and reference electrodes is confounded, we examined the effects of neuroleptic treatment on alpha power after transforming data to average reference (AVR) and current source derivation (CSD) format. Bilateral frontal, central, temporal, and parietal EEG, referenced to Fz or Cz, were recorded from 10 medication free schizophrenic patients during active and resting conditions. A second recording was obtained after one-four weeks of neuroleptic treatment. After transformation to AVR and CSD (central leads only), a Fourier analysis was performed and session effects on log alpha power and asymmetry analyzed by repeated measure ANOVA. AVR data revealed a significant interaction between session, placement, and side (p<.02); alpha power increased bilaterally but asymmetrically after treatment in frontal (greater on right) and central (greater on left) leads. CSD analysis of central lead power also demonstrated a bilateral increase in alpha power, greater on the left, after treatment (p < .05). These results suggest changes in the spatial distribution of EEG alpha activity associated with neuroleptic drug administration.

## **NR71**

## **REFERENCE EFFECTS ON EEG ALPHA ASYMMETRY**

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

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

Edward L. Merrin, M.D., Psychiatry, VA Medical Center, 4150 Clement Street 116N, San Francisco, CA 94121; Thomas C. Floyd, M.A., George Fein, Ph.D.

## Summary:

Task related shifts in EEG alpha activity have been widely described as evidence for hemispheric asymmetry of function. However, topographic localization is difficult with the common reference recording methods usually employed because activity at the recording and reference electrodes is confounded in such data. Reference effects may be reduced with the average reference (AVR), where all recording sites are referenced to their grand mean, or current source derivation (CSD), where the local potential gradient perpendicular to the scalp is estimated.

We used AVR and CSD techniques to reanalyze lateralization of alpha activity recorded from nine channels referenced to Cz in 13 normal right-handed men during performance of verbal and spatial tasks. With the common Cz reference, there was more left-sided alpha suppression during the verbal task and more right-sided alpha suppression during the spatial task (P<.05). However, after transformation to AVR or CSD (central leads only), there were no lateralized differences between tasks. Examination of AVR data suggested that changes in activity primarily at the Cz electrode site were responsible for the lateralized changes in the Cz referenced recordings. These results illustrate that common reference recordings may obscure the topography of the EEG and cannot be interpreted as evidence of activity localized at the putative recording electrodes.

## INCREASED HVA RESPONSE TO MUSCARINIC AGONIST IN ALZHEIMER'S DISEASE

Nunzio Pomara, M.D., Geriatric Psych, Nathan S. Kline Inst, Orangeburg, NY 10962; Michael Stanley, Ph.D., Matthew Galloway, Ph.D., Dennis Deputula, Peter A. LeWitt, M.D., Thomas B. Cooper, M.A.

#### Summary:

Introduction: Receptor binding studies suggest that the loss of presynaptic cholinergic markers in Alzheimer's disease (AD), is not accompanied by a loss of postsynaptic muscarinic receptors. However, it has been demonstrated that in the cholinergic system, functional responses can be altered in the absence of a change in the actual receptor number. To further explore the functional status of muscarinic receptors in AD, we conducted the following experiment in which we assessed central and peripheral effects of a muscarinic agonist (Arecoline) on biogenic amine turnover and neuroendocrine measures.

*Method:* Individuals meeting NINCDS-ADRDA criteria for probable AD (N=6) and normal controls of comparable age (N=4) participated in a double-blind study in which the following treatments were given 1 week apart, and in a random order: 1) Arecoline  $4mg/60 \min (I.V.) + glycopyrrolate (GLY) (0.1 mg I.V.) pretreatment, 2) GLY, 3) placebo. Blood and CSF samples were collected during each session.$ 

Findings: Arecoline infusion resulted in an 86% increase in CSF HVA relative to placebo in AD patients (p<.005), while controls showed no significant changes in HVA. There was no concomittant Arecoline induced increase in plasma HVA. Both AD and controls showed significant increases in plasma cortisol and prolactin in response to Arecoline. GLY had no effect.

*Conclusion:* These findings are consistent with the hypothesis that the functional status of muscarinic receptors may be altered in AD.

#### NR73

#### Tuesday, May 10, 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., Monroe Cullum, Ph.D., Robert Heaton, Ph.D.

#### Summary:

Hypofrontality is hypothesized to be an important factor in understanding the neurobiological substrate of schizophrenic patients. Evidence for hypofrontality includes data from electrophysiological, brain imaging, and neuropsychological studies. Weinberger et al's Wisconsin Cart Sorting Task (WCST) studies indicate that schizophrenics show "perseverative errors" in changing the strategies used to sort cards with stimuli of varying form, colors, or numbers, and that normals selectively activate the prefrontal cortex during the WCST. Goldberg et al reported that schizophrenic patients cannot normalize responding on the WCST, even when given repeated, corrective instructions. Results of the current study show that 1) during an acute psychosis due to bipolar or schizophrenic disorders (N = 10–20), patients show increased WCST perseverative errors, and 2) stabilized but still impaired outpatients show normal WCST functions but are abnormal on other parts of the Halstead Reitan Battery. The WCST dysfunction of at least some schizophrenic patients may correlate with a reversible, state-dependent frontal dysfunction rather than a fixed lesion or fixed frontally based deficit.

#### NR74

## TIOSPIRONE IN TREATMENT REFRACTORY SCHIZOPHRENICS

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

Jeffery N. Wilins, M.D., Psychiatry, VAMC Brentwood Divn, 11301 Wilshire Blvd, Los Angeles, CA 90073; Neil Hartman, M.D., Donald Freidenberg, M.D., April Clemens, R.N., Jeffrey L. Cummings, M.D.

#### Summary:

As part of a multi-center study, we administered Tiospirone (Bristol-Myers), a buspirone derivative reported to have antipsychotic activity to 11 treatment refractory male inpatients with schizophrenia. Using a single-blind, flexible-, multiple-dose design we performed serial measures of the BPRS, SANS negative symptom scale, AIMS, Simpson-Angus, and the Fahn-Marsden Dystonia Rating Scale. Following an 8 day washout period, 9 patients completed a minimum of 6 weeks of Tiospirone (maximum dose 500 mg/day). Matched T-test comparisons of the pre-medication baseline with week 6 of treatment across patients demonstrated statistically significant improvement in the total BPRS score (p = .0291, T = -2.65, df = 8), the Affective Blunting subscale of the SANS (p = .0138, T = 6-3.14, df = 8), and approached significance in the SANS Attention subscale (p = .0564, T = -2.23, df = 8). One patient manifested a psychotic exacerbation after 8 months of treatment, while another outpatient has remained stable on drug after 9 months. No patients manifested parkinsonism or exacerbations of existing tardive dyskinesia on any dose of Tiospirone. Two patients, 1 with moderate and 1 with severe focal dystonias, improved markedly on Tiospirone. Tiospirone may be useful in the treatment of patients with schizophrenia, including those who are refractory to traditional neuroleptics. In addition, Tiospirone does not appear to cause parkinsonism and may preferentially ameliorate dystonic symptoms.

## NR75 AIDS RISK BEHAVIOR IN ADOLESCENTS

Steven E. Keller, Ph.D., Psychiatry, Univ Med Dent of NJ, 185 S. Orange Ave MSB E561, Newark, NJ 07103; Steven J. Schleifer, M.D., Jacqueline Bartlett, M.D., Robert L. Johnson, M.D., Cheryl Thompson, Ph.D.

## Summary:

The considerable national effort promoting AIDS education in sexually active adolescents and young adults implies that with increased knowledge, individuals will opt for less risky behaviors. We have begun to test this hypothesis with an urban, inner-city adolescent/young adult population in an epicenter for HIV. A sexual HIV-transmission risk scale was constructed, accounting for abstinence, fidelity, contact with high-risk individuals, and condom usage. The Diclemente questionnaire assessed AIDS-related knowledge.

52 subjects, 37 male and 15 female, ages 12–25 (mean 16.6  $\pm$  3.5) were studied. The age of beginning sexual activity was 13.2  $\pm$  1.7. Nine of the subjects denied sexual activity. Only five of the active subjects utilized sex practices with low risk of HIV-transmission.

From a range of knowledge, behavioral, and psychological variables, prior sexual victimization alone predicted sex-risk behaviors (p < 0.05). Victimization was highly correlated with a diagnosis of depression and the occurrence of stressful life events (p < 0.01). AIDS-knowledge was consistently high, comparable to DiClemente's sample. Neither age nor sexual abstinence correlated with AIDS-knowledge. Rather, the highest scores for transmission/prevention-knowledge were found in subjects in the highest risk categories. These data suggest that specific psychological attributes and environmental factors rather than knowledge are critical in shaping AIDS-risk behaviors.

## **NR76**

## Tuesday, May 10, 12 noon-2:00 p.m.

# HYPERCORTISOLISM IN ALZHEIMER'S DISEASE

Isabella J.E. Heuser, M.D., Biol. Psych., NIMH, 9000 Rockville Pike, Bethesda, MD 20892; Jorge J. Juncos, M.D., Ijaz Khan, M.D., Mark A. Demitrack, M.D., Mitchel A. Kling, M.D., Philip W. Gold, M.D.

## Summary:

Postmortem studies in patients with Alzheimer's disease (AD) show decreased cortical CRH content varying inversely with CRH receptor number. Despite this cortical CRH depletion, patients with Alzheimer's disease have been reported to show evidence of pituitary-adrenal activation by indirect means such as the dexamethasone suppression test. In the present study, we have attempted to further study pituitary-adrenal activity in patients with AD (n = 13) by more direct means of measuring ACTH and cortisol levels every 15 minutes for 36 hours and compared the results with healthy age-matched controls (n = 12). Compared with controls, patients with AD showed significantly greater mean 36-hour ACTH ( $5.86 \pm 0.17$  vs  $5.11 \pm 0.20$  pg/ml, p<.01) and cortisol values ( $9.2 \pm 0.5$  vs  $6.9 \pm 0.5 \mu g/d1$ , p<.005). In contrast to previous assumptions, the principal hypersecretion of cortisol occurred during the hours from 6 AM to 6 PM rather than during the night. We conclude that patients with Alzheimer's disease show hypercortisolism. It is noteworthy that in contrast to a younger sample of depressed patients, the hypercortisolism of Alzheimer's disease is associated with a significant elevation in plasma ACTH. This finding suggests that Alzheimer disease patients may be somewhat less sensitive to glucocorticoid negative feedback, compatible with data in experimental animals showing loss of CNS glucocorticoid receptors with aging. Hypercortisolism, despite loss of cortical CRH content in AD, suggests separate regulation and function of cortical and hypothalamic CRH neurons.

# NR77 Tuesday, May 10, 12 noon-2:00 p.m. NEUROLEPTIC REINTRODUCTION FOLLOWING NEUROLEPTIC MALIGNANT SYNDROME

Patricia I. Rosebush, M.D., Psychiatry, Sunny Brook Medical Ctr., 2075 Bayview Avenue, Toronto, Ontario Canada M4N3M5; Thomas Stewart, M.D.

## Summary:

Neuroleptic malignant syndrome (NMS) occurs in patients who will often require neuroleptics again. The safety of reintroducing neuroleptics remains unknown. We studied 13 cases of NMS in which neuroleptics were reintroduced. This was successful in 9 instances and unsuccessful in 4.

Of 9 successful reintroductions, 8 were attempted 2 weeks or more after the syndrome resolved. A different neuroleptic was used in 8 of the 9 successful cases. Lower potency neuroleptics were used in 6 of 9 successful trials; higher potency in 2 and the same potency in one. Lower chlorpromazine (CPZ) equivalent dosages were used in 7 and similar CPZ equivalent dosages in 2 of 9 successful reintroductions. 4 cases of unsuccessful reintroduction included a patient given neuroleptics within 24 hours of the previous episode and 3 cases in which the same drug and dosage were used 1, 2, and 28 weeks later.

In summary, neuroleptics are safely reintroduced in the majority of cases. An interval of at least 2 weeks following an NMS episode, using a different neuroleptic and an equivalent or lower dosage initially may ensure success.

## NR78 SERUM ABNORMALITIES IN NEUROLEPTIC MALIGNANT SYNDROME

Patricia I. Rosebush, M.D., Psychiatry, Sunny Brook Med Center, 2075 Bayview Avenue, Toronto Ontario, Canada M4N3M5; Michael F. Mazurek, M.D.

## Summary:

Neuroleptic malignant syndrome (NMS) is a fulminant, life-threatening reaction to neuroleptic medication. While elevated muscle enzymes are a recognized part of the disorder, the other biochemical features of NMS have not been well characterized. We have had an opportunity to study 25 cases of NMS over the past 6 years. Of the 20 cases in which serum iron levels were determined, 19 were associated with values that fell below the normal range of 55–180 mg%. In 14 cases the serum iron fell below 40 mg%, and in 7 patients the values measured were below 20 mg%. In each case for which data were available the serum iron returned to normal levels upon resolution of the NMS. In the lone patient with serum iron values that remained within the normal range, the mean serum iron during the NMS was 83 + 4 mg%, while upon recovery it was  $132 \pm 6$  mg%. Abnormalities were also observed in serum calcium and magnesium levels. Calcium concentrations (corrected for a serum albumin of 4 gm%) fell below the normal range in 14 of 25 cases, while magnesium values were below the lower limit of normal in 10 of the 16 cases in which levels were measured.

These results indicate that the laboratory abnormalities associated with NMS are widespread. The reduction of serum iron concentration is particularly striking, and suggests that a low level of serum iron may be useful as a supportive biochemical marker for the disorder.

## NR79

## Tuesday, May 10, 12 noon-2:00 p.m.

CLINICAL RELEVANCE OF MAPPING EEG IN DEMENTIA

Trey Sunderland, M.D., SCN LCS, NIMH Bldg 10 3D41, 9000 Rockville Pike, Bethesda, MD 20892; Richard Coppola, D.Sc., James L. Hill, Ph.D., Fran Oakley, O.T.R., Robert M. Cohen, M.D., Herbert Weingartner, Ph.D.

## Summary:

Clinical EEG's have proved useful in the diagnosis of Alzheimer's disease (AD) primarily when they show clear evidence of diffuse background slowing. Computerized mapping EEG has the advantage of providing quantifiable data from multiple leads that can be compared to other clinical measures. In the current study, 43 medication-free patients with mild-to-moderate DSM-III-R AD (18 males and 25 females; mean age =  $67.6 \pm 7.9$  years) were administered 32-lead EEG's under resting, alert conditions. Baseline measures included the Blessed Dementia Rating Scale and other global dementia instruments, several ratings of mood and behavior, and an objective evaluation of activities of daily living (ADL). Cognitive testing included the Weschler Memory Scale, and measures of episodic and semantic memory in selected patients. EEG data were analyzed for magnitude in the alpha, beta, theta, and delta bands, as well as total power and mean frequency across all leads.

Of all measures, ADL functioning revealed the most significant correlations with EEG magnitude, but only in the slower theta and delta bands (r = -0.65 to -0.85; p $\sim$ 0.001); total power and mean frequency also revealed a strong association with ADL functioning (r = -0.55 to -0.70, p $\sim$ 0.001). Cognitive measures provided relatively few significant correlations with EEG findings; most correlations were modest (r = 0.35 to -0.45; p $\sim$ 0.02) and were found with delta and theta bands, *not* with alpha and beta bands as might have been expected. The clinical dementia ratings generally failed to reveal significant EEG correlations; however, the Blessed Rating Scale showed a positive correlation (r = 0.37 to 0.44; p $\sim$ 0.02) with slow wave activity across selected leads and a significant negative correlation (r = -0.40 to -0.60; p $\sim$ .01) with average wave frequency. These results indicate that the characteristic slow wave EEG changes of progressive AD may be linked more to clinically significant changes in ADL functioning than to mood state, specific cognitive abilities, or global measures of dementia severity.

## NR80 HOSPITAL UTILIZATION IN SCHIZOPHRENIA

Lloyd E. Rader, M.D., Psychiatry, VA Medical Center, North Little Rock, AR 72114; Daniel E. Rodell, Cornelia M. Beck, Steven C. Buchanan, M.D., T. Michael Kashner, Ph.D., Floyd Westendorp, M.D.

## Summary:

We examined the utilization of inpatient services by all patients meeting *DSM-III* criteria for schizophrenia (n=351) admitted to a large VA facility over a two-year period. For these patients, the mean cumulative length of stay was 93 days per patient with a mean of three admissions for each patient. One hundred nine patients exceeded the 75th percentile for either cumulative length of stay ( $\geq$ 116 days) or hospital admissions ( $\geq$ 4) and were classified as "high" utilizers. The "high" utilizers had a mean cumulative length of stay of 176 days compared with 35 days for the other schizophrenic patients. At a rate of \$200/day (the estimated daily cost for a VA psychiatric inpatient bed), the average cost of hospitalizing a "high" utilizing patient was \$35,000 in contrast to \$7,000 for other schizophrenic patients. A stratified randomized chart review of 121 of the above patients, 41 of whom were high utilizers, was then performed by two psychiatrists. Reasons for admission were identified for each patient and collapsed into four major categories: (1) exacerbation resulting from medication noncompliance, (2) exacerbation related to substance abuse, (3) inability of caretaker/or support system to maintain the patient in the community and (4) exacerbation not due to other categories. Exacerbations related to substance abuse involved in "high" utilization, this evidence suggests that efforts must be directed at designing special treatment programs for patients whose schizophrenia is complicated by substance abuse.

#### NR81

## PREMORBID FUNCTIONING AND OUTCOME IN SCHIZOPHRENIA

Richard S.E. Keefe, M.A., Psychiatry, VA Medical Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Richard C. Mohs, Ph.D., Miklos F. Losonczy, M.D., Michael Davidson, M.D., Thomas B. Horvath, M.D., Kenneth L. Davis, M.D.

## Summary:

Chronic schizophrenics with the most severe social deterioration have previously been shown by the authors to differ from less deteriorated schizophrenics by measures of left-to-right ventricular asymmetry, negative symptoms, and nonresponse to haloperidol. This study investigated the social antecedents of these characteristics of very poor outcome in 69 chronic schizophrenics. Patients meeting RDC or Feighner criteria for schizophrenia were assessed for level of premorbid sociosexual functioning with the Premorbid Asocial Adjustment Scale. Poor premorbid sociosexual functioning was associated with worse current social functioning as measured by the Levels of Functioning Scale (r=.26; p<.03), greater overall severity of psychopathology as assessed by the CGI (r=.25; p<.05), greater left-to-right ventricular asymmetry, determined by the left ventircular brain ratio (VBR) divided by the right VBR, more severe negative symptoms as determined by Negative Symptoms manifested (r=-.29; p<.03). Response to haloperidol, covaried for baseline BPRS score, was not significantly related to premorbid sociosexual functioning (partial r=-.20; p=.12). These data are consistent with the notion that the concurrent characteristics of very poor outcome schizophrenic patients are not solely a result of the chronicity of these patients, but are associated with antecedent factors.

#### NR82 PLASMA INTERFERON IN SCHIZOPHRENIA

## Tuesday, May 10, 12 noon-2:00 p.m.

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

Darrell G. Kirch, M.D., Neuropsychiatry, NIMH, William A White Building, Washington, DC 20032; Olivia T. Preble, Ph.D., E. Fuller Torrey, M.D.

## Summary:

As a potential marker for viral and/or autoimmune pathology, concentrations of alpha interferon were determined in 48 plasma samples from 19 subjects with *DSM-III* schizophrenia.

The samples were paired, drawn while the patient was on chronic neuroleptic treatment and then after neuroleptic withdrawal. One pair of samples was taken from each of 14 subjects, and two pairs from each of five subjects, the latter being withdrawn twice from neuroleptics. The BPRS mean item score for the group increased by 37% (P<0.01) after neuroleptic withdrawal. Of the 48 samples, 16 (33%) showed elevated interferon. Of the 19 subjects, 11 (58%) showed elevated interferon in one or more samples. In a normal population, less than 5% of individuals will show elevated interferon levels. Of the 24 samples collected on chronic neuroleptic treatment, 11 showed elevated interferon, while five of 24 collected after withdrawal were elevated (P-N.S.). The BPRS mean item score corresponding to the 16 samples with elevated interferon was 1.38, while that corresponding to the 32 samples with normal interferon was 1.59 (P-N.S.).

These data conform that a significant number of schizophrenic patients have increased plasma alpha interferon, but this does not appear to be associated with withdrawal from neuroleptics or increased psychopathology.

## NR83 AMPHETAMINE AND CT FINDINGS IN SCHIZOPHRENIA

Llewellyn B. Bigelow, M.D., William White Building, 2700 Martin L. King Jr. Ave SE, Washington, DC 20032; Terry E. Goldberg, Ph.D., David G. Daniel, M.D., Joel E. Kleinman, M.D.

## Summary:

Introduction: Amphetamine and other stimulants have in recent years been employed by many researchers as probes in the study of schizophrenia. Using a double-blind randomized crossover design, we have investigated the effect of oral amphetamine on the Wisconsin Card Sort (WCS) and the Continuous Performance Test (CPT). The relationship of mood changes to brain CT finding was also investigated.

Methods: To date eight subjects meeting DSM-III-R criteria for chronic schizophrenia from this center's voluntary inpatient research population have received 0.25 mg/kg body weight of amphetamine elixir or matching placebo on two occasions separated by a least four days. All were being maintained on haloperidol, 0.25 mg/kg/24 hours. Neuropsychological testing commenced one hour after drug administration and continued for about one hour. The POMS and 10mm line test are being used to document mood changes.

Results: Consistent with previous reports, there is no single pattern of response to amphetamine in this small group. Compared to placebo, under amphetamine some patients showed improvement and some deterioration of performance on the CPT. On the WCS there were four subjects with less than 70% and four with scores greater than 70% correct responses (a cutoff for normal performance). WCS scores were relatively unaffected by amphetamine as compared to placebo. Five patients by self-report and by report of blind research staff appeared to develop an improved mood on amphetamine. One commented spontaneously that her thoughts seemed much clearer; another with prominent negative symptoms who was too fearful to cooperate with a blood flow procedure on placebo, actively and cheerfully participated in the same procedure after amphetamine. Four of these five were found on review of existing CT scans to have enlarged lateral ventricles (VBR>7.0), while two without apparent mood change had normal VBRs. CT scans are not yet available for the remaining two subjects. A larger sample will be reported, along with an exploration of the relationship of amphetamine effect to CT findings.

## NR84

## Tuesday, May 10, 12 noon-2:00 p.m.

# AGE DISORIENTATION AND SCHIZOPHRENIC DEMENTIA

Terry E. Goldberg, Ph.D., CBDB, NIMH, 2700 Martin L. King Jr. Ave SE, Washington, DC 20032; Joel E. Kleinman, M.D., David G. Daniel, M.D., Michael S. Myslobodsky, M.D., Daniel R. Weinberger, M.D.

## Summary:

Introduction: The notion that dementia is part of the schizophrenia syndrome dates at least to Kraepelin. One aspect of dementia in the schizophrenia syndrome, age disorientation, is present in upwards of 25% of chronic elderly schizophrenic patients. The search for biological correlates of this phenomenon (age disorientation) has thus far been unsuccessful. This study attempts to examine a proposed relationship between age disorientation and brain ventriculomegaly in schizophrenia. *Method:* Thirty-nine patients (mean age of 35 years) with *DSM-III* diagnoses of chronic schizophrenia were assessed with the Mini Mental State Examination (MMSE) and CT scanning (n = 33) with ventricular-brain ratios (VBR) calculated. All patients were also asked to state their age. Age disorientation was considered present if the patient was unable to provide his chronologic age within two years of its actual vaue. An age delusion was considered present if the patient maintained in a fixed and consistent manner that he was more than two years younger or older than his actual age in the context of intact MMSE performance.

lts:	Group	<u>N</u>	VBR	MMSE
	Age disoriented	6	11.3*	13*
	Age delusional	2	2.7	25
	Age oriented	31	6.9	23

\*p<.05 relative to other groups

*Discussion:* In this study, patients with age disorientation invariably had ventriculomegaly. Moreover, when compared with a group of demented, but age-oriented patients, the age-disoriented patients still had a significantly larger mean VBR. The converse, that ventriculomegaly was invariably associated with age disorientation, was not true. Age disorientation appears to be part of a syndrome of cognitive failure and neuroanatomic abnormality that may represent true dementia praecox.

## NR85 MEDIAL PREFRONTAL CORTEX LESIONS IN THE RAT

George E. Jaskiw, M.D., CBDB, NIMH, 2700 Martin L. King Jr. Ave SE, Washington, DC 20032; Farouk Karoum, Ph.D., William J. Freed, Jr., Ph.D., Joel E. Kleinman, M.D., Daniel R. Weinberger, M.D.

## Summary:

The dorsolateral prefrontal cortex (DLPFC) has been implicated in the pathogenesis of schizophrenia, prompting studies of DLPFC homologues, such as the medial prefrontal cortex (MPFC) of the rat. Dopamine (DA) in MPFC appears to modulate DA turnover in nucleus accumbens septi (NAS) and the corpus striatum (CS). To elucidate the role of MPFC, we bilaterally lesioned intrinsic MPFC cells in male rats using ibotenic acid (5 $\mu$ g/.5 $\mu$ I). Locomotor activity was measured in photocells counters for 60 minutes after a 5 minute habituation. One cohort was tested repeatedly on days 3, 6 and 13 after lesion, while the other was tested only on day 13. On day 14, rats were sacrificed and MPFC, NAS and CS dissected out.

Compared to those vehicle treated, IA lesioned tested repeatedly were more active on days 3 and 6 as were the rats tested only on day 13. In both cohorts DA metabolite profiles suggested increased DA turnover in MPFC and CS. Noradrenaline was increased in NAS of unacclimatized rats. The results 1) confirm that intrinsic MPFC cells participate in habituation processes and 2) suggest that MPFC neurons may exert a tonic modulatory effect on subcortical catecholamine systems. By extension, it is possible that dysfunction of intrinsic DLPFC neurons could mediate some features of psychiatric illness.

#### NR86 STAGE FOUR SLEEP AND CT SCAN MEASURES IN SCHIZOPHRENIA

# Tuesday, May 10, 12 noon–2:00 p.m.

Jeffrey L. Peters, M.D., Psychiatry, VA Medical Center, Highland Drive, Pittsburgh, PA 15206; Welmoet B. van Kammen, M.D., Thomas C. Neylan, M.D., Kenneth L. Goetz, M.D., Daniel P. van Kammen, M.D.

## Summary:

Prior studies have shown a bimodal distribution of EEG slow wave sleep or an association between slow wave sleep and increased negative symptoms in schizophrenia (Hiatt *et al*, 1985; Ganguli *et al*, 1987).

In this study, 10 physically healthy males (mean age 32.3, range 24–50 years; *DSM-III* chronic schizophrenia) consented to 3 consecutive nights of polysomnography and head CT scans without contrast. The sleep record and CT scans were scored independently by established techniques. The lager negative symptom scale and the Cannon-Spoor Premorbid Adjustment Scale were used. Four patients had no prior neuroleptic exposure; the others were free of all medication at least two weeks before the sleep studies.

Stage-4 percent correlated negatively with VBR calculated by planimetry (r = 0.76, p = 0.005), premorbid functioning (r = 0.69, p = 0.009), and negative symptoms (r = 0.67, p = 0.01). There was no association between age and VBR or between age and Stage-4 sleep in this sample.

A small comparison group of 6 former Bataan/Corregidor Prisoners-of-War were studied in identical manner (mean age 69.3, range 65–73 years; *DSM-III* chronic PTSD). Many had chronic medical problems, but all were free of psychotropics at least two weeks. As expected from the age difference, slow wave sleep was markedly reduced or absent in this sample. No correlation was found between Stage-4 percent and VBR.

The results suggest that decreased Stage-4 sleep may be a trait variable secondary to brain atrophy in a subgroup of schizophrenic patients.

## **NR87** LITHIUM AND GROWTH HORMONE RESPONSE IN PSYCHOSES

Surendra Kelwala, M.D., Psychiatry, VA Medical Center, Southfield and Outer Drive, Allen Park, MI 48101; Anil Jain, M.D., Sheena Jenson, B.A., Vijaya Chilakamarri, M.D., Basivi Baddigam, M.D., Samuel Gershon, M.D.

## Summary:

We are conducting a large scale study to investigate Lithium (Li) efficacy in schizophrenic illnesses and to evaluate the significance of biological and clinical predictors of Li response. A previously reported biological predictor of Li response in schizophrenia is Apomorphine induced Growth Hormone Response (GHR). The peak level of GH in the plasma 60 ± 20 minutes following injection of .75 mg of Apomorphine is hypothesized to measure the sensitivity of post-synaptic dopamine receptors in drug free subjects. We currently have data on 22 inpatients who met the Research Diagnostic Criteria for schizophrenia or schizoaffective illness-predominantly schizophrenic and completed the GHR test and Li trial. Li was given for 2-6 weeks (mean duration 29 days) at levels 1.1-1.4 meg/L. Patients were classified as good responders by-40% improvement on either the New Haven Schizophrenia Index (NHSI) or BPRS, ≥2 improvement on CGI, and discharge from the hospital on Li: partial responders—10-40% improvement on NHSI/BPRS and ≥1 improvement on CGI; non responders -<10% improvement on NHSI/BPRS after a minimum of 14 days of Li trial or greater than 25% worsening on the NHSI or the development of neurotoxicity at any time of the trial. Three patients were good responders (GH peak value  $\bar{x} = 28.64 \pm 20.97$ ), 9 patients were partial responders (GH peak value  $\bar{x} = 29.51 \pm 23.12$ ) and 10 patients were non responders (GH peak value  $\bar{x} = 28.23 + 14.26$ ). A one way ANOVA (F = .0092) did not differentiate good, partial, or non responders. While the rate of good and partial response to Li in schizophrenic illnesses is consistent, the failure of GHR to differentiate responders from non responders is not concordant with other studies.

## **NR88**

Tuesday, May 10, 12 noon-2:00 p.m. A PARALLEL DISTRIBUTED PROCESSING MODEL OF ATTENTION DEFICIT IN SCHIZOPHRENIA

Jonathan D. Cohen, M.D., Psychology, Carnegie Mellon Univ, Pittsburgh, PA 15213

## Summary:

A theory is proposed that links the three most consistent findings concerning schizophrenic cognition: 1) schizophrenics suffer from an attentional impairment; 2) schizophrenics consistently demonstrate slower reaction times in a variety of psychomotor tasks (e.g., Nuechterlein, 1977); and 3) schizophrenics show a strong meaning bias in the interpretation of ambiguous linguistic stimuli (Chapman, Chapman and Miller, 1964). The theory is described in terms of a computational model, which uses the mechanisms of parallel distributed processing (Rumelhart, McClelland et al., 1986). The model provides a specific mechanism for the allocation of attention, and demonstrates that when the performance of this mechanism is limited or impaired, there is a slowing of processing in all pathways. This can provide an explanation of the increased reaction times observed in schizophrenics in terms of a specific attentional deficit. The model also shows that impairment of attention has a disproportionately larger effect on processing in weak as compared to strong pathways. This can be used to explain the strong meaning bias observed in schizophrenics. Thus, the model is able to provide a coherent account of several important empirical phenomena associated with schizophrenia, in terms of an attentional deficit in an explicit processing mechanism.

## **NR89**

# NEGATIVE SYMPTOMS IN SCHIZOPHRENIA AND DEPRESSION

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

Jacqueline A. Samson, Ph.D., Psychiatry, Brockton VA Med Center, 940 Belmont Street, Brockton, MA 02401; Alexander Young, B.S., Ming T. Tsuang, M.D., John C. Simpson, Ph.D.

## Summary:

Previous studies of negative symptoms in schizophrenia and depressive illnesses have failed to find clear differences between these diagnostic categories (1,2). To explore the specificity of negative symptoms in schizophrenia, we used a threestage analytic process to examine scores on the scale for the Assessment of Negative Symptoms (SANS) in samples of 37 DSM-III schizophrenic and 11 unipolar depressed male patients. Results: SAS General Linear Model procedures revealed that SANS items did not discriminate between the two DSM-III patient groups. However, when schizophrenic patients who presented with high scores on the depressive mood subscale of the SADS (group 1; N = 11) were eliminated, significant differences were found ( $R^2 = .68$ , F = 2.40, P = .03), with schizophrenics showing more inappropriate affect (P < .03), decreased intimacy (P < .01), and more impaired relationships (P < .01). When patients with inappropriate affect (group 2; N = .11) were removed from the sample the following SANS items discriminated schizophrenic from depressed patients (R<sup>2</sup> = 87, F = 3.77, P = .02): decreased movements (P<.01); increased latency (P<.005); decreased eye contact (P<.005); poverty of content of speech (P<.005); decreased intimacy (P<.02); impaired relationships (P<.002); and social inattentiveness (P<.02). Our findings suggest a possibility of at least three groups of schizophrenic patients: group 1 with depressive mood; group 2 with inappropriate affect; and group 3 with poverty of speech content, psychomotor retardation, and impaired social relations but with no depressive mood. Results will be discussed in terms of a categorical versus a continuum model of psychoses and affective illnesses.

William C. Wirshing, M.D., Psychiatry, UCLA Brentwood VAMC, Wilshire & Sawtelle 210 B151H, Los Angeles, CA 90073; George Bartzokis, M.D., Jeffrey L. Cummings, M.D.

## Summary:

Although tardive dyskinesia (TD) has been clinically well defined for many years, it has proved problematic to measure quantitatively. A battery of prototype electromechanical instruments has been developed by the Brentwood Movement Disorders Laboratory to measure and analyze the hyperkinetic movements of TD directly, objectively and non-invasively. Fifty patients with mild to moderate clinical TD (but who were devoid of other clinically apparent movement abnormalities) and 70 neurologically normal controls were assessed with this battery. The electromechanical features which most consistently characterized and differentiated the TD group were a greater variability of all movements; increased energy in the 1 Hz to 2 Hz frequency band in hand and foot movements; a marked increase in movements during distracting tasks; and an increase in the energy in the 4 Hz frequency band (3 Hz to 6 Hz) in a subset of the TD group. The authors conclude that this latter group, which constituted one-third of the total TD group were patients with combined TD and subclinical drug-induced parkinsonian tremor. They further concluded that this type of instrumentation would be useful in prospectively following individual patients to scan for subclinical movement away from an instrument-established baseline and in examining patients with combined movement abnormalities.

## NR91

#### Tuesday, May 10, 12 noon-2:00 p.m.

# CSF NOREPINEPHRINE AND RELAPSE IN SCHIZOPHRENIA

Kenneth L. Goetz, M.D., Psychiatry, Univ of Pittsburgh, VAMC Highland Drive 116A, Pittsburgh, PA 15206; Jeffrey L. Peters, M.D., David Shaw, Ph.D., Jeffrey K. Yao, Ph.D., Welmoet B. van Kammen, M.D.

## Summary:

There is considerable evidence for noradrenergic system disturbances in schizophrenia. In this study, we evaluated the relationship of CSF NE durng haloperidol treatment to relapse following haloperidol withdrawal. Thirty-two male schizophrenics *(DSM-III)*, age 21–51, underwent a lumbar puncture during haloperidol stabilization (2–40 mg/day) and again during a sixweek placebo-replacement period. Fourteen patients relapsed while 18 patients remained stable. CSF NE, MHPG, HVA and 5-HIAA were measured using HPLC.

Levels of CSF NE were significantly higher in haloperidol-treated patients who relapsed than in those who did not  $(0.79 \pm 0.36 \text{ vs.} 0.52 \pm 0.35 \text{ pmol/ml}$  respectively, p = 0.04). Levels of CSF MHPG, HVA and 5-HIAA, or measures of sleep and psychosis did not differ between the two groups during haloperidol treatment. However, CSF NE and MHPG were significantly higher in the drug-free relapsed patients than in the drug-free nonrelapsers. Additionally, CSF NE significantly correlated with psychosis only in the relapsed patients.

These data support the hypothesis that noradrenergic activity is increased in schizophrenic patients who will relapse following neuroleptic withdrawal. Also, the continued increase of NE in drug-free relapsed patients supports the concept that increased noradrenergic activity is a prerelapse condition rather than a response to neuroleptic treatment.

#### NR92 BIOLOGICAL MARKERS OF THE POSITIVE AND NEGATIVE SYNDROMES

# Tuesday, May 10, 12 noon-2:00 p.m.

Anand K. Pandurangi, M.D., Psychiatry, MCV Station, P.O. Box 710 MCV, Richmond, VA 23298; Solomon C. Goldberg, Ph.D., David Ross, M.D., Alfred L. Ochs, Ph.D., Douglas G. Brink, Pharm.D., Mark H. Hill, M.A.

## Summary:

There has been a recent surge in the positive and negative syndromes within schizophrenia. Neurobiological findings previously known to be relevant to schizophrenia have been reinvestigated as markers of these syndromes (1) We report here our investigation of three such measures in the context of the positive-negative dichotomy. Raters of each measure were blind to the results of the other measures.

36 subjects with schizophrenia by research criteria were assessed for the severity of their positive and negative symptoms. Lateral ventricle size was measured using the ventricle-brain ratio (VBR) by CT Scans. Smooth pursuit eye movement (SPEM) was assessed using intra-red laser detection and digital recording. 18 subjects underwent the amphetamine challenge test with placebo control, in a double blind fashion and their behavioral response was assessed using the BPRS. Mean age of subjects was  $30.9 \pm 9.7$  years. Mean total duration of illness was  $9.7 \pm 7.6$  years. There were 24 males and 12 females.

*Results:* Positive symptoms had a significant relation with the SPEM measures of velocity and position root mean square error score (VRMS and PRMS r = 0.51, p = 0.05, r = 0.55, p = 0.03, respectively). Negative symptoms showed a trend toward a negative relation with these measures of SPEM (r = 0.42 and -0.41). There was an insignificant relation between the positive and negative symptoms scores (r = 0.23, N.S.). The positive and negative symptoms had no relation with the amphetamine response or the VBR. Amphetamine response had a negative relation with VBR. (r = -0.54, p = 0.02). Deficits in SPEM tasks may be markers of the positive syndrome and resistance to amphetamine may mark the negative syndrome. Findings will be discussed in the context of Crow's Type I & II.

#### MEG AUDITORY SOURCES MAY DIFFER IN SCHIZOPHRENIA

Martin Reite, M.D., Psychiatry, Univ of Col Sch of Med, 4200 E. 9th Avenue, Denver, CO 80262; Peter Teale, M.S., Leigh Goldstein, M.S., John Whalen, B.A.

#### Summary:

We recorded the 100 msec latency magnetic evoked field (EF) component (M100) from both left (L) and right (R) hemispheres of six normals (N) and six schizophrenic patients (S), using a single channel, second, difference gradiometer with DC SQUID, 20mm coil diameter, and 6cm baseline. EFs were obtained by averaging 128 responses to 20msec, long 85dB 1 KHz tone pips. M100 amplitude from each of 28–43 recording points were used in a computer, generated least squares best fit to a single dipole model providing estimates of source dipole location, orientation, and depth. Comparing L and R hemispheres in normals, M100 sources were further posterior over the L hemisphere by  $2.1 \pm 1$  cm (t = 3.56, df = 10, p<.005), did not differ in height, and were oriented more nearly vertical by  $20^{\circ}$  (L =  $171 \pm 9^{\circ}$ ; R =  $151 \pm 9^{\circ}$ ; t = 4.04, df = 5, p<.01). In schizophrenics, left and right hemisphere sources did not vary significantly in height, antero-posterior location, or orientation. Comparing schizophrenics to normals, L hemisphere sources in patients were further forward by an average of 1.1cm (t = 2.45, df = 10, p<.03), and were tilted more posteriorly by  $22^{\circ}$  (N =  $171 \pm 9^{\circ}$ , S =  $149 \pm 6^{\circ}$ ; t = 4.95, df = 10, p<.006). These findings provide further evidence for differences in interhemispheric and especially L hemisphere function in schizophrenia. Supported by USPHS Grants No. RR03259, MH41396 and MH46335.

# ILLNESS, WELLNESS IN A LARGE SCHIZOPHRENIA PEDIGREE

## Tuesday, May 10, 12 noon-2:00 p.m.

Anne S. Bassett, M.D., Med Genetics, NY State Psych Inst, Box 58 722 West 168th Street, New York, NY 10032; Dolores Malaspina, M.D., Barry Jones, M.D., Pamela Forsythe, M.D., Angus Beck, M.D., Charles A. Kaufmann, M.D.

#### Summary:

**NR94** 

The examination of large pedigrees for linkage analysis studies provides the opportunity to determine the range of illness and health in these special families. Two psychiatrists evaluated 21 living members from an extensive Canadian pedigree segregating schizophrenia. Modified structured interviews (SCID-I,II), complete mental status examinations, positive and negative symptom ratings (PANSS), and movement disorder screens (AIMS, ESRS) were done. These data, supplemented by audio-tapes of the interviews, available hospital records, and collateral information, provided *DSM-III-R* multiaxial diagnoses and allowed an assessment of life stresses and coping skills. Deceased or lost family members from four generations (N = 25) were assigned *DSM-III-R* diagnoses from comprehensive clinical records dating back to 1857.

Direct interviews revealed wide-ranging diagnoses from severe (Schizophrenia, Chronic Disorganized Type), to mild (Avoidant traits), while functioning ranged from longterm hospitalization to very good overall functioning (GAS from 10 to 86). Tardive dyskinesia was evident in all neuroleptic treated subjects, and a movement disorder (grimacing, titubation) in one subject with Schizotypal personality but no drug treatment history. Preliminary results of linkage analysis using genetic markers from the long arm of chromosome 5 (a region implicated in schizophrenia) will be presented.

The results suggest that clinical data collected to determine psychopathology for linkage analysis studies may also provide a new view on potential buffers to severe psychiatric illness in families greatly at risk.

## NR95 GLOBAL AND FOCAL CEREBRAL ATROPHY IN SCHIZOPHRENIA

## Tuesday, May 10, 12 noon-2:00 p.m.

William R. Yates, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; Victor Swayze, M.D., Nancy C. Andreasen, M.D.

## Summary:

We evaluated a group of schizophrenics (n = 107) and a group of controls (n = 72) for neuropsychological performance and compared these results with CT scan ratings for global, frontal and temporal atrophy. Atrophy ratings were based on evidence of sulcal widening and made blind to diagnosis on a nominal scale using model scans. This method resulted in interrater reliability kappas of .62–.67. There was no difference between schizophrenics and controls for the presence of global atrophy (16.8% vs. 16.7%) or frontal atrophy (160.3% vs. 9.3%). Temporal atrophy was rated as present for 20.6% of the schizophrenics compared to 9.3% of the controls (chi-square = 4.15, p<.05, odds ratio = 2.57).

Schizophrenics with atrophy demonstrated specific neuropsychological deficits when compared to schizophrenics without atrophy. Global atrophy predicted increased impairment on several Wisconsin Card Sort measures including number of perseverative errors (57.3 vs. 31.3, F = 9.41, p < .01) and also predicted decreased performance IQ (83.2 vs. 97.7, F = 8.17, p < .01). Schizophrenics with temporal atrophy compared to those without temporal atrophy demonstrated increased impairment in trail-making time (253 seconds vs. 153 seconds, F = 4.17, p < .05), increased VBR (r = .234, p < .01) and evidence of a more severe and chronic illness. Control subjects with atrophy showed no neuropsychological impairment compared to controls without atrophy. These findings suggest an increased prevalence of temporal atrophy among schizophrenics and specific neuropsychological correlates of global and temporal cerebral atrophy.

## **TEMPORAL HORN AREA INCREASED ON SCHIZOPHRENIA CTS**

CONFOUNDS OF NEUROENDOCRINE CHALLENGE TESTS

Godfrey D. Pearlson, M.D., Psychiatry, Johns Hopkins, 600 N. Wolfe St Meyer 3-166, Baltimore, MD 21205; Jeremy Broadhead, M.D., Ashok J. Kumar, M.D., Pricilla Dorsey, B.S., Larry E. Tune, M.D.

#### Summary:

Recent neuropathological studies report structural brain changes in the temporal lobes of schizophrenics, including temporal ventricular horn enlargement. Although the temporal horns are frequently visible on CT scans (although small and obscured in some cases by bony artifact), we are unaware of any previous study attempting to quantify them from CT in schizophrenia.

Fifty DSM-III-R chronic schizophrenics and 50 cognitively and neurologically screened, sex- and age-matched normal controls aged 20-40 years, underwent non-contrast cranial CT scans on a Siemens Somatom DR3. Slice thickness (8mm), and scanning parameters were identical for patients and controls. Temporal horns, when unequivocally present in the relevant CT cut, (27 schizophrenics, 19 male; 31 controls, 15 male) were identified by a neuroradiologist, and their enlarged images traced using a radiologic projector by a rater blind to diagnosis. Temporal horn area (THA) was measured in cm<sup>2</sup> from the tracings using a planimeter. Exploratory data analysis for mean THA ( $\pm$  SD) in schizophrenics versus controls, respectively, showed a significant difference for the left side (.55 ± .374 versus .355 ± .354; t = 2.03, DF = 56, p < .05, 2-tailed), but not for the right (.485  $\pm$  .477 versus .451  $\pm$  .392; t = .31, DF = 56; p = NS). Overall these CT results are not dissimilar to previous neuropathological reports. Our schizophrenics had THA's that were 55% greater than controls on the left, and 7.5% greater on the right. These findings may be consistent with suggestions that temporo-limbic pathology is associated with the schizophrenic syndrome.

#### **NR97**

Tuesday, May 10, 12 noon-2:00 p.m. PLASMA HALOPERIDOL: GAS CHROMATOGRAPHY VERSUS RADIORECEPTOR ASSAY

Jack Hirschowitz, M.D., Psychiatry, VAMC, Middleville Road, Northport, NY 11768; Robert Hitzemann, Ph.D., Barbara Hitzemann, B.S., Beatrice Kovazsnay, M.D., Gail Brogini, B.S.N., Kathy Folkerts, B.S.N.

## Summary:

In previous studies (e.g., Hitzemann et al., Psychopharmacol. 90:280, 1986), we have examined the relationships among plasma neuroleptic levels as determined by gas chromatography (GC), total plasma neuroleptic activity as determined by the radio-receptor assay (RRA) and therapeutic response. The data obtained for three neuroleptics, thiothixene (THX), fluphenazine (FPZ), and haloperidol (HAL) suggest that total plasma neuroleptic activity correlates best with therapeutic response. The data also show that for HAL total neuroleptic activity is significantly less than that which would be predicted by the amount of parent compound present (see also Silverstone et al., J. Psych. Res. 18:255, 1984). We have continued our investigation of the HAL phenomenon on 40 chronic schizophrenic patients currently receiving one to 60mg/day (average dose = 19.5mg). In these subjects the correlation between the RRA and GC data was significant (r = 0.70, p < 0.001). However, the RRA detected on average 50% less neuroleptic activity than would have been predicted from the GC data. There were significant correlations between the dose administered and the GC data (r = 0.60, p < 0.01) or the RRA data (r = 0.44, p < 0.05). We conclude that these data provide evidence of a factor or factors present in plasma which decrease the receptor affinity of HAL. Such factors may be important in understanding the phenomenon of HAL non-response.

#### **NR98**

## Tuesday, May 10, 12 noon-2:00 p.m.

Barbara E. McDermott, M.A., Psychiatry, Univ of Cincinnati, 231 Bethesda ML 559, Cincinnati, OH 45267; Charles Beasley, M.D., Kathleen Kelly, M.S.N., Jack Hirshowitz, M.D., David L. Garver, M.D.

# Summary:

It has long been hypothesized that a hyperdopaminergic state plays a central role in the etiology of psychotic symptoms. To evaluate this hypothesis, the apomorphine growth hormone challenge test has been employed extensively as a postsynaptic D<sub>2</sub> dopamine receptor sensitivity probe. Some studies of the APO challenge test suggest that washout periods as short as seven days are sufficient to eliminate drug effects from this test. However, recent pharmacokinetic studies of haloperidol have suggested that months may be required for elimination. In order to evaluate the relationship between certain intrinsic disease variables and the APO challenge test, the extrinsic confounds must be assessed. Peak growth hormone response was evaluated for neuroleptic-naive patients (x = 28.6, n = 50) and those patients previously exposed to neuroleptics ( $\bar{x}$  = 18.9, n = 84). The results of a t-test reveal that GH response is significantly higher in naive patients ( $t_{(132)}$  = 2.996, p<.004). Length of time off medication (after seven days) did not influence GH response (t<sub>773</sub> = 1.31, p<.20). Patients off medication longer than 100 days exhibited a similar GH response ( $\bar{x} = 14.9$ , n = 26) to those off medication less than 100 days ( $\bar{x} = 19.6$ , n = 49). Age and length of illness were only related to GH response for those patients previously exposed to neuroleptics. These results suggest that neuroendocrine paradigms such as the APO challenge test may be significantly confounded by past neuroleptic exposure.

## **NR99** SIMPLE SCHIZOPHRENIA: THEN AND NOW

Todd J. Boffeli, B.S., c/o D.W. Black, M.D., University of Iowa, 500 Newton Raod, Iowa City, IA 52242; Donald W. Black, M.D., George Winokur, M.D.

#### Summary:

Fifty-two patients (29 men, 22 women) hospitalized between 1939 and 1964 had a chart diagnosis of simple schizophrenia. Their charts were reviewed for sociodemographic information and all were re-diagnosed using DSM-III-R criteria. The mean age was 25.8 years. Ninety-six percent of the patients had an onset of symptoms before age 30 years. Seventy-nine percent of the patients were single; sixty-nine percent of the patients lived with their parents. Fifty-one percent were unemployed.

Of the 52 patients, 35 (67.3%) had an Axis I disorder. These disorders included four (7.7%) with schizophrenia, 24 (46.2%) with major depressive disorder, two (3.8%) with delusional disorder, two (3.8%) with bipolar mania. An Axis II disorder was present in 35 of the 52 patients (67.3%). Axis II disorders included 23 (44.2%) schizotypal, 12 (23.1%) schizoid, one (1.9%) histrionic, one (1.9%) avoidant, two (3.8%) borderline. Five (9.6%) patients met criteria for both schizoid and schizotypal personality disorders. Fourteen of the 24 (58.3%) with major depressive disorder also had a personality disorder. Four (7.7%) of the patients were re-diagnosed during the follow-up as schizophrenic.

Although simple schizophrenia remains a popular diagnostic concept, we have demonstrated that it is diagnostically heterogeneous, and its exclusion from DSM-III appears justified.

#### **NR100** INPATIENT TREATMENT OF ALZHEIMER'S DISEASE BY THA

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

L. Jaime Fitten, M.D., Psychiatry Med, Sepulveda VAMC, 16111 Plummer St 116A-9, Sepulveda, CA 91343; Kent M. Perryman, Ph.D., Patricia Gross, Ph.D., Alan Steinberg, Ph.D., Harriet Fine, Pharm. D., Joseph Cummins, Ph.D.

#### Summary:

Ten inpatients with NINCDS-ADRDA probable Alzheimer's Disease (AD) GDS stages 3-6, completed a randomized, doubleblind, placebo-controlled, crossover trial of oral tetrahydroaminoacridine (THA) (IND 24,840), plus lecithin. Patients were admitted to the geropsychiatric unit for diagnosis, cessation of psychotropics, and behavioral stabilization (two-four weeks). Upon acceptance into the study, baseline measures were taken and lecithin (30mg/day) started. An optimal dose-finding period (two-three weeks) followed. Individual "best" doses were determined by increasing THA daily by 25mg/day as tolerated or to a maximum of 250mg/day. The "best" dose produced highest cognitive scores without side effects. Cognition and behavior were monitored by widely used neuropsychological and functional tests (e.g., MMSE, FAS, FULD, TRAILS, IADL, etc.). THA serum concentration was determined at time of testing. Clinical labs, SPECT and EEG were also serially obtained. After titration, patients were randomly assigned to either "best" THA dose or placebo (one week) followed by washout (one week), then THA or placebo (one week). Overall ANOVA for repeated measures revealed no significant difference in cognition or behavior between drug and non-drug conditions. Supplementary data analysis identified one potential mold responder. Significant liver enzyme abnormalities were noted in three patients. Conclusions: subchronic THA has no dramatic effect on cognition or behavior in AD and is potentially hepatotoxic.

#### NR101

## DENIAL AND PATIENTS WITH BREAST LUMPS

## Tuesday, May 10, 12 noon-2:00 p.m.

Rima Styra, M.D., Psychiatry, St. Michael's Hospital, 30 Bond Street, Toronto, Ont., Canda M5E1T4; Isaac Sakinofsky, M.D., Leo Mahoney, M.D., Nick Colapinto, M.D., Donald Currie, M.D.

#### Summary:

Psychiatric morbidity in cancer patients has been related to mental state (prediagnostic) and coping skills. Sixty-nine patients referred to a teaching hospital breast clinic for breast lumps were prospectively interviewed prior to their obtaining a diagnosis. Baseline measures of mental state and coping style were obtained at this time, as well as at one month and six months follow-up.

Our data indicate that denial (as determined by the Problem Solving Inventory) was used as a coping mechanism prior to diagnosis by 55 (80%) of the 69 patients. Even though 80% of patients used denial they still scored fairly high on the Spielberger Anxiety Scale (mean 40.27±11.88). Also it was noted that this "denial" was dissociated from practical measures, only two patients delaying their first assessment.

Identifiers of the breast lump as a problem showed a greater use of problem tackling and less use of problem avoidance than deniers in dealing with issues as determined by one way ANOVA. Those patients who cope through denial are less likely to have a family history of breast cancer than the identifiers (X<sup>2</sup>=10.46, df=1, p<.01). Emotion Focused Coping and Beck Depression scores were correlated (r=0.39); as were Wishful Thinking and the Spielberger Anxiety scores (r= 30); and Wishful Thinking and Beck Depression scores (r=.44).

We conclude that although denial is used by the majority of patients prior to diagnosis, anxiety levels are still high overall. Deniers cope by avoiding other problems in their lives, while identifiers tend to tackle problems as shown by measures of coping style.

# PLASMA DEBRISOQUIN LEVELS IN STUDIES OF HVA IN MAN

Mark A. Riddle, M.D., Child Study Center, Yale University, Box 3333, New Haven, CT 06510; James F. Leckman, M.D., George M. Anderson, Ph.D., Maureen T. Hardin, M.S.N., Soo C. Cho, M.D., Donald J. Cohen, M.D.

## Summary:

Plasma concentrations of homovanillic acid (pHVA) are used to estimate CNS dopaminergic activity in clinical studies of symptom severity (e.g., schizophrenia) and medication response (e.g., haloperidol). Debrisoquin sulfate (DBQ), a medication that blocks peripheral, but not NCS, production of HVA has been used to decrease the "noise" contributed by peripherally produced HVA in pHVA measurements. This report describes the first use of plasma DBQ levels to examine relationships between DBQ dose, pDBQ levels and decrease in pHVA. Nine normal controls and 12 subjects with Tourette's syndrome (TS), aged 14 to 40 years, were hospitalized and received 50-60mg of DBQ in 5 doses between 15:00 on study day 1 and 09:00 on study day 2. PHVA samples were obtained at 12:00, 13:00, 14:00, and 15:00 on study days 1 (pre-DBQ) and 2 (post-DBQ). PDBQ levels were obtained at 12:00 and 15:00 on day 2. No significant mean differences were observed between normals and TS patients for age, DBQ dose, pDBQ levels, pre-DBQ pHVA, post-DBQ pHVA, or % decrease in pHVA. There was a moderate relationship between pDBQ and DBQ dose (r = .44, p < .05, n = 21). All 9 subjects whose mean pDBQ levels were ≥64ng/ml had a decrease in pHVA (range = 48 to 67%) that may reflect complete blocking of peripheral HVA. For the 12 subjects whose mean pDBQ levels were ≤ 54ng/ml, the decrease in pHVA ranged from 9 to 58%. These data suggest that minimal pDBQ levels (perhaps > 60ng/ml) are necessary to adequately block peripheral HVA production.

## **NR103**

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

COMPUTER-ANALYZED EEG AND TREATMENT OF ALZHEIMER'S DISEASE Andrew F. Leuchter, M.D., Psychiary, UCLA, 760 Westwood Plaza, Los Angeles, CA 90024; Stephen Read, M.D., Jill Shapira,

M.N.C., Donald Walter, Ph.D., Cheryll Smith, Ph.D.

## Summary:

Three patients with Alzheimer's disease underwent intracranial administration of bethanechol through shunts in the ventricular system. Optimal dosage was determined through a seven-step dose response paradigm, with doses as high as 1.48 mg/day. Serial computer-analyzed EEG (CEEG) examinations were performed after the patient was stablized at each dose. There were strong linear correlations between global decreases in 2-6 Hz slow wave activity, cognitive improvement, and spousal ratings of global improvement. In two cases with good response to drug, optimal dose coincided with the fastest posterior dominant frequency and the highest spectral ratio from the left temporal region. Global 2-6 Hz slowing decreased with increasing dose until optimal dose was achieved, and increased dramatically with supraoptimal doses. In the patient with a poor drug response, slowing increased at all drug doses. The results suggest that CEEG may be useful in monitoring cholinergic treatment in Alzheimer's patients.

## **NR104**

## Tuesday, May 10, 12 noon-2:00 p.m. THE EFFECT OF DARK-ADAPTATION ON SMOOTH PURSUIT EYE TRACKING IN SCHIZOPHRENIA AND LITHIUM-TREATED AFFECTIVE DISORDER

Pam M. Cooper, Ph.D., Psychiatry, Univ of Ottawa, 501 Smyth Road, Ottawa, ON, Canada K1H8L6; R.T. Pivik, Ph.D.

## Summary:

This study attempted to replicate reports that: a) dark-adaptation normalizes impaired pursuit performance in schizophrenics; and, b) lithium disrupts tracking performance in patients with affective disorder. Interactive effects of dark-adaptation and lithium on tracking performance were also examined.

Pursuit tracking was recorded electrooculographically in 34 subjects [12 normal controls (C); 11 actively ill patients with bipolar affective disorder-six receiving lithium (ADL), five off lithium (AD); and 11 actively ill schizophrenics (Sc)] under both light and dark-adapted conditions. Eye movement data were electronically processed and computer analyzed for velocity arrest and root-mean-square error measures, and data were statistically analyzed using MANOVA with repeated measures and post-hoc Newman Keuls procedures. During light-adaptation, significant differences in tracking performance were not present between C and AD nor Sc and ADL groups. However, tracking performance for the latter groups was significantly inferior to that of C and AD subjects. Dark-adaptation markedly reduced tracking errors in Sc and ADL patients eliminating all significant between-group differences. These findings replicate previous reports of dark-adaptation-associated normalization of tracking in Sc subjects and lithium-associated tracking impairment in AD patients. The observation that dark-adaptation reduced tracking errors, medication-associated or not, suggests a common mechanism for pursuit dysfunction in Sc and ADL patients.

## Acknowledgements:

The Canadian Friends of Schizophrenics and the Ontario Mental Health Foundation.

## NR105 OXIRACETAM: TREATMENT IN ALZHEIMER'S DEMENTIA

EFFECTS OF NEUROLEPTIC REDUCTION IN SCHIZOPHRENIA

Maurice W. Dysken, M.D., GRECC-11G, Minneapolis Drive, One Veterans Drive, Minneapolis, MN 55417; Susan Anton-Johnson, R.P.H., Linda Klein, M.A., Michael Kuskowski, Ph.D., Frank Stallone, Ph.D., Richard Katz, Ph.D.

## Summary:

Oxiracetam (4-hydroxy-2-oxo-1-pyrrolidinacetamide), a recently synthesized nootropic agent (CIBA-GEIGY), was employed as a potential treatment for cognitive decline in patients with Alzheimer's dementia. Subjects consisted of 10 outpatients who were between 50 and 85 years of age and had a *DSM-III* diagnosis of Primary Degenerative Dementia (PDD), a Global Deterioration Scale (GDS) score ranging from 3 to 5, a Mini-Mental State (MMS) score ranging from 12 to 24, and a d' score on the Buschke Recognition Test (BRT) that was between -0.72 and 2.6. In addition, the predicted verbal IQ derived from the National Adult Reading Test had to exceed the verbal IQ score from the Wechsler Adult Intelligence Scale (WAIS) verbal subtest using the Duke/Satz-mobel modification. Following two weeks of placebo administration, patients received daily dosages of 400mg (4 weeks), 800mg (4 weeks), and 1200mg (4 weeks) of Oxiracetam. Efficacy measures were obtained at the end of each dosage period and consisted of the GDS, MMS, BRT, Brief Cognitive Rating Scale, WAIS, Word Fluency, and Road Map Test. Global Improvement ratings were determined by both a trained rater and by a family member. All ten patients (3M, 7F), who ranged in age from 57 to 84 (mean = 67), completed the 14 week study. Seven patients had a GDS of 4 and three patients scored 5. All CNS active medications were discontinued at least one week before study medication was begun. All outcome measures failed to show that Oxiracetam was more effective than placebo in treating PDD. No significant adverse experiences were reported. In one patient transient incomplete right bundle branch block was noted at 400mg and 800mg.

## NR106

## Tuesday, May 10, 12 noon-2:00 p.m.

Gerard Leblanc, M.D., Sante Mentale, Ctr Hosp Univ Laval, 2705 Boul Laurier Bureau 4211A, Sainte-Foy, Q, Canada GIV 4G2; Hugues J. Cormier, M.D., Sylvie Vaillancourt, MPs, Marie-Andree Gagne, Ph.D., Christian Gingras, B.Sc.

#### Summary:

The present open study evaluated the clinical effects of a reduction in neuroleptic (NL) medication on outpatients of a mental hospital. Thirty-nine subjects, who had been exposed to high dosages of NL (the equivalent of 18 mg or more of haloperidol per os per day) for at least six months and whose clinical condition had been stable for at least three months, were interviewed; 32 of them consented to having their medication reduced and 29 completed the reduction protocol, three having withdrawn. The mean age of the 29 study subjects was 37.2 (s=11.1); there were nine females and 20 males; 25 suffered from schizophrenia disorder and four from schizo-affective disorder; on average they were receiving the equivalent of 62–76 mg of haloperidol daily. During the first stage of the protocol, the subjects' clinical condition was evaluated monthly for three months without any change in their medication. During the following five months, dosages of NL were reduced by 50% at the rate of 10% per month. Then the reduced dosages of NL were maintained for five months. During the last three months of this stage, the subjects' clinical condition was again evaluated monthly. When the subjects' clinical condition is compared before and after the reduction in NL, one observes: 1) a reduction in schizophrenia negative symptoms (p=0.0001; Andreasen criteria, 1982); 2) a reduction in psychotic symptoms (p=0.002; Overall and Gorham criteria; 1962); and 3) an increase in tardive dyskinesia symptoms (p=0.0018; Chouinard criteria, 1978). After the reduction of NL, four subjects had to be hospitalized for a short period (17 days on average), but it was not necessary to increase their medication; two others presented a severe psychotic episode. Results of this study will be discussed.

## NR107 SCHIZOPHRENIA: FACTOR ANALYSIS OF MONOAMINE INDICES

19F MRI AND MRS OF FLUPHENAZINE IN VIVO AND VITRO

Ede Frecska, M.D., Clin Res Ctr, Natl Inst Ment Dis, PO. Box 1, Budapest 27 01281, Hungary; Mihally Arato, M.D., Csaba M. Banki, M.D., Gyorge Bagdy, Ph.D., Andras Perenyi, M.D., Arpad Bela, M.D.

## Summary:

Cerebrospinal fluid (CSF) dopamine (DA), dihydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA), norepinephrine (NE), 5-hydroxyindolacetic acid (5-HIAA), serum prolactin (PRL) levels and dopamine-beta-hydroxylase (DBH) activity were measured in 42 schizophrenic men who were subgrouped according to their scores on the Abnormal Involuntary Movement Scale (AIMS) and Brief Psychiatric Rating Scale (BPRS). Factor analysis was carried out on various combinations of the variables. In patients with symptoms of tardive dyskinesia (TD), CSF DA, DOPAC, HVA, NE, and serum DBH were distributed into three factors in contrast to the non-TD patients who had only one factor. CSF DA, DOPAC, and HVA were dispersed in two factors in patients with severe positive symptoms versus one single factor in subjects with mild productive signs. Factor structures diverged only when the above variables were included in the analysis. Omitting one of them or entering other ones (e.g. 5-HIAA or PRL) made the difference in factor pattern disappear. Subgroups did not differ in age and neuroleptic medication.

These findings favor the hypothesis that in TD there is a disintegration between the norepinephrine and dopamine system, and that positive schizophrenic symptoms are associated with dopaminergic dysregulation.

## **NR108**

## Tuesday, May 10, 12 noon-2:00 p.m.

David C. Arndt, M.S., Psychiatry, Stanford University, 177 Liberty Street, San Francisco, CA 94110; Adam V. Ratner, M.D., Kym F. Faull, Ph.D., Jack D. Barchas, M.D., Stuart W. Young, M.D.

## Summary:

The bulk biodistribution of a trifluorinated neuroleptic (pharmaceutical fluphenazine) was studied using <sup>19</sup>F NMR. Fifteen male Sprague-Dawley rats were injected with fluphenazine (120 mg/kg) and were scanned in a 2.0 tesla NMR system. The rats were killed following scanning, and the brains were removed. The excised brains were then scanned using <sup>1</sup>H and <sup>19</sup>F magnetic resonance techniques. The fluorinated neuroleptic was imaged at the injection site, spectroscopically detected in vivo in the head, and spectroscopically localized in the excised whole brain. It was possible to image a standard human clinical dose of fluphenazine deconoate as an intramuscular bolus. The capacity to image and to spectroscopically localize bulk biodistribution of fluorinated neuroreceptor ligands may prove to be a valuable, inexpensive, and noninvasive technique for monitoring the kinetics of neuroleptic uptake from the intramuscular injection site. The capacity to evaluate, in vivo, agents that interact with dopaminergic neuroreceptors would permit characterization of receptor densities, increase understanding of the metabolic pathways of neurotransmitters, and facilitate in vivo pharmocokinetic studies of neuroleptic drugs. These data suggest that in vivo <sup>19</sup>F NMR of fluorinated agents is possible and could have clinical and research applications to the neurosciences.

## NR109 CEREBRAL FUNCTION DURING COGNITION IN DOWN SYNDROME

Karen F. Berman, M.D., NIMH, CBDB, St. Elizabeths Hospital, 2700 Martin Luther King Ave., Washington, DC 20032; Mark Schapiro, M.D., Robert P. Friedland, M.D., Stanley I. Rapoport, M.D., Daniel R. Weinberger, M.D.

## Summary:

Prefrontal hypofunction in schizophrenia has been frequently demonstrated by regional cerebral blood flow (rCBF) and other measures of cerebral metabolism, particularly when such measurements are made during prefrontally linked cognitive activation tests on which patients with schizophrenia perform poorly. However, since few studies of other cognitively impaired patient populations have been reported, the specificity of "hypofrontality" to schizophrenia and its relationship to cognitive deficits has not been clear.

Using the xenon 133 inhalation rCBF method, we compared cortical function in 11 young, physically healthy, mild to moderately retarded patients with Trisomy 21 Down Syndrome (DS) (mean age 28 years; mean mental age on Peabody Picture Vocabulary Test 8 years, range 4 to 16) to that of a group of age- and sex-matched normal subjects. Following an initial resting state rCBF study on each of two days, patients had rCBF measured during four different cognitive activation conditions: on day 1, during Raven's Progressive Matrices, which is a posterior cortical activator, and during a nonspecific control task; and on day 2, during the prefrontally linked Wisconsin Card Sorting Test (WCS) and during a nonspecific control task.

Despite poor performance on the WCS and in contrast to schizophrenic patients, the DS patients increased prefrontal rCBF during the WCS compared to baseline (mean [ $\pm$ SEM] change in rCBF, 5.0 $\pm$ 1.7 IS units, p $\leq$ .02, paired T-test) in a fashion similar to normals (3.7 $\pm$ 1.8, p=.05). During Raven's Progressive Matrices there were no significant differences between the two groups, but DS patients did not activate posterior cortical areas as normals did.

These data suggest that cognitively linked hypofunction of prefrontal cortex, as is seen in schizophrenia, is not common to all impaired groups and that different pathophysiological substrates underly the cognitive dysfunction seen in schizophrenia and DS.

## NR110 GROWTH HORMONE AS TRAIT DISTURBANCE IN DEPRESSION

## Wednesday, May 11, 9:00 a.m.-10:30 a.m.

Samuel C. Risch, M.D., Psychiatry, Emory University, 1701 Uppergate Drive, Atlanta, GA 30322; Richard Hauger, M.D.

## **Educational Objectives:**

Overview of literature with respect to Growth Hormone abnormalities in depression with presentation of new data suggesting that reduced or "blunted" growth hormone respone to human Growth Hormone Releasing Factor may be a "trait" abnormality in affective illness.

## Summary:

Abnormalities of growth hormone secretion have been reported in depressed patients including elevations in daytime plasma concentrations and attenuated responses to central provocative challenges with insulin-induced hypoglycemia, clonidine and the tricyclic antidepressant desmethylimipramine. The recent availability of the hypothalamic peptide human growth releasing factor (hGRF) allows direct testing of pituitary growth hormone secretory response in depressed patients, remitted depressed patients, and age- and sex-matched normals.

All subjects received a complete history, physical, laboratory examination, and Schedule for Affective Disorder and Schizophrenia (SADS) interview. All subjects received hGRF (lug/kg) and placebo hGRF intravenously on separate days one week apart in a double-blind, randomized, counterbalanced paradigm. Blood samples were obtained every 15 minutes for 30 minutes prior to and for two hours subsequent to the infusions. Samples were subsequently assayed for growth hormone and other plasma neurohormones by RIA. Mean changes in Log growth hormone plasma concentrations from baseline to post hGRF timepoints were significantly (p=.001, Diagnostic Group  $\times$  Drug  $\times$  Time) attenuated in depressed patients (n=7, RDC Major Depression) and in remitted depressed patients (n=7, RDC Hx of Major Depression, remitted) as compared with age- and sex- (all male) matched normal controls (n=17). These results suggest that this neuroendocrine abnormality in depressed patients may persist for years after recovery from depression. Preliminary results from ongoing studies regarding the diagnostic sensitivity and specificity of this neuroendocrine disturbance will be presented.

#### References:

1. Mendlewicz J, Linkowski P, Kerkhofs M, Desmedt D, Goldstein J, Copinschi G and Van Cuter C: diurnal Hypersecretion of Growth Hormone in Depression. Journal of Clinical Endocrinology and Metabolism 60(3): 505-511, 1985.

2. Lesch K.-P., Laux G, Erb A, Pfuller H and Beckman H: Attenuated Growth Hormone Response to Growth Hormone-Releasing Hormone in Major Depressive Disorder. Biological Psychiatry 22: 1495-1499, 1987.

#### NR111 LOW CSF 5-HIAA DIFFERENTIATES SUICIDE ATTEMPTERS

Michael Stanley, Ph.D., Psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; Barbara Stanley, Ph.D., J. John Mann, M.D., Allen J. Frances, M.D., Lil Traskman-Bendz, M.D.

## **Educational Objectives:**

To learn about the role of biochemical factors in suicide.

## Summary:

Suicide and suicidal behavior remain one of the most persistent and serious mental health problems in the United States. Recent approaches to the study of suicide have examined the role of biochemical abnormalities in people who display this behavior. In particular, serotonergic dysfunction has been linked to suicide. The purpose of this study was to conduct a largescale investigation in order to further examine the role of serotonergic dysfunction in suicide attempts in psychiatric patients with diagnoses that put them at high risk for suicide. An additional goal was to determine the potential clinical utility of serotonergic dysfunction as measured by CSF 5-HIAA as an index of identification of individuals at risk for suicide.

The sample in the study was comprised of a total of 212 patients—143 suicide attempters and 69 non-attempters—which included 39 with Schizophrenic Disorder, 81 with Major Affective Disorder without Axis II diagnoses, 78 with Major Affective Disorder with Personality Disorders, and 14 with other disorders. Lumbar punctures were performed following a two-week drug-free interval and the 5-HT metabolite 5-hydroxyindoleacetic acid (5-HIAA) was measured by HPLC-electrochemical detector. It was found that 5-HIAA levels were significantly lower in the attempter than in the non-attempter group (t=2.27; p<.03). Furthermore, it was also found that very low levels of CSF 5-HIAA were associated with high likelihood of having attempted suicide. More specifically, using a cut-off point of 13.0 ng/ml of CSF 5-HIAA, 91% of the patients below this level were suicide attempters (30/33 patients). By contrast, high levels of CSF 5-HIAA (CSF levels  $\geq$  24.0), did not discriminate between attempters and non-attempters.

## **References:**

<sup>1</sup>Mann, J. and Stanley, M. (eds.). *Psychobiology of Suicidal Behavior*. New York: New York Academy of Sciences, Vol. 487, 1986.

<sup>2</sup>Stanley, M. and Mann, J.J.: Biological factors associated with suicide. *American Psychiatric Association Annual Review*, Vol. 7, 1988, in press.

#### NR112 TEMPORAL LOBE SIZE BY MRI IN AFFECTIVE DISORDER

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

Peter Hauser, M.D., BPB, NIMH Bldg 10 Rm 3S239, 9000 Rockville Pike, Bethesda, MD 20892; Lori Altshuler, M.D., Robert M. Post, M.D., Wade Berrettini, Ph.D., I.D. Dauphinais, M.D., Joel Gelernter, M.D.

## **Educational Objectives:**

Educational objectives include: 1) a review of brain morphological differences between subjects without a psychiatric history and patients with affective disorder, and 2) a discussion of the usefulness of MRI technology to elucidate these differences.

## Summary:

Alterations in temporal lobe function have been postulated in the affective disorders, and gross anatomical changes in temporal lobe structures have been reported in schizophrenic subjects. A group of 26 patients with primary affective disorder and a group of 26 normal subjects without medical or psychiatric illness were scanned using a Picker Vista 0.5 tesla scanner in order to investigate possible structural changes in this area. Twelve contiguous coronal slices were made at 10 mm intervals starting at the frontal pole. A slice through the temporal lobes at the level of the pons (interpeduncular cistern) was selected in each subject. Area measurements of the temporal lobe (including temporal lobe gray and white matter, hippocampal/parahippocampal complex and temporal horn) and cortex were traced by hand on a blind basis and computed directly from the original MRI tapes using the VAX/VMS computer system. Ratios between structures on the same scan were calculated to control for positional and other image artifacts. In a preliminary analysis of the first 13 affective patients (4 M, 9 F; mean age 38.5 years) and 13 normal subjects (6 M, 7 F; mean age 32.8 years) the ratio of temporal lobe area to hemisphere area was smaller in patients than controls both on the left (p < .046) and on the right (p < .009). Other ratios did not distinguish the groups.

While further analyses of the entire sample will be presented, these preliminary data suggest the possibility of relative decreases in the size of the temporal lobe in patients with primary affective disorder compared with normal controls. The data will be discussed in terms of the role of temporal lobes in the modulation of affect and cognition.

## **References:**

1. Brown R et al: Postmortem evidence of structural brain change sin schizophrenia. Arch. Gen. Psychiatry 43:36-42 1986.

2. Andreason N et al: Structural abnormalities in the frontal system in schizophrenia. Arch. Gen. Psychiatary 43:136-144 1986.

# NR113 MAOI TREATMENT OF IMIPRAMINE-RESISTANT DEPRESSION

Michael E. Thase, M.D., WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213; David J. Kupfer, M.D.

## **Educational Objectives:**

To present new evidence on the effectiveness of monoamine oxidase inhibiting antidepressants in depressed patients who have failed to respond to an adequate trial of a standard tricyclic.

## Summary:

While monoamine oxidase inhibitors (MAOIs) frequently are utilized in resistant depression, their effectiveness in this situation has not been well documented. We report on open clinical trial of MAOI treatment in 32 patients (7M, 25F; x age=40) years) with recurrent major depression (RDC/DSM-III) who had failed to respond to 8 weeks or more of treatment with imipramine at maximum tolerated dosages ( $\bar{x}$ =256.8 mg/d) and interpersonal psychotherapy. Unsuccessful treatment also had included prior attempts to augment response with  $T_3$  (n=13), lithium (n=8), and/or perphenazine (n=13). Treatment with phenelzine (n=4, 60 mg/d) or tranylcypramine (n=28; x=38.5 mg/d) was initiated after a 7-day washout, and dosage was titrated openly. Outcome was assessed weekly by independent evaluations. Thirty patients completed a 6-week trial. Significant reductions in Hamilton scores were noted by week 2, with an ultimate 53% repsonse rate (16/30). Mean Hamilton scores fell from 19.3 (3.8) to 9.5 (5.9) (p < .001). Response was associated with high severity level (p = .07), the presence of reversed neurovegetative signs (p=.01), and the failure to show a partial response during initial IMI treatment (p=.01). When compared to our prior studies of resistant depression, MAOI treatment appeared more useful than T<sub>3</sub> augmentation (25% response rate) and roughly comparable to Li<sup>+</sup> -augmentation (65% response rate). Consistent with prior clinical observations, there appears to be a subgroup of unipolar patients who are refractory to IMI but who are guite responsive to MAOIs. These findings provide further evidence of the utility of MAOIs in treatment-resistant depression. We suggest their consideration as the intervention of first or second choice when a patient fails to respond to an adequate trial of standard tricyclic antidepressant. **References:** 

<sup>1</sup>Thase ME, Kupfer DJ: Characteristics of treatment-resistant depression. In Zohar J, Belmaker RH (Eds): *Treating Resistant Depression*. New York: PMA Publishing, 1987

<sup>2</sup>Shawcross C, Tyrer P: The place of monoamine oxidase inhibitors in the treatment of resistant depression. In Zohar J, Belmaker RH (Eds): Treating Resistant Depression. New York: PMA Publishing, 1987

## NR114 CLONIDINE FOR MANIA: PLACEBO CONTROLLED TRIAL

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

Philip G. Janicak, M.D., Research, III St Psych Inst., 1601 W. Taylor Street, Chicago, IL 60612; Rajiv P. Sharma, M.D., Edward Altman, Ph.D., Javaid I. Javaid, Ph.D., Puskoor M. Kumar, M.D., John M. Davis, M.D.

## **Educational Objectives:**

To report recent preliminary findings on a placebo controlled trial with clonidine for the treatment of acute mania. Thus far, 20 patients have been studied and there appears to be no benefit with clonidine in comparison to placebo. Side effects with clonidine (up to .8 mg) are significant.

## Summary:

Since some have reported that clonidine may have antimanic properties, it would be of great theoretical significance to confirm clonidine's ability to reduce NE synthesis. Further, if clinically effective, employing clonidine could avoid the use of antipsychotics which may cause NMS and/or TD. We are conducting a double-blind study in which accutely ill manic patients receive either clonidine or placebo. After giving informed consent, 20 patients have completed a washout phase (mean = 6 days) and then received either placebo or clonidine (up to .8 mg/day). Patients were evaluated with the BPRS and the Young Mania Scale (YMS) at baseline and days 1,2,3,7,10,14 or when dropped from the study because of significant worsening of symptoms. More patients in the clonidine group failed to complete the study (primarily due to rash or hypotension) than did those on placebo. An end-point analysis was used to include values in those patients who did not complete the 14-day trial. The BPRS and YMS change scores were analyzed by a repeated measure analysis of variance. There were virtually no differences in improvement based on the BPRS or YMS in the clonidine versus the placebo treated groups. The main effect of clonidine versus placebo yielded (F = .03, df = 2/17, p = .97). The BPRS clonidine versus placebo difference yielded (t = .23, p = .82) and the YMS change score difference for clonidine versus placebo yielded (t = .03, p = .97). To our knowledge, this is the first report of a double-blind, placebo-control trial using clonidine as an antimanic agent. Based on our findings, we would conclude that clonidine produces exactly the same clinical effects on mania as does placebo, and that the doses used (0.2 to 0.8 mg/day) caused significant side effects and showed no clinical efficacy.

## **References:**

<sup>1</sup>Zubenko GS, Cohen BM, Lipinski SF et al: Clonidine in the Treatment of Mania and Mixed Bipolar Disorder. *Am J Psychiatry*, 1 141:1617-1618 1984.

<sup>2</sup>Giannini AJ, Extein I, Gold MS, et al: Clonidine in Mania. Drug Development Research, 3:101-103 1983.

## NR115 ECT'S EFFECT ON SLEEP IN MAJOR DEPRESSION

Henry W. Lahmeyer, M.D., Psychiatry, Univ of Illinois, 910 W. Wood Streeet, Chicago, IL 60612; Philip G. Janicak, M.D., Michael Easton, M.D., John M. Davis, M.D.

## **Educational Objectives:**

To inform clinicians regarding changes in sleep parameters during a course of ECT for major depression. In general, the changes were similar to those observed in studies using TCA's. However, since serial EEG's were obtained during treatment, some unexpected changes in REM latency were observed and may serve as an early predictor in ECT.

## Summary:

This is a preliminary report on a prospective study of ECT's effect on sleep. Five subjects meeting DSM-III/RDC criteria for major depression had various sleep parameters recorded serially, during a course of 8-12 ECT treatments, either unilateral, nondominant or bilateral ECT. Following a two-week washout period, two baseline sleep EEGs were obtained, and then were repeated weekly during treatment as well as at the end of the course of ECT. Recordings were done at least 48 hours after an individual treatment. The 24-item Hamilton Rating Scale for Depression (HRSD) was used, the average score at baseline was 32 and decreased to 8.2 after a course of ECT (p<.01). All subjects improved during treatment. The mean sleep parameters for all five subjects changed with ECT as follows: total sleep time increased 27%; awake minutes decreased by 45%; sleep efficiency increased by 24% and delta % increased by 11% (indicating improved sleep continuity and quality). REM parameters also normalized with REM latency increasing by 35% and REM density decreasing by 20%. By obtaining serial sleep recordings, we noted that the mean of all parameters moved in the direction of normalization except for REM latency which actually shortened early in treatment (i.e., total REM sleep decreased 12% by week two) and then normalized near the end of the course of ECT. This effect was most pronounced in the two subjects with the most rapid improvement and was reversed in the one partially recovered subject. This preliminary data indicate that: 1) improvements in the sleep parameters were striking in this small sample size and paralleled the improvements seen in the HRSD scores; 2) ECT (an effective nonpharmacological treatment) induces most of the same changes in sleep seen with a successful course of antidepressant therapy; and 3) to our knowledge the phenomenon of an initial shortening in REM latency early during the course of ECT has not previously been reported and may be a potential marker of the final treatment outcome.

#### References:

<sup>1</sup>Hoffman G, Linkowski P: Effect of ECT on sleep and CSF biogenic amines in affective illness. *Psychiatric Research* 16:99-206, 1985.

<sup>2</sup>Grunhaus L, Tiongco D:Serial monitoring of antidepressant response to electroconvulsant therapy with sleep recordings and dexamethasone suppression test. Biol Psychiatry 20:805-808, 1985.
#### NR116 SEROTONERGIC CORRELATES OF PERSONALITY DISORDER

Emil F. Coccaro, M.D., Psychiatry, Bronx VA Medical Center, 130 West Kingsbridge Road, Bronx, NY 10468; Larry J. Siever, M.D., Richard Kavoussi, M.D., Robert A. Trestman, M.D., Luana Howard, R.N., Kenneth L. Davis, M.D.

### Educational Objectives:

To present data from serotonergic pharmaco-challenge studies of patients with DSM-III personality disorder which suggest that central serotonergic function correlates inversely with measures of aggression and impulsiveness.

### Summary:

Data from CSF, receptor binding and pharmaco-challenge studies suggest a significant role of central serotonergic (5-HT) function in the regulation of aggressive and impulsive behaviors in man. To further explore the nature of this putative central 5-HT abnormality and its relationship to these behaviors in psychiatric patients, we examined the prolactin (PRL) response to the mixed 5-HT releaser/agonist fenfluramine (FEN: 60 mg po), as an index of overall central 5-HT function, in 20 male patients with a variety of *DSM-III* personality disorders (PD assessed by SIDP) and in 14 moral male controls. The peak delta PRL response to FEN discriminated PD patients from controls (p<0.05). PD patients meeting criteria for *DSM-III* borderline personality disorder (BPD) had reduced peak delta PRL responses to FEN when compared to PD patients with other *DSM-III* non-BPD PD diagnoses (p<0.05). Clinician-rated and self-rated measures of lifetime aggression and impulsiveness were inversely correlated with the PRL response to FEN in all patients. These finding were not accounted for by the presence of a life history of major affective disorder, alcohol/drug abuse, or of a past history of suicide attempt as noted in some of the patients. These results suggest that central 5-HT function may be diminished in a subgroup of patients with PD (e.g. BPD) and that it may be inversely correlated with behaviors related to physcial aggression and impulsiveness in patients with *DSM-III* PD.

### **References:**

1. Brown GL, Ebert MH, Goyer PF et al. Aggression, suicide, and serotonin: Relationships to CSF amine metabolites. *Am J Psychiatry* 139:741-746, 1982.

2. Siever LJ, Klar H, Coccaro EF. Psychobiologic substrates of personality. In: Klar H and Siever LJ (editors) *Biological Response styles: Clinical Implications*. APA Press Inc., Washington, D.C., 1985.

# NR117 DESIPRAMINE FACILITATION OF COCAINE ABSTINENCE

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

Frank H. Gawin, M.D., Psychiatry, Yale University 904 Howard Avenue Suite 2-E, New Haven, CT 06519; Herbert D. Kleber, M.D.

### **Educational Objectives:**

To promote an understanding of emerging pharmacological treatments for cocaine dependence.

### Summary:

Clinical consensus has until recently held that cocaine dependence is solely a psychological addiction. Recent clinical research, indicating that cocaine dependence produces distinct abstinence symtom patterns, converges with preclinical data to suggest that stimulant dependence is based in cocaine-induced neurophysiological subsensitivity in specific CNS systems that regulate hedonic responsivity <sup>1.2</sup>. In 1984 we reported that a pharmacological treatment, desipramine hydrochloride, targeted at this deficit markedly decreased cocaine abuse and craving in an open trial <sup>2</sup>.

We now describe a just completed, double-blind, random-assignment, eight-week comparison of desipramine hydrochloride, lithium carbonate, and placebo treatments for cocaine dependence. Subjects were 72 outpatient cocaine abusers who met *DSM-III-R* dependence criteria for cocaine, but not for other abused substances. Desipramine (N=24), lithium (N=24), and placebo (N=24) treated subjects were equivalent on prior cocaine and other substance abuse, cocaine craving, sociodemographics, and other Axis 1 comorbidity (based on SADS-RDC). Initial data analysis demonstrates that desipramine, compared to both other treatments, substantially decreased cocaine use (repeated measures ANOVA, F=2.93; p<.001). Lithium outcome did not differ from placebo. Statistically significant differences in cocaine use appeared by the second week. Endpoint cocaine use was reduced to less than 6% of baseline use in the desipramine cell, compared to 46% in the placebo cell and 36% in the lithium cell. Endpoint cocaine craving was reduced to 32% of baseline in the desipramine cell, compared to 77% (t=3.2; p<.001) and 70% (t=3.1; p<.002) in the placebo and lithium cells. Exclusion of subjects with any current RDC affective disorder (20% of the sample) did not affect these findings. These finding firmly indicate that desipramine is an effective general treatment for actively cocaine dependent individuals. Further data analyses will also be presented.

# **References:**

<sup>1</sup>Gawin F, Kleber H. Archives of General Psychiatry 43: 107-113, 1986.

<sup>2</sup>Gawain F, Kleber H. Archives of General Psychiatry 41: 903-910, 1984.

# NR118 CARBAMAZEPINE TREATMENT OF ALCOHOL WITHDRAWAL

Robert J. Malcolm, M.D., Psychiatry, Medical University of SC, 171 Ashley Avenue, Charleston, SC 29425; James C. Ballenger, M.D., Raymond F. Anton, M.D., Bruce Lydiard, M.D., E. Strugis, Ph.D., Linda Williams, B.S.

# **Educational Objectives:**

At the end of the program the attendee will be able to list four advantages that carbamazepine has over Oxazepam in the treatment of alcohol withdrawal states and compare the side effect profiles of both classes of drugs.

### Summary:

Benzodiazepines are the major treatment for alcohol withdrawal <sup>1</sup>. They are limited because of their risk of abuse, potential for interactions with alcohol and failure to ameliorate the long-term neurologic and psychiatric sequelae of alcoholism. The present study is the first, to our knowledge, to compare carbamazepine with a benzodiazepine in severely ill patients withdrawing from alcohol. The study was a double-blind, randomized-control trial (7 days) of carbamazepine (CBZ dose=800 mg/d) versus oxazepam (OXZ dose=120 mg/d). Eighty-one subjects (41 on CBZ and 40 on OXZ) were assessed before and during treatment with the Clinical Institute Withdrawal Assessment for Alcohol (CIWA-A), physiologic, neurologic, self-report measures, and psychological tests. Comparisons between treatment groups were made using a repeated measures ANOVA. The CIWA-A scores showed no significant group (CBZ vs. OXZ) or group-by-time interactions. Although both drugs demonstrated a significant reduction in withdrawal symptom severity (F1, 30=329.4; p<.001) by the end of seven days, CBZ more rapidly improved deep tendon reflexes, tremor, anger and anxiety (all p<.05). The global distress score n the SCL-90 was significantly reduced for CBZ at the end of the study (F 1,1=13.49; p<.001). Side effect profiles and dropout rate for both drug groups were similar. CBZ appears to be superior to OXZ in more rapidly reducing neurologic and psychiatric symptoms during alcohol withdrawal.

Since the antikindling properties of CBZ have been previously noted<sup>2</sup>, and since reported alcohol withdrawals may kindle more serious withdrawal symptoms, CBZ may be a useful agent in the repeatedly withdrawn alcoholic.

### **References:**

<sup>1</sup>Sellars E, Kallant H: Alcohol intoxication with withdrawal. Engl J Med 294:757-762, 1976.

<sup>2</sup>Ballenger JC, Post RM: Carbamazepine in alcohol withdrawal syndromes and schizophrenic psychoses. *Psychopharm Bull.* 20:572-584, 1984.

### NR119

# **OPIOID DETOXIFICATION USING BUPRENORPHINE**

### Wednesday, May 11, 9:00 a.m.-10:30 a.m.

Thomas R. Kosten, M.D., Psychiatry, Yale University, 904 Howard Avenue Suite 2-E, New Haven, CT 06519; John H. Krystal, M.D., Dennis S. Charney, M.D., Lawrence Price, M.D., Charles I. Morgan, M.D., Herbet D. Kleber, M.D.

# **Educational Objectives:**

To teach psychiatrists about a new treatment for opioid detoxification.

### Summary:

Ten opioid-dependent patients were treated with buprenorphine, a partial opioid agonist, for one month at either 2 mg/day (n=4), 3 mg/day (n=3) or 4 mg/day (n=3). Following outpatient buprenorphine, the patients were hospitalized for 4 to 7 days, and buprenorphine was discontinued abruptly by placebo substitution. The patients were then given the antagonist naltrexone (1 mg PO.) in a double-blind, placebo-controlled challenge and monitored for three hours. The naltrexone challenges produced no increase in opioid withdrawal symptoms, plasma MHPG, or blood pressure levels comapred to placebo, and significantly fewer symptoms, MHPG or blood pressure increases than similar naltrexone challenges in 15 methadone-maintained patients. During the 3 hours following naltrexone, withdrawal symptoms in the buprenorphine patients went from a baseline of 16 (±1) to a maximum of 16 (±1), while symptoms increased from 19 (±1) to a maximum of 38 (±2) in the methadone patients (F=97; df=1, 23; p<0.0001). Plasma MHPG rose from 3.2 (±2) ng/ml to 3.5 (±4) ng/ml in the buprenorphine patients and from 3.1±0.2 to 4.0 (±0.3) ng/ml in the methadone patients (t=2.3; p<0.5). Mean standing blood pressure rose from 97.7. (±3.7) mmHg to 106.5 (±3.7) mmHg in the buprenorphine patients and from 104.2 (±3.0) mmHg to 117.2 (±2.0) mmHg in the methadone patients (t=2.5; p<0.02). This method for a transition from the pure agonist methadone to the pure antagonist naltrexone via buprenorphine suggests a new detoxification approach for opioid addicts.

### **References:**

1. Kosten TR, Kleber HD. Buprenorphine detoxification from opioid dependence: A pilot study, *Life Sciences*, in press. 2. Lewis JW. Buprenorphine. *Drug Alcohol Abuse* 14: 363-372, 1985.

### NR120 FAMILIAL ALCOHOLISM IN OPIOID ADDICTS

Thomas R. Kosten, M.D., Psychiatry, Yale University, 904 Howard Avenue Suite 2-E, New Haven, CT 06519; Bruce J. Rounsaville, M.D.

### **Educational Objectives:**

To educate psychiatrists about familial transmission of substance abuse in opioid addicts.

### Summary:

The relationship of familial alcoholism to alcoholism and drug abuse was examined among 201 opioid addicts using direct interview and "best estimates" on a total of 877 first-degree relatives. We found a strong association of familial alcoholism with alcoholism in 121 alcoholic addicts compared to normals (chi squared=81, p<0.0001). This association was supported by proportional hazards adjustments for relatives' age, sex and interview status. The proportional hazard showed that alcoholic addicts had 3.2 times greater rates of familial alcoholism than did normals. Particularly strong associations occurred between paternal alcoholism and alcoholism in female addicts (56% vs 9%, chi squared=26, p<0.0001), and between maternal alcoholism and alcoholism in female addicts (56% vs 9%, chi squared=26, p<0.0001). The 477 addict siblings were used to assess the specificity of parental alcoholism for alcoholism versus drug abuse. We found that paternal alcoholism was associated with alcoholism in make siblings (53% vs 28%, chi squared=13.5, p<0.001), while maternal alcoholism was associated with drug abuse in female siblings (23% vs 8%, chi squared=9.9, p<0.001). These associations suggested a polygenic model of transmission with higher liability thresholds for females, and with opioid or stimulant abuse being a more severe form of expression of a general substance abuse liability. This was consistent with our earlier work based on family history data alone, but differed from Cloninger's work with the "pure" alcoholic.

### **References:**

1. Kosten TR, Rounsaville BJ, Kleber HD. Parental alcoholism in opiate addicts. *J Nerv Ment Disease* 173: 461-469, 1985. 2. Cloninger R. Neurogenic adaptive mechanisms in alcoholism. *Science* 236: 410-416, 1987.

# NR121 EVIDENCE FOR ALTERED CSF HVA LEVELS IN BULIMIA

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

David C. Jimerson, M.D., Psychiatry, Beth Israel Hospital, 330 Brookline Avenue, Boston, MA 02215; Walter H. Kaye, M.D., Michael D. Lesem, M.D.

### **Educational Objectives:**

This presentation will review evidence that brain dopamine pathways may significantly influence feeding behavior, in part through effects on hedonic responses to food. Results from a recent study suggesting altered central dopamine function in bulimia will be presented. Possible implications for pharmacological treatment approaches to bulimia will be considered.

### Summary:

Dysregulation of central neurotransmitter function may predispose to the onset or persistence of symptoms of bulimia nervosa. While the neurotransmitters serotonin and norepinephrine have been the focus of a number of studies in bulimic patients, preclinical studies suggest that dysregulation of mesolimbic dopamine pathways could contribute to altered eating patterns through changes in hedonic responses to food.

To obtain an index of central dopamine function in bulimia, we measured CSF levels of the major dopamine metabolite homovanillic acid (HVA) in 25 medication-free female patients meeting *DSM-II* criteria for bulimia (mean age= $22.9\pm3.9$  year; mean weight= $91.0\pm7.2\%$  population average body weight (ABW)). Patients were abstinent from bingeing and vomiting during their hospitalization, and participated in CSF studies during the first week (admission phase) and fourth week (abstinence phase) of hospitalization. The control group included 11 healthy female volunteers free of past history of major psychiatric illness (mean age= $25.3 \div 4.6$  years; mean weight= $98.8\pm8.9\%$  ABW).

For the group of bulimic patients, there was a trend toward lower CSF HVA values in the admission phase in comparison to control values (p<0.1). From admission to abstinence phase, CSF HVA levels increased significantly for the patient group (p<.01) to levels similar to control values. Patients with a history of bingeing more than an average of 14 times per week had subtantially lower admission phase HVA levels (145±35 pmol/ml) than less severely symptomatic patients (212 50 pmol/ml, p<.005) or the controls (p<.005). These results indicate that dysregulation of central dopamine function may play a role in the pathophysiology of bingeing behavior in patients with relatively severe bulimia. It is also possible that altered dopamine function could contribute to depressive symptoms observed in some bulimic patients.

### **References:**

1. Hoebel BG: Neurotransmitters in the control of feeding and its rewards: Monoamines, opiates, and brain-gut peptides. In Stunkard AJ, Steller E (eds): *Eating and its Disorders*, New York, Raven Press, pp. 15-38 1984.

2. Russell G: Bulimia nervosa: An ominous variant of anorexia nervosa. Psychol Med 9:429-448 1979.

### NR122 EVALUATION OF MIDAZOLAM IN CHRONIC INSOMNIACS

Paulo F. Alterwain, M.D., Psychiatry, School of Medicine, Blvd Artigas 1545, Montevideo, Uruguay; Jaime M. Monti, M.D.

# Summary:

Midazolam is an imidazobenzodiazepine which shares the pharmacological properties of the benzodiazepines. The compound is readily absorbed after oral administration. Peak plasma concentration after a single dose occurs in 30 min and declines rapidly owing to its wide distribution and rapid metabolic inactivation. The effects of midazolam in oral formulation of 15 and 30 mg on the sleep cycle of patients suffering from insomnia were assessed by means of polysomnographic recordings using a double-blind cross-over design. Both doses of midazolam were effective in improving sleep on short-term administration. In addition, significantly larger decrements of non-REM (NREM) sleep latency and of wake time through the third of night and nonsignificant trends toward smaller number of awakenings as well as shorter total wake time and longer NREM sleep time were induced by the 30 mg dose. Irrespective of the dosage sleep was almost exclusively increased at the expense of NREM sleep. Following treatment there was no rebound insomnia. These results suggest that the 15 mg dose could be appropriate in patients with difficulties in falling asleep, while the 30 mg dose would be more appropriate for patients who also experience difficulties in staying asleep.

### NR123 EFFECT OF ZOLPIDEM ON SLEEP IN INSOMNIAC PATIENTS

CONTINUATION TREATMENT FOR THE ELDERLY DEPRESSED

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

Jaime M. Monti, M.D., Pharmacology, Clinics Hospital, Av Italia sn, Montevideo, Uruguay; Paulo F. Alterwain, M.D., Daniel Monti, M.D.

### Summary:

Zolpidem is an imidazopyridine which interacts with the GABA receptor complex, showing selectivity for benzodiazepine receptors with the biochemical characteristics and regional distribution of the BZD<sub>1</sub> subtype. The effects of zolpidem on the sleep cycle of insomniac patients were assessed by means of polygraphic recordings. Baseline placebo nights were compared with drug (10 mg p.o.) and placebo withdrawal nights. In the morning, patients were interviewed about the efficacy of treatment and the presence of side effects. The compound was effective in inducing and maintaining sleep on short- and intermediate-term administration. Sleep latency and total wake time were decreased. Total sleep time increase was related to larger amounts of stage 2 NREM sleep. The baseline values of stages 3 and 4 (slow wave sleep) were below normal. However, in contrast to results obtained after benzodiazepine administration, stages 3 and 4 showed no further decrease during zolpidem treatment. REM sleep time in min was slightly but not significantly increased. During withdrawal nights sleep induction and maintenance variables showed no significant differences in comparison to baseline. Tolerance was not observed during the two weeks of drug use. Subjective evaluation showed a relatively good correlation with sleep laboratory findings. In addition, we found no evidence that zolpidem impaired task performance the morning after its administration. Side effects included drowsiness and headache.

# NR124

### Wednesday, May 11, 12:00n-2:00 p.m.

Anastasios Georgotas, M.D., Psychiatry, New York University, 560 First Avenue, New York, NY 10016; Robert E. McCue, M.D., Thomas B. Cooper, M.A., Narmada Nagachandran, M.D., Irene Chang, B.A.

### Summary:

Although there is ample evidence that for the majority of cases of major depression, antidepressants are an effective treatment, there is considerable uncertainty about how a patient should be managed once the depressive episode has resolved. How long should the patient be on medication? How does one know when to discontinue it? What is the chance of a relapse or recurrence, and how useful are antidepressants in preventing one? Sixty elderly depressed patients who had responded to either nortriptyline or phenelzine were followed under double-blind conditions during four to eight months of continuation treatment. Over 70% of patients remained well during this period. There was no significant difference in the relapse rate between patients on nortriptyline and those on phenelzine; however patients on the latter drug were more likely to require dose reductions or drop out because of side effects. The length of the index episode was a strong predictor of relapse during continuation treatment. Following this continuation treatment 19 of these patients were randomly switched under doubleblind conditions to placebo. At the end of eight weeks, three (18.8%) of the placebo patients had relapsed, three (27.3%) of patients kept on nortriptyline had relapsed, and none of the patients on phenelzine relapsed. Patients who had more prior episodes of depression had a greater risk of relapsing. We conclude that four months of continuation treatment may be adequate for most elderly patients.

### NR125 PREMENSTRUAL SYMPTOMS IN THE GENERAL POPULATION

Martine Lalinec-Michaud, M.D., Douglas Hospital Department of Psychiatry, 6875 Boul. Lasalle, Verdun, PQ, Canada H4H 1R3; Viviane Kovess, M.D.

### Summary:

The authors want to prove the existence of negative symptoms during the premenstrual period from a random population sample and furthermore want to explore the variation of the negative symptoms based on the variables.

Abstract: The present study shows the results of a general population survey recently conducted in the Province of Quebec. This is a random sampling covering rural and urban areas. The people answered the questionnaires relating to their general health and also filled out the Illfeld questionnaire (29 questions) derived from the Self-evaluation of the Derogatis symptoms (SCL-90). Information was thus collected from about 850 women aged 15 to 45, that is to say 85% of the selected population. The results show that the women in their premenstrual period differ markedly from the women in the intermenstrual period in the following manner: decrease of appetite (.001), irritability (.02), muscular pain (.04), negative attitude towards the others (.07), tension, nervousness (.07). Later analysis compare the negative effect to the following variables: rural or urban area, age, parity, marital status, education, use of oral contraceptives. The results confirm a greater prevalence of negative effects for women in general during the premenstrual period.

### NR126 THYROID HORMONE POTENTIATION OF ANTIDEPRESSANTS

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

Russell T. Joffe, M.D., Psychiatry, St. Michael's Hospital, 30 Bond Street 4M, Toronto Ont., Canada M5B1W8; William Singer, M.D.

#### Summary:

Tricyclic antidepressants are the primary treatment for major depression. However, up to one-third of patients fail to respond to these drugs. Several, but not all, open and double-blind studies have shown that small amounts of triiodothyronine (T3) will convert tricyclic nonresponders to responders. As thyroxine (T4) is converted to T3 to have its physiological effect, it has been assumed that T4 would have a similar antidepressant effect to T3. There are, however, no systematic studies of the antidepressant potentiating effects of T4. We carried out a randomized, double-blind, three-week study of the effects of 150 mcg of T4 versus 37.5 mcg of T3 in 38 patients (21–T4, 17–T3) with major depression according to Research Diagnostic Criteria who failed an adequate trial of desipramine or imipramine. Nine of 17 patients on T3 versus four of 21 patients on T4 had a 50% reduction in the 17-Item Hamilton Depression Scale score (p= 026, Fisher Exact Test). By repeated measures analysis of variance, there was a significant difference in the effect of the two thyroid hormones on depression scores. The relationship between thyroid function tests and behavioral measures will be detailed. The difference in antidepressant efficacy of these two thyroid hormones suggested by our study may be explained by differences in cerebral utilization of T3 and T4. The clinical relevance of these findings and their implication for the role of thyroid hormones in the pathophysiology of mood disorder will be discussed.

### THE DIAGNOSIS OF MAJOR DEPRESSION BY SELF-REPORT

Scott Wetzler, Ph.D., Psychiatry, Montefiore Hospital, 111 East 210th Street, Bronx, NY 10467; Rene Kahn, M.D., Alan Dubro, Ph.D.

### Summary:

Self-report psychological tests are commonly used for the assessment of Major Depression (MD). Little research has been conducted that examines the diagnostic efficiency of these tests in diverse psychiatric populations. This study compares the diagnostic efficiency of three popular psychological tests—the MMPI, SCL-90, MCMI,—with regard to the diagnosis of MD in a mixed inpatient and outpatient psychiatric sample. Two types of analyses were used: a multidimensional analysis examining profiles composed of all scales within a given psychological test (10 MMPI scales, nine SCL-90 scales, and 20 MCMI scales), and a unidimensional analysis examining diagnoses (of MD or no MD) based on the depression scales alone (the Depression scale and Mezzich index for the MMPI, the Depression scale for the SCL-90, and the Dysthymia and Psychotic Depression scales for the MCMI).

Patients with DSM-III MD (n=48) had different multidimensional profiles on each of the three tests (based on significant group by measure interactions within MANOVAs using the Greenhouse-Geisser correction) in comparison to patients with other psychiatric disorders (n=68). Discriminant function analyses revealed that when all scales are combined these tests correctly classified patients between 73% and 80% of the time.

The unidimensional analyses revealed that, at common cut-off scores, the MCMI Dysthymia (BR=85) and SCL-90 Depression (T=70) performed better that the MMPI Mezzich index (score=190) in contrast to previous findings reported in the literature. It was also the most sensitive (.92) of all the scales and most efficient at ruling out MD, although its specificity (.50) was mediocre. The MCMI Psychotic Depression scale (BR=85) was insensitive to the diagnosis of MD with very few patients scoring above the threshold.

These findings indicate that self-report tests may serve a useful purpose saving professional time and labor. Patients with MD have distinctive test profiles, and certain depression scales can diagnose patients at a rate significantly above chance. Although these figures are impressive, the tests are by no means perfect. It would be a mistake for these tests to be used in lieu of a clinical evaluation. However, certain scales may be used very efficiently as screening instruments in the initial stage of a clinical evaluation.

### NR128 THYROID FUNCTION IN LITHIUM MAINTENANCE TREATMENT

### Wednesday, May 11, 12 noon-2:00 p.m.

Julie A. Hatterer, M.D., Psychiatry, NYS Psychiatric Inst., 722 West 168th Street, New York, NY 10032; James H. Kocsis, M.D., Peter E. Stokes, M.D.

### Summary:

To determine the clinical significance of thyroid function abnormalities in patients maintained on lithium, the authors evaluated the relationships of thyroid function tests to clinical response to lithium and side effects from lithium in 20 outpatients meeting *DSM-III* criteria for major affective disorder. No significant relationships were found between baseline thyroid function tests and clinical response. Thyroxine ( $T_4$ ) and Triiodothyronine Uptake Ratio ( $T_3UR$ ) within the normal range were found to be associated with complaints of lethargy and cognitive impairment. Thirteen subjects were followed prospectively for six months with monthly evaluations of affective state, side effects and occurrence of relapse. Thyroid function tests were repeated at the final visit. Final and mean  $T_3$  within the normal range were found to be significantly lower in patients who relapsed, and mean  $T_3$  was inversely correlated with affective state as measured by mean scores on the Hamilton and Young Mania Rating Scales. The implications for clinical management of thyroid abnormalities in lithium maintenance patients are discussed.

#### ROLE OF PHOSPHOLIPASE A2 OVERACTIVITY

EFFICIENT ECT: TEMPOROPARIETAL PLACEMENTS DIFFER

Joseph R. Hibbeln, B.A., III. State Psych Inst., 1601 West Taylor Street, Chicago, IL 60612; June W. Palmer, Ph.D., John M. Davis, M.D.

#### Summary:

Current theories of affective disorders do not account for many of the biological markers replicated in patient studies. We link many biological findings in a reasonable physiological relationship, compatible with mechanisms of action of pharmacological and electroshock therapies for depression. We propose that excessive phospholipase A<sub>2</sub> (PLA<sub>2</sub>) activity disrupts lipid/protein interactions and, therefore, the activity of membrane-dependent proteins. Similar disruptions in these proteins are documented in depressed patients and can be accounted for by excessive PLA<sub>2</sub> activity. This paradigm accounts for disturbances in the activity of NA-K-ATPase, beta<sub>2</sub> and alpha<sub>2</sub> adrenergic receptors, norepinephrine and serotonin uptake, and imipramine binding. Interestingly, ethanol perturbs membrane fluidity and membrane-bound enzymes in a manner similar to excessive PLA<sub>2</sub> activity. Disturbances in other membrane-dependent proteins, tyrosine and tryptophan hydroxylase, can explain the biogenic amine hypothesis. Inhibition of glucocorticoid and TRH receptor binding to their respective ligands by PLA<sub>2</sub> may explain patient nonsupression in the DST and nonresponse in the TRH stimulation test. Physiological regulators of PLA<sub>2</sub> activity (calcium, cortisol, estrogen, progesterone and PGE<sub>2</sub>) are documented abnormalities in some patients with affective disorders and consistent with excessive PLA<sub>2</sub> activity. Thus, postpartum depression and premenstrual tension syndrome may also be described in the paradigm. The mechanisms of action of tricyclic antidepressants, lithium, electroconvulsive shock and some novel antimanic agents can be described in terms of alternations of PLA<sub>2</sub> activity. A hereditary factor predisposing patients to the disorders may be a gene defect at either PLA<sub>2</sub> or in its regulation.

#### NR130

#### Wednesday, May 11, 12 noon-2:00 p.m.

Helen M. Pettinati, Ph.D., Research, Carrier Foundation, PO. Box 147, Belle Mead, NJ 08502; Stephani M. Nilsen, R.N., Kenneth W. Willis, M.D., Richard D. Weiner, M.D.

#### Summary:

The use of unilateral ECT has recently increased in the United States. Improvements in equipment and technique have better prepared the clinician to give therapeutic dosages of unilateral ECT. One aspect that has received little attention is the exact placement of the stimulus electrodes on the nondominant side of the head. In clinical practice, at least seven different placements can be used (see d'Elia & Raotma, 1975). Weiner (1980) has discussed the potential for electrode placements with shorter distances between the two contacts to require more energy and raise seizure threshold since more current will be shunted through scalp tissues. Thus, certain electrode placements might result in more missed, focal and/or subtherapeutic seizures. The present study assessed 49 unilateral ECT patients, randomly assigned and blind to one of three temporoparietal placements. Of the 49, 17 had the d'Elia placement (the distance between the electrodes is 4" to 5"), 16 had the Lancaster (2"-3"), and 16 had the McAndrew (3"-4"). The d'Elia and Lancaster placements are the most commonly used in clinical practice. Significantly more missed and focal seizures (p=.01) were found using the McAndrew placement compared to the other two placements. While there were no differences in the therapeutic response across the three placements, the immediate restimulation that occurred at the time of a missed or focal seizure likely corrected the potential for reduced therapeutic response. In addition, the electrical dosage given during this study may be relatively higher than in other clinical settings. Results will be discussed in relation to restimulation and changes in dosage.

### NR131 METHYSERGIDE BLOCKS THE POSTICTAL PROLACTIN SURGE

Athanasios P. Zis, M.D., Psychiatry, University of BC, 2255 Wesbrook Mall, Vancouver BC, Canada V6T2A1; Ronald A. Remick, M.D., Campbell M. Clark, Ph.D., B.E.K. Grant, R.N., Gregory M. Brown, M.D.

### Summary:

Plasma prolactin (PRL) levels increase severalfold immediately following tonic-clonic seizure, complex partial seizures, and electroconvulsive therapy (ECT). Depth EEG recordings suggest that spreading of the ictal discharge to subcortical (limbic) structures is necessary for the observed PRL release. The neurochemical substrate of this neuroendocrine response remains unknown. There is considerable evidence that serotonin stimulates PRL secretion. Serotonin has long been implicated in the pathophysiology of depression and there is evidence that the administration of electroconvulsive shock to animals produces alterations in the serotonergic system. We report here that pretreatment with the classic serotonin receptor antagonist methysergide blocks the ECT-induced PRL surge. Eight drug-free patients undergoing a course of ECT received in a counterbalanced design methysergide (2 mg) or placebo twice daily for two days prior to treatment number three and in the morning two hours prior to their treatment. The same sequence was repeated prior to treatment number five with patients being crossed over from active drug to placebo and vice versa. Blood samples were drawn immediately before and at 15, 30, 45 and 60 minutes after the electrical stimulation. The postictal PRL surge was markedly restrained by pretreatment with methysergide. This effect of methysergide was clearly evident in all eight subjects and was nearly complete in six. We believe that the observed blockade of the postictal rise in PRL by methysergide is the result of the effect of this drug at serotonin receptor sites in the diencephalon. The relevance of the observed and heretofore unreported blockade of the ECT-induced PRL rise by the methysergide to the mechanism of action of ECT will be discussed.

# NR132 Wednesday, May 11, 12 noon-2:00 p.m. A LONGITUDINAL STUDY OF MOOD VARIATIONS AND IMMUNE DYSFUNCTION

William J. Lancee, M.Sc., Social & Community Psych, The Clarke Institute, 250 College Street, Toronto Ont., Canada M5T1R8; S.J.J. Freeman, M.D., Mary Kay O'Neil, Ph.D.

### Summary:

Psychiatric researchers are becoming increasingly interested in the interaction between the CNS and the immune system. This prospective study in psychoneuroimmunology elucidates causal and temporal relationships between the occurrence of life events, changes in mood states, changes in immunocompetence and recurrences of an opportunistic virus (Herpes Simplex Virus 1, or cold sore virus). Thirty-two undergraduate students having recurrent cold sores were followed for 84 consecutive days. The subjects completed a diary which contained a mood scale and a checklist of precipitating events and cold sore symptoms. Once a week, the subjects met with study staff to complete a life-events questionnaire and to provide a saliva sample in order to test for HSV-1 and antibodies to HSV-1. There were a total of 36 cold sore episodes. The relative risk for cold sores following a period of extreme mood days was found to be 9.6. The one-way Chi-squared statistic was 4.27 (1 df., p-.05). The 8th day prior to cold sores appears to be especially high in risk, indicating that the immune-viral mechanism triggered by extreme moods or physiological events takes 8 days to manifest itself in overt cold sores. Data from this study show that life experiences result in mood consequences that compromise the immune system and this, in turn, enables opportunistic viruses to replicate. The implications of the results to psychiatry will be discussed.

### NR133 DEPRESSION, CELLULAR IMMUNITY AND SUICIDALITY

David J. Borrelli, M.D., Westwood Lodge, 45 Clapboardtree Street, Westwood, MA 02090; Elinor Levy, Ph.D., Patricia Salt, Ph.D., Steven M. Mirin, M.D., Paul H. Black, M.D.

### Summary:

Twenty-seven depressed psychiatric inpatients and 27 sex-matched hospital staff volunteers serving as controls were compared on assays of cellular immune function. These assays included three measures of mitogen responsiveness (Concanavalin con A, Phytohemagglutinin PHA, and Pokeweed Mitogen PWA); T-cell subsets including helper T-cells (T4) and suppressor T-cells (T8); and natural killer cell (NK) activity. Only physically healthy subjects, drug-free for 14 days were included.

The depressed inpatients (mean score on 21 item HAM-D was  $26.3\pm6.3$ ) were further characterized with data collection that included demograhic, descriptive-diagnostic information, as well as biological characteristics (including "biological markers" of DST, urinary MHPG and free cortisol, platelet MAO activity) and psychosocial data (Rotter Internal-External Control Scale, Sarason Life Experience Survey, and Kobasa Hardiness Scale).

Paired comparisons of the immune measures of those patients with the *DSM-III* diagnosis of Major Depression (n=14) were revealing of statistically significant reduction of NK activity (paired t-test, p=0.05), as well as trend toward a lower response to PHA (p=0.10). Paired comparisons of those patients with other depressive disorders (Atypical Depression, Dysthymic Disorder, and Bipolar Disorder, depressed) did not demonstrate these differences in parameters of cellular immune function. A subsample of patients who had made a serious attempt prior to or during current hospitalization (n=8) were compared to those who had not made a recent suicide attempt. The "suicide attempters" had a statistically significant reduction of the responsiveness to the mitogens Con A (%) and PHA (cpm), as well as trend toward lower responsiveness to Con A and PHA.

# NR134

### Wednesday, May 11, 12 noon-2:00 p.m.

# PSYCHOSOCIAL FACTORS IN RECURRENT SUICIDALITY

Gabor I. Keitner, M.D., Butler Hospital, 345 Blackstone Blvd., Providence, RI 02906; Christine Ryan, Ph.D., Ivan W. Miller, Ph.D., Nathan B. Epstein, M.D., Duane S. Bishop, M.D., William H. Norman, Ph.D.

### Summary:

Research on suicidality tends to focus in the main on epidemiologic and/or psychological variables. In order to assess psychosocial aspects of suicidality, we examined suicidal and nonsuicidal patients with major depression during (n=118) and subsequent to (n=80) their hospitalization. Factors associated with suicidality at the index episode included age at onset of the depression, duration of the depressive episode, presence of an Axis II diagnosis, and discrepant views of family functioning between the patients and their family members. Suicidal patients viewed their family functioning more negatively than did their families, while nonsuicidal depressed patients perceived their family functioning more positively than did their families, while nonsuicidal depressed patients perceived their family functioning more positively than did their family members. Together these factors accounted for 48% of the variation between suicidal and nonsuicidal patients (p $\sim$ .001). Suicidality at follow-up (10–42 months, mean=27) was associated with a more negative perception of family functioning by suicidal than nonsuicidal patients as well as poorer posthospital interepisodic adjustment and more exits (moves, divorce, separation) from their family constellation. These results indicate that when assessing patients with major depression for recurrent suicidality, attention should also be paid to their family functioning and immediate social environment.

# NR135 DESIPRAMINE BLOOD LEVEL AND THERAPEUTIC RESPONSE

### Wednesday, May 11, 12 noon-2:00 p.m.

Mahmoud N. Musa, M.D., Psychiatry, Chicago Medical School, 3333 Green Bay Road, North Chicago, IL 60064; Bahjat Qaqish, M.D.

# Summary:

Studies of the relationship between plasma concentration of desipramine and antidepressant response have produced contradictory results. Various groups reported linear, curvilinear and no relationship. In this study, fifty nine patients with edogenous depression received a fixed dose of desipramine for four weeks. Plasma levels were determined by high-pressure liquid chromatography and the range was between 12 and 684 mg/ml. Therapeutic response was determined by Hamilton depression scale weekly. The data were analyzed utilizing a computer-assisted graphing procedure called LOWES: Locally weighted scatter plot smoothing. It is a model-independent exploratory data analysis procedure. The plot of depression emelination score vs. Plasma concentration resulted in an oscillatory pattern of three maxima alternating with two response minima. These results are consistent with and lend support to current hypothesis pertaining to the pharmacodynamics of desipramine and noradrenergic receptor subtypes. This study will be compared with previous studies which may explain the contradictions in previous studies and help with utilization of blood levels of desipramine and other antidepressants and increase our understanding of the mechanism of action of antipressants.

### NR136 PSYCHOLOGICAL MODULATION OF CELL-MEDIATED IMMUNITY

G. Richard Smith, M.D., Psychiatry, University of Arkansas, 4301 W. Markham Slot 554, Little Rock, AR 72205; Diane F. O'Rourke, Ph.D., Carolyn Conger, Ph.D., Ronald K. Charlton, Ph.D., Russell W. Steele, M.D., Susan S. Smith, M.S.W.

### Summary:

The purpose of this experiment was to test the hypothesis that antigen specific cell-mediated immunity could be modulated by a psychological process. Twenty eight meditators were recruited for the study. After obtaining baseline venous blood for in-vitro lymphocyte assays, subjects were randomized into an Enhancer or Suppressor group. They were then skin tested with varicella-zoster (VZ) skin test antigen which elicits a delayed type hypersensitivity reaction. Subjects meditated alone and in groups for 48 hours attempting to either enhance or suppress their response. Skin tests were then read and venous blood obtained for in-vitro analysis. The in-vitro analysis included lymphocyte stimulation to VZ antigen and phytohemoglutinin (PHA), as well as quantification of lymphocyte subsets using monoclonal antibodies.

As hypothesized, the Enhancer group had larger skin test reactions (7.3)cm vs 5.4cm) at 48 hrs by t test (p<0.05). Further, when the pre- and post-lymphocyte stimulation values (blastogenic index and/or counts per minute) were blindly classified as an enhanced reaction, a suppressed reaction, or no change, the groups differed in the predicted direction (x<sup>2</sup>=10.8, df=2, p<0.01). Finally, there were no differences in PHA stimulation nor lymphocyte subsets.

The data support the hypotheses that immunological responses may be intentionally modified via a psychological process. The present data suggest that this may occur via antigen recognition.

#### NR137 MULTIPLE HORMONE RESPONSES TO CLONIDINE INFUSION

### Wednesday, May 11, 12 noon-2:00 p.m.

Jay D. Amsterdam, M.D., Psychiatry, Hospital Univ of Penna, Dep Res Unit: 3400 Spruce St, Philadelphia, PA 19104; Brett Skolnick, Ph.D., Greg Maislin, M.S., Jennifer Phillips, B.S., Neil J. Berwish, M.D., Andrew Winokur, M.D.

### Summary:

There is evidence that some hormonal response abnormalities after neuroendocrine challenge tests in patients with major depression may reflect alterations in CNS neurotransmitter systems regulating limbic-system hypothalamic function. In particular, the  $\alpha$ 2 adrenergic receptor modulates noradrenalin turnover and has been implicated in several neuroendocrine abnormalities in depression. For example, diminished growth hormone (GH) response has been observed by several investigators after clonidine administration (an  $\alpha$  2 adrenoceptor agonist). However, few studies have examined disturbances in multiple endocrine axes after clonidine administration.

We administered an intravenous clonidine (2.5  $\mu$  g/kg) challenge test and examined GH, prolactin (PRL), and cortisol responses over 210 minutes in 18 depressed patients (12 melancholic and six nonmelancholic) and nine healthy controls, with mean  $\pm$ SD ages of 33 $\pm$ 9, 37 $\pm$ 8, and 33 $\pm$ 12 years, respectively.

Basal concentration of GH, PRL, and cortisol were similar in patients and controls. However, after clonidine, the mean GH response over the 210-minute period was significantly diminished in melancholic (p=0.02) and nonmelancholic (p=0.04) patients compared to controls. Overall, PRL responses to clonidine were highly variable; however, the mean PRL response over 210 minutes was significantly greater in melancholic patients (p=0.02) compared to controls. Finally, there was a slight decrease in the mean cortisol concentrations after clonidine infusion, that failed to achieve statistical significance because of the large cortisol response variability between subjects. In conclusion, these data suggest the presence of altered  $\alpha 2$  adrenoceptor activity in some depressed patients.

### NR138

# LONG-TERM CONTINUATION ANTIDEPRESSANT TREATMENT

### Wednesday, May 11, 12 noon-2:00 p.m.

Thomas A. Aronson, M.D., Psychiatry, Suny at Stony Brook, HSC-T10, Stony Brook, NY 11794; Sashi Shukla, M.D.

### Summary:

This retrospective, naturalistic study examines the clinical characteristics and course of illness of 26 patients with major affective disorders who demonstrated a robust antidepressant (AD) response but repeatedly relapsed in temporal relation to an AD tape at the usual 6–12 month intervals. These patients were not chronic treatment-refractory depressives. Rather, they required long-term ( $\bar{x}$ =36.6 months) *continuation*, not preventive, treatment to maintain their euthymia. In comparison to 15 randomly selected patients with more typical recurrent illness and response to intermittant 6–12 month treatment, the long-term group was more likely to be younger, married, have a longer duration of depression prior to entering treatment, and meet *DSM-III* criteria for coexistent dysthymic, panic or personality disorder, or psychotic features. Symptomatically, they presented with more agitation, severe anxiety, panic attacks, and psychotic symptoms. They appeared to have thymoleptic-responsive dysthymic and personality disorders which improved with medication and worsened upon withdrawal. Patients who require long-term continuation AD treatment may not be uncommon in a tertiary care Affective Disorders Clinic. The findings suggest that concomitant Axis I and II diagnoses in AD responsive patients may be associated with the need for long-term therapy, and suggest limitations to the standard 6–12 month recommendation. They also support the idea that AD's control symptoms without curing or shortening the episode.

### NR139 IMIPRAMINE BINDING IN ADOLESCENT SUICIDE ATTEMPTERS

Lee S. Cohen, M.D., Psychiatry, NYS Psychiatric Inst., 722 W 168th St., Div Child Box 78, New York, NY 10032; Michael Stanley, Ph.D., Paul D. Trautman, M.D., Sarah Mack, B.A., David Shaffer, M.D.

# Summary:

Recent biochemical research in adult suicide attempters/completers has indicated a dysregulation in the serotonergic system as manifest by lowered cerebrospinal fluid 5-hydroxyindoleacetic acid, and decreased brain <sup>3</sup>H imipramine binding as compared with nonsuicidal controls. Platelet <sup>3</sup>H imipramine binding sites have been used as a measure of presynaptic serotonergic functioning and have been found to be decreased in density in adult depressed patients, prepubertal conduct disordered patients and in aggressive adolescents. To investigate the serotonergic dysregulation hypothesis, we measured platelet <sup>3</sup>H imipramine binding in eight female and two male suicide attempters (N=10, age range 12–18: six adjustment disorders, two with major depression, one dysthymic disorder and one separation anxiety disorder) within 14 days of their attempt. Forty percent of the sample had a family history of suicidal behavior. Patients were rated for depression, anxiety, hopelessness and psychosis. A negative correlation was found betwen scores on the Hamilton rating scale for depression and density of platelet <sup>3</sup>H-imipramine binding (r=–.7296, p=.01) as well as a trend towards a negative correlation on depression related items (dysthymia r=–.5152, p=.064, helplessness r=–.4697, p=.085). No correlation was found among Bmax and measures of conduct disorder, anxiety and hopelessness. These preliminary data suggest the need for further research to assess the role of a lowered density of platelet <sup>3</sup>H-imipramine binding sites as a risk factor in adolescent suicidal behavior.

### NR140 A CONTROLLED TRIAL OF FLUVOXAMINE IN MAJOR DEPRESSION

JYUAAWINE IN WAJUR DEPRESSION

John P. Feighner, M.D., Feighner Research, 1011 Devonshire #E, Encinitas, CA 92024; William F. Boyer, M.D.

### Summary:

Fluvoxamine, a selective serotonin reuptake inhibitor, was investigated in a six-week double-blind study among inpatients with *DSM-I/I* major depression.

Following a three-day placebo wash-out patients were randomly assigned 2:2:1 to fluvoxamine, imipramine or placebo. Demographics and treatment history were comparable across groups. All but one patient fulfilled criteria for melancholia.

Sixty of 81 patients completed at least two weeks following wash-out and were evaluated for efficacy; 12 on placebo, 21 fluvoxamine, and 27 imipramine. The median daily doses were 145 mg of fluvoxamine and 159 mg of imipramine.

Analysis of covariance (controlling for baseline) showed significant (p < 0.05) differences on CGI severity and BPRS total and a trend (p=0.08) on the Hamilton Depression Scale. Fluvoxamine was superior ( $p \le 0.02$ ) to both placebo and imipramine on these measures.

The average number of reported adverse events per patient was 3.6 for placebo, 3.4 for fluvoxamine, and 3.9 for imipramine. Fluvoxamine's most common adverse effects were nausea and agitation. The number of fluvoxamine patients withdrawn for side effects was not significantly different than placebo. There were no significant changes in vital signs, ECG or laboratory tests.

### NR141 COGNITIVE EFFECTS OF CORTICOSTEROIDS IN MAN

# Wednesday, May 11, 12 noon-2:00 p.m.

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

Owen M. Wolkowitz, M.D., Psychiatry, Univ of California, 401 Parnasus Avenue, San Francisco, CA 94143; Victor I. Reus, M.D., Herbert Weingartner, Ph.D., Raymond Deicken, M.D., Karen Thompson, B.S., Alan Breier, M.D., Allen Doran, M.D., David Pickar, M.D.

### Summary:

Excessive circulating levels of endogenous and exogenous corticosteriods are associated with cognitive impairment. Few studies have prospectively examined this relationship. We report the results of three studies which convergently suggest that corticosteriods produce highly specific cognitive deficits in man. In Study 1, a recognition memory test was administered to depressed patients and normal controls. Depressed dexamethasone nonsuppressors, compared to suppressors and to controls, made significantly more errors of commission (p<0.05) with no difference in correct recognition scores. In Study 2, dexamethasone (1 mg p.o. at 11 p.m.) administration was associated with a focal cognitive deficit in normal controls, viz., a significant increase in "intrusions" into free recall (p=0.05), with no change in correct free recall. In Study 3, prednisone (80 mg p.o. daily x 5 days, double-blind) administration in healthy volunteers was associated with a significant and specific decrease in the ability to identify "distractors" in a test of recognition memory (p<0.05).

Our findings with dexamethasone and prednisone in normals and with endogenous hypercortisolemia in depressed patients provide a consistent picture of corticosteroid-related cognitive effects, namely a failure to discriminate previously presented relevant information from related but irrelevant new information. These finding will be discussed in the context of the effects of arousal on cognition.

### A PILOT CLINICAL TRIAL OF M-CHLOROPHENYLPIPERAZINE IN DEPRESSION

Alan M. Mellow, M.D., Lab Clin Sci, NIMH, NIH Clinical Ctr Room 3D-41, Bethesda, MD 20892; Brian A. Lawlor, M.D., Trey Sunderland, M.D., Edward A. Mueller, M.D., Susan E. Molchan, M.D., Dennis L. Murphy, M.D.

### Summary:

M-chlorophenylpiperazine (m-CPP), a metabolite of the antidepressant trazodone, is a serotonin receptor agonist that is currently being used with the acute pharmacologic challenge strategy to examine the functional status of the serotonergic system in several patient populations. Because of m-CPP's distinct biochemical properties and documented serotonergic dysregulation in affective disorders, we initiated a study with a small group of patients to examine the efficacy of daily oral m-CPP as a possible treatment for depression.

In this first clinical trial with m-CPP, five depressed inpatients (mean age  $62.0\pm8.2$  years) received oral m-CPP over 14 days at a maximum dose of 80 mg/day in a double-blind, placebo-controlled crossover design. Two of five patients showed considerable clinical improvement in depression and anxiety (as measured by HDRS, NIMH Global Ratings, and NIMH Self-Ratings), as well as rebound worsening of symptoms when crossed back to placebo. The remaining three patients showed minimal improvement, but some evidence of rebound worsening. Although preliminary, these observations are of interest, particularly given the purported role of serotonin in aggression, because both m-CPP responders had a history of aggressive, impulsive behavior when depressed. The observed short-term response and immediate rebound worsening upon withdrawal are consistent with receptor stimulation as a mechanism of action for the drug. This clinical trial suggests that further study of m-CPP as a therapeutic agent in selected patients may lead to a greater understanding of the role of serotonin in psychiatric disorders.

### NR143

# ESMOLOL INFUSION CONTROLS RISE OF HR AND BP IN ECT

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

Anthony L. Kovac, M.D., Anesthesiology, KU Medical Center, 39 and Rainbow Boulevard, Kansas City, KS 66103; Manuel Pardo, M.D., Hiroshi Goto, M.D., Kasumi Arakawa, M.D.

#### Summary:

Electroconvulsive therapy (ECT) normally causes a transient but significant hyperactivity of the sympathetic nervous system resulting in tachycardia and hypertension. These increases in heart-rate (HR) and blood pressure (BP) have no therapeutic effect for ECT and are potentially harmful to the patient. In this study, all patients (N=9) received both esmolol and "no treatment," in a randomized, crossover design. During the esmolol treatment, a bolus (80 mg) and intravenous infusion of esmolol (24 mg-min) were started 2 minutes prior to induction of anesthesia (oxygen, methohexital, and succinylcholine) and continued for approximately 5 minutes after induction. HR and BP measurements were taken before infusion, during the ECT treatment and every minute throughout the infusion period; then at 2, 5, 10, 15 and 30 minutes after the infusion was discontinued. Esmolol was found to blunt the increase in HR by 28% (p <0.05, ANOVA) systolic blood pressure (SBP) by 17%, maximal diastolic blood pressure by 11%, and rate pressure product (HR×SBP) by 41%. Graphs of results are presented. Esmolol infusion appears to be a safe and useful agent for attenuating the HR and BP effects of ECT.

### NR144 MAGNETIC RESONANCE BRAIN STUDY IN BIPOLAR PATIENTS

### Wednesday, May 11, 12 noon-2:00 p.m.

Henry A. Nasrallah, M.D., Psychiatry, Ohio State University, 473 West 12th Avenue, Columbus, OH 43210; Stephen C. Olson, M.D., Jeffery A. Coffman, M.D., Steven B. Schwarzkopf, M.D., Judy A. McLaughlin, M.S., Judith Brandt, R.N.

### Summary:

In a previous magnetic resonance imaging (MRI) study (Andreasen, et al., 1986), we reported a smaller cranial, cerebral, and frontal size in schizophrenia. We have attempted to replicate those findings in a new sample of schizophrenics, and in a sample of patients with bipolar affective psychoses.

Method: 40 schizophrenic and 15 bipolar patients (DSM-III-R) aged 20 to 45 years have consented to participate in the study so far. MRI was done with a G.E. 1.5 Tesla scanner using inversion recovery pulse sequence (TI=800 and TR=1500 MS). The midsagittal areas of the cranium, cerebrum, frontal area, VBR and callosal dimensions were measured with computerized planimetry and a digitizing tablet.

Results: After controlling for height, schizophrenic and affective groups did not differ on measures of cranial, cerebral, frontal, and callosal area or VBR. A significant negative correlation between height and cerebral area emerged in the schizophrenic group (p < .05) compared to a positive correlation in the bipolar group. The results suggest that while no MRI differences emerged between schizophrenia and affective disorder patients, the unusual negative correlation between height and cerebral size in schizophrenia suggests some neurodevelopmental differences between the two groups. This abnormal finding was noted in the male but not the female schizophrenics, suggesting that pathological neural development in schizophrenia may be gender-specific.

### NR145 ALTERED SEROTONIN BINDING IN SUICIDE VICTIMS

Larry D. Sparks, Ph.D., Psychiatry, University of Kentucky, 800 Rose Street Annex II Rm 203, Lexington, KY 40536; Karley Little, M.D.

### Summary:

Decreased serotonin, decreased presynaptic 3H-imipramine Bmax, and increased postsynaptic serotonin-2 Bmax have been demonstrated in the brains of suicide victims. In a preliminary study we have examined serotonin binding in the pineal of ten suicide victims, all dying of highly lethal means (not drug over-dose). Twenty-six controls were matched for sex, age, sudden or traumatic death, absence of underlying medical diagnosis or treatment, and level of alcohol present at autopsy. *DSM-3R* diagnoses were assigned retrospectively by an experienced psychiatrist, blind to autopsy and biochemical results, after interviewing available family or physician. Pineal glands were harvested within 24 hours of death in subjects and controls. Binding assays were done using tritiated serotonin. Complete analysis is pending, but results at the 2nM concentration show a reduction in binding in suicides (controls  $4.2\pm1.8$ , p. 5). Controls with gunshot wounds of the head (N=12) averaged  $4.35\pm.53$  fmol/mg protein vs.  $1.16\pm.39$  fmol/mg protein in suicides (N=6) with gunshot wounds to the head (p, 01). The clinical correlations of these changes, their pathophysiologic significance and the possible role of serotonin receptors in the pineal will be discussed.

### NR146 MUSCARINIC/NICOTINIC-EVOKED CATECHOLAMINE RELEASE

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

Marvin A. Oleshansky, M.D., Med. Neurosci., Walter Reed Inst. Resch., Div. of NP WRAIR, Washington, DC 20307; Yoshikazo Nakazato, Ph.D., Peter Chiang, Ph.D.

### Summary:

Recent evidence has demonstrated that acetylcholine (A Ch) binds to both nicotinic and muscarinic receptors in the CNS. The neurochemical and functional correlates of A Ch binding to these receptors remains unclear. The effects of cholinergic receptor activation on isolated-perfused guinea pig adrenal glands was studied as a model neuronal system.

Both adrenal glands were perfused with Locke solution through a cannula inserted into the lower aorta; perfusates were collected from a cannula in the caudal vena cava. Drugs were perfused for one or two minutes. Catecholamines released from the adrenal medulla for five minutes following drug infusions were assayed by HPLC with electrochemical detection.

A Ch evoked catecholamine release in a dose-dependent manner with an ED<sup>50</sup> of 7×10<sup>-5</sup>M. Nicotine or oxotremorine, a muscarinic agonist, each independently stimulated catecholamine secretion. Oxotremorine potentiated nicotine-evoked catecholamine release nearly double that expected from the additive actions of the individual secretagogues.

SECRETAGOGUE	CATECHOLAMINES (nmol±SEM/5min)
A Ch (10 <sup>-5</sup> )	3.1±0.6
Nicotine (2×10 <sup>-5</sup> M)	1.4 <u>+</u> 0.2
Oxotremorine (10 <sup>-5</sup> M)	0.2 <u>+</u> 0.2
Nicotine+oxotremorine	2.9 <sup>+</sup> <u>+</u> 0.1

The synergistic effects of oxotremorine and nicotine on catecholamine secretion suggests that A Ch may stimulate adrenomedullary catecholamine release through activation of both muscarinic and nicotinic receptors. These findings raise the possibility that cholingeric mechanisms in the CNS may be under duel regulation of nicotinic and muscarinic receptors.

# EFFECT OF NALOXONE ON PROLACTIN LEVELS WITH ECT

Trevor R.P. Price, M.D., Psychiatry, Hosp of Univ of PA, 3400 Spruce Street, Philadelphia, PA 19104; Michael R. Sperling, M.D., Thomas W. McAllister, M.D., Shlomo Melmed, M.D.

### Summary:

Endogenous opiate and prolactin levels are elevated following ECT and spontaneous seizures (Aminoff, et al., 1984). Since opiates may stimulate prolactin release, and naloxone can block this response, post-ECT prolactin elevations could be due to ECT-induced opiate release. This research reports the effect of high dose naloxone on prolactin secretion, seizure duration, and immediate post-ictal behavior in patients receiving ECT.

*Methods:* Seven patients were given 8 mgm. of naloxone or 1 cc. of saline IV, immediately prior to ECT. Each patient was studied twice, receiving saline or naloxone prior to two consecutive treatments out of the first three in a series, with the order of administration being randomized. Seizure durations were monitored with a one-channel EEG, and post-ictal behavior, level of consciousness, and orientation were assessed during the first 15 minutes after ECT. Immediately before and 15 minutes after each ECT, 5 cc. of blood were drawn for prolactin levels.

*Results:* No significant differences were found in seizure duration nor post-ictal behavior with naloxone as compared to saline. Mean post-ECT prolactin levels with naloxone and saline were not significantly different at 127 ( $\pm$ 82) and 106 ( $\pm$ 86) respectively.

*Discussion:* These results extend the work of Papakostas, et al. (1985), who reported failure of low doses of naloxone to block ECT-induced prolactin release. They indicate that this phenomenon is not significantly related to endogenous opiates, and suggest that it is probably dependent on other neurotransmitters such as GABA and/or 5-HT.

### NR148

# CHRONOBIOLOGICAL INFLUENCE IN TRH-TSH CHALLENGE

#### Wednesday, May 11, 12 noon-2:00 p.m.

Fabrice Duval, M.D., Specialise, Centre Hospitalier, Service Du Dr Macher, Rouffach, France 68250; Luc-Andre Granier, M.D., M. Antoine Crocq, M.D., Marien Claude Mokrani, Ph.D., Michel Toussaint, Comp. Eng, Jean-Paul Macher, M.D.

### Summary:

We studied the TSH response to TRH challenge (200  $\mu$ g IV) at 8 AM and 11 PM after a minimum wash-out period of 10 days in 29 patients (12 M, 17 F, aged 20–56 years, mean 38.9±10.8 SD yrs) with a Major Depressive Episode (*DSM-III-R*) (24-item Hamilton Depression rating scale score: 33±8.2 SD) and 20 controls (10 M, 10 F, aged 20–56 years, mean 34.7±9.3 SD yrs).  $\Delta$ TSH (difference between peak TSH after TRH injection and baseline TSH) was significantly greater at 11 PM than 8 AM both in patients (p < .001) and controls (p < .00001). However, the difference between 11 PM  $\Delta$ TSH minus 8 AM  $\Delta$ TSH ( $\Delta\Delta$ TSH) was significantly lower in patients (mean  $\Delta\Delta$ TSH=1.1± 1.5 SD  $\mu$  U/ml) compared to controls (mean  $\Delta\Delta$ TSH=4.8±1.9 SD  $\mu$ U/ml) (p. < .00001). In the total sample,  $\Delta\Delta$ TSH correlates with the mesor (rho=.518; p=.0003) and amplitude (rho=.55, p=.0001) of TSH secretion over the 24 hour period. Both diagnostic sensitivity and specificity derived from  $\Delta\Delta$  (viz. 89.6% and 95% with a cut-off value of <3  $\mu$ U/ml) are greater than the corresponding values obtained from the TRH/TSH challenge performed at either 8 AM (viz. 41.4% and 75% with a cut-off value of <7  $\mu$ U/ml) or 11 PM alone (viz. 62% and 80% with a cut-off value of <10  $\mu$ U/ml). We suggest that  $\Delta\Delta$ TSH has the advantage of taking into account the chronobiological influences in the interpretation of the TRH/TSH challenge.

#### NR149 LINKAGE OF BIPOLAR | DISORDER TO CHROMOSOME 11

### Wednesday, May 11, 12 noon-2:00 p.m.

John C. Kluznik, M.D., Specialise, Centre Hospitalier, Service Du Dr Macher, Rouffach, France 68250; Harry Orr, Ph.D., Stephen Rich, Ph.D., Beverley Koller, Ph.D., Lisa Duvick, M.D.

### Summary:

Bipolar disorder has recently been shown in one pedigree (1) to be linked to chromosome 11. We have previously reported a five-generation bipolar pedigree with an autosomal dominant pattern of transmission (2). Using recombinant techniques we have found data suggesting linkage to the proximal end of the short arm of chromosome 11.

Method: All family members were examined by a psychiatrist (JCK). Diagnoses were made by Research Diagnostic Criteria. There were 31 individuals in the pedigree. Initial probes with HRAS and INS have been made for the 10 samples obtained so far.

*Findings:* The lod score is +0.6 with theta=0.2. There are two recombinants who separate INS and HRAS from the illness. There are three samples not yet analyzed. If these samples follow true, the lod score will reach + 1.2 with theta=0.15. We are presently searching for other family members. The findings of a positive lod score in this pedigree suggests that this is an additional family with linkage of bipolar illness to the 11th chromosome.

### NR150 QUANTITATIVE EEG CORRELATES OF DEPRESSIVE PHENOMENOLOGY

Kenneth R. Alper, M.D., Psychiatry, NY Univ Med Ctr, 550 First Avenue, Brain Res., New York NY 10016; A.L. Lieber, M.D., Leslie S. Prichep, Ph.D.

# Summary:

Neurometric quantitative EEG (N-QEEG) data and a scale listing the common phenomenologic manifestations of depression were obtained on 50 psychiatric inpatients with *DSM-III* Major Unipolar and Bipolar Depression. The first two factors obtained by factor analysis of the phenomenology data accounted for 18% and 9% of the variance and were readily interpretable as atypical and endogenous depression (Leibowitz et al 1984). The N-QEEG data were divided into domains of multivariate and univariate measures of coherence, asymmetry, and absolute and relative power and also factor analyzed. Multiple regression analysis revealed significant association with the two factor sets, particularly with respect to the endogenous factor and factors representing delta and theta coherence in the temporal regions (B=.34 p=.017) and delta absolute power in all regions (B=.42 p=.002). The data appear to support the validity of an endogenous depression as a biological subtype.

# NR151 BRAIN MRI BEFORE AND AFTER ELECTROCONVULSIVE THERAPY

# Wednesday, May 11, 12 noon-2:00 p.m.

Laszlo Gyulai, M.D., Psychiatry, Hosp of Univ of PA, 3400 Spruce Street, Philadelphia PA 19104; Trevor R. P. Price, M.D., Thomas W. McAllister, M.D., Robert I. Grossman, M.D., Bruce H. Braffman, M.D., Anish U. Shah

# Summary:

Electroconvulsive therapy (ECT) is an effective treatment of severe depression. Adverse effects of ECT include transient memory impairment, temporary changes in the blood-brain barrier, and acute elevation of blood pressure (1). Based on animal studies, adverse effects might also include neuropathologic changes such as petechial hemorrhages, gliosis, and neuronal loss (2). To assess this possibility, magnetic resonance imaging (MRI) has been performed thus far on 15 patients with major affective disorder treated with various types of ECT (Bilateral Sinusoidal, n=6; Bilateral Brief Pulse, n=5; and Unilateral Non-Dominant Brief Pulse, n=4). Short and long TR sequences of brain images were taken using the GE 1.5 Tesla, 1 meter bore magnet within a maximum of six weeks prior to and following ECT. The pre- and post-ECT MR scans were blindly evaluated for foci of abnormal signal intensity, morphological abnormalities, and focal or diffuse parenchymal loss. A comparison of the scans revealed no discernible differences in MRI findings of the nine cases comprehensively evaluated to date (the results of the preliminary evaluation of an additional six scan pairs, which are currently in the final evaluation process, are consistent with the first nine). Thus, as assessed by the most sensitive clinical method of brain-imaging currently available, ECT does not appear to cause detectable structural changes in the CNS within six weeks following treatment according to this preliminary evaluation.

# NR152

# EKG CHANGES WITH HYDROXYNORTRIPTYLINE METABOLITES

### Wednesday, May 11, 12 noon-2:00 p.m.

Lon S. Schneider, M.D., Psychiatry, Univ of Southern Calif, 1934 Hospital Place, Los Angeles CA 90033; Thomas B. Cooper, M.A., James Severson, Ph.D., Bruce R. Sloane, M.D.

# Summary:

Pharmacokinetic factors may contribute to altered nortriptyline (NT) effects in the elderly. Plasma concentrations of NT's principal metabolite, the E-10-hydroxynortriptyline isomer (E-10-OHNT), tend to be greater than NT, increase with age, and may contribute to cardiotoxicity <sup>1</sup>(Young et al 1985). ECG changes were evaluated in 21 ambulatory, elderly, major depressed outpatients (RDC; mean age 64 yr±6SD, range 60–83) who were treated with therapeutic doses of NT. Resting ECGs were obtained before and after six weeks of treatment. All but two had no pretreatment conduction defects. Plasma was assayed simultaneously for NT, the E-10-OHNT and Z-10-OHNT isomers. Three developed 1° AV block and one developed right BBB during treatment. Daily nortriptyline dose and steady state plasma levels did not differ from controls in these subjects (94±11 ng/ml vs 84±27), but E-10-OHNT levels were significantly higher (220±67 ng/ml vs 128±58, p < .02). Overall, there were significant correlations between changes in the PR interval and QRS duration with plasma concentrations of NT, E-10-OHNT, Z-10-OHNT and the sum of NT and both of its metabolites. Multiple regression analyses suggested that PR interval increases were associated with increasing NT concentration, while QRS duration and QTC interval increases were associated with higher Z-10-OHNT concentration. E- and Z-10-OHNT may contribute substantially to cardiac effects of NT treatment, and may be of particular importance in the elderly.

# IMIPRAMINE BINDING IN PRIMARY AND SECONDARY MAJOR DEPRESSION

Lon S. Schneider, M.D., Psychiatry, Univ of Southern Calif, 1934 Hospital Place, Los Angeles, CA 90033; James Severson, Ph.D., Bruce R. Sloane, M.D., Eric R. Frederickson, B.S., Ronald Gleason, M.D.

# Summary:

Platelet <sup>3</sup>H-imipramine binding density ( $B_{max}$ ) and MAO activity, putative biological markers of major depression, were investigated in elderly medical outpatients with primary major depression (DSM-III-R;n=18, 72yr±7SD), in patients with depression secondary to medical illness (organic mood disorder, depressed;n=15, 75yr±8), and in controls (n=14, 73yr±10).  $B_{max}$  was decreased significantly in subjects with major depression compared to subjects with 2° depression and to controls (Tukey's p <.01), with no difference between 2° depression subjects and controls ( $F_{2,44}$ )=9.74, p<.001). K<sub>d</sub> (affinity) was not significantly different among the groups. MAO activity was increased in the 2° depression group (p<.05), but not in the major depression group ( $F_{2,41}$ )=4.38, p<.05). Medication status and medical diagnosis did not affect  $B_{max}$  results. A discriminant analysis confirmed that  $B_{max}$  and MAO activity were the only significant predictors. These results provide evidence for the relative specificity of platelet <sup>3</sup>H-imipramine  $B_{max}$  as a marker for primary major depression compared with depression secondary to medical illness, support the concept of biological heterogeneity in 2° depression, and extend the findings of decreased  $B_{max}$  values in two previous studies in non-medically ill depressed elderly patients to medically ill patients. (Schneider et al 1985, Nemeroff et al 1988).

#### NR154 PERSONALITY TRAITS IN RECOVERED DEPRESSED ELDERLY

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

Lon S. Schneider, M.D., Psychiatry, Univ of Southern Calif, 1934 Hospital Place, Los Angeles, CA 90033; Mary F. Zemansky, Ph.D., Vicki E. Pollock, Ph.D., Bruce R. Sloane, M.D., Ronald Gleason, M.D., Michael S. Bender, Ph.D.

### Summary:

Personality, social adjustment, and sensation seeking were assessed in euthymic, elderly subjects who had recovered from a major depressive episode (MDE) in order to identify dysfunctional patterns which may relate to risk for depression in late life. The structured clinical interview for *DSM-III-R* (SCID) was used to identify 20 subjects who had recovered from a MDE (mean 17 yr previously) and 30 controls without a past psychiatric history. Personality was assessed with the SCID-II, interpersonal relations with the Social Adjustment Scale SR (SAS), and sensation seeking with the Zuckerman Sensation Seeking Scale (SSS). Age (mean 64.4yr±6.8SD), marital state, living situation, Beck Depression Inventory (5.0 vs 3.9), Geriatric Depression Scale (3.9 vs 2.6), and Dysfunctional Attitudes Scale (101 vs 103) did not distinguish recovered subjects from controls. Recovered subjects had significantly more *DSM-III-R* dysfunctional personality traits than controls (17.7 vs 11.1; p < .02). Clusters B and C tended to distinguish the groups ( $F_{3.46} = 3.64$ , p < .02), particularly narcissistic (p < .02), borderline (p < .01), histrionic (p < .01), and passive aggressive (p < .02) traits. 8 subjects vs 3 controls met *DSM-III-R* criteria for at least one personality disorder (p < .05). Recovered subjects were more impaired on the SAS Social and Leisure Activity Subscale (p < .05) and showed greater experience seeking (p < .05) and socially disinhibited behavior (p < .01) on the SSS. These results indicate that recovered MDE subjects endure significant lifetime personality dysfunction, in the absence of depressive symptomatology, which may represent residue of past depression, a risk factor toward recurrence, or possibly, traits associated with recovery from a depressive episode.

# NR155

# TOPOGRAPHIC EEG'S IN RECOVERED DEPRESSED ELDERLY

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

Vickie E. Pollock, Ph.D., Psychiatry, Univ of Southern Calif, 1934 Hospital Place, Los Angeles, CA 90033; Lon S. Schneider, M.D., Bruce R. Sloane, M.D., Ronald Gleason, M.D.

### Summary:

Quantitative EEG measures are reported to distinguish depressed patients from normal controls, but it is unclear whether these characteristics persist beyond the patients' clinically depressed mood states. In this report, topographic EEG parameters are used to compare elderly subjects with and without past histories of a major depressive episode. The structured clinical interview for *DSM-III-R* (SCID) was used to identify 18 euthymic, physically healthy subjects who had recovered from a major depressive episode and 18 controls without a past psychiatric history, matched for age, sex, and handedness. A Neuro Science Brain Imager was used to acquire EEG amplitudes from 28 scalp sites, while subjects relaxed with their eyes closed.

Analyses revealed that topographic alpha amplitudes of recovered depressed subjects were significantly greater than those of controls, but the groups did not differ in delta, theta, or beta activity. These results are conceptually consistent with prior studies in which the waking EEG characteristics of actively depressed patients have been compared to control subjects, and suggest that increased alpha amplitude may function as a trait marker associated with major depression.

### NR156 GLYCOPYRROLATE VERSUS ATROPINE IN POST-ECT AMNESIA

Barbara R. Sommer, M.D., Psychiatry, Univ of California, 401 Parnassus Avenue Box 39C, San Francisco, CA 94143; Andrew Satlin, M.D., Loren M. Friedman, M.S., Jonathan O. Cole, M.D.

### Summary:

Although the mechanism of electroconvulsive therapy (ECT)-induced amnesia is unknown, the cholinergic system in the brain has been implicated in other disorders of cognition. For example, atropine, the APA-recommended preanaesthetic for ECT patients is a centrally acting anticholinergic drug known to cause amnesia, confusion, and delerium. Our hypothesis was that atropine may further exacerbate amnesia and/or confusion resulting from ECT, and that a peripherally acting preanaesthetic such as glycopyrrolate would by comparison decrease these side effects.

We randomly administered glycopyrrolate versus atropine in equivalent doses as the preanaesthetic agent to 20 consecutively admitted patients with major depression, for whom ECT was the clinical treatment of choice. Patients were matched for age, Hamilton Scale for Depression (Ham D), and baseline performance on the verbal Learning Task of Buschke. We found no significant difference in outcome between patients treated prior to ECT with glycopyrrolate versus atropine, as measured by scores of retrieval, recognition, or storage on the Buschke and on the Mini-Mental State Exam. Both groups had large and nearly identical improvement on the Ham D.

These results may be interpreted as follows: (1) either our testing was not sensitive enough or the number of patients not great enough to detect differences in the two drugs' effects; (2) during the seizures induced by ECT, even glycopyrrolate is able to penetrate the blood brain barrier in sufficient quantities to be as deleterious as atropine; or (3) the mechanism of cognitive impairment does not involve acetylcholine.

### NR157 BIPOLARITY AND HIGH ACHIEVEMENT: A FAMILIAL ASSOCIATION

William H. Coryell, M.D., Psychiatry, Univ of Iowa, 500 Newton Road, Iowa City, IA 52242

### Summary:

Previous studies have inconsistently shown links between high social class, creativity or "genius" and affective disorder, particularly bipolar affective disorder. Almost all studies have been proband focussed, however; few data exist to describe familial links between bipolar illness and achievement.

The NIMH Collaborative Study on the Psychobiology of Depression—Clinical Branch evaluated 442 non-bipolar, 64 bipolar II, and 88 bipolar I probands as they presented for treatment at any one of five tertiary care centers. Although bipolar II males exhibited relatively high levels of occupational achievement, there were otherwise no significant group differences in educational or occupational achievement among probands. The 273 interviewed relatives of bipolar I probands exhibited substantially higher levels of educational and occupational achievement than did the 1028 interviewed relatives of non-bipolar probands. This advantage was particularly striking for the female relatives. Ratings for the 165 interviewed relatives of bipolar II probands were intermediate. Moreover, these relationships held for both affected and unaffected relatives.

### NR158 PROGNOSIS OF MAJOR DEPRESSION IN THE COMMUNITY

# Wednesday, May 11, 12 noon-2:00 p.m.

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

J. Kent Sargeant, M.D., Clin Gen EPI, NY Psychiatric Inst, 722 West 168th Street Box 14, New York, NY 10032; Martha L. Bruce, Ph.D., L. Florio, M.S.

# Summary:

Evidence from outcome studies of Major Depression indicates a high frequency of relapse and chronicity, and that prior chronicity, recurrent episodes, and the presence of psychosocial stressors are associated with poor outcome(1). The generalizability of these findings, however, is limited for two reasons: 1. Most investigations have focused on treated samples and so may be biased towards more chronic or severe illness. 2. Community studies have also selected from special populations(2), restricting the clinical applicability of findings. The Epidemiologic Catchment Area (ECA) study offers the opportunity to investigate prognosis in depression without these problems. In surveying a large probability sample of the general population with a standardized diagnostic instrument (the DIS) at two points in time, prognostic factors may be identified independent of treatment status. In this study, ECA subjects with a *DSM-III* diagnosis of Major Depressive Disorder at first interview (n=423) were categorized according to their diagnostic status one year later. The results confirmed a high rate of non-recovery, particularly among women over 30 where 28% were depressed after one year. In contrast, for women ages 18–29 and men of all ages the rate of Major Depression was 15%–17%. Comorbidity and symptom patterns also differentiated outcome groups. The implications of these results for understanding the natural history of Major Depression are discussed.

### **BRAIN CT FINDINGS IN LATE-ONSET DEPRESSION**

George S. Alexopoulos, M.D., Psychiatry, Cornell Univ Med Coll, 21 Bloomingdale Road, White Plains, NY 10605; Robert C. Young, M.D., Robert C. Abrams, M.D., Charles A. Shamoian, M.D.

### Summary:

Depressives with onset of first episode in late life (LOD) have less family history of affective disorder than depressed patients with earlier onset (EOD). This suggests that other factors play a more important pathogenetic role in LOD. Earlier we observed an association between LOD and dementing disorders. We, now, hypothesize that brain CT scan measures distinguish LOD from geriatric EOD.

Geriatric psychiatric inpatients (N=63) with primary major depression or primary degenerative dementia were studied. Diagnosis was assigned by two psychiatrists using DSM-III criteria. All the subjects were older than 60 years of age. Non-contrast brain CT scans were performed with an Elscint-Exel 2002 CT scanner. Depressed patients with onset of illness at age 60 years or older (LOD; N=26) had greater ventricular-brain ratio (VBR) (P < 0.05), and more cortical atrophy (CA) (P < 0.05) than geriatric depressives with earlier age of illness onset (EOD; N=16). EOD patients had lower VBR (P < 0.004),  $V_3R$  (P < 0.02) and CA (P < 0.0001) than subjects with primary degenerative dementia (PDD; N=21). There were no differences in CT measures between LOD and PDD patients.

The findings suggest that brain changes play an important role in LOD. The association between brain CT findings and depression may be biologically meaningful since we have observed relationships between VBR and post-dexamethasone plasma cortisol and VBR and response to antidepressant treatment.

#### **NR160** CAFFEINE AUGMENTATION OF ECT

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

C. Edward Coffey, M.D., Psychiatry, Duke Medical Center, Box 3920, Durham, NC 27710; Gary S. Figiel, M.D., Richard D. Weiner, M.D., Terry Clark, M.D., Martha Cress, R.N.

### Summary:

A decline in seizure duration occurs frequently during a course of ECT and may result in brief or missed seizures and limited clinical benefit. In a series of open clinical studies we have demonstrated that pretreatment with caffeine i.v. is an effective and safe technique for maintaining the duration of ECT-induced seizures. We now describe the results of a randomized, double-blind, placebo-controlled study which confirms and extends our original findings.

Results: In contrast to placebo, the use of caffeine allowed ECT to be administered without any increase in stimulus intensity during the therapy. There were no differences between the placebo and caffeine groups, however, with respect either to clinical response or mean seizure durations. In general, caffeine was well-tolerated and there were no adverse cardiovascular effects; the major side effect was transient anxiety.

By allowing a course of ECT to be administered at significantly reduced stimulus intensities, caffeine may lessen the potential for encephalopathic side effects from the therapy. Data on this issue will be discussed. The observation that caffeinemodified ECT was therapeutically effective even at reduced stimulus intensities may have important theoretical implications for the mechanism of action of ECT.

#### NR161 Wednesday, May 11, 12 noon-2:00 p.m. UNILATERAL VERSUS BILATERAL ECT: LONG-TERM MEMORY FOLLOW-UP

Richard D. Weiner, M.D., Psychiatry, Duke University, Psych Service (116-A), Durham, NC 27705; C. Edward Coffey, M.D., Jonathan Farber, Ph.D., Rebekka Arias, B.S., Jonathan Davidson, M.D.

### Summary:

Although it is widely recognized that unilateral nondominant electrode placement (UL) is associated with less memory impairment than bilateral electrode placement (BL), the persistence of these differences following ECT has been unclear. Previously, we reported the presence of greater autobiographic memory loss with BL ECT for as long as six months following completion of the ECT course. The present investigation was designed to corroborate and extend these findings in a new population. As part of a larger study, 39 right-handed melancholic inpatients were randomly assigned to either UL or BL ECT. Subjects were tested prior to ECT and at two or three days and both one and six months post ECT, using a variety of outcome measures. UL ECT was associated with better memory function on objective testing than was BL ECT at all follow-up intervals. At six months post ECT, measures of retrograde memory function (i.e. covering material learned prior to ECT) continued to show evidence of such differences (famous events and autobiography memory recall [p=0.005, 0.03]). In contrast to these memory effects, no intergroup differences were observed in terms of therapeutic response. The significance of these findings will be discussed, particularly in regard to the subjects' own perceptions of memory function post ECT, as well as their attitudes concerning this treatment modality.

#### NR162 SEASONALITY AND PHOTOTHERAPY IN THE GENERAL PUBLIC

Siegfried Kasper, M.D., Clinical Psychobiology Br, Natl Inst of Men Hlth, 9000 Rockville Pk B110 Rm 4S239, Bethesda, MD 20892; Susan L. B., Rogers, R.N., Thomas A. Wehr, M.D., Pamela A. Madden, M.S., Norman E. Rosenthal, M.D.

### Summary:

In a survey conducted in Montgomery County, Maryland we administered a telephone version of the SPAW (Seasonal Pattern Assessment Questionnaire, Rosenthal et al., 1986) to 416 people called at random from a computer-generated list of telephone numbers (completion rate 92%). We found that 92% of the population noticed seasonal changes of mood and behavior to varying degrees. These changes included energy (66% of the population), mood (6%), social activity (60%), weight (47%), appetite (47%) and sleep (42%). 68% of the population reported seasonal changes in food preference, with 81% indicating a preference for starchy foods and 66% a preference for sweet foods in the winter. 94% of the population expressed a preference for high-protein foods in the summer months. For 27% of the population seasonal changes were a problem and approximately one-third (8% of the total population) of this group rated it as marked, severe or disabling, a degree of impairment equivalent to that of patients with seasonal affective disorder (SAD). The seasonal pattern of "feeling worst' revealed a bimodal distribution with a greater winter and a substantially lower summer peak. To establish a bridge between the clinical and epidemiological literature on SAD, 40 subjects from this representative sample of the Montgomery County population have been selected at random and invited to participate in a study of the efficacy of light therapy. In order to determine whether phototherapy (two hours of bright light in the morning) is effective in an unselected population not seeking treatment, we are investigating the responses of 20 subjects with varying degrees of seasonal changes (from mild to severe) in mood and behavior in winter. A control group (n=20) matched for the degree of seasonality, age and sex is being treated with dim light. We will present the results of the epidemiological survey and this ongoing treatment study. We predict that the propensity to respond to bright light is a continuous variable dependent on the degree to which an individual is adversely affected by the change of the seasons.

#### NR163 FAMILIAL ASSOCIATION BETWEEN ADD AND MDD

### Wednesday, May 11, 12 noon-2:00 p.m.

Joseph Biederman, M.D, Child Psych, Mass General Hospital, 15 Parkman St ACC-625, Boston, MA 02114; Stephen Faraone, Ph.D.

### Summary:

The purpose of this analysis is to examine the possible etiologic relationship between ADD and MDD. If ADD and MDD share common genetic determinants, several testable predictions follow 1) the frequency of MDD among the relatives of patients with ADD should be significantly higher than the rate in relatives of not-ill comparison children or population rates; 2) The risk of MDD should be the same among the relatives of probands with and without MDD, unless ADD+MDD represents a genetically distinct form of the disorder. The study population consisted of Caucasian non-Hispanic males derived from the same outpatient hospital setting. The ADD study population consisted of 73 consecutive outpatient referrals. ADD subjects met the following inclusion criteria: (i) Age, 6-17; (ii) Sex, Male; (iii) Diagnosis, Attention Deficit Disorder according to DSM-III confirmed by a structured psychiatric interview with the mother; (iv) Full scale IQ above 70. The normal comparison group consisted of 26 non-adopted, Caucasian, non-Hispanic, healthy children and adolescents of comparable age and socioeconomic status (SES), screened for absence of medical or psychiatric disorders. Only biological relatives and full siblings were included. Raters were blind with respect to the clinical status of the probands. Psychiatric assessments of probands and their siblings were based on interviews with the mothers using the DICA-P, and of parents were based on direct interviews with both parents using the NIMH-DIS to cover adult disorders and an addendum based on the DICA-P to cover childhood disorders. Only definite diagnoses were used to determine rates of disorders. The familial risk analyses was estimated using the Kaplan-Meier estimate from survival analysis. In addition, specific hypotheses about familial transmission were tested using loglinear models. Twenty-six percent (N=19) of ADD probands had comorbid MDD. To test the study predictions, we separated the families into two groups, those with (ADD+MDD) and those without (ADD+MDD) comorbid MDD. We found that the risks for ADD (morbidity risk (MR)=15% and 28% respectively) and for MDD (MR=20% and 28% respectively) significantly differed from those of relatives of normal comparison children (MR=5% and 4% for ADD and MDD respectively), and that the two traits did not cosegregate within families. These findings support the hypothesis that ADD and MDD share common vulnerabilities and suggest that ADD with comorbid MDD may represent a different expression of the same etiologic factors responsible for the manifestation of ADD.

### NR164 TRYTOPHAN DEPLETION ALTERS MOOD IN DEPRESSION

Pedro L. Delgado, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06508; Lawrence Price, M.D., Dennis S. Charney, M.D., George K. Aghajanian, M.D., Harold Landis, George R. Heninger, M.D.

### Summary:

Reduction of dietary tryptophan (TRP) decreases plasma TRP, brain TRP and brain serotonin (5-HT) in laboratory animals. In humans it produces mild impairment of attentive performance, reports of negative mood, enhancement of the prolactin response to I.V. TRP, and reduction of CSF 5-HIAA. This study investigates the effects of TRP depletion on mood in depressed patients before and after antidepressant treatment. Method: A 24-hour, 160 mg/day, low-TRP diet followed the next morning by a TRP-free amino acid drink (TFD) was administered in balanced, placebo-controlled fashion (within subject) to 16 patients (nine depressed, drug free, seven remitted on antidepressant) to acutely lower plasma TRP. Ratings of mood and plasma for free and total TRP were obtained at 9 am before starting the diet, 15 minutes prior to the drink, and three, five, and seven hours after. Normal TRP intake began eight hours after the drink. Ratings were obtained at 12 pm the next day. Four patients were tested single-blind, the rest double-blind. Results: Total and free TRP decreased 92% and 95% five hours following the TFD (p < .0001 and p < .004). Ratings of mood did not change the day of the TFD, but seven of nine depressed patients demonstrated a mean decrease in Hamilton Depression Scale score of 50% (25%-74%) the day following the TFD. Five of seven remitted depressed patients relapsed two to seven hours after the TFD with gradual (48-72 hours) return to remitted state. Discussion: TRP deprivation may alter the function of the 5-HT system, leading to rapid improvement of depressive symptoms upon resuming normal TRP intake. Relapse of remitted patients suggests the therapeutic effects of some antidepressants may depend on maintenance of 5-HT availability. Acute TRP depletion is a useful method with which to evaluate 5-HT function in humans.

### NR165

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

# EFFECTS OF THYMOLEPTIC DRUGS ON SEROTONIN FUNCTION

Lawrence H. Price, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06508; Dennis S. Charney, M.D., Pedro L. Delgado, M.D., George R. Heninger, M.D.

### Summary:

Serotonergic (5-HT) function may be abnormal in affective disorders, since depressed patients show blunted prolactin (PRL) responses to the 5-HT precursor, i.v. tryptophan (TRP). Long-term treatment with the tricyclic antidepressants (TCAs) desipramine (DMI) and amitriptyline, and short- and long-term treatment with the monoamine oxidase inhibitor (MAOI) tranylcypromine, enhance net PRL responses in depressed patients. We used the PRL response to i.v. TRP to assess the effects of short- and long-term treatment with several thymoleptic drugs on 5-HT function in affective disorder patients. Methods: A total of 84 patients, most with DSM-III major depression, participated. After a minimum 2 weeks of placebo (>3 weeks drugfree), patients received TRP 7 grams i.v. Samples for plasma PRL were obtained at intervals before and after the TRP infusion. The test procedure was reported after  $\sim$ 1 week and after  $\sim$ 3 weeks of treatment with lithium (LI) (n=23), DMI (n=25), or the selective 5-HT reuptake inhibitor fluvoxamine (FLUV) (n=36). Results: As in previous studies, TRP increased PRL. The PRL response was enhanced after short-term, but not long-term, LI treatment. DMI enhanced the PRL response after long-term, but not short-term, treatment. FLUV markedly enhanced the PRL response after both short- and long-term. Conclusion; These findings are consistent with evidence that enhancement of 5-HT function may be a necessary, but not sufficient, condition for efficacy for some antidepressant drugs, such as TCAs, MAOIs, and 5-HT reuptake inhibitors. Homeostatic responses of the 5-HT system to long-term LI treatment may limit that drug's antidepressant efficacy. The mechanism of action of atypical antidepressants that do not enhance the PRL response, such as trazodone and mianserin, remains to be determined.

### NR166 SAD: VARIED SCHEDULE PHOTOTHERAPY AND CATECHOLAMINES

Janis L. Anderson, Ph.D., Psychiatry, Harvard Medical School, Mass Mental Hlth, 74 Fenwood Rd, Boston, MA 02115; Russell G. Vasile, M.D., Kerry L. Bloomingdale, M.D., Joseph J. Schildkraut, M.D.

### Summary:

Phototherapy for 2 weeks with >2000 lux incandescent light on a varying schedule (1 h at morning, noon, or night changing from day to day at the patient's convenience), is being compared to a morning schedule (1 h between 6–8 am) in randomly assigned, unmedicated outpatients with fall/winter Seasonal Affective Disorder (SAD). Clinical state is assessed before and after phototherapy, by raters blind to treatment group, using the 21-item Hamilton Rating Scale for Depression (HRSD) and, since the time it became available, the SIGH-SAD1, which adds ratings of specific symptoms of SAD not reflected on the HRSD. All patients had pretreatment HRSD scores  $\geq$  10 and SIGH-SAD scores  $\geq$  16.

Both schedules of phototherapy have been effective in treating SAD. Mean SIGH-SAD scores to date are: morning schedule pretreatment  $23.03\pm2.1$ , posttreatment  $12.3\pm3.4$ , n=6, P<.001; varying schedule—pretreatment  $21.5\pm2.6$ , posttreatment  $5.3\pm2.7$ , n=4, p<.01. Mean HRSD scores (n=12) showed similar changes. An additional patient became hypomanic on the varying schedule.

Preliminary data on urinary catecholamines and metabolites assayed in 3 daily 24-h urine collections are currently available in a limited sample of SAD patients. Some of these patients show low urinary MHPG and NE, similar to values previously observed in patients with Bipolar I Depression; but in contrast to Bipolar I depressions, low scores on a discriminant function equation (D-type scores)<sup>2</sup> based on urinary catecholamines and metabolites, were *not* found in these SAD patients. Catecholamine data from the entire preliminary sample of SAD patients, however, are similar to data from patients with Bipolar II or Unipolar Endogenous nonseasonal depression. Further clinical and biochemical data are currently being collected and will be presented.

# NR167

# PLASMA MHPG IN MAJOR DEPRESSIVE DISORDER

### Wednesday, May 11, 12 noon-2:00 p.m.

Larry J. Siever, M.D., Psychiatry, Bronx VA Med Ctr, 130 W. Kingsbridge Road, Bronx, NY 10468; Emil F. Coccaro, M.D., Kim Owen, M.D., Richard Kavoussi, M.D., Richard C. Mohs, Ph.D., Ren-Kuy Yang, M.D., Peter J. Knott, Ph.D., Kenneth L. Davis, M.D.

# Summary:

In order to evaluate possible abnormalities in the noradrenergic system in depression plasma, 3-methoxy-4-hydroxyphenylglycol (MHPG), a major noradrenergic metabolite, was measured at hourly intervals over an eight-hour period under basal conditions and/or over three hours in response to the  $\alpha$ -2-adrenergic agonist clonidine in 45 acutely depressed patients, 24 remitted depressed patients and 26 age- and sex-matched controls. Under basal, resting conditions, the acute depressed patients showed an earlier MHPG peak (13:08±2.43 hours.) in comparison to normal controls (15.32±2.27 hours), with remitted patients peaking close to the normals (14.54±1.36 hours) (f=5.2, p <0.01). Although mean plasma MHPG at 10 hours did not differ between groups, the variance between acute depressed individuals was also greater than in the remitted patients and normal controls (F-test, p <0.05). The percent MHPG fall in response to clonidine was reduced in the acute depressed patients (0.8±10.9%) compared to normal controls (9.6±10.7%), with remitted patients close to normal controls (8.3±11.3%). These results suggest a state-dependent disturbance in the regulation of release/metabolism of norepinephrine.

### NR168 FAMILY HISTORY OF DEPRESSED PERSONALITY DISORDERS

# Wednesday, May 11, 12 noon-2:00 p.m.

Jeremy M. Silverman, Ph.D., Psychiatry, Bronx VAMC-116A, 130 W. Kingsbridge Road, Bronx, NY 10468; Larry J. Siever, M.D., Lynn Pinkham, M.A., Steven Greenwald, M.A., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

# Summary:

This study investigated a possible increased risk for major affective disorder (MAD) in 134 1° relatives of 30 personality disorder (PD) probands with a history of RDC or *DSM-III* depression compared to 82 1° relatives of 16 PD probands with no depression. Multiple family informants were blindly interviewed using the Family History RDC to assess MAD and axis I schizophrenia-related disorders in relatives; supplementary criteria were used to assess affective, impulsive and schizophrenia-related personalities. The morbid risk for MAD to relatives of depressed PD probands was 27.6% compared to 7.5% among relatives of nondepressed PDs (p < .01). The risk for schizophrenia-related personality was also significantly increased among relatives of depressed PDs (11.2% v. 1.5%, p < .05), though this disorder was clustered in relatives of the two probands groups for affective and impulsive personality or for axis I schizophrenia-related disorders. Furthermore, there were no significant differences in risk for depressed of depressed non-borderline PDs (23.0%); both groups of relatives showed significant increases (p < .05) compared to the relatives of non-borderline PDs (5.0%). These data suggest that the frequently reported increased risk for MAD to relatives of depressed personality disorder patients.

### NR169 FENFLURAMINE CHALLENGE IN MAJOR DEPRESSION

EFFECT OF ECT ON BETA-ADRENERGIC RECEPTORS

Michael D. De Meo, M.D., Psychiatry, NY Hospital Cornell, 525 East 68th Street, New York, NY 10021; P. Anne McBride, M.D., J. John Mann, M.D., John Keilp, M.S.

### Summary:

Introduction: Alterations in central serotonergic (5-HT) systems in depression and suicide are suggested by CSF, neuroendocrine and postmortem brain studies. Serotonergic stimulation increases prolactin (PRL) secretion. *Methods:* We studied central serotonergic responsivity in 26 medication-free inpatients with Major Depression and 26 healthy controls by assessing plasma PRL levels prior to and following the 5-HT releaser/agonist fenfluramine (FEN:60 mg, PO) and placebo. *Results:* Peak FEN-induced PRL response correlated negatively with age in controls (r=-.52, p < .007) and the decrease appeared to occur sharply around age 30 (<30yrs: PRL=22.7 $\pm$ 9.5, n=12;  $\geq$ 30 yrs:PRL=68 $\pm$ 3.5 ng/ml, n=14; p < .000). A significantly smaller decrease in peak PRL response after age 30 was observed in the depressed subjects (ANOVA F=11.6, df=1,44;p <.001). Among subjects under age 30 mean peak PRL response was blunted in depressed patients compared to controls (PRL=14.0 $\pm$ 66, n=9 vs PRL=22.7 $\pm$ 9.5 ng/ml, n=12; p < .03). There were no significant differences in mean peak PRL responses between older depressives and controls or between suicide attempters and nonattempters in each age group. *Conclusions:* There appears to be a significant age effect on PRL response to FEN challenge. Diminished FEN-induced PRL response observed in our younger depressed patients is consistent with decreased central 5-HT function in Major Depression. Characteristics of the depressed groups, correlations with psychopathology measures and their implications will be discussed.

### NR170

### Wednesday, May 11, 12 noon-2:00 p.m.

John C. Mahler, M.D., Psychiatry, NY Hospital Cornell, 525 East 68th Street, New York, NY 10021; James P. Halper, M.D., Richard P. Brown, M.D., Michael De Meo, M.D., John A. Sweeney, Ph.D., J. John Mann, M.D.

### Summary:

Introduction: Animal studies have demonstrated induction of subsensitivity in central beta-adrenergic receptors after repeated electroconvulsive shocks, and investigators have postulated that this effect may mediate the antidepressant action of ECT. We have previously found decreased responsivity of lymphocyte beta-adrenergic receptors in patients with endogenous depression and psychomotor agitation. This study examined the effects of ECT on lymphocyte beta-adrenergic receptor function. *Methods:* Unmedicated, physically healthy patients with major depressive disorder (MDD) 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:* Preliminary results indicate that isoproterenol-generated cyclic-AMP levels were significantly lower (4.95 versus 9.58, p < 0.035) in five patients following a course of ECT. ECT produced a pronounced improvement in the patients' clinical condition; pretreatment Hamilton Depression Scale mean of 37.6 versus posttreatment mean of 7.0. *Conclusion:* ECT has qualitatively similar effects on lymphocyte beta-adrenergic responsivity in patients with MDD as has been reported in rodent brain. The implications of the finding will be discussed.

# NR171 AUTORADIOGRAPHY OF BRAIN 5-HT2 BINDING IN SUICIDE

Victoria Arango, Ph.D., Psychiatry, Cornell Univ Med Col, 411 E 69th Street, New York, NY 10021; Paul Ernsburger, Ph.D., Peter M. Marzuk, M.D., D.J. Reis, M.D., J. John Mann, M.D.

### Summary:

There is a 28% increase in the number of  $5-HT_2$  binding sites in frontal cortex homogenates of suicide victims (1). Since there are reduced brainstem levels of the 5-HT metabolite 5-HIAA, the results may represent postsynaptic receptor up-regulation secondary to reduced presynaptic serotonergic activity. Using quantitative autoradiography, we sought to determine whether the increased receptor number in frontal cortex was localized to specific cortical layers and restricted to frontal cortex.

Slide-mounted sections (15  $\mu$  m) of prefrontal (PFC) and temporal (TC) cortex of suicide victims and matched controls (PFC N=8 pairs, TC N=5 pairs) were incubated in 2nM <sup>125</sup>I-LSD for 90 minutes. Nonspecific binding was determined by 5  $\mu$  M ketanserin. Autoradiograms were exposed (9–15h) with <sup>3</sup>H-standards calibrated for <sup>125</sup>I and quantified by computer-assisted image analysis.

In PFC and TC of both groups 5-HT<sub>2</sub> receptor binding differed between cortical layers: intermediate > outer, inner (repeated measures MANOVA p <0.01). In all cortical layers TC had greater binding than PFC. An increase in 5-HT<sub>2</sub> receptor binding was found in suicide brains compared to controls. This increase varied between regions: in PFC the binding in suicide brains was 44% above controls while in TC was 22% above. The increased binding in individual layers of PFC, and across all cortical layers, was significant (p < 0.01). In TC the increase in 5-HT<sub>2</sub> receptors was significant across all cortical layers (I–VI, p < 0.01) and in the outer layers (I–II, p=0.02). There was no difference in <sup>125</sup>I-LSD binding to white matter between the suicide and the control groups.

We conclude that a) 5-HT<sub>2</sub> receptors are differentially distributed across cortical layers, b) there are regional differences in 5-HT<sub>2</sub> receptor binding, c) 5-HT<sub>2</sub> receptors are increased in the gray matter of PFC and TC of suicide victims compared to controls, and d) this increase may be unequal between cortical regions.

# NR172

# SINGLE VISIT DEXAMETHASONE SUPPRESSION TEST

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

Naveed Iqbal, M.D., Psychiatry, Albert Einstein Col Med, 15000 Waters Place, Bronx, NY 10461; Gregory M. Asnis, M.D., Jill Friedman, Ph.D., Herman M. van Praag, M.D.

### Summary:

Although originally thought to be a highly specific test for the diagnosis of Major Depressive Disorder (MDD) it is now clear that the traditional Dexamethasone Suppression Test (DST) is rather not so specific. Various factors appear to influence the DST such as stress, dose of dexamethasone, time of administration, compliance and the bioavailability of dexamethasone. To avoid these problems such as acute stress of venepuncture and pharmacokinetic differences several hours later, we modified the traditional DST in an attempt to look at the acute effects of dexamethasone within one halflife. The SVDST is an afternoon procedure (12–5 PM). An angiocatheter was inserted in a forearm vein at 1200 hours with sampling of plasma cortisol every 30 minutes; at 1300 hours, 1 mg. dexamethasone (elixir) or placebo was given. The cortisol results on eleven normal controls (M=9, F=2), ages (20–23 years old), were analyzed by repeated measures ANOVA, showing significant test by time interaction F (8,80)=10.38, p < .001. Significant differences between active versus placebo were noted 60 minutes post dexamethasone administration (P < .05). This suggests that dexamethasone can suppress cortisol acutely during day-light hours. Data with different dosages on controls and patients will also be presented.

### NR173 LONG-TERM FOLLOW-UP OF TREATED CHRONIC DEPRESSIVES

Bruce M. Sutton, M.D., Psychiatry, Payne Whitney Clinic, 525 East 68th Street, New York, NY 10021; James H. Kocsis, M.D., Allen J. Frances, M.D.

### Summary:

*Goal:* We recently reported the first placebo controlled trial demonstrating the short-term efficacy of imipramine for outpatients with chronic depression. The current report is of a follow-up on patients entered into the above controlled trial to investigate long-term implications of the acute response to treatment. The specific hypothesis tested was that imipramine responders would continue to have a more favorable long-term outcome than nonresponders or patients who had not completed an adequate medication trial.

*Method:* Follow-up was "naturalistic" in design and employed a structured clinical interview. Mean follow-up interval was 3.5 years. Groups compared were imipramine responders (n=9) versus imipramine nonresponders, placebo nonresponders and drop-outs (n=16).

*Results:* The majority of imipramine responders continued on imipramine throughout the follow-up interval and as a group had a significantly better clinical course compared to the nonresponding group (p=.01). On follow-up none of the imipramine responders met criteria for *DSM-III* Dysthymic Disorder while 75% of those in the other groups continued to be dysthymic (p=.005). Eighty-nine percent of the imipramine responders still met the stringent criteria for "recovery" as defined in the original medication trial compared to 12% in the comparison group (p=.005). Imipramine responders also fared significantly better at follow-up on a variety of measures of depression, global severity of illness, and social/vocational functioning.

Significance: These results support a favorable long-term outcome in chronic depressive patients who have responded to antidepressant medication. This is important because many of these patients were previously considered to be "characterologic" and had received extensive psychotherapy but very limited drug therapy. The theoretical and clinical implications of these findings will be discussed.

#### NR174

### Wednesday, May 11, 12 noon-2:00 p.m.

### FIVE- TO SEVEN-YEAR FOLLOW-UP OF LATE-LIFE MANIA

Upma Dhingra, Psychiatry, Johns Hopkins, Meyer 279 600 N. Wolfe St., Baltimore, MD 21205; Peter V. Rabins, M.D.

### Summary:

We were able to obtain five- to seven-year follow-up information on 38 of 42 patients 60 years and older who had been hospitalized for mania. Thirteen (34%) had died. Twenty-three of the 25 still alive were examined. Sixteen (70%) reported at least one episode of affective disorder requiring rehospitalization. Five (13%) scored 24 or below on the Mini Mental State Exam indicating that they had become demented. Patients with onset of bipolar disorder before age 45 were more likely to have a family history of affective disorder than those with onset after 44 (p=.03). Age of onset of affective disorder or of mania was unrelated to becoming demented, having a relapse or having died.

These patients were compared to 38 patients with unipolar depression who were 60 years old or older and were hospitalized during 1982. The bipolar and unipolar patients were similar demographically and had similar fatality rates and rates of dementia. Bipolar patients had an earlier mean age of onset (p=.04).

These results demonstrate that bipolar disorder in late life has the same prognosis as unipolar depression. There is little evidence that mania first occurring after age 60 is a precursor to dementia.

### MELATONIN ADVANCES CIRCADIAN RHYTHMS IN HUMANS

Robert L. Sack, M.D., OHSU, 3181 Sam Jackson Park Road, Portland, OR 97201; Alfred J. Lewy, M.D.

### Summary:

We administered melatonin 5 mg orally at bedtime to totally blind people with free-running rhythms (circadian periods greater than 24 hours) in an attempt to entrain them to a 24-hour day. *Methods:* Five men (average age 35.4 years), who were in good health but without any light perception, had blood drawn hourly for 24 hours once every one to two weeks. Plasma melatonin was measured by a gas chromatographic negative ionization-mass spectrographic method. The onset of melatonin production was used to determine circadian phase position on each sampling day, and the period of the melatonin rhythm was determined by fitting a regression to the successive melatonin onset. Melatonin was administered in a single-blind, placebo-controlled trial (5 mg at bedtime for three weeks). Throughout the study, the subjects had full access to social cues, slept at night and were awake during the day. *Results:* All five subjects had free-running melatonin rhythms during the pretreatment period (average circadian period: 24.6±0.6 h). After three weeks of treatment, the endogenous melatonin rhythm, had advanced three to 12 hours in four of the five subjects. Following active treatment, their circadian rhythms reverted to the previous free-running period. Melatonin was well-tolerated by all the subjects. *Discussion* Melatonin previously has been shown to entrain the activity rhythms of free-running rodents. Although we have not yet been able to entrain free-running rhythms in blind people, we have been able to show that melatonin has significant chronobiologic activity in humans. Melatonin holds promise as a treatment for symptoms arising from abnormal circadian rhythms such as jet lag, shift work syndrome and certain sleep and mood disorders.

### NR176

# RISK FACTORS FOR DSM-III DEFINED DEPRESSIONS IN WOMEN

### Wednesday, May 11, 12 noon-2:00 p.m.

Alan J. Romanoski, M.D., Psychiatry, Johns Hopkins Univ, 600 N Wolfe St Meyer Bldg 4-119, Baltimore, MD 21205; Gerald Nestadt, M.D., Marshal F. Folstein, M.D., Ernest M. Gruenberg, M.D., Paul R. McHugh, M.D.

### Summary:

This paper describes the prevalence of specific *DSM-III* depressive disorders in the adult, female household population in Eastern Baltimore, as well as several putative risk factors for their development. These findings differ from other available data on risk factors for the development of depression in women in that they are based on standardized clinical examinations performed by psychiatrists who ascertained specific *DSM-III* depressive disorders, as opposed to data based on question-naires or depression-assessment scales not specific to a clinical diagnostic system.

Four specially selected and trained research psychiatrists examined a multi-stage stratified probability sample (N=512) (75% completion rate) of 95,500 female Eastern Baltimore residents over 18 years of age for which they had no clinical responsibility. Their mission was to identify each woman's *DSM-III* defined disorder after conducting a Standardized Psychiatric Examination (SPE) which averaged two hours in duration. The SPE format and record was developed as a validation study of the NIMH Diagnostic Interview Schedule in the Eastern Baltimore site of the Epidemiologic Catchment Area studies, and included a systematic review of the family, developmental, psychosocial, and recent life event histories for each study subject.

By weighting the data on each subject according to the strata and response rates, and adjusting to the 1980 census, the authors present the first direct estimates of specific factors that place women at risk for the development of *DSM-III* depressive disorders in the U.S. Putative risk factors explored include employment status, presence of an intimate confidant, children living at home, income and antecedent life events.

### EPIDEMIOLOGY OF DSM-III DEPRESSIVE DISORDERS IN THE UNITED STATES

Alan J. Romanoski, M.D., Psychiatry, Johns Hopkins Univ, 600 N Wolfe St Meyer Bldg4-119, Baltimore, MD 21205; Gerald Nestadt, M.D., Raman Chahal, M.D., Marshal F. Folstein, M.D., Ernest M. Gruenberg, M.D., Paul R. McHugh, M.D.

#### Summary:

This paper describes the distribution of specific *DSM-III* depressive disorders in an adult household population in Eastern Baltimore. These findings are different from other available data in that they are based on standardized clinical examinations performed by psychiatrists to ascertain discrete *DSM-III* clinical entities (Major Depression, Dysthymic Disorder, Atypical Depression, Adjustment Disorder with Depression, Organic Affective Syndrome, Substance Affective Disorder, Bereavement), as opposed to data based on lay-administered schedules or clinician-administered interviews which do not lead to *DSM-III* categories of depressive disorder.

Four specially selected and trained research psychiatrists examined a multi-stage stratified probability sample (N=810) of 175,000 Eastern Baltimore residents over 18 years of age. Their mission was to identify each subject's *DSM-III* defined disorder after conducting a Standardized Psychiatric Examination (SPE) which averaged two hours in duration. The SPE format and record was developed as a validation study of NIMH Diagnostic Interview Schedule in the Eastern Baltimore site of the Epidemiologic Catchment Area Studies and included a systematic review of the family, developmental, psychosocial, and recent life event histories for each study subject. The SPE format also included a detailed psychosocial history review for each study subject. The psychiatrists had no clinical responsibilities for the study subjects. A 75% completion rate was obtained among designated respondents.

By weighting the data on each subject according to the strata and response rates and adjusting to the 1980 census, the authors present the first direct estimates of the age-, sex-, and race-specific rates for each of the DSM-III Depressive Disorders in the U.S., as well as data on risk factors for their development.

### NR178 ANTIDEPRESSANT RESPONSE IN AUTOIMMUNE THYROIDITIS

#### Wednesday, May 11, 12 noon-2:00 p.m.

John J. Haggerty Jr., M.D., Psychiatry, Univ North Carolina, CB# 7160 Medical School Wing B, Chapel Hill, NC 27599; Jerry Browne, M.S., Robert N. Golden, M.D., Cort Pedersen, M.D., Dwight L. Evans, M.D.

### Summary:

Symptomless autoimmune thyroiditis (SAT) occurs in 9%-20% of depressed patients. In order to test whether SAT affects response to antidepressant medication, we blindly evaluated treatment response by means of chart review in 44 euthyroid psychiatric inpatients receiving antidepressant treatment for *DSM-III* major depressive episode (MDE). Our sample included 7 patients with positive serum titers of either antimicrosomal or antithyroglobulin antibodies and 37 patients with negative titers. All received standard clinical treatment with antidepressant drugs for 2 or more weeks. Patients with antithyroid antibodies had a significantly lower mean response rating than did patients without antibodies (p<.05). Our data support previous findings indicating that relatively small decrements in thyroid reserve might adversely affect recovery from affective disorder.

### NR179

# NATURAL KILLER CYTOTOXICITY IN DEPRESSIVE ILLNESS

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

Ziad Kronfol, M.D., Psychiatry, Univ of Michigan, 1500 E. Med Ctr Dr UH 9C B0120, Ann Arbor, MI 48109; Kavita Goel, M.P.H., Joann Goodson, R.N., Madhavan Nair, Ph.D., Stanley Schwartz, M.D.

#### Summary:

Immunological abnormalities have frequently been observed in patients with psychiatric disorders. We have earlier reported a decrease in mitogen-induced lymphocyte proliferation in patients with depressive illness. Natural killer (NK) cytotoxicity has been reported to be impaired in patients with schizophrenia. We now report on NK cytotoxicity in patients with major depression.

We compared NK cytotoxicity to K562 target cells, using four different effector:target (E:T) ratios, in seven hospitalized depressed patients and seven age- and sex-matched normal controls. Depressed patients had a mean Hamilton score of 21.0. They all met RDC criteria for major depression. They were all drug-free for at least two weeks prior to immune testing. Both patients and controls were free of medical illness or drugs known to interfere with immune regulation. Fresh blood samples from patients and their respective controls were assayed simultaneously to control for day-to-day variation in the assay.

Mean percent NK cytotoxicity was lower in depressed patients compared to their matched controls for each of the E:T ratios investigated. These results were statistically significant (t=14.6; p<.001). Although still preliminary, these finding suggest an impairment in NK cytotoxicity in major depression. Mechanisms of immunosuppression should now be investigated.

# NR180 DEPRESSIVE NONSEASONAL RESPONSE TO BRIGHT LIGHT

Daniel F. Kripke, M.D., Psychiatry, Univ of Cal San Diego, M-003, La Jolla, CA 92093; J.C. Gillin, M.D., Daniel J. Mullaney, M.S.

### Summary:

Evening bright white light treatment has a significant antidepressant effect among hospitalized veterans with major depressive disorders. Thirty-four drug-free veterans with *nonseasonal* major depressions were randomly assigned to treatment with either bright (2000 lux) white light or dim red control light. Treatments were provided from 2000-2300 or from 1900-2200 for 7 evenings. After 5-7 days of treatment, the reduction from baseline in Hamilton Depression Ratings was significantly greater among the bright-light treated group (p < 0.05). Almost all patients treated with bright white light improved, whether their depressions were primary or secondary, and whether their depressions were endogenous or melancholic or neither. Considering the net improvement (active treatment benefit minus the improvement observed in the control group), benefits obtained with 1 week of evening bright light were about twice the benefits reported in the literature for one week of imipramine. Indeed, 1-week results with treatment of inpatients with bright light were similar to 4-week imipramine benefits. If these results can be replicated and extended, bright light may prove to be a valuable alternative treatment for hospitalized patients with major depressive disorders.

#### NR181 AGGRESSION SUICIDE CSF 5-HIAA AND FAMILY INSTABILITY

### Wednesday, May 11, 12 noon-2:00 p.m.

Gerald L. Brown, M.D., Biol Psych Branch, NIMH Bldg 10 RM 3N204, 9000 Rockville Pike, Bethesda, MD 20892; Peter F. Goyer, M.D., Danuta M. Lamparski, Ph.D., Markku Linnoila, M.D., Frederick K. Goodwin, M.D.

### Summary:

How aggressive and suicidal behaviors may be attributed to CSF 5HIAA levels as opposed to family instability was investigated in 36 inpatient military men (mean age,  $22.0 \pm 4.4$  yrs.) from whom aggression ratings, suicidal history, CSF 5HIAA, and histories of eight factors thought to be related to family instability were available. Data were subjected to parametric and nonparametric analyses as appropriate. Results indicated that mean ratings of aggressive history were significantly higher in those with suicidal history and lower levels of CSF 5HIAA. Those with mean aggressive ratings above a normal range (from a sample of age-matched, military males without a history of psychiatric difficulty) showed a significantly higher frequency of family instability factors. Further, those with a history of suicidal attempt had significantly lower levels of CSF 5HIAA and a significantly higher frequency of family instability factors; finally, levels of CSF 5HIAA, per se, were not significantly related to frequency of family instability factors. Thus, decreased CSF 5HIAA is not necessarily associated with increased family instability, but is associated with an increased likelihood of aggressive and suicidal behaviors; those individuals who are aggressive or suicidal usually do come from more unstable families. Low CSF 5HIAA or family instability alone may not necessarily predispose towards aggressive or suicidal behaviors, but, if both are present, the individual is considerably more at risk to evince destructive (toward others, property, or self) behaviors. Data will be further subjected to discriminant function analyses.

### NR182 COGNITIVE PERFORMANCE AND PERCEPTION IN LLPDD

# Wednesday, May 11, 12 noon-2:00 p.m.

Peter J. Schmidt, M.D., BPB, NIMH Bldg 10 Rm 3N238, 9000 Rockville Pike, Bethesda, MD 20892; Birgitta Both-Orthmann, Kari L. Muller, M.D., David R. Rubinow, M.D.

### Summary:

In order to investigate whether reported changes in cognition in LLPDD were a product of change in performance or perception, we administered the Raven Progressive Matrices to women with prospectively confirmed LLPDD (n=40) and asymptomatic controls (n=30) during the follicular (non-symptomatic) and late luteal (symptomatic) phases of the menstrual cycle. Additionally, at the time of testing all subjects completed visual analogue scales rating perceived performance, distractibility during testing, and perceived level of difficulty in completing the test. No significant differences were observed in performance between patients and controls, nor were differences observed in the patients' performance during the luteal phase compared with the follicular phase. However, significant differences were observed in the patients' perception of their performance during the luteal phase compared with the follicular phase (p<.01) that were not observed in the control group. In other words, patients reported that their performance was impaired and they were not distractible during the luteal phase testing. These findings compliment other evidence of luteal phase-related state-dependent changes in women with LLPDD including significant alterations of the perception of life events, body image, locus of control, and trait measures such as MMPI. The implications of these changes for future studies of LLPDD will be discussed.

### ABNORMAL SYMPATHETIC NERVOUS SYSTEM RESPONSES IN MDD

Philip J. Wilner, M.D., Psychiatry, New York Hospital, 525 East 68th Street, New York, NY 10021; Richard P. Brown, M.D., James P. Halper, M.D., John A. Sweeney, Ph.D., Katherine Johnson, R.N., J. John Mann, M.D.

### Summary:

Goals: Excessive Norepinephrine (NE) release has been found in Unipolar Depressed patients 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 and healthy controls rested supine for 30 minutes after insertion of IV catheter. EPI, NE, BP, and HR 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:* We found no difference in mean supine EPI levels in patients compared to controls. However, patients had a greater rise in EPI after three minutes of standing and controls had a greater rise from three to five minutes (p<.05). Patients and controls had the expected rise in HR upon standing but there was no statistically significant difference in HR between the two groups at any time. *Significance:* (1) At rest patients do not have elevated catecholamines (CA); (2) the lower than expected HR response to the exaggerated early CA release on standing observed in depressed patients may be explained by subsensitivity of cardiac beta-adrenergic responses; (3) both lymphocytes and cardiac betaadrenergic responsivities may be blunted in endogenous depression; (4) the changes in EPI indicate that patients had a faster SNS response to a postural challenge that may be due to altered central regulation.

### NR184

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

# EEG SLEEP AND LONGITUDINAL DST RESPONSE

Shashidhar M. Shettar, M.D., Psychiatry, University of Mich, 1500 E. Med Ctr Dr. Box 0118, Ann Arbor, MI 48109; James E. Shipley, M.D., Roger F. Haskett, M.D., Leon J. Grunhaus, M.D., Suzanne Bahadosingh, Atul C. Pande, M.D.

### Summary:

Depressed patients with DST nonsuppression have been reported to show more marked sleep EEG disturbances than DST suppressors. We attempted to determine whether baseline EEG sleep would be related to the classification of patients based on their pattern of change or lack of change from the baseline DST to a repeat DST prior to discharge.

The sample consisted of 47 inpatients diagnosed as MDD by SADS/RDC with a Hamilton rating (17 item scale) of  $\geq$ 15. EEG sleep data were averaged from two consecutive nights after a minimum of 13 days drug free (mean  $\pm$  SD=20.5  $\pm$  8.0 days). The baseline DST was done within seven days of the sleep study.

At baseline there was no significant difference in age or severity between DST suppressors and nonsuppressors. As has been reported, nonsuppressors had a lower REM latency (p < .001) and sleep efficiency (p < .02) and no difference in REM density compared to suppressors.

On the basis of the first DST and a DST done prior to discharge, patients were categorized as: a) persistent supressors (n=26); b) those normalizing (n=14); and c) those failing to normalize (n=7). There was no difference in any baseline sleep measure between those normalizing and those failing to normalize. We conclude that while DST and sleep measures may be associated at baseline, these sleep measures were not associated with the pattern of change or lack of change between the baseline and predischarge DSTs.

### NR185

# SLEEP, FATIGUE AND MOOD IN PREMENSTRUAL SYNDROME

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

Margaret F. Jensvoid, M.D., Biol. Psych., NIMH NIH Bldg 10 Rm 3N234, 9000 Rockville Pike, Bethesda, MD 20892; Kari L. Muller, M.D., David R. Rubinow, M.D.

# Summary:

The DSM-III criteria for Late Luteal Phase Dysphoric Disorder (LLPDD) contain a variety of symptoms that should demonstrate marked menstrual cycle phase dependent variability. In this study, we examined the presence of two of these symptoms, "hypersomnia or insomnia" and "easy fatiguability or marked lack of energy," in 10 patients with prospectively confirmed LLPDD and 10 controls with prospectively confirmed absence of LLPDD. All subjects recorded sleep characteristics and completed self-ratings of fatigue and mood. Sleep and emotional characteristics were analyzed using two cycles of twice-daily analogue scale data from each subject.

The sleep characteristics, numbers of hours of sleep, and number of interruptions, showed no significant difference between premenstrual and follicular phases for either patients or controls. However, measures of fatigue (energy, tiredness) and mood (sadness, anxiety, and global) were significantly different premenstrually compared with postmenstrually in patients but not controls. Measures of fatigue correlated with mood and global measures but showed no correlation with sleep characteristics. In summary, despite the fact that the sleep characteristics showed no significant difference premenstrually compared to postmenstrually in PMS patients or controls, tiredness, energy levels, and mood were significantly worse premenstrually compared to postmenstrually in PMS patients.

### **NR186** MELATONIN SECRETION AND SLEEP IN THE ELDERLY

Clifford M. Singer, M.D., Psycyhiatry, Portland, OR 97201; Robert L. Sack, M.D., Duane Denney, M.D., Mary L. Blood, B.S., Robert F. Vandiver, M.D., Alfred J. Lewy, M.D.

### Summary:

Introduction: The pineal hormone melatonin is secreted mainly at night and appears to have some capacity to induce sleep.<sup>1</sup> Production of melatonin declines with age although there is great variation in this.<sup>2</sup> We undertook this study to determine if this age-associated decline in melatonin could be correlated with changes in sleep that are also attributed to aging. Methods: Twenty-five healthy volunteers over the age of 65 (average age = 76 years) were recruited. Three overnight urine collections per subject were assayed for 60H melatonin (the main metabolite of melatonin). Based on their average melatonin production, subjects were divided into "high" secretors (>7500 ng) and "low" secretors. The sleep records were scored using conventional criteria by a sleep technician blind to the 60H melatonin data. Results: The average 60H melatonin content of the overnight collection was 5246 ± 3986 ng. Melatonin production was positively correlated with total REM sleep (r=0.88, p=0.01) and REM latency (r=0.74, p =0.05). Total sleep time, sleep efficiency, percent of stage 3 and 4 sleep and delta count did not show statistically significant correlation with melatonin production. Conclusion: Low melatonin production in the elderly is associated with shorter REM latencies and less total REM sleep.

### **NR187**

Wednesday, May 11, 12 noon-2:00 p.m. THE TIMING OF SLEEP AND BRIGHT LIGHT EXPOSURE IN TREATING WINTER DEPRESSIVES

Clifford M. Singer, M.D., Psychiatry, OHSU, 3181 SW Sam Jackson Road, Portland, OR 97201; Robert L. Sack, M.D., Alfred J. Lewy, M.D.

### Summary:

Background: We have investigated the possibility that winter depressives<sup>1,2</sup> whose sleep is being shifted can be treated with two hours of bright (2500 lux) light, providing it is scheduled close to sleep offset. Methods: Eight patients with winter depression spent two weeks in the Clinical Research Center with rigorously controlled light exposure; their sleep was gradually delayed one hour per day and then advanced one hour per day so that by middle of the second week of the study they were again sleeping between midnight and 0800. Subjects were in dim (150 lux) light conditions for 22 hours a day, maintained by restriction to light-tight rooms or by wearing welders' goggles. Patients were randomly assigned to two groups, four patients per group. By the middle of the second week, bright light exposure at noon was gradually delayed to 1600 (eight hours after sleep offset) in the "afternoon light" group and was gradually advanced from noon to sleep offset (0800) by the middle of the second week in the "morning light" group. Clinical symptoms were assessed every two-to-three days by 21-item Hamilton Depression Ratings done by two clinicians who were blind to the protocol. Results; On Day 1, the average Hamilton ratings for the afternoon light group were 17.0 + 3.4 and 18.1 + 3.3 for the morning light group. By Day 15, the afternoon light group had an average Hamilton of 19.0  $\pm$  5.0, whereas the morning light group had an average rating of 4.3  $\pm$  0.9 (p=0.03, Student's t-test). In the morning light group, depression ratings on the last day of the study were significantly lower than on the first day (p=0.005, paired t-test). Conclusion: Winter depressive patients respond to as little as two hours of bright light per day, providing it is scheduled close to sleep offset.

#### **NR188** Wednesday, May 11, 12 noon-2:00 p.m. CARBAMAZEPINE INHIBITS SIGNAL TRANSDUCTION THROUGH THE PHOSPHATIDYLINOSITOL CYCLE

Robert E. Vadnal, M.D., Psychiatry, LSU Medical School, 1542 Tulane Avenue, New Orleans, LA 70112; Nicolas G. Bazan, M.D.

### Summary:

Male Sprague-Dawley rats were prelabelled by intraventricular injection with 14 uCi [3H]-myoinositol per brain (15 Ci/mmol), 20-24 hours prior to sacrifice. Rats were pretreated with carbamazepine (50 mg/kg) or vehicle (ethanol) intraperitoneally 90 minutes prior to either electroconvulsive shock (ECS) or sham. The seizures produced in the carbamazepine rats were rated at 3/4 compared to control rats rated at 4/4. ECS (120 V, 155 cps, 750 msec) was produced using stainless steel scalp electrodes. Rats were sacrificed after either real ECS or sham ECS after 30 seconds by head-focused microwave irradiation (6.5 KW, 1.5 sec). The cerebral cortex and hippocampus were dissected and homogenized in 20 vols of chloroform: methanol (2:1). After an acidified extraction, the phosphoinositides were separated by thin layer chromatography (TLC) and the inositol phosphates separated by ion exchange chromatography. [3H]-myoinositol incorporation in cerebral cortex was increased in PIP<sub>2</sub> with the carbamazepine-ECS  $\rightarrow$  carbamazepine  $\rightarrow$  ECS (37%  $\rightarrow$  17%  $\rightarrow$ 7%). In hippocampus, carbamazepine-ECS >carbamazepine=ECS (37% > 9% =9%). [3H]-IP1 levels were reduced in the carbamazepine-alone group by 15% in the cortex and 18% in the hippocampus. This is in marked contrast to the significant elevations caused in lithium. ECS-alone caused a 55% increase in [3H]-IP<sub>3</sub> in cortex and a 48% increase in the hippocampus. Pretreatment with carbamazepine completely inhibited this effect. This is the first report demonstrating effects of carbamazepine on signal-transduction in the inositol lipid cycle.

# CIRCADIAN RHYTHMS IN DEPRESSION AND RECOVERY

Eric Souetre, Psych Biol, NIMH, 9000 Rockville Pike, Bethesda, MD 20892; Edouard Salvati, M.D., Jean-Luc Belugou, M.D., Dominique Pringuey, M.D., Bernard Krebs, M.D., Guy Darcourt, M.D.

### Summary:

Circadian rhythms of body temperature, plasma cortisol, norepinephrine (NE), thyrotropin (TSH) and melatonin were compared in endogenous depressed patients (MAD *DSM-III*) (11 Bipolar, five Unipolar) (n=16), before and after three weeks of antidepressant treatment as well as in healthy subjects. Plasma hormone profiles were estimated using hourly blood samples and RIA for cortisol, TSH and melatonin and HPLC for NE. Data analysis was based on the chornogram method as well as the use of fitted function such polynomial regression and cosine function. Paired 1 test and ANOVA were used for group comparisons.

Clear abnormalities of the circadian rhythms were found in depression, consisting mainly in a significant reduction of the amplitude of the temperature (p<0.01), cortisol (p<0.05, NE (p<0.01), TSH (p<0.01) and melatonin (p<0.001) circadian rhythms. However, no phase abnormalities were detected. Normal circadian profiles were restored after recovery, in particular by increasing amplitude. Whereas features of the circadian rhythms observed in remission may be associated with antidepressant drug effects, those observed in depression resemble the circadian rhythms observed in normal subjects living under temporal isolation and those of blind subjects. Our findings suggest that depression may be related to a weakening of the entrainment processes of the internal clocks by environmental factors.

### NR190

### Wednesday, May 11, 12 noon-2:00 p.m.

# SEASONAL CHANGES IN MOOD AT THREE LATITUDES

Normal E. Rosenthal, M.D., Psych Biol, NIMH Bldg 10 Rm 4S239, 9000 Rockville Pike, Bethesda, MD 20892; Steven D. Targum, M.D., John P. Docherty, M.D., Howard A. Hoffman, M.D., Joel R. Hamovit, M.S.W., Michael J. Bryant, B.A., Siegfried F. Kasper, M.D.

### Summary:

Seasonal changes in mood and behavior were determined by administering the Seasonal Pattern Assessment Questionnaire (SPAQ) to all patients visiting selected internist and dental offices in Nashua, New Hampshire (43°N), Washington, D.C. (39°N) and Sarasota, Florida (27°N) during a certain period of time. The number of subjects screened were 189, 218 and 217 at the above sites, respectively. The proportion of subjects who noted that the changing seasons affected their wellbeing to a problematic degree were 24%, 20% and 27%, respectively, and this reached marked to disabling proportions in 7%, 6% and 9% of cases. Although the proportion of subjects who complained of seasonal difficulties were similar at the three sites, the distribution of these difficulties across the year was different. In New Hampshire, the most northern site, the distribution of responses to the question, "When do you feel worst?" was virtually unimodal, with a major winter peak, and only a small number of individuals complaining of summer difficulties. In Washington, D.C., although the majority of people noted that they felt worst during the winter months, there was also a sizable peak of people with summer difficulties. In Sarasota, Florida, there was also a bimodal distribution but more people complained of summer difficulties than of winter difficulties. These data may have implications for the relative proportion of patients with summer and winter depression in the population. Further details from this survey will be discussed at the meeting.

#### NR191 SEIZURE THRESHOLD DURING ECT IN MANIC PATIENTS

# Wednesday, May 11, 12 noon-2:00 p.m.

Sukdeb Mukherjee, M.D., CL Neuropsych, NYS Psych Inst, 722 W. 168th Street Box 72, New York, NY 10032; Harold A. Sackeim, M.D.

### Summary:

Studies of seizure threshold in depressed patients undergoing ECT have demonstrated that initial seizure threshold (IST) is higher with bilateral than with unilateral (D'Elia) electrode placements, that IST is significantly correlated with age, that bilateral ECT is associated with a greater cumulative increase in seizure threshold than is unilateral ECT, and that the degree of cumulative increase in seizure threshold may be associated with therapeutic response to ECT. We examined these issues in 24 manic patients undergoing ECT in an ongoing research protocol. All patients were drug free during the course of ECT. Mean IST was significantly higher with bilateral than with unilateral (D'Elia) electrode placements (105.6 vs 36.7 mA-sec, respectively), with a range across all patients from 12 to 168 mA-sec. Treatment responders showed a 95% cumulative increase in seizure threshold in contrast to the 41% increase in the nonresponders (p. 01). In 11 patients receiving bilateral ECT, IST was significantly lower in the 5 nonresponders (mean 78.0 mA-sec) than in the 6 responders (mean 122.0 mA-sec). Across the sample, IST was significantly correlated with age (r=.618; p. 02). Thus, the earlier findings from our studies of depressed patients are replicated in these preliminary findings in manic patients. The significance of these findings to antimanic properties of ECT will be discussed, particularly with reference to the proposed hypothesis involving anticonvulsant properties of ECT.

### NR192 PERSONALITY TRAITS IN GERIATRIC DEPRESSION

Robert C. Abrams, M.D., Psychiatry, Cornell Univ Med Col, 21 Bloomingdale Road, White Plains, NY 10605; Robert C. Young, M.D., Jonathan H. Holt, M.D., George S. Alexopoulos, M.D.

### Summary:

The role of personality traits and disorders in the pathogenesis of major depression has not been clairified and may differ in mixed-age versus geriatric populations. Previously we administered the Personality Disorder Examination (PDE), a structured interview for diagnosing *DSM-III-R* personality disorders, to geriatric patients recovered from major depression and to never-ill elderly controls. The recovered depressives received significantly higher dimensional scores for all Axis II disorders except antisocial personality. We now administered the Eysenck Personality Inventory (EPI)-Form A, a 57-item self-rated instrument, to 16 of the original recovered patients (mean age 70.1 years + 6.3 S.D.) and 14 of the controls (mean age 75.7  $\pm$  7.0). Subjects with cognitive impairment or residual depression were excluded using the Mini-Mental State Examination (MMS) and the Hamilton Depression Rating Scale (HDRS), respectively. Patients scored significantly higher on the EPI Neuroticism subscale than controls (t=5.7, df=28, P<.001), while their mean Extraversion scores were not significantly different. In the controls, PDE scores for the Borderline and Masochistic Disorders correlated significantly (p<.001) with Neuroticism. Patients' PDE scores had no significant correlations with Extraversion or Neuroticism scores. The EPI Neuroticism Subscale appears to discriminate history of unipolar depression in an elderly population, as do PDE dimensional scores based on *DSM-III-R* Personality Disorders. If stable, these differences provide increasing evidence for an association of dysfunctional personality traits with geriatric depression.

### NR193

# HEAT SHOCK PROTEINS IN SUICIDE

### Wednesday, May 11, 12 noon-2:00 p.m.

Joel E. Kleinman, M.D., CBDB, NIMH, 2700 Martin L. King Jr. Ave SE, Washington, DC 20032; David Goldman, M.D., Chitra Rajagopal, M.D., Markku Linnoila, M.D.

### Summary:

Introduction: Although suicide accounts for approximately 25,000 deaths annually in the USA, neurochemical mechanisms remain unclear. Protein abnormalities in suicide victims reported in the past have not gained widespread acceptance or led to further understanding. The following study examines heat shock proteins (HSP) (70 kd; proteins transcribed in response to a variety of stresses such as heat) in suicides and controls. *Methods:* Using two-dimensional electrophoresis, HSP from human postmortem parietal cortex were analyzed in 21 suicides, 28 other psychiatric controls, and 16 normals after storage at  $-70^{\circ}$ C. There were no significant differences in age, gender, or postmortem intervals (PMI) between the three groups. *Results:* HSP existed in more than one form in 13 of 65 subjects, but none of the suicides (p<05). An association between HSP in more than one form and PMI was found (p<05), but did not account for the difference between suicides and controls in the expression of HSP has been found in postmortem brain specimens. Implications of this research will be discussed.

### NR194

# HOPELESSNESS AS A PREDICTOR OF ULTIMATE SUICIDE

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

Aaron T. Beck, M.D., Psychiatry, Univ of Pennsylvania, 133 S. 36th Street Rm 602, Philadelphia, PA 19104; Gary Brown, M.S., Robert J. Berchick, Ph.D., Robert A. Steer, Ed.D.

### Summary:

A longitudinal study of 1,958 outpatients who were evaluated at the Center for Cognitive Therapy between 1978 and 1985 was conducted to ascertain whether or not the Hopelessness Scale (HS) was related to eventual suicide. The mean HS score for the eventual suiciders was signifiantly higher than that of the non-suiciders. In addition, an optimal cutting score on the HS identified 15 of 16 (93.8%) eventual suicides. The results replicate an earlier study with psychiatric inpatient suicide ideators (Beck, Steer, Kovacs, & Garrison, 1985) which also found a high prediction rate and low false negative rate for the HS in prediction of eventual suicide. Further, the HS has advantages over other risk factors for eventual suicide in that it is in an ongoing index of risk and can be a target of therapeutic intervention.

### NR195 OPTIMIZING DIAGNOSTIC TESTS USING ROC ANALYSIS

CORTISOL AND EPINEPHRINE AFTER ACTH IN DEPRESSION

Douglas Mossman, M.D., Psychiatry, Med Univ of SC, University Services Building, Charleston, SC 29425; Eugene Somoza, M.D.

### Summary:

This presentation will demonstrate how receiver operating characteristic (ROC) analysis may be used to assess, describe, and optimize the performance of psychiatric diagnostic tests. Re-evaluated data from published studies of the dexamethasone suppression test (DST) provide examples of how ROC analysis can greatly improve the accuracy measures used to describe and compare diagnostic systems. The presentation also shows how the DST and other diagnostic tests may be optimized for clinical use.

Among the specific topics to be discussed: (1) Adjusting the DST's sensitivity and specificity to maximize information yield while incorporating pre-test estimates of disorder prevalence. (2) Examples of the variation in cortisol cut-offs for non-suppression necessitated by assumptions about pre-test probability of affective illness. (3) Use of cut-off variation to optimize utility (i.e., minimize costs and risks, maximize benefits). (4) Assessing improvements in DST technology, e.g., using a 0.5-mg dexametha-sone dose, or using a dexamethasone-cortisol product as a diagnostic index.

### NR196

### Wednesday, May 11, 12 noon-2:00 p.m.

Peter E. Stokes, M.D., Psychiatry, Cornell Univ Med Col, 1300 York Avenue, New York, NY 10021; Peter M. Stoll, M.A., Carolyn R. Sikes, M.A., Melissa A. Yu, B.S., Irene Gurvits, B.S.

### Summary:

We measured plasma cortisol at intervals after a 250  $\mu$  g i.v. bolus of ACTH 1-24 given to 16 depressed patients shortly after hospitalization and again before discharge, and to four healthy controls, to confirm a heightened adrenocortical response to ACTH in hypercortisolemic depressed patients, and to evaluate its state-relatedness. We also collected preliminary data on plasma epinephrine (E) response to i.v. ACTH 1-24 in two depressed patients and two controls, to test whether high ACTH levels may stimulate E release from the adrenal medulla, in view of data that depressed patients with high cortisol also have high urinary E excretion. Plasma cortisol was assayed at 0, 30, 60, 90, 120, and 180 minutes after ACTH at 9 a.m. Peak plasma cortisol increment above baseline and area under the curve from 0-180 minutes were greater in depressed patients at admission than in controls (p<.01). Within patients, peak cortisol response and area under curve were greater in 11 dexamethasone nonsuppressors than in five suppressors (p<.05). Despite reversion to DST suppression by hospital discharge in most nonsuppressors, cortisol response to ACTH at discharge was relatively unchanged. Two depressed patients with plasma E obtained before and at 30 minute intervals after ACTH showed no clear E response to ACTH. One patient and one control with frequent early plasma sampling each showed a transient plasma E increment at six minutes after ACTH. More data on early E response to ACTH are being collected and will be discussed.

### NR197

### ECT PHASE-DELAYS HAMSTER CIRCADIAN ACTIVITY RHYTHMS

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

John D. Hallonquist, Ph.D., Psychiatry, Mt. Sinai Hospital, 600 University Avenue, Toronto, Ontario, Canada M5G1X5; Jack S. Brandes, M.D.

#### Summary:

Circadian dysfunction has been reported in major affective disorders. For some patients, abnormally phase-advanced circadian rhythms may be etiologically important, rather than mere state-markers. In these cases, clinically effective therapies might be expected to correct relationships between different rhythms and with 24-hour environmental cues by phase-delaying the advanced rhythms. Antidepressant drugs and lithium are reported to phase-delay and slow some circadian rhythms in animals, but to date there are no reports that electroconvulsive therapy (ECT) has similar effects. Demonstrations of chronotypic properties for all three therapies would add support to the circadian dysfunction hypothesis of affective disorders. We now have evidence that under brief anesthesia, a single administration of ECT (but not sham-ECT) can significantly (p<.01) phase-delay free-running circadian activity rhythms of hamsters housed in constant light. Furthermore, this effect appears to be limited to administrations during the subjective day of these nocturnal animals. The finding that a phase delay depends on when ECT is administered at a specific time relative to their circadian rhythms. Our research also supports the development of other, less invasive, alternate therapies which normalize circadian function.

### NR198 DEPRESSION, CORTISOL SECRETION AND LEUKOCYTE TRAFFIC

Andrew H. Miller, M.D., Psychiatry, Montefiore Hospital, 111 East 210th Street, Bronx, NY 10467; Gregory M. Asnis, M.D., Christine Lackner, B.S., Allen J. Norin, Ph.D.

# Summary:

Alterations in the relative composition of the circulating leukocyte pool including decreases in lymphocyte percentage and increases in neutrophil percentage have been found in patients with Major Depression (MD). In a similar fashion, oral glucocorticoid administration is associated with decreases in circulating lymphocyte and monocyte percentages and increases in both the neutrophil percentage and white blood cell (WBC) count. Since MD is characterized by hypersecretion of the glucocorticoid, cortisol, the relationship between cortisol metabolism and leukocyte traffic in depressed patients has been of interest.

In order to study this relationship, continuous blood samples were obtained from subjects between 1 p.m. and 4 p.m., yielding an integrated plasma cortisol value which correlates highly with 24-hour cortisol secretion. Circulating leukocyte determinations were made using an electronic particle counter and hemacytometer. Compared to normal controls (N=15), MD patients (N=31) exhibited an increased neutrophil percentage (65.5 vs 58.9 p=.05) and a decreased monocyte percentage (3.3 vs 6.7 p ...001). Additionally, cortisol secretion was negatively correlated with lymphocyte percentage (-0.41 p=.01) and positively correlated with neutrophil percentage (0.38 p=.02) in both groups. Finally, subjects with hypercortisolemia (plasma cortisol 11ug/d1, N=9) were noted to have a decreased lymphocyte percentage (24.4 vs 31.2 p=.06), a decreased ratio of lymphocytes to neutrophils (.38 vs .54 p=.037) and an increased neutrophil percentage (68.6 vs 62 p=.097) compared to the normosecretor group (N=37). In summary, these findings suggest that alterations in cortisol secretion may have significant effects on leukocyte traffic in depressed patients. Redistribution of peripheral leukocytes during MD may be relevant to the disturbances in immune function seen in this disorder.

### NR199

# AN IN VITRO ASSAY FOR GLUCOCORTICOID RESISTANCE

### Wednesday, May 11, 12 noon-2:00 p.m.

Andrew H. Miller, M.D., Psychiatry, Montefiore Hospital, 111 East 210 Street, Bronx, NY 10467; Gregory M. Asnis, M.D., Christine Lackner, B.S., Allen J. Norin, Ph.D.

### Summary:

Major Depressive Disorder (MDD) is characterized by abnormalities in hypothalamic-pituitary-adrenal activity as evidenced by hypersecretion of cortisol and nonsuppression of dexamethasone (in vivo glucocorticoid resistance). These abnormalities may be related to altered responsiveness to feedback inhibition by glucocorticoids at the level of the hypothalamus and/or pituitary. Recently, however, the dexamethasone suppression test (DST) has been questioned due to observations that the bioavailability and pharmacokinetics of dexamethasone are significantly associated with DST status. We report preliminary findings of the use of an in vitro assay for glucocorticoid resistance which circumvents the problem of variable steroid bioavailability following oral dexamethasone. We assaved the in vitro effect of the glucocorticoid, cortisol, on Natural Killer (NK) cell activity of peripheral blood lymphocytes from patients with MDD (N=10) and controls (N=10). NK cells are a lymphocyte subpopulation that are known to be inhibited by both cortisol and dexamethasone in vivo and in vitro. Concentrations of cortisol ranging from 0.08 to 1.25 mg/ml were added to separate lymphocyte cultures and NK cell activity was determined after three hours at 37°C in a standard <sup>51</sup>chromium release assay. Comparison of mean inhibitory dose response cures between patients and controls revealed that NK activity was significantly less inhibited (glucocorticoid resistance) at the five highest cortisol concentrations in the patient group. At the three lower cortisol concentrations, less inhibition was observed in the patient group, however the values were not statistically significant. In summary, we present findings of peripheral glucocorticoid resistance in MDD patients using an vitro assay system that circumvents issues of steroid bioavailability that has plaqued the DST.

# HIGH DA D2 RECEPTORS IN PSYCHOTIC BIPOLARS ON PET

DOES TREATMENT INFLUENCE MORTALITY IN DEPRESSIVES?

Godfrey D. Pearlson, M.D., Psychiatry, Johns Hopkins, 600 N. Wolfe St Meyer 3-166, Baltimore, MD 21205; Dean F. Wong, M.D., Christopher Ross, M.D., Larry E. Tune, M.D., Mary J. Bascom, B.A., Henry N. Wagner, Jr., M.D., Robert F. Dannais, M.D., Jonathan Links, Ph.D.

### Summary:

Using PET scanning, we have previously reported increases in Bmax of dopamine (DA) D2 receptors in the caudate/putamen of both drug-naive and drug-free schizophrenic patients (1). Because psychotic symptoms can also occur in affective disorder, we examined 15 currently ill, drug-naive and drug-free patients with affective disorder (nine psychotic, six nonpsychotic), using the same techniques as employed for schizophrenics (1). These were use of C11-N-Methyl-Spiperone as a ligand and two PET scans (one drug-free, a second four hours after 7.5 mg of PO Haldol) to calculate Bmax. Because Bmax values of DA D2 receptors decline with age (2), comparisons were made with normal screened controls after a median split on age, at 45 years.

In both young and old affectively ill patients those who were nonpsychotic had Bmax values not significantly different from those of controls. Psychotic manic and depressed patients had Bmax values 200-300% higher than age-appropriate controls, and, for younger individuals, values similar to those we previously reported in comparably aged drug-naive schizophrenics (1). We conclude that the presence of psychotic symptoms is associated with increased Bmax of D2 receptors in both schizophrenia and affective disorder.

### NR201

#### Wednesday, May 11, 12 noon-2:00 p.m.

Donald W. Black, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; George Winokur, M.D., Amelia Nasrallah, M.A., Mohandoss Emmanuel, M.S., Robert Woolson, Ph.D.

### Summary:

Mortality risk among 1.076 subjects with major affective disorders (705 primary unipolar, 302 secondary unipolar, and 160 bipolar depressives) was compared to that of age- and sex-matched controls from the general population. Patients were divided into four treatment groups, depending on primary mode of therapy during the index hospitalization. These groups included electroconvulsive therapy (ECT), adequate antidepressants, inadequate antidepressants, and neither treatment. Risk of death from all causes was increased for the entire sample. Increased risk for suicide was found for each treatment group during the entire follow-up, but especially the first two years when 25 (69.4%) suicides occurred. There were no significant differences in the risk for suicides, or deaths from all causes combined, among the four treatment groups. Furthermore, there was no difference in mortality when we compared patients who have had ECT at anytime during their lives with patients who have never received ECT. We conclude from a short-term follow-up of depressives that mode of therapy received in the hospital has little influence on subsequent mortality, including suicide.

### NR202

Wednesday, May 11, 12 noon-2:00 p.m. ALDOSTERONE IN LATE LUTEAL PHASE DYSPHORIC DISORDER: EFFECTS OF ATENOLOL

Jeffrey L. Rausch, M.D., Psychiatry, UCSD, M-003, La Jolla, CA 92093; David S. Janowsky, M.D., Shahrokh Golshaan, Ph.D., Karen Kuhn, B.A.

### Summary:

Luteal activation of the mineralocorticoid axis has been postulated as a potential etiologic factor in premenstrual mood symptoms. We measured serum aldosterone and plasma renin activity twice weekly for two months in 16 women meeting provisional DSM-III-R criteria for Late Luteal Phase Dysphoric Disorder. The women were treated during the latter 10 days of their cycles with either atenolol (50 mg qAM) or placebo, in a placebo-crossover, double-blind randomized design. Two way analysis of variance for repeated measures indicated significant increases in serum aldosterone levels during the menstrual cycle, with significantly (F=9.28, p=.01) higher luteal aldosterone levels in comparison to the follicular phase of the menstrual cycle. There was a trend toward an increase in luteal plasma renin activity (F=4.52, p=.06). There was no significant drug X time interaction between atenolol and placebo for either aldosterone (F=.25, n.s.) or plasma renin activity (F=1.05, n.s.); luteal increases in aldosterone and plasma renin activity were found during both active and placebo months. However, aldosterone was lower at one time point, 3 (±2) days prior to menstruation during the atenolol month. The results suggest that premenstrual women may undergo subtle shifts in fluid balance during the luteal phase of the menstrual cycle, but that low doses of atenolol may not be sufficient to dramatically blunt the increased luteal activity of the mineralocorticoid axis. Most premenstrual symptoms were not significantly improved with the 50 mg dose of atenolol, although premenstrual irritability was significantly better on atenolol.

#### NR203 MOTILITY RHYTHMS IN PSYCHOTIC INPATIENTS

Martin H. Teicher, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Andrew Sussman, B.A., Ross J. Baldessarini, M.D., Harris Lieberman, Ph.D.

# Summary:

Locomotor activity levels and rhythms were studied in hospitalized psychotic patients with schizophrenic (n=5), schizoaffective (n=4), or bipolar (manic) disorders (n=9). Activity was monitored under normal illumination with a wrist-worn microprocessorcontrolled portable activity monitor with solid-state memory (PCD Actigraph). Activity was monitoried continuously over 72 hr, stored in 5 min periods, and analyzed as sequential hourly epochs for circadian rhythms using non-linear cosinor analysis, and in 15 min epochs for ultradian rhythms using variance spectra. Schizophrenic and schizoaffective patients showed similar levels of mean activity, percent diurnal activity, and circadian amplitude; all of these parameters were significantly lower than those observed in bipolar patients. Schizoaffective and bipolar patients were readily distinguished from schizophrenic subjects, however, by the presence of a robust 2 cycle per day (cpd) ultradian rhythm in the former groups, and by subtle differences in circadian acrophase. This 2 cpd rhythm accounted for 15.1 and 13.6% of the total variability in the activity of schizoaffective and bipolar patients, respectively, but only accounted for 5.3% in schizophrenics (p<0.0001). This ca. 12 hr rhythm may be a useful marker for the presence of affective illness, and probably corresponds to the clinical concept of *"diurnal variation."* 

#### NR204 MEMBRANE MOLECULAR STUDIES IN BIPOLAR DEPRESSION

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

Alan G. Mallinger, M.D., Western Psych Inst, 3811 O'Hara Street, Pittsburgh PA 15213; Clareann H. Bunker, Ph.D., Jonathan M. Himmelhoch, M.D., Michael E. Thase, M.D., Christine S. Dippold, B.S., Steven Knopf, B.S.

### Summary:

To investigate possible cell membrane abnormalities in bipolar depressed patients, we studied the maximum transport rate ( $V_{max}$ ) and exchange stoichiometry (STO) of sodium-lithium countertransport (Na-Li CT). A molecular alteration in this mechanism could affect the transport rate, or cause deviation from the usual (1 Na:1 Li) exchange ratio. Therefore, in the first reported study of this type, we measured both Na influx and Li efflux in erythrocytes (RBCs) from 33 drug-free patients. The assays performed were highly reliable; coefficients of variation for duplicate flux measurements were 4.2% for Li and 6.2% for Na. Observed rates of Na and Li flux via Na-Li CT were similar (means  $\pm$ SDs= 0.286 $\pm$ .161 vs 0.262  $\pm$ .121 mmoles/liter RBCs/hr, respectively; t=1.3, p>0.15). The mean  $\pm$ SD ratio for Na: Li transport was 1.09  $\pm$ .46, which closely approximates a 1:1 exchange. There were no patient subgroups with abnormal Li or Na flux values, and the correlation between these measures was strong (Spearman rho= 0.70, p<10<sup>-3</sup>). Thus, we found no evidence for abnormal STO of Na-Li CT. However, comparison of Li-loaded with Li-free cells demonstrated a 45% increase of mean Na influx due to coupled Na-Li CT (t=10.2, p<10<sup>-4</sup>). We compared Na-Li CT V<sub>max</sub> findings from bipolar patients with two control studies that used identical methods. The healthy controls were 55 male college students and 160 middle-aged women. Na-Li CT V<sub>max</sub>ranged from 0.070- 0.684 mmoles/liter RBCs/hr among controls, as compared to 0.073- 0.716 in patients and the means were similar. Thus, we found no abnormatility in the STO or V<sub>max</sub> of Na-Li CT among bipolar depressed patients. However, Li interactions with Na-Li CT can affect cellular Na dynamics, and may thus have a role in the clinical actions of this agent.

### NR205 PANIC AND CHILDHOOD TRAUMA IN DEPRESSED WOMEN

### Wednesday, May 11, 12 noon-2:00 p.m.

Gregory Gillette, M.D., Research Unit, Dorothea Dix Hospital, South Boylan Avenue, Raleigh, NC 27611; James Garbutt, M.D., Kevin Robertson, M.A.

### Summary:

Numerous recent studies have reported that 50-68% of panic disorder patients suffer major depression sometime in their lives and, conversely, that 15-38% of patients with major depression suffer panic attacks. Geneaologic, pharmacologic, and neuroendocrine overlap between the disorders have been repeatedly documented.

For theoretical reasons, an association between childhood loss experiences and adulthood depression has often been assumed, although empirical evidence is not definitive.<sup>1</sup> Similarly, recent reports have attempted to associate adulthood panic disorder with childhood loss experiences and separation anxiety, again with inconsistent correlation.<sup>2</sup>

We have examined childhood traumatic life events (parental separation, paternal death, maternal death, physical abuse, incestuous abuse) reported by a consecutive series of 27 women referred to an inpatient research unit for depression. Loss event histories were obtained by semi-structured psychosocial history interview, and abuse event histories from inpatient psychotherapy sessions. The only category of childhood trauma that showed statistically significant correlation with presence of concurrent panic attacks in adult depressed female inpatients was incestuous abuse: 11 of 15 patients with incest history had panic and 11 of 14 patients with panic had incest history (p<0.05, Yates corrected Chi square). Clinical and theoretical implications will be discussed.

### NR206 FLUOXETINE VERSUS DOXEPIN IN DEPRESSION

Eric C. Dessain, Psychopharm, Harvard Medical School, 115 Mill Street, Belmont, MA 02178; Ann P.C. Merzel, B.A., Susan J. Dugan, B.S., Paul W. O'Neil, M.Ed., Loren M. Friedman, M.S., Jonathan O. Cole, M.D.

### Summary:

Fluoxetine was compared to doxepin in a double-blind study of 60 depressed outpatients. Ages ranged from 19-62 years. After a seven day placebo washout, patients were randomly assigned to fluoxetine or doxepin for a six week trial. Symptoms of depression were evaluated weekly using the Hamilton Depression Rating Scale (HDRS) and the Clinical Global Impresison Scale (CGI). Vital signs and adverse effects were recorded weekly. Dosage regimens varied according to tolerance and clinical response.

Sixteen of the 30 patients receiving fluoxetine completed this study; only six of the doxepin group did.

This study suggests that both drugs were equally potent as antidepressants. Repeated measures analyses of variance, with baseline covaried, yielded a significant time effect for both HDRS (p<.0001) and CGI ratings (p<.0001), but failed to demonstrate significant effects for drug or a significant drug X time interaction. Adverse events were reported with equal frequency in both groups except for more dry mouth with doxepin (p<.01). Patients on fluoxetine lost 2 ± 4 lbs.; those on doxepin gained 4 ± 5 lbs. (p<.001). The dosage schedule of doxepin in this study was poorly tolerated. Fluoxetine had no measurable cardiac effect; doxepin increased heart rate slightly.

### NR207

### Wednesday, May 11, 12 noon-2:00 p.m.

# DAYTIME AMNESIA WITH TRIAZOLAM

Edward O. Bixler, Ph.D., Psychiatry, Penn State Univ, 500 University Avenue, Hershey, PA 17033; Rocco L. Manfredi, M.D., Constantin Soldatos, M.D., Caroline Kamper, B.S., Eric Fee, B.S.

### Summary:

Two studies were conducted to evaluate the effects of triazolam on memory. In the first, a systematic sleep laboratory study (N=8), the effects of triazolam 0.5 mg cn delayed recall were evaluated 22 hours after bedtime administration when direct sedative effects are not present due to triazolam's short elimination half-life. A double-blind, placebo controlled, parallel-group design was utilized. The findings demonstrate clearly that some degree of impairment of daytime recall was present daily and that quite often it was severe. Memory impairment of a severe degree was observed on 55% of the days following triazolam administration compared to only 5% following placebo administration. In addition, episodes of amnesia were spontaneously reported by three of the four subjects on several occasions following triazolam administration and none following placebo. In the second study, based upon data collected through the spontaneous reporting system of the FDA, the rates of reported adverse drug reactions involving the CNS were compared among patients taking either flurazepam, temazepam, or triazolam during the first full year that each drug was commercially available. Amnesia was reported almost exclusively with triazolam (a rate of 47.5 vs 1.0 for temazepam and 0.0 for flurazepam). Rates of other side effects including hyperexcitability, withdrawal effects, and cognitive as well as affective and other behavioral effects were also much greater with triazolam. The above findings are consistent with the increasing number of reports of a wide range of behavioral side effects related to the administration of the triazolobenzodiazepines (triazolam and alprazolam).

# NR208

# BENZODIAZEPINE ANXIOLYTICS AND REBOUND INSOMNIA

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

Anthony Kales, M.D., Psychiatry, Penn State Univ, 500 University Avenue, Hershey, PA 17033; Antonia Vela-Bueno, M.D., Alexandros Vgontzas, M.D., Marianne McCormick, B.S., Charles Falcone, B.S.

### Summary:

Anxiolytics often are used as hypnotic agents, yet the literature is sparse regarding their effects on sleep. In response to this need, using a double-blind, placebo-drug-placebo parallel groups design, we conducted sleep laboratory studies of two rapidly eliminated benzodiazepines, lorazepam, 2 mg(L), alprazolam, 1 mg(A), and one slowly eliminated, diazepam, 10 mg(D), administered nightly at bedtime. Results show that all three drugs have considerable hypnotic efficacy for the first three nights (total wake time reduced by 61% with D, 58% with A, and 36% with L). By the end of one week of administration, however, a degree of tolerance had developed for A, which lost 37% of its efficacy. Moreover, for both L and A there was a strong indication for the development of early morning insomnia (combined rate 33.2 vs 0.0% of subject nights for D) and daytime anxiety (combined value 123.6 vs 20.0 for D) along with other side effects (memory impairment with L and disinhibitory behavior with A), while administration of D was associated with more intense daytime sleepiness. Following with-drawal, rebound insomnia was noted for L and A (total wake time 124.5% and 63.0% above baseline, respectively, both on the third night) and a degree of rebound anxiety for L (57.1% above baseline on the sixth night) was observed with D. These findings along with those from previous studies of benzodiazepines demonstrate that rebound phenomena, including the occurrence of interdose rebound anxiety are more frequent and intense with the more rapidly eliminated benzodiazepines. Thus, the more slowly eliminated anxiolytics have a major advantage in the treatment of anxiety disorders.
#### **NR209 REBOUND ANXIETY WITH SHORT HALF-LIFE HYPNOTICS**

Rejean Fontaine, M.D., Psychiatry, Allan Memorial Inst, 1025 Pine Avenue West, Montreal Que, Canada H3A1A1; Paul Beaudry, M.D., Patrick Le Morvan, Ph.D., Linda Beauclair, M.D., Guy Chouinard, M.D.

#### Summary:

Daytime anxiety was reported with short half-life hypnotics. To further investigate the between-dose R.A. we carried out a double-blind, placebo controlled trial with triazolam and zopiclone.

Method: 75 outpatients with generalized anxiety (DSM-III-R) with severe insomnia were included. Following a washout period of at least one week, they were randomly assigned to triazolam 0.5 mg or zopiclone 7.5 mg or placebo. At weekly intervals, sleep inventories, Hamilton Anxiety Rating Scale, CGI for insomnia and anxiety were completed. Also, blood levels for both drugs were done.

Results: Covariance analysis showed both drugs to be superior to placebo for insomnia. Also, analysis for daytime anxiety showed that zopiclone was significantly better than triazolam (p < .05) while the placebo group fell between the two drugs. We also assessed daytime R.A. defined as a 10% increase in anxiety above baseline ratings at inspection of cases. There were more cases for triazolam (10/30) as compared to placebo (1/15) (p < 10) while zopicione was intermediate (5/30).

Discussion; Both drugs are efficacious hypnotics, but triazolam induced more daytime rebound anxiety. These findings are relevant in the use of hypnotics especially in anxious patients and could explain dependence with triazolam.

## NR210 VALIDITY OF THE INVENTORY TO DIAGNOSE DEPRESSION

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

Mark Zimmerman, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; William Coryell, M.D.

#### Summary:

Six hundred and thirteen first-degree relatives of schizophrenics, depressives, and normal controls were interviewed with the Diagnostic Interview Schedule (DIS) and completed the Inventory to Diagnose Depression (IDD), a self-report scale to diagnose major depressive disorder (MDD). The current point prevalence of MDD was nearly identical according to the two measures (DIS 2.8%, IDD 2.6%). Diagnostic concordance varied according to the interval between the evaluations. When the two measures were completed within two days of each other the agreement was as high as can be expected between two instruments with less than perfect reliability (kappa=.80, Yule's y=.87). We used a family study approach to examine validity, and found that both the DIS and IDD cases of depression were two or three times more frequent in the relatives of depressed patients than the relatives of schizophrenics and controls.

## NR211

Wednesday, May 11, 12 noon-2:00 p.m. DELAYED SLEEP PHASE SYNDROME: PRELIMINARY EFFECTS OF PHOTOTHERAPY

Jean R. Joseph-Vanderpool, M.D., NIMH, 9000 Rockville Pike, Bethesda, MD 20892; Eric Souetre, M.D., Karen Kelly, M.D., Patricia M. Schultz, M.S.W., Richard Allen, Ph.D., Norman E. Rosenthal, M.D.

#### Summary:

Delayed sleep phase syndrome (DSPS) is a condition characterized by chronic inability to fall asleep at the desired clock time and to maintain alertness in the morning. The problems have persisted for at least six months and in most cases many years. There is evidence that bright light may be capable of shifting circadian rhythms, which are believed to be abnormally delayed in DSPS. We are conducting a crossover study in which the active treatment is bright (2500 lux) light in the morning and dark goggles in the evening; and the control treatment involves the use of dim (300 lux) light in the morning and transparent goggles in the evening. Each treatment is administered daily for two weeks with at least two weeks of washout in between to permit relapse to occur. Light treatments were administered from 7 a.m. and goggles from 4 p.m. to nightfall. Sleep latency studies were performed at 11:00 a.m. in 10 patients. Data are available on six patients before and afer bright light treatment and on four patients before and after dim treatment. There were significant differences in morning sleep latencies before and after bright light treatment. Values were 12.3 ± 7.5 minutes versus 18.3 ± 6.4 minutes, respectively (P less than .02, Wilcox sign rank). There was no significant difference between pre- and post-treatment morning sleep latencies in the dim condition. Post-treatment morning sleep latencies in the bright condition were significantly higher than those in the dim condition (18.3+6.4 minutes versus 13.0+3.7 minutes, (P less than .02, Mann Whitney U Test).

## NR212 MOOD DISORDERS IN PARKINSON'S DISEASE

Ijaz Kahn, M.D., Biol. Psychiatry, NIMH, 9000 Rockville Pike, Bethesda, MD 20892; Jorge J. Juncos, M.D., Isabella J.E. Heuser, M.D., Mitchel A. Kling, M.D., Harvey Whitfield, M.D., William Gallucci, B.S., Tom Chase, M.D., Philip W. Gold, M.D.

## Summary:

A number of studies have documented a high prevalence of depression in patients with Parkinson's Disease (PD) when compared with patients suffering from other similar incapacitating illnesses. Whether depression in patients with PD is an understandable reaction to a chronic, disabling disorder or is secondary to the biochemical abnormalities associated with PD is less clear. To explore whether PD patients show neuroendocrine features typical of endogenous depression, we measured plasma adrenalcorticotropic hormone (ACTH) and cortisol secretion at 30-minute intervals for a 24-hour period. The PD patients were on L-dopa therapy and were divided into two groups: one that had a history of "on-off" episodes and one that did not. These groups were compared to each other and to an age-matched, drug-free control population.

Compared to the control group, the PD patients with "on-off" had increased levels of ACTH and cortisol. These differences were most evident in the 12-hour period from 6 PM to 6 AM.

The hypercortisolism seen in PD patients with the "on-off" phenomena suggests an alteration in the set point for ACTH and cortisol secretion, an abnormality also seen in psychiatric patients with endogenous depression. Altered glucocorticoid receptor function may play a role in these disturbances.

#### NR213 ELEVATED CSF CRF IN COMPLETED SUICIDES

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

Mihaly Arato, M.D., Disease, Nat'l Inst Nerv Mental, OIE, Budapest 27 01281, Hungary; Csaba M. Banki, M.D., Garth Bissette, Ph.D., Charles B. Nemeroff, M.D., Erzsebet Demeter, Ph.D., Aniko Faluks, Ph.D.

## Summary:

Several indices of the enhanced hypothalamic-pituitary-adrenal axis, including dexamethasone nonsuppression, have been suggested as indicators/predictors of suicidality. In a previous study, obtaining postmortem cisternal CSF samples in the first few hours after death from violent suicides and controls, we have found no difference in the cortisol and ACTH levels between the two groups. We have extended this study assaying the CSF level of immunoreactive corticotropin-releasing factor (CRF). Investigating 19 suicides and 19 controls—who were matched in age, sex, postmortem interval, and clock-time of death—we have found significantly elevated CRF levels in suicides compared with controls:  $207.1 \pm 42.1$  vs  $80.8 \pm 9.9$  pg/ml, t=2.32, p<.05. These findings, i.e. elevated CSF levels of CRF together with "normal" ACTH and cortisol, suggest the possibility of the downregulation of CRF receptor sensitivity at the pituitary level. This assumption is supported by recent findings of CRF challenge tests showing blunted ACTH response to CRF. In clinical investigations we have repeatedly found elevated CSF CRF levels in depressed patients compared with neurologic and psychiatric controls, but no difference between suicidal and nonsuicidal patients. The increased CRF secretion may be related to the underlying affective disorders in completed suicides.

## NR214

## ANTIDEPRESSANT ACTIVITY OF ACE-INHIBITORS

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

Angelo Bosio, M.D., Assoc. Advan. of Neurosci, and Clin. Pharmacol., Via Vivanti g, Brescia 25100, Italy; Rosangela Rosola, Daniela Canini, M.D., Carlo Abbati, M.D., Lidia Sorlini

#### Summary:

On the basis of preliminary clinical reports suggesting the usefulness of captopril in improving quality of life through an antidepressive activity this trial was developed on 30 patients with diagnosis of mild hypertension and depression in accord with *DSM-III-R*. The trial was performed in double-blind, cross-over. After a period of ten days without any treatment (washout) the patients, matched for sex and age, were divided into two groups receiving captopril 25 mg per os **T.I.D.** for a period of five weeks or Enalapirl 20 mg per os once a day and placebo B.I.D. for the same period; after a second washout period of ten days the treatment for the two groups was crossed for a second period of five weeks.

Evaluation was performed after the washout period and every week during the treatment in accord with Hamilton Rating Scale for depression and anxiety, Zung Rating Scale for anxiety and depression and a Life Satisfaction Index; BP was monitored during the trial. Side effects were recorded.

The results of the trial indicate a good therapeutic activity for both the molecules on hypertension but a significant antidepressant activity only for captopril. These results indicate that ACE inhibitor activity is not related to psychotropic effects; at this level captopril antidepressant action may be related to a peculiar pharmacological profile on enkephalinase or other central active neurotransmitters and related enzymes.

## NR215 RCBF EFFECTS OF SCOPOLAMINE COMPARED TO DEMENTIA

William G. Honer, M.D., Psychiatry, Columbia University, Box 105 NYSPI 722 W 168th St, New York, NY 10032; Isak Prohovnik, Ph.D., Gwenn Smith, M.A., Louis R. Lucas, M.Sc.,

## **Educational Objectives:**

At the end of the presentation, the learner should be able to describe the effects of anticholinergic blockade on cerebral blood flow and memory in humans and contrast these effects with Alzheimer's disease and other forms of dementia.

## Summary:

While the cognitive deficits of Alzheimer's disease (AD) are considered related to a cholinergic deficit, no attempt has yet been made to test the hypothesis that the characteristic regional cerebral blood flow (rCBF) pattern of AD may also relate to such a deficit. We therefore measured rCBF using the 133-Xe inhalation technique in 15 young normal subjects before and after induction of reversible cholinergic blockade with scopolamine at doses of 6.1 and 7.3 ug/kg iv. rCBF was measured at baseline and then five, 25 and 60 minutes post-injection. As expected, significant memory impairment (Buschke Selective Reminding Test) was observed 30 minutes after both doses of scopolamine ( $F_1$ ,  $_{13}$ =65.85, p<.001). Significant reductions in rCBF occurred at 25 minutes in the high dose group, with a substantial average decrease in global flow of 12.7 ml/100mg/min, or 17% ( $F_{2,12}$ =8.54, p<.01). In contrast to the focal parietotemporal flow deficit seen in AD, after scopolamine we observed a maximal deficit averaging 20% in the five frontal detectors (time X region interaction;  $F_{2,12}$ =9.89, p<.001). These results suggest that the frontal, but not the parietotemporal, flow deficits seen in several dementing conditions may be related to cholinergic dysfunction.

## References:

<sup>1</sup>Risberg J, Gustafson L; Regional cerebral blood flow in psychiatric disorders, In Handbook of Regional Cerebral Blood Flow. Edited by Knezevic S, Maximilian VA, Mubrin Zet al., Hillsdale, Lawrence Erlbaum, 1988.

<sup>2</sup>Sunderland T., Tariot PN, Cohen RM et al.; Anticholinergic sensitivity in patients with dementia of the Alzheimer type and age-matched controls. Arch Gen Psychiatry 44:418-426, 1987.

## NR216 SCOPOLAMINE AND CNS METABOLISM: A MODEL FOR SDAT?

Thursday, May 12, 9:00 a.m.-10:30 a.m.

Michael Gross, M.D., Lab. of Cerebal Metabo., NIMH NIH, Bldg 10 Rm 4N317, 9000 Rockville Pike, Bethesda, MD 20892; Thomas E. Nordahl, M.D., Trey Sunderland, M.D., William E. Semple, Ph.D., Susan M. Dowling, B.A., Robert M. Cohen, M.D.

## **Educational Objectives:**

To compare the metabolic changes in regional brain metabolism induced by anticholinergic blockade to those associated with Alzheimer's disease.

## Summary:

The loss of cholinergic neurons may be the principal source of the cognitive deficits of early alzheimer's disease (SDAT). To evaluate the metabolic features of this hypothesis, positron emission tomography with FDG was used to determine the alterations of regional brain metabolism induced by scopolamine (0.5-0.75 mg IV) in 18 normal adults as compared to seven controls, and a comparison made with the alterations reported for SDAT. Performance on cognitive measures including an auditory discrimination task during the scan was impaired in the scopolamine group. Comparisons of metabolic rates between the two groups for global, lobar cortical and subcortical structures showed no differences except for a bilateral decrease in normalized thalamic metabolism in the scopolamine group (p=0.01). This contrasts with findings recently reported for SDAT by a number of investigators, including decreased global and absolute parietal and temporal rates, and decreased ratios of parietal/(caudate + thalamus), parietal association/sensorimotor and lateral temporal/occipital cortex. Mean lateral asymmetry did not differ between groups. Overall, scopolamine significantly decreased thalamic metabolism and induced few of the metabolic alterations reported for SDAT. This suggests that cognitive impairment from scopolamine, although similar in form to that seen in SDAT, may primarily involve a thalamic rather than cortical mechanism.

#### **References:**

<sup>1</sup>white PJ, Price DL et al.: Alzheimer's disease and senile dementia: Loss of neurons in the basal forebrain. Science 215:1237-1239, 1982.

<sup>2</sup>Haxby JV, Grady CL et al.: Neocortical metabolic abnormalities precede nonmemory cognitive defects in early Alzheimer'stype dementia. Arch. Neurology 43:882-855, 1986.

#### NR217 NEUROPEPTIDES IN ALZHEIMER'S DISEASE

Michael F. Mazurek, M.D., Medicine, McMaster University, 1200 Main Street West, Hamilton Ontario, Canada L8N 3Z5; M. Flint Beal, M.D.

## **Educational Objectives:**

To know that the various neuropeptides in cerebral cortex, even though they are all contained in morphologically similar intrinsic neurons, are affected to different degrees in Alzheimer's disease.

## Summary:

The neuropeptides somatostatin, neuropeptide Y (NPY), cholecystokinin (CCK), vasoactive intestinal peptide (VIP), substance P and corticotropin releasing factor (CRF) are synthesized in morphologically similar populations of locally projecting neurons in cerebral cortex. One might expect that each of these peptides would be affected in a similar manner in Alzheimer's disease (AD), but some evidence suggests that this might not be the case. We have studied this issue in a single set of postmortem cerebral cortex samples that we dissected from 14 histologically confirmed cases of AD and 17 age-matched controls. Pooled aqueous and acid extracts of tissue were measured for each of the peptides by radioimmunoassay. Concentrations of both somatostatin and CRF were significantly reduced by 42%-65% in nine of 11 cortical areas examined, and by 18%-33% in the remaining two cortical regions. The other neuropeptides were much less dramatically affected. NPY, which is almost 100% colocalized with somatostatin in cerebral cortical neurons, was significantly reduced by 24%-44% in five of the 11 cortical regions and normal in the others. Substance P levels were decreased by 21%-35% in eight of the 11 areas.

These results indicate that the Alzheimer disease process produces highly similar reductions in cortical concentrations of somatostatin and CRF, while levels of the other cortical peptides, despite their being contained in morphologically similar neurons, are less markedly affected.

#### References:

1. Mazurek MF, Beal MF, Martin JB: Neuropeptides in Alzheimer's disease: clinical implications. Neurologic Clinics 4: 753-768, 1986.

2. Mazurek, MF, Beal MF, Bird, ED, Martin, JB: Vasopressin in Alzheimer's disease: a study of postmortem brain concentrations. Annals of Neurology 20:665-670, 1986.

## NR218

Thursday, May 12, 9:00 a.m.-10:30 a.m.

# OPTIC NERVE HEAD IN ALZHEIMER'S DISEASE

Michael Davidson, M.D., Psychiatry, Bronx VA Medical Center, 130 W. Kingsbridge Road, New York, NY 10468; Clark Tsai, M.D., Robert Ritch, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

## **Educational Objectives:**

Investigation of a potential antemortem biological marker in Alzheimer's Disease

#### Summary:

Degeneration of the optic nerve (1) and occasional visual decline have been reported in Alzheimer's disease (AD) patients in addition to the well-established cholinergic neuronal degeneration and cognitive decline. This investigation examines the optic nerve head in vivo in 30 patients meeting NINCDS criteria for "probable AD" and 20 elderly normal controls (NC). Both patients and controls had normal opthalmic history and examination. Image analysis of the optic nerve head (optic disk), which is of diagnostic value in assessing structural neural damage in glaucoma, was performed using the Rodenstock Optic Disc Analyser (RODA)<sup>2</sup>. The RODA records the topography of the optic nerve head by recording simultaneously stereoscopic video images which are stored and analysed with the help of a microcomputer. The condition of the optic nerve is assessed by measuring the optic disk, the size of the cup, the ratio between cup and disc (C/D) and the neuroretinal rim. The cup consists of astroglial cells which provide support to the nerve fibers. The rim is defined as the area between the cup edge and the disc edge. Increased C/D, increased cup volume or decreased rim as demonstrated in the present investigation, are suggestive of neural structural alteration and have been reported in glaucoma. C/D: AD=.49, NC=.38 (t=2.5, df=48, p<.01). Cup volume: AD=.48, NC=.28, (t=2.2, df=48, p<.02). RIM: AD=.98, NC=1.2, (t=-2.6, df=48, P<.01). Disc: AD=.1.5, NC=1.6, (t=0.6, df=48, P=NS). These preliminary results should be viewed with considerable caution due to the investigative nature of the optic nerve head analyser technique. Further investigation should establish if this technique could be utilized to provide an antemortem biological marker for AD.

#### **References:**

<sup>1</sup>Hinton DR, Sodun AA, Blanks JC. Optic nerve degeneration in Alzheimer's disease. New England J Med, 315:485-487 1986. <sup>2</sup>Shields MB, Martone JF, Shelton AR. Reproducibility of topographic measurements with the optic nerve head analyser.

#### NR219 SPECT SCAN CHANGES IN HIV-RELATED DEMENTIA

Godfrey D. Pearlson, M.D., Department of Psychiatry, Johns Hopkins, 600 N. Wolfe St. Meyer 3–166, Baltimore, MD 21205; Frederick Schaerf, M.D., Norman D. LaFrance, M.D., Justin McArthur, M.D., Mary J. Bascom, B.A.

#### **Educational Objectives:**

To demonstrate cortical and subcortical changes in SPECT scan are associated with HIV infection, and HIV-related dementia.

#### Summary:

A previous PET study<sup>1</sup> identified cortical and subcortical changes in demented AIDS patients, but not nondemented patients. We SPECT scanned 13 HIV-seropositive individuals and five matched normal controls. Seven of the 13 had early HIVrelated dementia (HIVRD); six were HIV positive with *no* neuropsychological symptoms. Paired (right and left) ROI's were placed on the frontal, temporal, parietal and occipital cortex, and over basal ganglia, and counts/pixel/minute assessed. We analyzed the basal ganglia:cortex ratio and cortical asymmetry measures where for paired right and left ROI's, XR and XL we used the formula  $\frac{XR - XL}{(XR + XL)/2}$ . When all SPECT measures were considered, six of seven HIVRD patients had one or

more values 2 SD or more outside the normal range. The exception was an individual with early and mild HIVRD. Unexpectedly, four of six nondemented HIV patients also had abnormalities in BG:CX ratios or asymmetries  $\geq$ 2SD from normals. The highest frequency of abnormalities was seen in the parietal area, where nine of 13 HIV-positive patients (69%) had an asymmetry index <sup>2</sup> more than 2 SD's from the normal mean of  $-0.95\pm2.0$ . We interpret these data as reflecting diffuse brain involvement by HIV, even in the absence of dementia. As patients are in a longitudinal protocol, repeat cognitive and SPECT measures will be available to examine predictive validity of SPECT in cognitive decline.

**References:** 

<sup>1</sup>Rottenberg DA *et al.* Ann Neurol 22:700-706, 1987.

<sup>2</sup>Haxby JV et al. Arch Neurol 43:882-885, 1987.

#### NR220

## AIDS IS ASSOCIATED WITH A HIGH RATE OF SUICIDE

Thursday, May 12, 9:00 a.m.-10:30 a.m.

Peter M. Marzuk, M.D., Pyschiatry, Cornell Univ Med Col, 1300 York Avenue, New York, NY 10021; Helen Tierney, M.D., Kenneth J. Tardiff, M.D., Edward B. Morgan, M.P.H., J. John Mann, M.D.

#### **Educational Objectives:**

To alert physicians and health care policy planners to the high rate of suicide associated with AIDS. 2) To increase understanding of the epidemiological characteristics and psychiatric status of individuals with AIDS who commit suicide.
To stimulate discussion of the implications of a high AIDS-related suicide rate for psychiatric management and longer-term public policy issues, including HIV antibody testing.

#### Summary:

The acquired immunodeficiency syndrome (AIDS) is associated with a wide range of psychiatric syndromes including depression, psychoses, delirium and dementia. <sup>1</sup> It has been suggested anecdotally, that while AIDS patients have suicidal ideation, the risk of suicide attempts is low.<sup>1</sup> In a comprehensive case review of medical examiner records and a cross-match of the suicide registry with AIDS surveillance data in New York City, we have found that the rate of suicide among men with AIDS aged 20 to 59 is 680.56 per 100,000 person-years. <sup>2</sup> This represents a relative risk in males with AIDS in this age group 36.30 times that of males in this age group without this diagnosis (95% C.I. 20.45 to 64.42). The overall relative risk of suicide in the AIDS population based on age and gender specific rates is 66.15 times that of the general population (95% C.I. 37.38 to 117.06). Individuals with AIDS who committed suicide tended to be single, white, homosexual males, mean age 37.5, who used violent means (jumping, hanging, firearms) and who had the diagnosis for less than six months. We will present data on an additional 24 cases of suicide totalling 36 cases occurring in a three-year period in New York City. Data to be presented include the circumstances of the suicides, epidemiologic characteristics and psychiatric status of these individuals including diagnoses, recency of psychiatric contact, and history of prior suicide attempts. Comparisons of the AIDS-related suicide rate with suicide rates of other medical illnesses as well as the biological, psychosocial, and demographic factors contributing to suicide risk will be discussed. The implications for psychiatric management of AIDS patients and long-term public policy issues, especially HIV antibody testing, will be addressed.

#### References:

<sup>1</sup>Holland JC, Tross S: The psychosocial and neuropsychiatric sequelae of the acquired immune deficiency syndrome and related disorders. *Ann Intern Med* 103:760-764 1985.

<sup>2</sup>Marzuk PM, Tierney H, Tardiff K, Gross EM, Morgan EB, Hsu Ma, Mann JJ: Increased risk of suicide in persons with AIDS. JAMA in press 1988.

# PSYCHIATRIC CORRELATES OF BEHAVIORAL INHIBITION IN CLINICAL AND EPIDEMIOLOGIC SAMPLES OF YOUNG CHILDREN

Joseph Biederman, M.D., Child Psychiatry, Mass General Hospital, 15 Parkman Street ACC-625, Boston, MA 02114; Jerrold F. Rosenbaum, M.D., Jerome Kagan, Ph.D.

#### **Educational Objectives:**

Clinicians will learn that the termperamental characteristic of behavioral inhibition confers to the child a risk for psychopathology, particularly anxiety disorders.

#### Summary:

"Behavioral inhibition to the unfamiliar" as defined in the work of Kagan and colleagues as well-defined early temperamental characteristic found to be highly prevalent in young children of parents with panic disorder and agoraphobia. We have examined the psychopathological correlates of behavioral inhibition in this sample of children at risk, as well as in an epidemiologically derived sample of children identified at 20 months of age as inhibited or uninhibited. In the clinically derived sample ("children-at-risk"), comparisons were made between 4- to 7-year-old children of parents with psychiatric disorders identified as inhibited (N=18) and non-inhibited (N=12). In the epidemiologically derived sample, comparisons were made between 4- to 7-year-old children identified at 20 months of age as inhibited (N=22) and uninhibited (N=19). Psychiatric assessments of the children were based on structured interviews (DICA-P) with the mothers conducted blindly and independently to the temperamental classification of the child. In the children-at-risk sample, the overall rate of DSM-III-defined disorders (77.8% vs 41.7%, p<0.05) and overanxious disorder (27.8% vs 0.0%, p<0.05) were significantly higher than in those without behavioral inhibition. The rates of all diagnosable disorders were higher in behaviorally inhibited children compared with non-inhibited ones, including anxiety disorders (33.3% vs 8.3%), affective disorders (22.2% vs 0.0%), encopresis/enuresis 22.2% vs 0.0%), and attention deficit disorder (33.3% vs 16.7%) and more inhibited children had at least four DSM-III diagnosable disorders per child (33% vs 0%, p<0.05), suggesting that these children may have clinically significant pathology. In the epidemiological sample, the rates of psychopathology among behaviorally inhibited children were circumscribed primarily to the anxiety disorders (45% vs 26%), particularly phobic disorders (simple and social phobia 32% vs 5%, p<0.05). In this sample, uninhibited children had higher rates of attention deficit disorder and oppositional disorder (63% vs 27%, p<0.1) and enuresis (37% vs 18%, p<0.05) compared with the inhibited children. These findings indicated that behavioral inhibition to the unfamiliar, as defined and measured in the previous work of Kagan et al., is an identifiable risk factor for psychopathology, particularly anxiety disorders, in young children. Behavioral inhibition in a child of a psychiatric patient seems to confer a serious risk for a wide range of psychopathology beyond the anxiety syndromes. These finding have implications for the development of preventive and early intervention strategies for children risk.

#### **References:**

1. Kagan J, Reznick JS and Snidman: The Biology and Psychology of Behavioral Inhibition in Young Children. Child Dev (in press).

2. Rosenbaum, JF, Biederman J, Gersten M, Hirshfeld D, Meminger SR, Herman JB, Kagan J, Reznick JS, Snidman N. Behavioral Inhibition in Children of Parents with Panic Disorder and Agoraphobia. Arch Gen Psyc (in press).

## DEPRESSION, DYSPHORIC AFFECT AND MOTHER/CHILD INTERACTION

Grazyna Kochanska, Ph.D., Lab. Dev. Psych., NIMH, 9000 Rockville Pike Bldg 15K, Bethesda, MD 20892; Leon Kuczynski, Ph.D.

## Educational Objectives:

This study provides some evidence on differences between well and affectively ill mothers regarding interactions with their children. The lifetime diagnosis of depression, as well as dysphoric affect immediately proceeding the interaction, were found to have impact of mothers' control strategies directed at their children.

## Summary:

Mother's depression has been often linked to impairments in her interactions with her child, such as lack of involvement, hostility, punitiveness, and general increased coercion. Opposite processes, such as fear of confrontation and impaired ability to reach compromise when faced with child's resistance have also been implied. However, direct observational evidence is still scarce. In this study every episode of mothers' interventions directed at their 16- to 51-month-old children during 90 minutes of naturalistic videotaped interactions was coded. The sample consisted of 33 nondepressed, 37 unipolar depressed and 17 bipolar depressed mothers (SADS-L, RDC). In order to understand better the impact of mothers' lifetime diagnosis and immediate dysphoric mood on interactions with children, their affect was measured prior to interaction (self-report of current mood-Profile of Mood States). The use of verbal strategies (direct, indirect and unclear commands, hints, explanations, bargains, alternatives, reprimands and positive incentives) was analyzed. Compared to nondepressed women, affectively ill women were less direct with their children and used more explanations. Negative mood affected well and depressed mothers differently. Normal women who reported negative mood prior to interaction were less direct and used fewer reprimands while controlling their children than those who reported positive mood and, therefore their behavior supported the hypothesis of the link between dysphoric affect and fear of confrontation. In depressed women negative affect prior to interaction impaired the use of explanations and of polite indirect commands and increased use of nonclear commands, thus lending some support to the coercion model. The findings are examined in relation to existing models of depressions, affect and social interaction.

## **References:**

1. Kochanska, G., Kuczynski, L., Radke-Yarrow, M., & Welsh, J.D. Resolutions of control episodes between well and affectively ill mothers and their young children. *J. of Abnormal Child Psychology*, Vol. 15, No. 3, pp. 441-456 1987.

2. Kuczynski, L., Kochanska, G., Radke-yarrow, M., and Girnius-Brown, O. A developmental interpretation of young children's noncompliance. *Developmental Psychology*, Vol. 23, No. 6, 799-806 1987.

## NR223 SOCIAL DEPRIVATION AND LONG-TERM VULNERABILITY

Thursday, May 12, 9:00 a.m.-10:30 a.m.

William T. McKinney, M.D., Psychiatry, Clinical Sciences, 600 Highland Avenue, Madison, WI 53792; Gary W. Kraemer, Ph.D., Michael H. Ebert, M.D., Dennis E. Schmidt, Ph.D.

## Educational Objectives:

1) To present new data from experimental studies in nonhuman primates regarding the role of early developmental experiences in predisoposing to differential reactions to later stressors. 2) To discuss these data in the context of theories regarding the developmental origins of human psychopathological syndromes.

## Summary:

Recent work demonstrates that rhesus monkeys with short periods of social deprivation, even though behaviorally rehabilitated and behaving normally under baseline conditions, respond differently to challenges later in development as compared to socially reared monkeys. These differences are manifest in both neurochemical and behavioral parameters. If monkeys are reared and maintained in socially rich environments, CSF NE increases over the course of development. Social isolation for periods during the first six months of development reduces CSF NE. Introduction to social groups during the second year leads to return of CSF NE, and the level remains higher even when later introduced to social groups. In monkeys with a history of social deprivation, both amphetamine and alcohol produce CSF NE increases as well as increases in self-directed and stereotypic behaviors and alcohol-induced convulsions. The significance of this work is in the context of developmental vulnerability and how alterations of the attachment system early in development affect longer-term responses to stressors. Newly emerging data document an important neurobiological substrate to this long-term vulnerability but one that only becomes apparent following challenge.

#### **References:**

<sup>1</sup>Bowlby, John "Developmental Psychiatry Comes of Age" American Journal of Psychiatry 145:1, 1-10, 1988 <sup>2</sup>Kraemer, Gary W. "Effects of Differences in Early Social Experience on Primate Neurobiological-Behavioral Development" The Psychobiology of Attachment and Separation Reite, M.; Field, T. (eds) Academic Press: New York, 135-161, 1985.

## NR224 PSYCHIATRIC SEQUELAE OF CHILDHOOD DISABILITY

Thursday, May 12, 9:00 a.m.-10:30 a.m.

Naomi Breslau, Ph.D., Psychitary, Henry Ford Hospital, 2799 West Grand Blvd., Detroit, MI 48202; Glenn C. Davis, M.D.

## Educational Objectives:

(1) To understand the contribution of organic and environmental factors influencing psychopathology of children. (2) To understand the complex causes of psychopathology secondary to physical disability.

## Summary:

Previous research demonstrated that children with physical disabilities involving brain dysfunction are at increased risk for psychopathology. Because these conditions involve neurological as well as physical abnormalities, afflicted children may be at risk for psychopathology of organic origin as well as for dysphoric reactions to their handicap. We compared 230 children with cystic fibrosis, cerebral palsy (CP) myelodysplasia or multiple handicaps and 335 non-disabled random controls on symptoms elicited from the children in structured diagnostic interviews. Disabled children, irrespective of medical diagnosis, were significantly more depressed than controls (t=3.34; p<.005). Additionally, children with CP, myelodysplasia and multiple handicaps, all conditions involving the brain, reported significantly more symptoms of attention deficit than children with CF or controls. (F=6.91; p < .0001). A multivariate analysis revealed that, in children with conditions involving the brain (excluding those with mental retardation who were unable to be interviewed), depressive symptoms were associated with family discord, a factor that increases the risk for psychopathology in all children, whereas symptoms of inattention were unrelated to family discord. These findings suggest that children with conditions involving the brain manifest dysphoric reaction seen also in children with other physical disabilities and excess in inattention symptoms, uniquely associated with brain dysfunction and unaffected by environmental factors.

## **References:**

1. Breslau N: Psychiatric Disorder in Children with Physical Disabilities. *Journal of the a American Academy of Child Psychiatry*, 24, 1:87-94, 1985.

2. Rutter M: Psychological Sequelae of Brain Damage in Children, American Journal of Psychiatry, 138:1533-1534.

#### NR225

# SEROTONERGIC FUNCTION IN AUTISTIC YOUNG ADULTS

P. Anne McBride, M.D., Psychiatry, Cornell Medical Col, 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 preliminary results of an ongoing research study.

#### Summary:

*Introduction:* Altered serotonergic function has been postulated in autistic disorder. Physiological responses mediated by serotonin were evaluated in 6 male young adults with autistic disorder versus 6-8 age- and gender-matched normal controls. *Methods:* The responsiveness of serotonergic pathways in the CNS was assessed by neuroendocrine challenge with a single 60 mg oral dose of fenfluramine, an indirect serotonin agonist. The magnitude of serotonin-amplified platelet aggregation, mediated by the platelet 5-HT<sub>2</sub> receptor complex, was measured in conjunction with assay of platelet 5-HT<sub>2</sub> receptor binding indices. *Results:* Compared to controls, autistic subjects exhibited blunted prolactin release following fenfluramine administration (repeated measures ANOVA, F=6.72, p<.03; following adjustment for plasma drug levels, F=20.77, p.<0.001). Furthermore, the mean serotonin-amplified platelet aggregation response was significantly reduced in autistic subjects (t=2.82, p<0.02), as was the mean number of platelet 5-HT<sub>2</sub> receptor sites (t=2.40, p<0.04); the mean ratio of the aggregation response to the number of platelet 5-HT<sub>2</sub> receptor sites did not differ between groups (t=0.72). Among autistic subjects, fenfluramine-induced prolactin release correlated postively with the serotonin-amplified platelet aggregation response (r=0.93, p<0.01) and negatively with whole blood serotonin content (r=0.83, p<0.05). *Conclusions*. The results of the fenfluramine challenge test are compatible with the hypothesis that central serotonergic responsiveness is decreased in male autistic young adults. Correlations between central and peripheral serotonergic measures suggest systemic alterations in serotonergic function in autism, which may include changes in the responsivity of 5-HT<sub>2</sub> receptor populations.

#### References;

<sup>1</sup>McBride, PA, Mann, JJ, Polley, MJH, Wiley, AJ, Sweeney, JA: Assessment of Binding Indices and Physiological Responsiveness of the 5-HT<sub>2</sub> Receptor on Human Platelets. Life Sci, 40: 1799-1809 1987.

<sup>2</sup>Anderson, GM, Hoshino, Y: Neurochemical Studies of Autism, in Cohen DJ, Donnellan Am, Paul, R (eds). Handbook of Autism and Pervasive Developmental Disorders, New York, J. Wiley & Son, pp 161-191 1987.

## NR226 PANIC DISORDER IN CHILDREN: DOES IT EXIST?

Donna Moreau, M.D., Child Psychiatry, NYS Psychiatric Inst, 722 West 168th Street Box 14, New York, NY 10032; Virginia S. Warner, M.P.H., Myrna M. Weissman, Ph.D.

## **Educational Objectives:**

At the end of the session, the participant will be able to: Recognize the symptoms of panic disorder as they present in childhood; diagnose panic disorder in children; be familiar with comorbidity of panic disorder in childhood.

## Summary:

The conventional clinical wisdom has been that Panic Disorder does not occur in children. Recently, there have been isolated clinical reports on the existence of Panic Disorder in childhood and adolescence (Herskowitz 1986, Van Winter 1984). However, these reports are not based on systematic diagnostic assessment. The only two studies using structured interviews in small samples failed to show the presence of Panic Disorder in 33 children hospitalized on an inpatient psychiatric unit (Livingston 1985) and in 102 children referred for outpatient psychiatric evaluation (Herschberg 1982). Retrospective histories taken from adults with Panic Disorder, studies on parents of children with anxiety disorders, and studies of children with depressed and anxious parents have lent support to an association between adult and childhood forms of anxiety disorders (Berg 1976, Weissman 1984, Breslau 1987). Specifically, adults with Panic Disorder have reported either early histories of Separation Anxiety Disorder (Klein 1964, Gittleman & Klein 1984, Raskin 1982) or early onset of their Panic Disorder, 14% 14 years or younger and 4% nine years or younger (Sheehan 1981). This paper presents seven cases of Panic Disorder based on direct structured diagnostic assessment (K-SADS) of the mother about the children and of the children themselves who were part of a study of 220 children at high risk or low risk for depression followed for a two-year period. The final diagnoses were made blindly by a child psychiatrist based on all available information. The age of onset of Panic Disorder ranged from five years to 18 years with a mean of 10.4 years. This paper will describe the symptoms, age of onset and comorbidity of Panic Disorder in these children. The finding from this study suggest that Panic Disorder, which is similar in symptom pattern to the adult disorder, does occur in children.

## **References:**

1. Sheehan DV, Sheehan KE, Minichiello WE: Age of onset of phobic disorders: A reevaluation. *Comp. Psychiatry* 22:544-553 1981.

2. Weissman MM, Leckman JF, Merikangas KR, et al.: Depresison & Anxiety disorders in parents and children. Arch Gen Psychiatry 41: 845-852 1984.

## NR227

# PTSD IN VIETNAM VETERANS: CLINICAL-EEG FINDINGS

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

Marion E. Wolf, M.D., Psychiatry, Veterans Administration, Buckley Road, North Chicago, IL 60064; Afshin Alavi, M.D., Aron D. Mosnaim, Ph.D.

## Summary:

In a study of forty-four Vietnam Veterans treated at the Stress Disorder Unit at the North Chicago VA Medical Center, it was found that over 75% of the patients had a concomitant substance abuse diagnosis. The predominant PTSD symptom constellation involved poor impulse control (56% of cases); Anxiety or depressive related symptoms were found in 44% of patients. Eighteen veterans had electroencephalographic studies. The EEGs, sleep and awake were found to be within normal limits in all of the patients studied.

In preliminary findings we have found that carbamazepine may be helpful in the symptomatic relief of many PTSD manifestations. The beneficial effects of this drug in PTSD may be attributed to therapeutic effects in seizure foci which cannot be identified by routine EEG diagnostic techniques. Alternatively, the therapeutic effects of carbamazepine may be related to the ability of this drug to reduce poor impulse control, angry outbursts and aggression. The clinical implications of these findings will be discussed.

## NR 228 FURTHER EMPIRICAL RESEARCH ON DEFENSE STYLES

Michael P. Bond, M.D., Psychiatry, Inst. of Comm & Fam Psych, 4333 Cote Ste. Catherine Road, Montreal, Quebec, Canada H3T 1E2; J. Christopher Perry, M.D., Maryse Gautier, M.Ed., Marilyn Goldenberg, M.S.W., Joan Oppenheimer, B.A., Joan Simand, M.S.W.

## Summary:

Further validation of a self-report questionnaire designed to measure defense styles was tested by correlating 156 subjects' responses to the questionnaire with their scores on the Defense Mechanism Clinical Rating Scale which involves judges rating defense mechanisms from a videotaped clinical assessment. There were significant positive correlations between the use of the maladaptive defense style yielded by the questionnaire and the rating of immature defenses by the clinical rating scale, as well as with low scores on the Health Sickness Rating Scale. There was a significantly negative correlation between the maladaptive defense style and the clinical rating of mature defenses. However, there was no evidence to support the validity of the measure for separate image-distorting and self-sacrificing defense styles. The authors speculate that the lack of evidence for cross-validity with the intermediate styles results from differences in the construction of the two measuring scales as well as in the context in which they are administered. A six month follow-up showed stability of defense styles over time, with a shift toward greater maturity.

#### NR229 BORDERLINE AND ANXIETY DISORDER COEFFECT ON OUTCOME

H. George Nurnberg, M.D., Psychiatry, Queens Hospital Center, 82-68 164th Street, Jamaica, NY 11432; Marjorie Raskin, M.D., Philip E. Levine, M.D., Simcha Pollack, Ph.D., Robert Prince, Ph.D., Ozzie Siegel, Ph.D.

## Summary:

This study investigates the coeffect of Borderline Personality Disorder (BPD) and Anxiety Disorder (AD) on outcome. Sixtytwo AD and 48 non-Anxious outpatients were identified in an Anxiety-Personality Disorder Study Project. All patients received Axis I and II diagnoses conforming to *DSM-III-R*. Personality Disorder (PD) diagnosis is established by inventory where each item in every personality disorder set is rated for each patient. Multiple diagnoses are recorded. Evaluation of outcome was determined by the Global Assessment Scale (GAS) after entry and exit or extended treatment.

BPD prevalence was 20%. Analysis showed a significant effect of BPD comorbidity with lower treatment outcome in both anxious and non-anxious patients. Anxiety had a small but consistent effect on outcome within the three personality groups— BPD, other PD, non-PD.

BPD appears to be a strong factor in poor treatment outcome and must be recognized as a potential source of variance in studies on the treatment of anxiety and other clinical disorders. We intend to pursue this finding further with more specific analyses of individual BPD criteria and outcome.

## NR230

## CAFFEINE DEPENDENCE IN MODERATE COFFEE DRINKERS

John R. Hughes, Psychiatry, Univ. of VT, 1 SO Prospect Street, Burlington, VT 05401; Stephen T. Higgins, Ph.D., Suzy Gulliver, M.S., Gina Mireault, B.A.

#### Summary:

To test caffeine withdrawal, 10 moderate coffee drinkers (three-seven cups/day) were given decaffeinated coffee or caffeinated coffee (decaffeinated coffee plus 100 mg caffeine) for one day each in a crossover design. To test for pyschological dependence on caffeine, subjects were then given concurrent access to caffeinated and decaffeinated for two days and the rates of self-administration of each examined. Assignment to coffees was randomized and double-blind. The procedures were repeated weekly for five-six independent tests for each subject. Subjects reported more withdrawal symptoms (p < .05) and especially more headaches (p < .006) on decaff only days. In the concurrent access test, 61% of the coffees self-administered were caffeinated and 39% were decaffeinated (p < .002). Eight of the ten subjects self-administered more caffeinated coffee than decaffeinated coffee. Headaches on decaff days predicted subsequent preference for caffeinated coffee (p < .03).

Our results indicate cessation of caffeine reliably produces withdrawal and coffee drinkers use coffee to self-administer caffeine.

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

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

## NR231 SCHIZOTYPAL GENDER DIFFERENCES

Thomas H. McGlashan, M.D., Reseach Inst., Chestnut Lodge, 500 West Montgomery Avenue, Rockville, MD 20850

#### Summary:

Gender differences in psychopathology are well known and studied in the pyschoses,<sup>1</sup> but such research in the *DSM-III* Axis *II* disorders has just begun. This report looks at gender differences in clinical profile and long-term course for an inpatient sample with *DSM-III* schizotypal personality disorder (SPD: male N=17, female N=16) from the Chestnut Lodge followup study.<sup>2</sup> *Method:* Outcome data were collected by interview with adequate reliability between 2-32 years post index discharge. Baseline and *DSM-III* diagnostic assessment involved independent and reliable rating of the patients' abstracted medical records. Gender analysis compared male versus female SPD patients across this battery using multivariate techniques to minimize type 1 error. *Results:* Men were more socially and sexually isolated up to index admission. Women were superior in symptom severity and global functioning at fifteen-year follow-up. This pattern of gender differences echoed, to a muted degree, the pattern found among the study's schizophrenic patients. *Significance:* This is a first investigation of gender differences for *DSM-III* SPD. It tests for these differences from both cross-sectional and longitudinal perspectives and employs stringent analytic procedures to screen out spurious findings. Results constitute yet another line of evidence placing SPD within the schizophrenic spectrum.

#### NR232 DEFENSES AND PARENTAL BONDING IN EATING DISORDERED WOMEN

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

Howard Steiger, Ph.D., Eating Disorders Program, Douglas Hospital, 6875 LaSalle Blvd, Verdun PQ, Canada H4H 1R3; Julie Vanderfeen, B.Sc., Pierre P. Leichner, M.D.

## Summary:

There is increasing interest in the "interface" between personality disturbances and the eating disorders (ED's) anorexia nervosa and bulimia. Studies that have compared personality and related features of ED patients to those of controls have found eating disorders to exhibit more pathology than controls, bulimics more so than anorexics. This study compared 53 anorexic or bulimic women, to 25 age-matched controls on well-validated scales measuring cognitive style, defensive organization, early "object relations" and developmental traumata (including separations, and physical and sexual abuse). Most measures reliably differentiated the eating- and non-eating-disordered groups, but not the ED subtypes. ED patients endorsed more maladaptive beliefs, used more primitive defenses, rated parents as less empathic, and reported more developmental traumata, than did controls. Bulimics alone reported higher incidences of childhood sexual abuse. Primitive vs. mature defensive organization were associated with identifiable patterns of early relations. ED's may thus be associated with difficulties in the personality that suggest a defect in self-development, and our data link the latter to identifiable developmental experiences. New data on outpatient psychiatric controls suggest, however, that such disturbances are not specific to ED's, and indicate the need to view the etiology of eating disorders through a biopsychosocial model.

# NR233 Thursday, May 12, 12 noon-2:00 p.m. SLEEP ENCEPHALOGRAPHY OF PANIC DISORDER PATIENTS AND NORMAL CONTROLS

Robert B. Lydiard, M.D., Psychiatry, Medical University, 171 Ashley Avenue, Charleston, SC 29424; Michele T. Laraia, M.S.N., James C. Ballenger, M.D., Elizabeth Howell, M.D., Victor Prockow, John Gross, M.D.

#### Summary:

There has been much controversy over the relationship between panic disorder and depression. One characteristic commonly associated with major depression is an abnormal sleep architecture, particularly the shortened latency to the onset of rapid eye movement (REM) sleep. Accordingly, encephalographic sleep recordings were compared in patients with panic disorder and normal control subjects on the second of two consecutive nights. Patients were panic disorder patients (14 females, four males) age  $35.6\pm8.8$  years (range 22-56) and controls were seven females and seven males, age  $30.7\pm7.6$  (range 22-46). No differences in night two measures were found in sleep latency, REM latency (patients:  $64.3\pm18$  minutes vs controls:  $75.6\pm26.5$  minutes), time asleep, stage I time or percent of sleep, REM time, number of episodes or percent of sleep, delta time or percent of sleep. There was a significant difference in sleep efficiency (patients:  $87.9\pm9.4^{\circ}$  vs controls:  $93.5\pm3.9^{\circ}$  p <0.03) and stage II duration (patients:  $195\pm36$  minutes vs controls:  $226\pm37$  minutes; p <0.02).

Hamilton Depression ratings were significantly higher in patients ( $15.3\pm5.6$ ) than in controls ( $3.6\pm3.4$ ); p < 0.0001. There was no correlation between Hamilton scores and REM latency in patients or controls. There was no differences in REM latencies between the eight depressed ( $63.3\pm11.2$  minutes) and 10 nondepressed ( $64.0\pm22.1$  minutes) panic disorder patients.

These data add to the growing body of literature supporting the distinction between panic disorder and depression.

#### PREVALENCE OF ANXIETY DISORDERS AMONG ALCOHOLICS

Robert B. Lydiard, M.D., Psychiatry, Medical University, 171 Ashley Avenue, Charleston, SC 29425; Elizabeth Howell, M.D., Robert J. Malcolm, M.D., James C. Ballenger, M.D.

#### Summary:

There has been increasing interest in the anxiety disorders in recent years, particularly in the panic-related disorders agoraphobia and social phobia.

Some studies have suggested that a substantial proportion of these anxious patients may abuse alcohol. We assessed 49 males admitted consecutively to the Charleston Veterans Administrative Medical Center Alcohol Detoxification Unit in order to assess whether there was a greater than expected prevalence of anxiety disorders in this population.

Method: We used the Structured Clinical Interview for DSM-III (SCID) for affective and anxiety disorders. Patients who had anxiety symptoms preceding the onset of alcohol abuse or had symptoms after at least one year of abstinence were given a "definite" diagnosis; 49 consecutively admitted male veterans were assessed after acute detoxification.

*Results:* Fourteen percent of patients assessed had definite panic disorder. Twenty-two percent had definite social phobia. A substantial proportion of patients also had affective disorders.

Conclusions: We found a greater than expected prevalence of anxiety disorders in this population of alcoholics. Treatment of alcoholism should include a careful evaluation for the presence of associated psychiatric diagnoses.

#### NR235 GABAMINERGIC MECHANISMS IN ANTIPANIC DRUG EFFICACY

ARREST HISTORY OF HYPERACTIVE BOYS GROWN UP

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

Michael F. Breslow, M.D., Psychiatry, Univ of Arizona, 1501 N. Campbell Avenue 70PC, Tucson, AZ 85724; Martha Fankhauser, M.S., Rebecca L. Potter, M.D., John Misiaszek, M.D., Keith M. Meredith, Ph.D., Deane G. Hope, Jr., M. Ed.

#### Summary:

The authors hypothesize that enhancement of gabaergic transmission is a key pharmacologic component in antipanic drug efficacy. To support this hypothesis they review the gabaergic properties of current antipanic medications and present data from their trial of the selective GABA agonist, baclofen, in the treatment of panic disorder (PD).

Effective pharmacologic treatments for panic disorder (benzodiazepines, tricyclic antidepressants, monoamine oxidase inhibitors) all up-regulate GABA receptors. Antidepressant and antianxiety drugs that lack gabaergic activity are not effective in PD (bupropion, buspirone). The authors thus hypothesized that enhancement of gabaergic transmission may be the mechanism of action that results in antipanic drug efficacy.

To test this hypothesis the authors treated nine medication-free PD subjects with baclofen (30 mg/day) in a double-blind, placebo-controlled, crossover trial. Baclofen was significantly more effective than placebo in reducing panic attacks and clinical measures of anxiety (Hamilton Anxiety Scale, Zung Self Rating Anxiety Scale, Symptom Checklist-90 Anxiety and Interpersonal Sensitivity subscale scores)—p < 0.05 on all measures. Implications for understanding the mechanism of action responsible for antipanic drug efficacy are discussed.

#### NR236

## Thursday, May 12, 12 noon–2:00 p.m.

Salvatore Mannuzza, Ph.D., Psychology, NYS Psychiatric Inst., 722 West 168th Street, New York, NY 10032; Rachel Klein, Ph.D., Paula Konig, B.A. Noreen Bonagura, M.S.W., Tina Giampino, B.A.

#### Summary:

We report on a prospective follow-up of 103 male adolescents (ages 16-23) who were diagnosed as hyperactive between ages 6 and 12, and 100 normal controls. The official arrest records of all subjects who resided in New York State during the follow-up interval were obtained. *DSM-III* diagnoses (based on interviews with adolescents and their parents) were made on 98% of the initial cohort as follow-up. Although other investigators have reported on the arrest history of hyperactive children in a prospective design (Weiss, Satterfield), this is the first account relating follow-up mental status to official arrest records. Significantly more probands than controls had been arrested (39% vs. 20%, p < .01), convicted (28% vs. 11%, p < .01), and incarcerated (9% vs. 1%, p < .03). About two-thirds of arrested probands (vs. one-third of controls) were charged with a felony (p < .10). Arrest history was significantly associated with follow-up diagnoses of conduct and substance use disorders, but not ADDH. We conclude that: (1) hyperactive children are at an increased risk for criminal activities leading to arrest in early adulthood; (2) the association between arrest history and childhood hyperactivity is almost entirely explained by the concurrent presence of a young adult conduct disorder. Our findings stress the importance of early identification of conduct problems in ADDH youths.

## NR237 RELIABILITY OF ANXIETY DIAGNOSES AND SYMPTOMS

Salvatore Mannuzza, Ph.D., Therapeutics, NYS Psychiatric Inst, 722 West 168th Street, New York, NY 10032; Abby J. Fyer, M.D., Lynn Y. Martin, R.N., M.S. Gallops, M.Ph., Jack M. Gorman, M.D., Michael R. Liebowitz, M.D., Donald F. Klein, M.D.

## Summary:

Test-retest reliability of lifetime disorder diagnoses and symptoms was determined using the Schedule for Affective Disorders and Schizophrenia-Lifetime anxiety Version (SADS-LA). Subjects were 104 patients seen at an anxiety research clinic. Diagnostic reliability ranged from good to excellent (kappas ±.60-+ .90) for generalized anxiety, social phobic, panic, agoraphobic, and obsessive-compulsive disorders. Simple phobia showed poor agreement. The *DSM-III-R* distinction of panic disorder with and without agoraphobia improved reliability. Subdisorder symptoms were defined as symptoms central to an anxiety diagnosis, but which did not meet disorder criteria due to insufficient frequency, intensity, associated features, distress, or impairment (e.g., panic attacks with three instead of four associated symptoms). Good to excellent reliability was found for any panic attack, the spontaneous and situational subtypes of panic, two social and three nonsocial irrational fears (asking directions; social affairs; traveling; driving oneself; dead bodies, death, funerals). In contrast, limited symptom attacks, stimulus bound panics, and most social and nonsocial fears had only fair to poor reliability. Major sources of disagreement (e.g., information variance, threshold for impairment attributing the same or similar symptoms to different disorders) are reviewed for each diagnosis and symptom. The significance and implications of these findings for other research investigations (e.g., treatment, family, biological, and epidemiological studies) are discussed.

#### NR238 STRATEGIC SELF-THERAPY FOR PERSONALITY DISORDERS

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

John O. Beahrs, M.D., Psychiatry, Ore Health Sci University, VA Med Ctr Outpatient Clinic, PO. Box 1036, Portland, OR 97207; John L. Butler, M.D., Stanley G. Sturges, M.D.

## Summary:

Strategic Self-Therapy (SST) is a new psychology protocol utilizing limited intensity, rigorus therapeutic boundaries, and contextual reframing as the vehicle for change. It is presented to encourage research on a safe and effective treatment for personality disorders that is more cost-efficient than intensive psychotherapy. SST theory is derived from systems and hypnosis research showing intrapsychic structure to vary with its psychosocial context, which can be altered strategically by assigning different meanings to otherwise invariant entities and events. Regressive dependency is minimized by explicitly differentiating the roles of patient, therapist, and system. Patients do the "work" of defining/redefining their identity and direction, and agree to refrain from destructive acting out. Therapists serve as catalyst/consultant, prescribing self-therapy projects that enable patients to reframe/redirect discordant aspects of themselves. Available social systems are used as a crisis resource. Ongoing research utilizes case study, convergent inquiry and independent group design. Current data supports the hypotheses that, compared to intensive psychotherapy, SST is comparably effective, more efficient in time and cost, and accompanied by less regression and acting out; hence its value for conditions with high regressive potential such as dissociative and borderline disorders.

#### NR239 ADRENERGIC DYSFUNCTION IN ANXIETY DISORDERS

Oliver G. Cameron, M.D., Psychiatry, University of Michigan, 900 Wall Street, Ann Arbor, MI 48109; Charles B. Smith, M.D., George C. Curtis, M.D., Myung A. Lee, M.D., Peggie J. Hollingsworth, Ph.D., George N.M. Gurguis, M.D.

We reported previously that people with panic attacks have fewer alpha-2 adrenoreceptors on platelets than normal subjects when determined by binding (Bmax) of the specific antagonist vohimbine, but had normal levels when measured by the specific agonist clonidine. Further decreases in vohimbine binding were observed after 3.5, 14, and 26 weeks of imipramine treatment (average dose=96 mg); clonidine binding also showed reductions during impramine treatment. Impramine also increased circulating catecholamines (which were normal before treatment). We now report that we have replicated our finding of decreased vohimbine binding in panic patients, and found a similar decrease in people with generalized anxiety disorder. However, in contrast to our prior finding of normal clonidine binding in panic patients, in this study we found decreased clonidine binding in both panic and generalized anxiety. Again, pretreatment circulating (supine and standing) catecholamines, as well as blood pressure and pulse, were normal. Additionally, despite normal catecholamine and blood pressure and pulse levels, patterns of intercorrelations among binding parameters, catecholamines, and blood pressure and pulse were similar for panic and generalized anxiety patients but different than normal subjects. Impramine treatment (mean dose=102 mg) again produced a small reduction in clonidine binding after 3 and 8 weeks; in contrast to our prior result, however, in this study vohimbine binding was increased after 3 weeks of impramine treatment despite a rise in circulating norepinephrine levels, but returned to approximately normal levels after 8 weeks. Alprazolam (mean dose=4.0 mg) produced a reduction in vohimbine binding at 3 weeks and a return toward normal at 8 weeks: clonidine binding showed minimal change in response to alprazolam. Thus, these results confirm that there are fewer vohimbine binding sites in drug-free panic patients, and suggest that the number of clonidine binding sites may also be reduced somewhat. Additionally, drug-free patients with generalized anxiety appear to have fewer sites. Effects of antianxiety drugs were small or inconsistent, and will require further study. These results support the hypothesis of adrenergic dysregulation in people with anxiety disorders.

#### NR240 DEPRESSION AND PREVIOUS ALCOHOLISM IN THE ELDERLY

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

Brian L. Cook, D.O., Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; George Winokur, M.D., Vickie Beach, R.N.

#### Summary:

The purpose of this paper is to evaluate whether a past history of alcoholism in geriatric depressives is clinically relevant. This project consisted of an historical prospective study of male non-bipolar depressives over age 55 years hospitalized during a five year period. Subjects were included if they met Feighner Criteria for a major depressive episode, regardless of alcohol history. Sixty-two subjects met this criteria, and 58 were available for follow-up interview three to five years after this index admission. On this follow-up, current psychiatric symptomatology, illness course, family history of psychiatric illness, and alcohol use history were systematically collected.

Among the 58 subjects with complete follow-up information, 16 were noted to have a history of alcoholism prior to their index admission. These past alcoholic geriatric depressives were noted to have a presentation at index with more agitation and suicidal ideation. Both their pre- and post-index course of illness were remarkable for clearly more chronic patterns. Family history of alcoholism was more common in the alcoholic group.

This study supports a past history of alcoholism in the elderly as being a risk factor for chronicity of depression. Such depressives rarely achieve satisfactory remission of their symptoms, and appear to share qualities of those seen in depression spectrum disorder.

## NR241 SEASON OF BIRTH AND CHILD TEMPERAMENT: NEW FINDINGS

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

Michel Maziade, M.D., Laval Robert-Giffard, Centre de Recherche, 2601 de la Canardiere, Beauport QC, Canada G1J2G3; Robert Cote, Ph.D., Jacques Thivierge, M.D.

## Summary:

The epidemiological relationship between month of birth and child temperament was studied in three large random samples (N=2103) of children in the general population from infancy to twelve years, taking into account socioeconomic status, age, and sex. As previously reported, two temperamental factors were derived from principal component analysis. Subjects were characterized by their factor scores; the type of relationship between these factor scores and month of birth, SES, sex were analysed through three factor ANOVAs. Analyses in the extremes of the temperament distribution were also performed. A significant statistical effect of month of birth on child temperament was observed (ANOVA, df=6, F=5.23, p=.0001 for temperament Factor 1; ANOVA, df=6, F=5.09, p=.0001 for temperament Factor 2) and data suggest that this effect decreases with age. The association with month of birth is not general but specific to some temperamental traits and aggregation of traits. Three types of implications are discussed: (1) etiological, concerning potential biological correlates of temperament that are linked to seasons (2) methodological, for avoiding in future temperament studies the possible bias created by a season of birth effect (3) epidemiological, regarding the formulation of new causative hypotheses possibly underlying the well documented birth seasonality effect on psychiatric disorders, especially schizophrenia.

## NR242 EXTREME TEMPERAMENT IN A CHILD PSYCHIATRIC SAMPLE

Michel Maziade, M.D., Laval Robert Giffard, Centre De Recherche, 2601 de la Canardiere, Beaupot, Que, Canada G1J2G3; Chantal Caron, M.D., Robert Cote, Ph.D., Pierrette Boutin, M.Ps., Jacques Thivierge, M.D.

## Summary:

This paper reports on a new epidemiological-clinical study of the NYLS temperament model in a consecutive sample of children (N=814) referred to a regional child psychiatric hospital. Temperament comparisons in this clinical population were made by using temperament normative values obtained in previous random samples of the general population of the Quebec city area (Maziade et al, 1984)<sup>1</sup>. Different clinical diagnostic groups were derived from an operationalized review of the whole hospital chart whose interrater reliability was tested and which was performed blind to temperament scores. The diagnostic groups were confirmed through discriminant function analyses. The results 1) replicate through principal component analyses in this child psychiatric population the same two factors of temperament as those previously found at different age levels in random samples of our general population; 2) show in the psychiatric population of children an overproportion of extremely adverse temperaments on both factors; 3) confirm an absence of equivalence between an extremely adverse temperament and clinical disorder; 4) suggest a specific relationship between particular temperament factors and the type of diagnosis. Findings provide promising leads for future clinical research on temperament, family functioning, and child psychiatric diagnoses. 1 Maziade M. et al. *Journal of the American Academy of Child Psychiatry*, 23, 5:582–587, 1984.

## NR243

## DST AND TRH TESTS IN POST-TRAUMATIC STRESS DISORDER

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

Thomas R. Kosten, M.D., Psychiatry, Yale University, 904 Howard Avenue Suite 2-E, New Haven, CT 06519; Victor S. Wahby, M.D., Earl Giller, Jr., M.D., John W. Mason, M.D.

## Summary:

Recent work by our group showed that veterans with post-traumatic stress disorder (PTSD) had low urinary cortisol levels and high adrenergic activity coupled with downregulated alpha adrenergic receptors. In this study we compared male veterans with PTSDI (n=11) and major depression (MD) (n=18) to 30 well controls (C). We confirmed our earlier report of low 24 hour urinary cortisol in PTSD (50 ± 16mg/24 hrs) compared to both MD (70 ± 35mg/24 hrs) and controls (69 ± 26mg/24 hrs) (F=3.8 with PTSD contrast; df=1,55; p<0.05). After a 1 mg DST, the mean 4 PM plasma cortisol levels were: 1.9 (± 2) ug/dl for controls, 1.8 (± 2) ug/dl for PTSD, 4.1 (± 5) ug/dl for MD (F=5.6 with MD contrasts; df=1,58; p<0.02). Using a cutoff of 5 ug/dl for DST suppression, 90% of C and PTSD and 78% of MD suppressed. On the TRH test, the MD patients had lower TSH levels (7.1 ± 3.3 uU/ml) than the control (9.5 ± 4.4 uU/ml) or PTSD (10.7 ± 6.0 uU/ml) patients (F=5.1 with MD contrasts; df=1,58; p<0.03). Using a cutoff of 5 uU/ml for TRH blunting yielded: 7% of C, 18% of PTSD, 17% of MD. Although 9 patients (4 MD, 5PTSD) were on medications, mean chlorpromazine dosage (340(n=2) vs 309(n=4) mg/day) and number of patients on antidepressants (2 vs 1) did not differ between the MD and PTSD patients. When analyses were repeated excluding medicated patients, the DST (F=5.5; p<0.02) and TRH (F=3.6; p<0.05) findings remained significant. Thus, PTSD patients showed no difference from normals in DST and TRH testing, but differed from major depression.

Susan Evans, R.N., Psychiatry, Payne Whitney Clinic, 525 East 68th Street, New York, NY 10021; Richard P. Brown, M.D., Marc Glassman, Ph.D., Kenneth H. Larson, R.N.

## Summary:

Goals: To report on the reliability of the Cornell Nurses' Rating Scale (CNRS) designed to assess a broad range of psychopathology in patients with depression, mania, schizophrenia and personality and adjustment disorders. To assess the CNR's construct and concurrent validity.

Methods: A pair of nurses were trained in reliability sessions consisting of viewing and rating five patient interviews followed by discussion. Twenty-two psychiatric inpatients were rated at two time intervals by the two nurses based on observations and data collected over an eight-hour shift. Diagnostic evaluation utilizing the Structured Clinical Interview for DSM-III (SCID) and Global Assessment Scale (GAS) and Clinical Global Impression (CGI) ratings were conducted by an independent rater.

Results: Intra-class correlations (ICC's) on individual items ranged from .46 to 1.0 with 88% of items >.70 Grouped into subscales, correlations were highly significant (r=.74-.99; p < .001). Pearson correlation coefficients among the global rating on the CNRS, GAS and CGI proved highly significant (r=.81, -.65; p=.001, p=.001; r=.81, .71; p=.001, p=.001). Moderately significant correlations occurred between ratings and diagnosis in clusters with sufficient N's to permit analysis (schizophrenia; r=.55; p=.008, r=.40, p=.05 and schizoaffective illness r=.50; p=.02, r=.40; p=.05).

Significance: Results demonstrate a high level of inter-rate agreement (reliability) and support for the CNR's validity. Future studies will include measuring the scale's sensitivity to changes in patients' mood and behavior. Since the CNRS is programmed for computer use and can be completed in two minutes, it is an efficient method for nurses to assess patients and is a valuable data resource to clinicians and researchers.

#### NR245 Thursday, May 12, 12 noon-2:00 p.m. DIAGNOSIS AND PREDICTING AGAINST MEDICAL ADVICE DISCHARGE STATUS

Robert K. Heinssen, Ph.D., Research Inst. Chestnut Lodge, 500 West Montgomery Avenue, Rockville, MD 20850; Thomas H. McGlashan, M.D.

## Summary:

The empirical literature reports few distinctive features among regularly and irregularly discharged inpatients.<sup>1</sup> None of these studies, however, consider diagnosis. This investigation uses data from the Chestnut Lodge Follow-up Study to test for predictors of discharge with medical advice (WMA), against medical advice (AMA), and by transfer for inpatients with Schizophrenia (N=132), Schizoaffective Disorder (N=61), Borderline Personality Disorder (N=69), and Unipolar Affective Disorder (N=42). Methods: Ratings of baseline variables (history and admission clinical picture), as well as current diagnosis, were made from patients' abstracted medical records with adequate reliability.<sup>2</sup> Baseline variables were included from six categories: diagnostic, demographic, family, premorbid functioning, illness up to and including admission, and signs and symptoms. Results: Results suggest diagnosis plays a critically interactive role with the variables predicting discharge status and the processes that influence patient-initiated discharges. Discriminant function analyses show that indices of chronic psychoses predict transfer for all diagnoses. Angry, impulsive behavior and unstable relationships predict AMA discharge in all but unipolar patients. For unipolars, being married is most powerfully associated with AMA status. The timing of AMA discharges suggest that self discharge requests reflect disharmony in the therapeutic relationship, and that the treatment crises precipitating AMA discharges vary among the diagnostic cohorts. The nature of these crises, as well as their treatment implications, will be discussed.

## NR246

# PLASMA CATECHOLAMINES IN SOCIAL PHOBIA

Andrew P. Levin, M.D., Psychiatry, Holliswood Hospital, 87-37 Palermo Street, Holliswood, NY 11423; Diana Sandberg, M.D., Jon Stein, M.S., Barry Cohen, M.S., Tim Strauman, Ph.D., Michael R. Liebowitz, M.D.

#### Summary:

Although several reports document greater physiologic arousal in socially anxious and social phobic subjects compared to normals during performance challenge, no studies include biochemical measures. Plasma epinephrine is known to increase in normals during performance. It was hypothesized that peripheral epinephrine response to performance challenge might be greater in social phobic subjects than controls. Twenty-three patients meeting DSM-III social phobia criteria and 14 controls were monitored during a 10 minute simulated speech. Although patients reported significantly more subjective complaints and demonstrated more anxious behaviors than controls, there were no differences in heart rate, or plasma epinephrine, norepinephrin, or cortisol. In addition, there was no correlation between subjective or behavioral measures and physiologic or biochemical responses. There findings suggest that social phobic symptomatology is not mediated by peripheral autonomic arousal.

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

## NR247 PERSONALITY DISORDERS IN EATING DISORDER PATIENTS

EATING DISORDERS IN SUBSTANCE ABUSE PATIENTS

Ronald N. Marcus, M.D., Psychiatry, New York Hospital W.D., 21 Bloomingdale Road, White Plains, NY 10605; Kathrine A. Halmi, M.D., Alison Gartner, Ph.D., Armand Loranger, Ph.D.

## Summary:

*Goals:* The literature on comorbidity of personality disorders with eating disorders is sparse and contradictory. This is one of the first studies to systematically assess the presence of *DSM-III-R* personality disorder diagnoses in eating disorder patients using a standardized structured interview. *Methods:* Thirty-five hospitalized subjects with diagnoses of anorexia nervosa, bulimia nervosa. or anorexia nervosa/bulimia were administered the Personality Disorder Examination (PDE), a reliable, structured interview designed to assess Axis II disorders. *DSM-III-R* Axis I diagnoses were established using the Structured Clinical Interview for *DSM-III-R* (SCID). Patients also received the Beck Depression Inventory, Hamilton Rating Scale and Clinical Anxiety Scale. *Results:* Of Axis II diagnoses, 57% of the subjects met criteria for at least one diagnosis, 40% met criteria for two or more diagnoses and 17% of the patients had 5-7 Axis II diagnoses. There were no differences in the number or distribution of Axis II diagnoses between the three eating disorder groups. There was significant Axis I comorbidity. Lifetime prevalences of affective illness, anxiety disorders and substance abuse were 73%, 30%, and 21%, respectively. There were no differences between eating disorder groups on the Beck or Cas, but the anorectic/bulimic group had significantly lower scores on the Hamilton compared to the anorectic and bulimic groups. *Significance:* This study indicates that there is significant comorbidity between eating disorder diagnoses and personality disorders. The implications of this finding for treatment strategies and prognosis will be discussed.

## NR248

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

Ronald N. Marcus, M.D., Psychiatry, New York Hospital W.D., 21 Bloomingdale Road, White Plains, NY 10605; Katherine A. Halmi M.D.

## Summary:

*Goals:* Growing and compelling evidence suggests an association between eating disorders and substance abuse. The study described below is one of the first *controlled* studies to systematically assess the prevalence of eating disorder diagnoses, anorexia nervosa and bulimia nervosa in substance abuse patients.

Methods: Thirty women who were consecutive admissions to a substance abuse unit were given a structured interview for eating disorder behavior, eating disorder diagnoses and affective illness. Substance abuse diagnoses were established using the Structured Clinical Interview for DSM-III-R (SCID). The control group consisted of 20 women who were consecutive admissions to the same psychiatric hospital without the diagnosis of substance abuse or psychosis.

Results: There was a significant increased prevalence of eating disorder diagnoses and aberrant eating behavior in the substance abuse group compared to the control group. Forty-seven percent of the women with a diagnosis of substance abuse met *DSM-III-R* criteria for anorexia nervosa and/or bulimia nervosa. Forty-seven percent of the substance abuse patients had an affective disorder diagnosis. Six patients (43%) with an eating disorder diagnosis also had an affective disorder diagnosis.

Significance: These findings suggest that specific attention should be paid to a diagnostic assessment and counseling for eating behavior as part of a substance abuse rehabilitation program.

## NR249 DEPRESSION IN ADOLESCENTS WITH CONDUCT DISORDER

Catherine A. Martin, M.D., Psychiatry, Univ of Kentucky, 820 S. Limestone Annex #4, Lexington, KY 40536; William Martin, M.D., Lisa M. White, B.S., William Workman, B.S., Laurie L. Humphries, M.D.

## Summary:

A battery of questionnaires examining the association of mood and antisocial feelings and behavior was developed and administered to 131 adolescents seen in a university-based adolescent psychiatric in- and out-patient service. This battery included the Beck Depression Inventory (BDI), the Kovacs and Beck's Child Depression Inventory (CDI), the Addiction Research Center Maturation Scale (ARCMS) (Martin et al, 1977), and the Modified Personal History Questionnaire (MPHQ) (Hewitt and Martin, 1980). The ARCMS measures feelings and attitudes related to impulsivity, egocentricity, need, hypophoria, and sociopathy, and the MPHQ measures sociopathic behavior and associated disorders. The following significant correlations were seen. The BDI and CDI scores correlated with the Impulsivity ( $p<10^{-4}$ ), Egocentricity ( $p<10^{-5}$ ), Need ( $p<10^{-3}$ ), Hypophoria ( $p<10^{-11}$ ), and Sociopathy ( $p<10^{-7}$ ) subscales and the composite ( $p<10^{-13}$ ) scores of the ARCMS and with alcohol use (p<0.02), drug use (p<0.015), delinquency/sociopathy (p<0.04), sexual activity (p<0.4), ADD ( $p<10^{-4}$ ), and depression ( $p<10^{-4}$ ) subscale scores and the composite score ( $p<10^{-4}$ ) of the MHPQ. Sixty percent of the adolescents with conduct disorder had a mean BDI score of 18.9 and CDI of 18.9. Adolescents with conduct disorder also scored significantly higher on the Egocentricity, Hypophoria, and Sociopathic subscales and the composite score ( $p<10^{-5}$ ) of the ARCMS than 124 control adolescents. This study demonstrates the close relationship between depression and antisocial feelings and behaviors in adolescents.

#### NR250

## MALPRACTICE PHYSICIAN STRESS REACTION

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

Catherine A. Martin, M.D., Dept. of Psychiatry, Univ. of Kentucky, 820 So. Limestone, Lexington, KY 40536; John F. Wilson, Ph.D., N. Donald Feibelman, M.D.

#### Summary:

Charles et al (1984, 1985) are the first to describe the psychological sequelae of malpractice in sued physicians. A study to further investigate the stress of malpractice in sued physicians was conducted. The largest insurer of physicians in a southern rural state facilitated a mailing of a questionnaire to physicians at various stages of litigation and randomly selected insurees who had never been sued. Forty percent of 1200 questionnaires were returned. The questionnaire investigated symptoms of stress and attitudes about the practice of medicine. Physicians who had been sued reported higher levels of stress including symptoms of post-traumatic stress disorder (38%), anxiety (28%), depression (33%), drug use (5%), and feelings of bitterness and anger. Symptoms were highest in the case-pending group. Physicians who had been sued more than once were more symptomatic while physicians whose cases were settled out of court were less symptomatic. These symptoms declined over five years but never returned to the level of the non-sued physician. The practice of ''defensive medicine'' remained above 50% after five years. The malpractice experience was not extraordinarily stressful for a subgroup of physicians. Further description of the symptoms and time course of the malpractice stress reaction and identification of successful coping mechanisms of sued physicians are needed.

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

# THE INTERACTION OF PROLONGED TOTAL SLEEP DEPRIVATION AND D-AMPHETAMINE ON AROUSAL, COGNITION AND MOOD

Paul A. Newhouse, M.D., Behav Biology, Walter Reed Inst Res, Bldg 189 Walter Reed Inst Rsch, Washington, DC 20307; Gregory L. Belenky, M.D., Maria L. Thomas, M.A., David Thorne, Ph.D., Helen Sing, M.S., Joanne Fertig, Ph.D., David Penetar, Ph.D.

## Summary:

The neurobiological effects of total sleep deprivation (TSD) and stimulant drugs on alertness, cognition, and emotion remain not well understood, in part because previous studies in patients or normals have examined subjects for short periods of TSD or during normal states of arousal. We examined the effects of a range of doses of d-amphetamine in an experiment using prolonged TSD to produce measurable and replicable decrements in arousal and cognitive functioning. Thirty-six healthy males, mean age 27 ± 7.5, were sleep deprived for 60 hours. As a measure of arousal, the subjects' latency to Stage 2 sleep (SL) was measured using the Multiple Sleep Latency Test; subjects completed a computerized battery of cognitive tests known to be sensitive to TSD as well as subjective and observer behavioral ratings at two-hour intervals. After 48 hours of TSD, subjects were administered either placebo, 5, 10, or 20 mg of oral d-amphetamine in a double-blind fashion (9 Ss per dosage group). Forty-eight hours of TSD produced highly significant (p < .01) declines in sleep latency (14.9 to 1.5 min), cognitive performance, and measures of vigor, but no other mood changes. Amphetamine produced a significant (p<.01) dose-related increase in SL with 20 mg and 10 mg producing a 106% and 51% recovering of pre-SD values which lasted 2-3 hours and then declined linearly. An attentional arithmetic task showed a rapid and significant (p < .05) improvement on 20 and 10 mg which was maintained on 20 mg for 12 hours post drug. Reasoning tasks also showed a gradual but significant improvement on 20 mg, peaking at 6 hours post drug. There was a significant (p<.01) increase in ratings of vigor on 20 mg which was maximal at 1-2 hours and declined to baseline by 6 hours. The dissociation of the arousing, cognitive, and behavioral effects of amphetamine after TSD suggests that they may be mediated by different neurochemical mechanisms and that the neurobiological effects of sleep deprivation may be partially reversed by amphetamine.

## NR252

## MAGNETIC RESONANCE IMAGING IN OBSESSIVE DISORDER

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

Jordan Garber, M.D., Psychiatry, Harbor UCLA Medical, 1000 West Carson Avenue, Torrance, CA 90509; Jambur V. Ananth, M.D., Lee Chiu, M.D., Armen Djenderedjian, M.D.

#### Summary:

Hydrogen Magnetic Resonance Imaging (MRI) was conducted on 20 male and 12 female patients with *DSM-III* OCD of two years duration and 14 normal controls matched for age and sex. All were free of other illnesses and sustance abuse. Severity and symptoms were rated using the Yale-Brown Scale (mean score 19.3). T-1 and T-2 weighted images were obtained in sagittal and axial orientation at 1.5 Tesla. T-1 values were computed and compared for brain regions of interest. Radiological evaluations did not demonstrate MRI abnormalities specific to OCD. Mean T-1 values for right frontal white matter (RFWM) were longer in patients than in controls (P 0.004). Patients with contamination obsessions and/or cleaning compulsions compared to patients with other symptoms had shorter mean T-1 values for RFWM (P 0.02) and right temporal gray matter (P 0.002). Differences between left and right frontal orbital cortex T-1 values correlated with total severity scores for unmedicated patients without family history of OCD (R=- 96, p 0.0002). Clomipramine response was weakly correlated to RFWM T-1 (R=0.53, p 0.02). These implications will be discussed later.

#### NR253 NICOTINE GUM, TOBACCO DEPENDENCE AND WITHDRAWAL

Michael G. Goldstein, M.D., Psychiatry, The Miriam Hospital, 164 Summit Avenue, Providence, RI 02906; Kenneth Ward, B.S., Raymond Niaura, Ph.D.

## Summary:

The efficacy of nicotine chewing gum as a treatment for cigarette smoking may be mediated by its ability to control symptoms of tobacco withdrawal. Several questions remain concerning the optimal method of administration to control withdrawal, and those psychobiological factors that contribute to the severity of the withdrawal syndrome. Eighty-nine smokers were randomly assigned to chew Nicorette (2 mg) on a fixed (1 piece/hr) or ad-libitum schedule. Withdrawal symptoms and craving for cigarettes were monitored on a daily basis for two weeks. Schedule of gum use did not affect withdrawal. However, during the first week, average withdrawal symptoms were related significantly to a combination of pre-treatment measures of tobacco dependence including baseline smoking rate, years smoking, levels of saliva cotinine, the Fagerstrom Tolerance Questionnaire, and the Smoking Patterns Scale (r squared=.34; p=.02). Of these variables, the Stimulation subscale of the Smoking Patterns Scale was most strongly related to withdrawal (partial r=.23; p<.05). These results were independent of the amount of gum chewed per day. Tobacco craving scores were not affected by schedule of gum use or other individual characteristics. Individual characteristics are more strongly related to withdrawal symptoms than schedule of nicotine gum use, and withdrawal symptoms may be more severe among those who report that smoking has a stimulating effect for them. Craving was not affected by the factors that influenced other withdrawal symptoms.

## NR254

## LACTATE RESPONSE IN PURE GENERALIZED ANXIETY

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

Deborah S. Cowley, M.D., Psychiatry, Univ of Washington, Harborview ZA-99 325 Ninth Ave, Seattle, WA 98104; Stephen R. Dager, M.D., Jon McClellan, M.D., Peter P. Roy-Byrne, M.D., David L. Dunner, M.D.

## Summary:

Lactate infusion provokes panic symptoms in patients with panic attacks at a significantly higher rate than in controls or psychiatric patients without panic attacks. Generalized anxiety disorder (GAD) is the diagnosis most difficult to differentiate from panic disorder (PD) and studies of GAD have been flawed by inclusion of patients with infrequent panic attacks, who respond to lactate similarly to PD patients. In this study, 12 patients with GAD without any history of panic ("pure" GAD), 24 PD patients, and 10 controls received a 15-minute saline infusion and then 10 cc/kg. 0.5 M sodium lactate over 20 minutes. Responses were rated as negative, positive (increased anxiety and physical symptoms meeting *DSM-III-R* criteria for a panic attack, but not full-blown panic), or panic (meeting criteria for a positive response AND sudden terror or panic). GAD patients had a significantly lower rate of panic responses than PD patients (1 of 12 versus 10 of 24;  $x^2$ =4.2, df=1, p<0.05), but the same proportion of GAD and PD patients had either a panic or a positive response (7 of 12 versus 14 of 24). Both patient groups differed significantly from controls. The significance of these results for lactate specificity and for the separation of PD from GAD will be discussed.

## NR255

## PERSISTENT ENDOCRINE ABNORMALITIES IN BULIMIA

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

Alan B. Levy, M.D., Psychiatry, Ohio State University, 473 W. 12th Avenue, Columbus, OH 43210; William B. Malarkey, M.D., Katherine Dixon, M.D.

#### Summary:

We have previously demonstrated a delayed (>30 min) Thyrotropin (TSH) response to Thyrotropin Releasing Hormone (TRH), elevated basal Growth Hormone (GH), abnormal GH response to TRH, diminished basal Prolactin (PRL) and an exaggerated PRL response to TRH in normal weight bulimics. This hormone profile, however, has not been previously examined in bulimics after treatment. We studied six normal-weight women with bulimia with a 500  $\mu$ g TRH stimulation test—before and after hospitalization. Basal TSH, GH, and PRL were determined at 10:00 AM as well as 15, 30, 45, and 60 minutes post-TRH. They were compared with 8 age- and sex-matched healthy controls. The TSH response to TRH, delayed in 3 of 6 bulimics on admission, was delayed in 4 of 6 upon discharge. Mean basal GH, significantly higher (p<.01) in bulimics on admission (6.4 ng/ml) than controls (1.7 ng/ml) remained elevated in bulimics on discharge (6.7 ng/ml). Mean basal PRL, significantly lower (p<.01) in bulimics (2.8 ng/ml) on admission than controls (4.7 ng/ml), remained low on discharge (3.2 ng/ml). The mean PRL response to TRH, significantly greater (p<.05) in bulimics (1945% above baseline) than controls (858%) on admission, continued to remain exaggerated at discharge (1113%) though thee was a trend toward normalization. Paired t-tests performed on bulimics before and after hospitalization showed no differences for basal TSH, GH, or PRL or their responses to TRH. Neuroendocrine abnormalities present in some bulimics may persist after a one month hospitalization despite the elimination of binging and purging.

#### NR256 OBSESSIVE COMPULSIVE DISORDER WITH PSYCHOTIC FEATURES

Jane L. Eisen, M.D., Psychiatry, Bulter Hospital, 345 Blackstone Blvd, Providence, RI 02906; Steven A. Rasmussen, M.D.

## Summary:

The relationship of OCD to psychotic states has received little systematic study to date. In the past, this has been attributed to the relative rarity of these coexisting conditions. We have identified 30 such patients from a total of 250 patients in our OC clinic (12%). The epidemiologic and clinical features of the probands were systematically collected using structured (SADS-LA) and semistructured interviews. There appears to be considerable diagnostic heterogeneity within this group. We identified four major subtypes that were differentiated by their clinical features, course, and treatment response: I. Probands who met criteria for OCD and schizophrenia (35%). II. Probands with OCD who presented with marked magical thinking, delusional obsessions, the need for symmetry and precision, and a deteriorative course (20%), III. Probands with delusional paranoia as well as OCD (15%), IV. Probands with transient obsessional delusions (OCD) (30%). When compared to OC patients without psychotic features, this proband group had a lower GAS on admission, earlier age of onset, a higher male/female ratio, a greater likelihood of having a deteriorative course, and poorer premorbid function. Patients with co-existing schizophrenia and OCD and deteriorative OCD (Subtypes I, II) responded poorly to neuroleptics and serotonin uptake antagonists, and were similar to the schizophrenic patients described by Fenton et al (1). Patients with delusional paranoia and OCD psychosis (Subtypes III, IV) were much higher functioning, had a positive response to serotonergic uptake antagonists, and showed no significant differences in clinical features and course from OCD patients without psychotic symptoms. These findings suggest OCD probands with psychotic features can be differentiated into distinct subtypes that have significant prognostic and therapeutic implications.

## NR257

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

## FAMILY FUNCTION IN OBSESSIVE COMPULSIVE DISORDER

Barbara Livingston, M.S.W., Psychiatry, Bulter Hospital, 345 Blackstone Blvd. Providence, RI 02906; Jane L. Eisen, M.D., Lois McCartney, M.S.W., Robert L. Lindsey, M.D., Steven A. Rasmussen, M.D.

## Summary:

Although rapid advances in the biologic and behavioral treatment of OCD have been made, the role of psychosocial factors has been relatively neglected. We report findings from preliminary studies that examine the impact of family dynamics on the course of illness, as well as how the symptoms of OCD influence family functioning. Fifty OCD probands and their families completed the Family Assessment Device (FAD), a self-report inventory (1). The clinician rated McMaster Clinical Rating Scale (McCRS) was also given to 20 of these families. Data analysis of baseline FAD scores showed that 76% of the respondents have a global family function score that indicates significant dysfunction in comparison to 22% of control families. Affective responsiveness, affective involvement, and communication were significantly more pathologic in the OC families than controls, while roles, behavioral control, and problem solving showed less significant differences. Fifty percent of families reported they were involved in aiding patients' rituals at baseline assessment. Two types of families that were commonly associated with treatment resistant patients were identified; 1. those who had problems setting limits and who often participated in rituals to decrease the probands' anxiety, 2. those who were inflexible and who were unable to control the level of hostility and frustration directed towards the proband. The identification of specific areas of family dysfunction in OCD have led us to develop multifamily educational groups based on the model of Anderson as an adjunct to pharmacologic and behavioral treatment. Twenty families have completed an eight-week time limited multifamily group. Assessment of treatment outcome has shown improvement in patient symptoms as well as in family function following completion of the groups.

#### NR258 DO BORDERLINE PATIENTS REGRESS IN THE HOSPITAL?

Alexis A. Giese, M.D., Psychiatry, Georgetown University, 3800 Reservoir Road NW, Washington, DC 20007; Ellen Leibenluft, M.D., David L. Gardner, M.D., Richard C. Filson, Ed.D., Elizabeth Zimmerman, B.A.

#### Summary:

A common assumption in the treatment of patients with borderline personality disorder (BPD) is that they are particularly prone to regression in the inpatient setting and that hospitalization should therefore be avoided. The literature provides case examples of regression in inpatients with BPD and discussion of the psychodynamics of their regression. However, the likelihood of clinical worsening of symptoms has not been previously studied empirically. This research operationalizes the concept of regression and examines the likelihood of symptomatic deterioration in the hospital.

The short-term hospital courses (mean length=23 days) of a group of nine patients with BPD were compared to a control group of nine patients with affective illness. Standard rating scales (BPRS, Beck, Ham-A, Ham-D, SCL-90R, global scales, etc.) were administered three times over the course of hospitalization. Patients with BPD were indeed found to be significantly more impaired on admission on almost all measures (for example, mean Hamilton—anxiety=21.9 for BPD vs. 17.1 for controls, p<0.05). However, no regression was noted for either groups; in fact, significant improvement (p<0.001) was found to occur for most scales in both groups. Further, the ANOVA multivariate analysis for repeated measures revealed *no* main effect of diagnostic group on the degree of improvement experienced. These results challenge the suggestion of the case illustrations reported thus far that patients with BPD are much more likely than others to regress in the short-term hospital.

#### NR259

## FOLLOW-UP STUDY OF INPATIENTS WITH ANOREXIA NERVOSA

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

David Greenfeld, M.D., Psychiatry, Yale Univ Sch Med, 333 Cedar Street, New Haven, CT 06510; Marie Hobart, M.D., Walter R. Anyan, M.D., Margaret Plantes, M.A., Donald M. Quinlan, Ph.D., Elaine Glass, M.S.W.

#### Summary:

Thirty female patients previously hospitalized at Yale-New Haven Hospital who met *DSM-III* criteria for anorexia nervosa (AN) were interviewed one to 10 years after hospitalization (mean 4.3 years). At follow-up 11 subjects (37%) had recovered from AN, 8 (27%) had significant eating symptoms but were not anorectic, 8 met *DSM-III* criteria for AN, and 6 (20%) met *DSM-III* criteria for bulimia. Sixteen subjects (53%) had no additional hospitalizations for AN; 14 subjects had one or more additional hospitalizations. Eleven subjects (37%) had no menses. Weight scores revealed 5 subjects (17%) in the low range, 8 (27%) in the borderline range, 12 (40%) in normal range, and 5 (17%) were overweight. Subjects with lowest weight scores at time of first hospitalization had the most subsequent hospitalizations for AN (p < .01) and the most anorectic symptoms at follow up (p < .05). Diagnostic assessment at follow up revealed 13 subjects (43%) with major depression, 6 (20%) with dysthymic disorder, 5 (17%) with separation anxiety and 5 (17%) with phobias. Subjects' insight was assessed using a previously developed scale. Assessment of subjects' insight into their condition revealed that subjects who can acknowledge that they suffered an illness have significantly better outcome than those who cannot: they have briefer episodes of AN (p < .05), and at follow-up have (a) higher weight scores (p < .001), (b) are less impaired by eating symptoms (p < .02), (c) are less likely to meet *DSM-III* criteria for AN (p < .05) and (d) have better overall level of function as reflected in higher GAS rating (p < .05). In addition, the ability to describe anorectic symptoms is also correlated with higher current weight score (p < .05).

#### NR260 SUBSTANCE USE, SUICIDE AND BORDERLINE PERSONALITY DISORDER

Rebecca A Dulit, M.D., Psychiatry, Payne Whitney Clinic, 525 E. 68th Street, New York, NY 10021; Minna R. Fyer, M.D., Steven, W. Hurt, Ph.D., Allen J. Frances, M.D., Timothy Sullivan, M.D., John F. Clarkin, Ph.D.

*Purpose:* Although parasuicidal and suicidal behavior are clinically recognized as common in borderline personality disorder (BPD) and included within the *DSM-III* criteria, the limited available evidence suggests that BPD patients with comorbid substance use disorders may be at particularly high risk for serious suicidal behavior. This study examines the impact of comorbid *DSM-III* substance use diagnoses on suicidal behavior in *DSM-III* BPD.

Method: Diagnostic, demographic, and course data were gathered on 168 DSM-III BPD inpatients. Systematic ratings of DSM-III Axis I disorders and lifetime suicidal behavior were made. Interrater reliability for diagnostic and suicide categories were acceptable.

Results: 17% of BPDs had no history of suicidal behavior, 33% had made gestures, and 50% had made serious attempts. BPDs with comorbid substance dependence (SD) other than alcohol dependence (AD) had a significantly higher rate of serious attempts (70%) than BPDs without substance use diagnoses (43%) or BPDs with AD (27%). BPDs with AD had a significantly higher rate of no suicidal behavior (45%) than BPDs without substance use diagnoses (17%) or BPDs with other SD (10%). The rate of affective disorder with similar in BPDs without substance use diagnoses (65%) and BPDs with SD (63%), but lower (36%) in BPDs with AD.

Significance: Although suicide gestures and attempts are common in DSM-III BPD, these data suggest that comorbidity with SD other than alcohol greatly increases the risk for serious suicidal behavior in BPD and that AD is associated with a decreased risk for suicide. Clinicians should be particularly concerned about BPDs with comorbid SD since treatment of concurrent SD may decrease the risk of completed suicide in BPD.

#### NR261 YALE-BROWN OBSESSIVE COMPULSIVE SCALE: VALIDITY

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

Wayne K. Goodman, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06508; Lawrence Price, M.D., Steven A. Rasmussen, M.D., Carolyn Mazure, Ph.D., George R. Heninger, M.D., Dennis S. Charney, M.D.

The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) was designed to remedy the problems of existing rating scales by providing a specific measure of the severity of symptoms of OCD (as defined by DSM-*III*-*R*) that is influenced by the type of obsessions or compulsions present. The Y-BOCS is a clinician-rated, 10-item scale, each item rated from 0 = "no symptoms" to 4 = "extreme symptoms" (total range = 0 to 40). The following psychometric studies were conducted: *Reliability*—(1) Interrater Reliability: Intraclass correlation coefficients revealed excellent agreement between four raters of 40 OCD patients for the Y-BOCS totals and individual items (e.g., for total Y-BOCS score r=0.98, P < .0001). (2) Internal Consistency: The Y-BOCS was found to be highly homogeneous with an alpha coefficient = 0.89 (N=40). *Validity*—(1) Convergent and discriminant validity was studied in three cohorts of OCD patients (total N=81). Y-BOCS scores were highly convergent with two out of three other OCD scales tested and there were weak correlations between the Y-BOCS and depression ratings (HAM-D) in OCD patients without secondary depression. (2) Sensitivity to Change: Based on a trial of fluvoxamine in 42 OCD patients, the Y-BOCS was sensitive to drug-induced changes (mean change in Y-BOCS = -25% on fluvoxamine vs. +2% on placebo). Point biserial correlations between OCD response category (as per CGI ratings) and mean score changes showed that decreases in Y-BOCS scores (r=0.65, (p < .01) but not in HAM-D scores (r=0.26, p=.30) specifically reflected improvement in OCD symptoms. *CONCLUSION:* These findings suggest that the Y-BOCS is a reliable and valid instrument for assessing the severity of OCD. It is also a sensitive and selective measure of changes in OCD symptoms.

## BENZODIAZEPINE RECEPTOR ANTAGONIST EFFECTS IN PANIC DISORDER

Scott W. Woods, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06508; Dennis S. Charney, M.D., Jonathan M. Silver, M.D., John H. Krystal, M.D., George R. Heninger, M.D.

#### Summary:

The anxiolytic efficacy of the benzodiazepine receptor (BZR) agonist drugs suggests that abnormal regulation of BZR function may relate to the pathophysiology of anxiety. To begin to evaluate this possibility, the BZR antagonist flumazenil (Ro 15-1788) and placebo was administered to panic disorder patients. *Methods:* Eleven patients (age 37+7 yrs) drug-free for four weeks participated. All received flumazenil 600 mg, ten flumazenil 200 mg, and eight matching placebo orally in random sequence on separate test days seven days apart. Subjective visual analog scale (100 mm) mood ratings, heart rate, blood pressure, and plasma cortisol and 3-methoxy-4-hydroxyphenylglycol (MHPG) measurements were obtained before and at multiple points following drug administration. Results: On placebo days, anxiety ratings decreased from baseline by 11±14 mm (p < .10) at 30 minutes and by 29 to 44 mm at each time point (p < .05) thereafter. On 200 mg days, anxiety ratings increased by  $19\pm39$  mm (p < 0.5 vs. placebo) at 30 minutes and then fell below baseline by 5 to 23 mm (all N.S. vs. placebo). On 600 mg days, anxiety ratings decreased by 3±18 mm at 30 minutes (N.S.) and then to levels similar to those on placebo days. Panic attacks occurred on placebo, 200 mg, and 600 mg days in 0/8, 4/10, and 0/11 patients, respectively. Netiher dose of flumazenil significantly altered heart rate, blood pressure, or plasma cortisol or MHPG in comparison to placebo. Discussion: The significant anxiogenic effect of flumazenil at the 200 mg dose strengthens evidence implicating a role for BZRs in the pathophysiology of anxiety. Future work with a control group is necessary to evaluate the diagnostic specificity of this effect. That no anxiolytic effects were observed suggests that flumazenil at these doses does not antagonize a tonic increased interaction of BZRs with an endogenous BZR inverse agonist in panic patients.

#### NR263

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

## CHARACTERISTICS OF SELF-DEFINED PANIC ATTACKS

John H. Krystal, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06508; Scott W. Woods, M.D., Candy L. Hill, M.S., Dennis S. Charney, M.D.

#### Summary:

For diagnostic, therapeutic, and research purposes, it is critical to understand the characteristics of panic attacks. *DSM-III-R* specifies panic attack criteria which, of necessity, are primarily based on clinical experience due to a paucity of objective data. We report results of a preliminary analysis of daily journal descriptions of 790 panic attacks from 59 drug-free patients with panic disorder.

*Method:* The daily journals consisted of standardized rating forms which were completed for each attack which permitted the quantitative evaluation of many panic attack characteristics such as severity (rated 0-10), the presence of 20 symptoms, and duration. Patients were instructed only that panic attacks were "sudden surges of anxiety."

*Results:* The *DSM-III-R* specified symptoms for panic occurred with frequencies ranging from sweating (58% of attacks) to choking (16%). However, other symptoms, not listed in *DSM-III-R*, occur equally frequently such as restlessness (40%), weakness (36%), and headache (31%). Situational and spontaneous attacks appeared quite similar over a number of characteristics including peak diurnal incidence, frequency per week, the number of symptoms per attack, severity, the duration of attacks, and the frequency of 19/20 associated symptoms. However, "feeling that you are going to die" was over 1.5 times more common in spontaneous than situational attacks (24% vs. 14%, p=.019). Overall, the sense of impending doom occurred in shorter-lasting attacks of greater severity, with more panic associated symptoms/attack. Limited symptom attacks, self-defined attacks with fewer than four symptoms, were less severe than attacks with four or more symptoms (4.7 +/- 1.3 vs. 5.9 +/- 1.4, p=.008) and showed a trend for shorter duration. However limited symptom attacks occurred at every level of severity.

Discussion: These data suggest that most DSM-III-R symptoms of panic occur frequently in self-defined panic attacks, but that other symptoms should be included in this criteria. The data also generally support the similar DSM-III-R treatment of limited symptom attacks, situational panic attacks, and spontaneous panic attacks. Based on these journal data, we will also report comparisons of self-defined panic attacks and pharmacologically elicited panic-like states in these patients.

#### NR264 BROMOCRIPTINE VERSUS DESIPRAMINE IN COCAINE WITHDRAWAL

Irl L. Extein, M.D., Fair Oaks Hopsital, 5440 Linton Blvd, Delray Beach, FL 33484; Sharman S. Allen, M.D., Mark S. Gold, M.D., Aldo Marales, Jr., M.D., Paul J. Goodnick, M.D., David A. Gross, M.D.

#### Summary:

To compare directly the efficacy of the dopaminergic agonist bromocriptine and the noradrenergic tricyclic antidepressant desipramine (DMI) in cocaine abstinence, we studied within 72 hours of hospital admission 12 young adults (three women, nine men) with *DSM-III-R* cocaine dependence (predominantly crack) and clinically significant cocaine withdrawal symptoms. Patients gave written informed consent for oral administration of single doses of bromocriptine 1.25 mgs and DMI 50 mgs on consecutive days utilizing a double-blind, random-assignment, crossover design. Craving, mood, and energy were self-rated before and 1, 3, 6, 8, and 12 hours after each medication on 100 mm lines. Though variability was high, baseline symptoms on bromocriptine and DMI days did not differ. Peak medication effects were noted at three-six hours. At six hours, bromocriptine reduced mean craving 48% (p<.05, paired t-test), improved depressed mood 38% (p<.10), and increased energy 21% (NS); whereas DMI reduced craving 41% (p<.10), had no effect on mood, and reduced energy 19% (p<.10). In patients with higher baseline symptomatology, both medications reduced craving (p<.05) but only bromocriptine significantly improved depressed mood and energy (p<.05). There was a trend (p<.10) for bromocriptine to improve depressed mood and energy compared to DMI, but no difference on craving. Results suggest superiority for bromocriptine over DMI in the acute treatment of cocaine withdrawl symptoms, which can lead to premature treatment drop-out and relapse. This study addressed only initial single-dose effects, and hence the findings are not inconsistent with other reports of efficacy of DMI manifest several weeks after initiation of medication in abstinent cocaine addicts.

#### NR265 DISCRIMINANT VALIDITY OF SCHIZOTYPAL PERSONALITY

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

Elizabeth Squires-Wheeler, Ph.D., Medical Genetics, Psychiatric Inst., 722 West 168th Street, New York, NY 11201; Andrew E. Skodol, M.D., L. Erlenmeyer-Kimling, Ph.D.

#### Summary:

The agregation of disorder in families identified by a schizophrenia disorder proband (index case) has provided indirect clues to the question of diagnostic boundaries. The Danish Adoption Studies provided quasiexperimental evidence for the range of expression of a putative schizophrenic spectrum disorder which was subsequently denoted schizotypal personality traits and disorder in *DSM-III-R*. This category is currently being used as an "affected phenotype" in genetic analyses including segregation and linkage studies. Several geneticists have noted the loss in precision and power (and the introduction of bias in estimators) in such studies if error is present in the designation of affected individuals. Thus, it is desirable to examine the discriminant validity of the hypothesized spectrum category prior to its use in genetic analyses. We report here rates of STPD traits and disorder from follow-up Axis II assessments of first-degree relatives (young adult offspring) of three groups of parent probands interview by a trained clinician blind to parental group status using the PDE (Personality Disorder Examination, Loranger, 1986). Rates of 4 or more STPD features (probable or definite STPD disorder) among offspring of schizophrenic disorder parent probands (n=63), affective disorder parent probands (n=62), and no disorder parent probands (n=135) are 7.9%, 11.3%, and 1.5%, respectively. This pattern replicates a distribution of STPD traits among these offspring assessed more than five years ago. We further extend the question of discriminant validity by examination of the rates of STPD traits in the "well parent" and in the maternal and paternal grandparents and aunts and uncles of these offspring.

## BEHAVIORAL AND PROLACTIN REPSONSES TO FENFLURAMINE IN OCD

Michael D. De Meo, M.D., NY Hospital Cornell, 525 East 68th Street, New York, NY 10021; P. Anne McBride, M.D., M. Katherine Shear, M.D., James P. Halper, M.D., Jaw-Sy Chen, Ph.D., J. John Mann, M.D.

#### Summary:

Introduction: A serotonin (5-HT) hypothesis of the pathophysiology of Obsessive-Compulsive Disorder (OCD) has been suggested by the therapeutic effects of 5-HT reuptake blockers and alterations in CSF and peripheral measures of 5-HT function. *Methods:* Using fenfluramine (FEN), and indirect 5-HT agonist, we investiaged whether FEN would affect symptoms of OCD, and whether patients would differ from healthy controls in their neuroendocrine response. Serotonergic stimulation increases prolactin (PRL) secretion. Plasma PRL levels prior to and following FEN (60mg, PO) and placebo were assessed in 14 medication-free patients with *DSM-III-R* diagnosed OCD and 12 age- and gender-matched healthy controls. Blind ratings of obsessions, compulsions, anxiety, and depression were assessed at baseline and hourly following FEN and placebo in the the OCD group. *Results:* FEN significantly reduced obsessions (p<.001) and depression (p<.02) in the OCD group with the time course paralleling serum drug levels, and did not affect compulsions or anxiety. There was no statistically significant difference between control and OCD subjects' mean peak PRL response after FEN (PRL=11.1 ± 8.5 vs PRL=15.4 ± 13.5 ng/ml, p=NS) although interpretation is complicated by potential age and gender effects. In our sample, female OCD patients exhibited a trend of higher mean peak PRL response compared to female controls (PRL=27.6 ± 16.5, n=5 vs PRL=9.1 ± 10.3 ng/ml, n=4; T= -1.94, p<.08). These preliminary findings and their implications for a 5-HT hypothesis of OCD will be discussed.

#### NR267

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

## EYE TRACKING IN OBSESSIVE COMPULSIVE DISORDER

John A. Sweeney, Ph.D., Psychiatry, Cornell Med College, 525 East 68th Street, New York, NY 10021; M. Katherine Shear, M.D., James P. Halper, M.D., Michael De Meo, M.D., Brett Clementz, M.S., Virginia Walsh, B.S.

#### Summary:

Eye tracking deficits are probably the most promising psychobiological and familial marker for schizophrenia but their diagnostic specificity remains poorly characterized. We studied patients with obsessive compulsive disorder (OCD) because their marked anxiety, severe functional impairment, and fixed ideas that can border on delusions might be associated with poor eye tracking performance. *Method:* 19 patients with OCD and 21 schizophrenic patients (*DSM-III* diagnosis by SCID interview) and 16 normal controls performed pursuit eye tracking tasks. Infrared (IR) recordings of eye movements were digitized at 250 HZ. and the frequency of corrective saccades and overall tracking error (RMS error) were determined by computer analysis. *Results:* Eye tracking performance was unimpaired in OCD patients relative to controls; however, their tracking error was significantly correlated with severity of obsessions (Yale scale; r=.46) and depression (Hamilton Depression Scale; r=.54) Schizophrenic patients showed significantly more frequent corrective saccades and greater tracking error. *Discussion:* The results contribute to the determination of the diagnostic specificity of eye tracking impairments. Consistent with earlier studies, our findings indicate that eye tracking abnormalities are rare in nonpsychotic patients, though some mild impairments may occur in OCD patients who manifest the most severe symptomatology. It seems likely that disturbed attentional processes in severely disturbed OCD patients probably cause some disturbance on the tracking task, and we are conducting longitudinal studies to confirm that the abnormalities are state dependent by beginning treatment with clomipramine in these OCD patients tested initially off all medication and retesting them.

#### NR268 CO-ALCOHOLISM IN PSYCHIATRIC OUTPATIENTS

Donna A. Vaughan, M.D., Psychiatry, Univ KS Sch of Med, 1010 North Kansas, Wichita, KS 67214; Beryl Silkey, Sc.M., Julie A. Parsons, M.D.

#### Summary:

Co-alcoholism is a newly identified, treatable diagnostic entity, described as ill-health or dysfunctional behavior that is found in famly members of an alcoholic<sup>1,2</sup>

One hundred adult psychiatric outpatients completed Whitfield's 31-question Family Drinking Survey (WFDS), the Brief Michigan Alcoholism Screening Test (BMAST)<sup>3</sup>, and a question concerning their use of sedatives or hypnotics. Clinic charts were reviewed for diagnosis.

One half of participants met criteria for co-alcoholism, (a WFDS score of  $\geq$ 4). Of these, 29.4% also met criteria for alcoholism in themselves (BMAST score of  $\geq$ 6) compared to only 12.0% of the non-co-alcoholics. Compared to non-co-alcoholics, co-alcoholics were slightly overrepresented among the diagnostic categories of anxiety, somatization, and personality disorders.

The proportion using sedatives or hypnotics among the co-alcoholics was nearly twice that of the non-co-alcoholic group (70.6% vs. 38.0%), even after removing anxiety disorders (69.0% vs. 37.0%); and the differences increased further with removal of alcoholism cases (86.1% vs 27.3%).

These findings, in the absence of *DSM-III-R* criteria for this disorder, support the need to establish diagnostic criteria and to screen for co-alcoholism in psychiatric patients, particularly since it is likely that the symptoms will persist without specific treatment for co-alcoholism. In addition, higher frequency of sedative hypnotic use among the co-alcoholics, raises the question of the appropriateness of using these medications in this population.

#### NR269

## PET STUDY OF BULIMIC NORMAL DIFFERENCES

Joseph C. Wu, M.D., Psychiatry, University of California, Medical Sciences I Room D404, Irvine, CA 92717; Monte S. Buchsbaum, M.D., Barton J. Blinder, M.D., Melissa Derfler, M.D., Jennifer Hagan, M.D.

## Summary:

Positron emission tomography (PET) scans of eight bulimic and eight normal control women were done to ascertain regional cerebral metabolic differences that characterize bulimia.

Eight bulimic women who met *DSM-III-R* criteria for bulimia were studied (mean age  $28.6 \pm 6.5$  years). Eight normal control women (mean age  $28.9 \pm 7.7$  years) were also studied. Scans were done on a NeuroEcat IV scanner with an in-plane resolution of 7.6 mm. Four to five millicuries of 18-F-2 deoxyglucose were administered. The continuous performance test (CPT) was done during the 30-minute uptake.

Three PET slices were chosen by our previously described methods (Buchsbaum et al, 1984). Briefly, a supraventricular, midventricular and infraventricular slice was chosen, and a 2.2 cm thick cortical peel was taken and subdivided into four quadrants per hemisphere.

A significant hemisphere by quadrant by group interaction was found when ANOVA was performed (F=2.82, d.f.=3, 42, p=.05). The bulimics had decreased frontal lobe activity and had a greater left/right ratio than normal controls.

Subcortical structures were also examined uisng a stereotactic coordinate system. A significant hemisphere by group interaction (F=4.80, d.f.=1, 12, p=.04) was found. Bulimics had decreased right and increased left hemisphere metabolism for subcortical structures.

These findings suggest that bulimia is associated with disorderd hemispheric activity.

## NR270

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

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

## PANIC DISORDER: CLONEZEPAM VERSUS ALPRAZOLAM AND PLACEBO

George E. Tesar, M.D., Psychiatry, Mass General Hospital, 15 Parkman Street ACC 715, Boston, MA 02114; Jerrold F. Rosenbaum, M.D., Mark H. Pollack, M.D., Gary S. Sachs, M.D., John B. Herman, M.D., Joseph N. Sidari

#### Summary:

We have completed a random assignment, parallel, double-blind, flexible dose study comparing clonazepam (0.5 mg), alprazolam (1.0 mg) and placebo in well diagnosed patients with panic disorder (or agoraphobia with panic attacks). Sixty subjects, of 74 randomized, completed at least three weeks of drug trial. Following the screen (placebo lead-in) and baseline (randomization) visits, patients were assessed at six weekly intervals while keeping dialy diaries of severity and duration of panic attacks and degree of anticipatory anxiety. Major outcome measures were: frequency and intensity of panic attacks, duration and intensity of anticipatory anxiety, extent of phobic avoidance, clinical global impression and patient global improvement, degree of generalized anxiety, work and social disability scores and depression ratings. Both end point and completer analyses are presented. At end point, patients on both active drugs improved significantly over placebo; further, there were no meaningful clinical or statistical differences between alprazolam and clonazepam in efficacy. The conclusions of the study are that clonazepam and alprazolam appear to be equally effective for the management of panic disorder. Potential relative advantages and disadvantages of alprazolam and clonazepam will be reviewed.

#### NR271 RELATIONSHIP BETWEEN CSF CRH AND MHPG IN ANOREXIA NERVOSA

Michael D. Lesem, M.D., Psychiatry, UTMSH, P.O. Box 20708, Houston, TX 77225; Philip W. Gold, M.D., Arlene P. Hegg, M.D., David C. Jimerson, M.D.

## Summary:

Based on preclinical studies showing that hypothalamic norepinephrine (NE) increases feeding and corticitropin releasing hormone (CRH) decreases feeding, it has been proposed that the functional activity of these substances may be altered in anorexia nervosa (AN). Previous studies have shown elevated CSF levels of CRH in low weight patients with AN, but normal CSF levels of NE and its major metabolite MHPG in these patients. We now report replication of these previous results, and demonstrate that activity levels in these two systems appear to be interrelated in AN.

Subjects included medication-free female patients (N=21) who met *SDM-III* criteria for AN. Of these pateitns, 14 had bulimic symptoms (age=25.1  $\pm$  6.0 years; weight=62.9  $\pm$  6.4% average body weight (ABW)), and 7 were nonbulimic (age 24.0  $\pm$  4.7 years; weight=58.6  $\pm$  6.1% ABW). CSF CRH levels for the patient group (43.3  $\pm$  12.2 pg/ml) were significantly higher than for the controls (35.4  $\pm$  10.4 pg/ml, p<.05); values were not significantly different for bulimic and non-bulimic patients. CSF MHPG levels for the patients 45.5  $\pm$  7.3 pmol/ml) were not significantly different from control values (49.2  $\pm$  11.4 pmol/ml). CSF CRH levels were significantly correlated with MHPG concentrations for bulimic AN (r=.63, p<.03), non-bulimic AN (r=.98, p<.005), and for the combined patient group (r=.58, p<.02), but not for the control group. The correlation between CSF levels of CRH and MHPG in AN patients will be discussed with reference to preclinical studies showing major interactions between central NE and CRH.

## NR272 NEUROPSYCHOLOGICAL FUNCTIONING AND BRAIN GLUCOSE METABOLISM IN NORMAL WEIGHT BULIMICS

Melissa A. Rooney-Chiles, M.A., Psychiatry, Univ of California Irvine, Capistrano Bysea Hosp Box 398, Dana Point, CA 92629; Barton J. Blinder, M.D., Joseph C. Wu, M.D., Monte S. Buchsbaum, M.D., Robert A. Leark, Ph.D.

#### Summary:

This study investigated the relationship between neuropsychological functioning and brain glucose metabolism as measured by PET scans, in normal weight bulimics. A relationship between eating disorders and affective disorders has been suggested. We hypothesized that bulimic subjects would exhibit brain glucose metabolic rates similar to that reported in depressives, namely hypometabolism in the frontal cortex and caudate nucleus. The PET scan yields metabolic rates for multiple brain regions; thus neuropsychological tests that tapped a broad arena of functioning were selected. Eight bulimic subjects and eight age-matched controls were administered a battery of 15 separate tests, and were given a PET scan following standardized procedures.

Differences between bulimics and controls on the neuropsychological and neurophysiological data were evaluated. Bulimics showed deficits in attention and in delayed visual memory. Additionally, bulimics exhibited hypometabolism in the frontal cortex. Correlations between mean frequency of bulimic episodes/week and neuropsychological data are also presented.

Relationship of findings to CNS involvement in eating disorders, as well as implications of the research for the hypothesized link between eating disorders and affective disorders are discussed. This represents preliminary results of a pre- and post-study involving an experimental antidepressant medication.

#### NR273 ELEVATED PRODUCTION OF LACTATE IN PANIC DISORDER

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

Richard Maddock, M.D., Psychiatry, UC Davis Med Center, 4430 V. Street, Sacramento, CA 95817; Jose Mateo-Bermudez, M.D.

#### Summary:

Early reports suggested that 'Anxiety Neurotics' produced more lactate during exercise than control subjects. Though Pitts and McClure based their original lactate infusion experiments on these observations, the original studies of lactate production during exercise were flawed by lack of control for differences in fitness. To date, no adequately controlled replications have been reported. We now report excess lactate production in panic disorder using a protocol unaffected by fitness.

Intracellular alkalosis combined with excess substrate (glucose) stimulates lactate production. Eight panic patients and six controls received intravenous infusions of glucose and saline in counterbalanced order under double-blind conditions. During each infusion subjects hyperventilated sufficiently to sustain a pCO<sub>2</sub> of 20mm Hg for seven minutes. Serum lactate increased significantly more in panic patients than controls in the glucose-hyperventilation condition. The two groups did not differ in the saline-hyperventilation condition. Anxiety levels were equal in both hyperventilation conditions and did not correlate with changes in lactate.

Although recent studies have focused on exogenous lactate as a precipitant of panic, these findings support the earlier observations of abnormal endogenous lactate metabolism in patients with panic symptoms. Further studies may identify underlying metabolic abnormalities possibly related to the pathogenesis of panic disorder.

# ADULT CHILDREN OF ALCOHOLICS: PERSONAL AND TRANSGENERATIONAL PATTERNS

Vicki L.C. Weatherford, Ph.D., Psychiatry, Univ of Calif Irvine MC, 101 City Dr South Bldg 53 Rt81, Orange, CA 92668; Edward Kaufman, M.D.

## Summary:

This adult children of alcoholics (ACA) study examined: 1) the prevalence of Axis II personality disorders in ACAs, 2) transgenerational family cohesion and adaptability patterns across ACA families, 3) transgenerational substance abuse patterns, as well as physical, sexual, and emotional abuse patterns, and 4) transgenerational communication patterns in ACA's families of origin and current marital systems. Fifty ACAs were recruited by flyer from a broad general community sample. The Structured Clinical Interview (SCID II) and Comprehensive Drinker Profile (CDP) were administered by trained clinicians. Objective measures included: the Family Adaptability and Cohesion Evaluation Scale (FACES III), Children of Alcoholics Screening Test (CAST), Michigan Alcoholics Screening Test (MAST), and Perceived Confirmation Scale (PCS). Sixty-seven percent of the ACAs met *DSM-III-R* criteria for Axis II personality disorders. Several predominent personality disorders emerged as well as a revealing composite of personality characteristics. Analyses of variance and chi-square analyses revealed specific and significantly dysfunctional (p<.001) cohesion and adaptability patterns in the ACA's family of origin, as well as in their current marital relationships. Significant (p<.001) dysfunctional communication patterns were also found. Seventy-two percent of the ACAs chose spouses who replicated their parents' physical, sexual, and/or emotional abuse towards them. Results are discussed in terms of prior clinical literature and research.

#### NR275 ALCOHOLISM AND MENTAL COMORBIDITY IN THE HOMELESS

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

Alan J. Romanoski, M.D., Psychiatry, Johns Hopkins Univ, 600 N Wolfe St Meyer Bldg4-119, Baltimore MD 21205; Gerald Nestadt, M.D., Alan Ross, Ph.D., Pamela J. Fischer, Ph.D., William R. Breakey, M.D.

## Summary:

This paper describes the distribution of *DSM-III* Alcohol Abuse and Dependence and the Alcohol Dependency Syndrome (ADS) among the homeless in Baltimore City. These findings are different from other available data on the distribution of alcoholism among the homeless in that they are based on standardized clinical examinations performed by psychiatrists and they are based on the diagnosis of *DSM-III* Alcohol Abuse and Dependence and ADS as discrete clinical entities, as opposed to data based on lay-administered questionnaires or criteria based upon the quantity, frequency, or consequences of drinking.

Three specially selected and trained research psychiatrists examined a multi-stage stratified probability sample (N=205) of homeless persons randomly selected from Baltimore City missions, shelters, and the jail, for which they had no clinical responsibility. Their task was to identify subject's *DSM-III*-defined disorder and the presence or absence of ADS after conducting a standardized psychiatric examination which averaged 90 minutes in duration. The Standardized Psychiatric Examination (SPE) format and record enables psychiatrists to reliably diagnose *DSM-III* Substance Use Disorder (K=0.84) and other specific *DSM-III* diagnostic categories (K=0.79-1.00).

The authors present direct estimates of the age-, sex-, and race-specific rates of *DSM-III* Alcohol Use Disorders and ADS among homeless adults, and data on the clinical characteristics of those so afflicted, including their rates of *DSM-III*-defined mental comorbidity. Over 50% of the sample had an alcoholism diagnosis, of which over 40% had major mental comorbidity. Implications for treatment resources are discussed.

#### NR276 DIMENSIONS OF CONDUCT DISORDER AMONG ADOLESCENTS

Spyros J. Monopolis, M.D., Psychiatry, University of Maryland, 645 West Redwood Street, Baltimore, MD 21204; George U. Balis, M.D.

#### Summary:

This report presents a comparison between male adolescents exhibiting aggressive conduct disorder (CD, N=26) and those without such disturbance (NON-CD, N=38). Subjects were drawn from a cohort of patients with episodic dyscontrol acts (usually violent) and various psychiatric diagnoses. The two groups did not differ significantly in race, age, and referral source. However, CD patients tended to have elementary and junior high school education, while the NON-CD subjects had high school education. We used self-reported questionnaire, physician reports, and EEG recordings (baseline and alpha-chloralose activated).

The *CD* group was significantly different from the NON-CD group (p<.05, Tukey's test) in regard to: epileptic symptoms; epileptoid dyscontrol acts; paroxysmal delta and theta EEG changes; childhood behavior problems, petty stealing, violent and antisocial behavior; school suspension, court involvement; enuresis, chorea, insensitivity to punishment, anhedonia, difficult to please; learning difficulties; developmental years and perinatal brain insult; family history of epilepsy (maternal side), and dyscontrol acts.

The NON-CD group was significantly different from the CD group in reference to: affective disorders, intermittent explosive disorder; angry suicidal outbursts, uncontrollable crying.

In summary, adolescents with aggressive conduct disorder and various psychiatric disorders were characterized by family history of epilepsy and episodic dyscontrol; perinatal brain insult, developmental, neuropsychiatric and childhood behavior disturbances; epileptoid symptoms and EEG changes.

## NR277

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

# EFFECTS OF CHILD SEXUAL ABUSE ON ADULT INTIMACY

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Sherry Stewart, M.A., Psychiatry, Southwest Psych Ser, 4710 Bellaire Blvd, Bellaire, TX 77401; Jenny G. Stadler, M.A., Pamela M. Cole, Ph.D.

## Summary:

While difficulties in intimate heterosexual relationships are reported frequently by women in therapy with a history of child sexual abuse, there is little systematic research on the specific nature of this longterm effect. In this study, 64 women (ages 22-40) with a history of child sexual abuse by an adult man completed questionnaires on their current relationships with men and on the quality of relationships in their families of origin. Their responses were compared statistically with those of 75 same-aged women without such a history. We found that sexually abused women reported significantly lower levels of trust in their male partners than nonabused women (p's<.0005) and fewer experiences of emotional, social, intellectual, and sexual intimacy (p's<.0005). Also, 14.7% of the total group of abused women were unable to complete the intimacy and trust questionnaires because they had never had a relationship with a man compared to 2.6% of the total group of non-abused women. Low levels of trust and intimacy were also moderately correlated with low levels of cohesiveness in the family of origin and of emotional support in the mother-daughter relationship. These relationships are further analyzed to present difference between cases of incestuous and nonincestuous child sexual abuse. Finally, difficulties with intimacy and trust were significantly related to the number of depressive symptoms reported on the Beck Depression Inventory. The findings are discussed in terms of the greater risk for adult interpersonal problems and psychopathology among sexually abused girls who lack a supportive relationship with their mothers and implications for the treatment of both child and adult sexual abuse victims.

#### NR278 GUILT IN OFFSPRING OF DEPRESSED MOTHERS

COMORBIDITY OF SOCIAL PHOBIA IN PANIC DISORDER

EFFECTS OF OPIOID BLOCKADE IN THE EATING DISORDERS

M.D., David Pickar, M.D., Timothy D. Brewerton, M.D., David C. Jimerson, M.D.

Carolyn Zahn-Waxler, Ph.D., LDP, NIMH 15K LDP, 9000 Rockville Pike, Bethesda, MD 20892; Grazyna Kochanska, Ph.D., Janice Kurpnick, L.S.W., Donald McKnew, M.D.

#### Summary:

The development and interrelations of guilt, empathy, anxiety, and hostility were compared in five nine-year-old children of well mothers (N=35) and children of SADS-screened, unipolar and bipolar depressed mothers (N=52). Assessments included a psychiatric interview (Childhood Assessment Schedule), the Achenbach Child Behavior Check List, and a semiprojective measure of emotions and interpretations of situations of interpersonal conflict and distress. On the projective measure, offspring of depressed mothers failed to show normative, age appropriate changes in guilt seen in children of well mothers (i.e. explicit concern over wrongdoing, remorse, reparation). Guilt expressions were more distorted or disguised with more bizarre and violent themes in interpretations of children of depressed mothers. Guilt was correlated with hostility in children of depressed mothers whereas guilt was correlated with empathy and anxiety symptoms in children of well mothers, suggesting different dynamics and meaning of guilt in the two groups. Consistent with other research, guilt was unrelated to mood disturbances in children at these ages. Discussion focuses on the role of guilt in depression, and why maternal depression might sometimes lead to different forms of guilt in their children and hence, different trajectories in this aspect of affective development.

#### NR279

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

Murray B. Stein, M.D., BPD, NIMH Bldg 10 Rm 3S239, 9000 Rockville Pike, Bethesda, MD 20892; Cheryl A. Shea, M.A., Thomas W. Uhde, M.D.

#### Summary:

In order to further study the relationship between panic disorder (PD), agoraphobia (Ag), and social phobia (SP), we systematically evaluated 35 patients meeting *DSM-III-R* criteria for PD (21 females and 14 males, mean age  $37 \pm 9$  yrs); 23 of the 35 patients also met criteria for Ag. Interestingly, 16 of the 35 patients (45.7%) met *DSM-III-R* criteria for a concurrent diagnosis of SP. Of these 16 patients with co-existing PD and SP ("PD-SP subgroup"), 11 had the onset of social phobia prior to the onset of their panic attacks.

Overall the PD-SP subgroup could be distinguished from the PD-non-SP subgroup on a number of parameters. The PD-SP subgroup scored higher on the Social Avoidance and Distress Scale ( $18.6 \pm 7.0 \text{ vs} 6.5 \pm 6.2, p < .0001$ ), the social phobia subscale of the Fear Questionnaire ( $16.7 \pm 6.5 \text{ vs} 7.5 \pm 5.0, p < .0001$ ), and the self-rated Zung Anxiety Scale ( $61.7 \pm 10.3 \text{ vs} 50.1 \pm 9.7, p < .01$ ). Fifteen of the 16 (93.8%) PD-SP patients had a lifetime history of major depression, compared with 9 of the 19 (47.4%) PD-non-SP patients (Fisher's Exact Test, p < .005). Taken together, these observations suggest that a sizeable subgroup of patients with panic disorder may suffer from significant social phobic symptomatology. Theoretical and practical implications of these findings will be further discussed.

#### NR280

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

Harry A. Brandt, M.D., DIRP/LCS/SBP, NIMH BLDG 10 RM 3S231, 9000 Rockville Pike, Bethesda, MD 20892; Arlene P. Hegg,

#### Summary:

The endogenous opioid system (EOS) is involved in the regulation of appetite, energy metabolism, mood, menstrual cyclicity and reproductive function, processes that are disturbed in anorexia nervosa (AN) and bulimia (B). To assess whether dysregulation of the EOS may contribute to the symptoms of eating disorder patients, we conducted a double-blind, placebocontrolled pharmacological challenge study with the opiate antagonist naloxone (0.5 mg/kg i.v.).

Eating disorder patients met *DSM-III* diagnostic criteria, and included 17 patients with bulimia, nine low weight anorexic patients at discharge weight (83% expected body weight). Patients were metabolically stable, medication free, and binge abstinent for at least four weeks prior to study. Results from 10 healthy female volunteers demonstrated the expected naloxone-induced decrease in consumption of a test meal, and post-naloxone rise in serum cortisol. In comparison to these results in controls, naloxone administration showed no apparent decrease in test meal consumption in the low-weight anorexic patients (p<.01), in the weight-restored anorexic patients (p<.01), or in the bulimic patients (p<.05). Similarly, cortisol responses (placebo-corrected, area under curve) to naloxone were significantly blunted in the low-weight anorexic patients (p<.005), in weight-restored anorexic patients (p<.0001), and in the bulimic patients (p<.0005). These preliminary results show blunted responsivity to the behavioral and neuroendocrine effects of an opioid antagonist in eating disorder patients and suggest that dysregulation of the EOS may be of pathophysiological significance in these disorders.

## PLATELET SEROTONIN UPTAKE IN BULIMIA NERVOSA

David S. Goldbloom, M.D., Psychiary, Toronto General Hosp. EN8-219 200 Elizabeth Street, Toronto, Ontario, Canada M5G2C4; Lisa Hicks, B.A., Paul E. Garfinkel, M.D.

#### Summary:

In the last decade, the importance of hypothalamic serotonin in the central regulation of satiety has been increasingly recognized. At the same time, clinical studies have implicated serotonin dysfunction in the context of depression, suicidality, aggression, impulsivity, alcoholism, and obsessive compulsive disorders. Aspects of these clinical disorders are common in bulimia nervosa (BN), and recent neuroendocrine studies in BN suggest serotonin dysfunction. This is of interest in view of the failure in BN of the normal satiety mechanisms. Assessment of central serotonin function includes neuroendocrine, CSF, post-mortem, and platelet strategies. Platelet serotonin uptake may provide a peripheral model of CNS synaptosomal uptake. This has not previously been studied in BN. We assessed 26 BN subjects and 16 controls matched for age, weight, and sex. All subjects completed the Eating Disorder Inventory, Eating Attitudes Test, Hamilton Rating Scale for Depression, and had a clinical intereview. Two morning samples, 30 minutes apart, were drawn for each subject and analyzed for platelet serotonin uptake for BN subjects was 605.7 + 28.2 picomoles per 10<sup>9</sup> platelets in 4 minutes (X + SEM), and for controls was 498.4 + 35.0 picomoles per 10<sup>9</sup> platelets in 4 minutes (X + SEM). This difference was found to be statistically significant [t(40)=2.37, p=0.02]. Limitations to this methodology and implications for a hypothesis of serotonin dysfunction in BN are discussed.

#### NR282

## EATING DISORDERS AND ALCOHOLISM: COPREVALENCE

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

David S. Goldbloom, M.D., Psychiatry, Toronto General Hosp, EN8-219 200 Elizabeth Street, Toronto, Ontario, Canada M5G2C4; Lisa Hicks, B.A.

#### Summary:

A clinical association between alcohol abuse and eating disorders has long been recognized. Hypotheses about this association have included such diverse explanations as oral needs, affective regulation through substance abuse, genetic vulnerability, cultural modulation of biological drives, and opiate and serotonergic dysfunction. In order to establish the prevalence of and characterize this association, we surveyed 100 consecutive female referrals to a specialized eating disorders programme for alcoholism. Measures included a drinking diary of the previous three months, the Michigan Alcohol Screening Test, and the Alcohol Dependence Scale, as well as the Eating Attitudes Test, Eating Disorder Inventory, Diagnostic Survey of Eating Disorders, and a clinical interview. The recent drinking history identified only 3% of the sample as having a concurrent drinking problem. The MAST, however, identified 12% as having had significant social sequelae of alcohol abuse, and the ADS revealed that 24% had met criteria for alcohol dependence. Symptoms of the eating disorder and degree of its associated psychopathology did not predict alcohol abuse, nor did family history of alcholism or affective disorder on the DSED. Preliminary data from a parallel survey of 100 consecutive female referrals to a specialized alcoholism treatment centre will be presented to examine the prevalence and characteristics of eating disorders in that sample. Implications of comorbidity will be discussed. The high ADS scores in the eating disordered sample are discussed in the context of a more general diathesis toward dependency.

#### NR283 CSF OXYTOCIN IN ANOREXIA NERVOSA

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

Mark A. Demitrack, M.D., Biol Psych, NIMH, 9000 Rockville Pike, Bethesda, MD 20892; Michael D. Lesem, M.D., Harry A. Brandt, M.D., Teresa A. Piggot, M.D., David C. Jimerson, M.D., Philip W. Gold, M.D.

#### Summary:

We have previously reported (Gold, et al., *N Eng J Med* 308:1117, 1983) that CSF vasopressin (VP) levels are increased in underweight patients with anorexia nervosa (AN), and tend to return to normal following correction of weight loss. This finding was of interest because VP has been shown to delay the extinction of behaviors acquired during aversive conditioning, and patients with anorexia nervosa show an exaggerated sense of the adverse consequences of eating. We report here on the CSF levels of oxytocin (OT) in AN. OT is structurally similar to VP and has central effects opposite to those of VP, including enhanced extinction of behaviors acquired during aversive conditioning.

Anorexic patients were studied longitudinally while at less than 65% ideal body weight and one-three weeks after correction of weight loss. CSF OT levels were significantly lower in underweight anorexics  $(5.7 \pm 0.4 \text{ pg/ml})$  compared either to their weight recovered state  $(7.1 \pm 0.4 \text{ pg/ml}, \text{ p} < .004)$  or to age-matched female controls  $(8.0 \pm 1.0 \text{ pg/ml}, \text{ p} < .05)$ . Although the causes and consequences of this defect are not definitively known, it may be of significance that anorexic patients show reciprocal abnormalities in the secretion of CSF VP and OT. We speculate that the reduction in centrally-directed OT secretion in AN may intensify the possible functional consequences of increased centrally-directed VP in these subjects.

#### NR284 SUBSTANCE ABUSE IN SCHIZOPHRENICS AT ADMISSION

Jeffery N. Wilkins, M.D., Psychiatry, VAMC Brentwood Divn, 11301 Wilshire Blvd, Los Angeles, CA 90073; Andrew I. Shaner, M.D., David A. Gorelick, M.D.

## Summary:

Substance abuse is a significant problem in schizophrenic patients during treatment, but there have been few systematic studies of substance abuse (verified objectively) in schizophrenics at admission. In this study, 29 of 30 consecutive schizophrenics (all males) admitted for inpatient treatment had urine samples tested for cocaine, phencyclidine (PCP), opiates, delta-9-tetrahydrocannabinol (THC), amphetamines, and barbiturates by fluoresence polarization immunoassay (positives confirmed by gas-liquid chromatography or high pressure liquid chromatography). Seventeen (59%) patients had a positive test; the commonest being cocaine (48%). Polysubstance abuse was common. Nine patients denied any history of substance abuse, although five (56%) had a positive urine test. Sixteen patients denied using any substance of abuse in the previous weeks (10 of these had a positive urine test). The evaluating physician judged that 19 patients were not under the influence of a substance of abuse at the time of admission (12, 60%) had a positive urine test and that 10 patients were under the influence (five, 50%) had a positive urine test. These data suggest the unreliability of patient self-report and physician assessment in determining recent substance use or acute intoxication in schizophrenic patients. This may lead to the misdiagnosis of a substance-induced psychotic disorder as schizophrenia or to the failure to appreciate the contribution of substance use to an exacerbation of schizophrenia.

#### NR285 SOCIAL STATUS-SETTING ALTERS PCP EFFECTS IN MONKEYS

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

James E. Dillon, M.D., Child Psychiatry, Univ of Mich Med Ctr, 1500 E. Medical Center Drive, Ann Arbor, MI 48109; Jeffery N. Wilkins, M.D., Michael J. Raleigh, Ph.D.

## Summary:

We investigated the effects of social status and environmental stimulus conditions on PCP-induced behaviors in adult male vervet monkeys (*Cerocopithecus aethiops sabaeus*). Eight adults, the dominant and one subordinate from four groups, were observed under two conditions. In one they were exposed to a provocative stimulus (potential predator, unfamiliar adult male, or noxious tactile stimulation) and in the other to a non-provocative stimulus (an unfamiliar juvenile vervet). Subjects were treated in a cross-over design with vehicle or PCP (0.2mg/kg). Dominance rank significantly affected PCP-elicited aggression and vigilance. Subordinate males showed larger increases in these behaviors (176 and 184% of baseline) than did dominant males (99 and 100%) across both stimuli ( $f_{1,6}$ >9.33, p<05 for each behavior). Stimulus condition also influenced PCP's effects on vigilance, stereotypes, and resting. Relative to the nonprovocative conditions, PCP induced larger increases in vigilance and stereotypies and greater decrements in resting under provocative conditions ( $f_{1,6}$ >17.31, p<05 for the condition by drug interaction for all behaviors). Finally, there was a significant (three-way) rank by condition by drug interaction for aggression. Relative to subordinate males, when given PCP, dominant males were more aggressive in provocative but less aggressive in non-provocative settings (f 1,6=6.26, p<05 for this interaction). Thus PCP, social, and individual behavioral effects of PCP, including aggression, are strongly influenced by social factors, such as dominance rank, environmental conditions, the degree of provocation, and the complex interactions among these factors.

## NR286

## STRESS AND DEPRESSION IN INNER CITY ADOLESCENTS

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

Steven J. Schleifer, M.D., Psychiatry, Univ Med Dent of NJ, 185 S. Orange Ave MSB E501, Newark, NJ 07103; Jacqueline Bartlett, M.D., Barbara J. Scott, Robert L. Johnson, M.D., Steven E. Keller, Ph.D.

#### Summary:

The association between life stress and depression has occasioned much discussion. Inner city adolescents are likely to be exposed to highly stressful conditions; however, depression has not been systematically investigated in this population. As part of a study of health risk factors in inner city adolescents and young adults, 37 males and 15 females attending an adolescent health clinic for routine examinations or minor health problems were interviewed in relation to psychiatric symptomatology and life stress. Sixteen met criteria for current major depression using the Diagnostic Interview for Children and Adolescents, and 38% met criteria for lifetime major depression. Modified Coddington-scale life events during the preceding year were three times that reported by a normative adolescent population; 19% had been arrested, 43% had a family member who had been arrested, and 60% had witnessed serious crimes. Elevated scores were not found, however, on the Cohen Perceived Stress Scale. Multiple regression independently. Levels of perceived stress were associated with depressive symptoms but not with syndromal depression. Stressful life experiences may contribute to the development of depression despite the absence of persistent high levels of perceived stress.

#### Thursday, May 12, 12 noon-2:00 p.m. THE TRIDIMENSIONAL PERSONALITY QUESTIONNAIRE: A VALIDITY STUDY WITH ALCOHOLICS

Danuta M. Lamparski, Ph.D., DHHS, NIAAA DICBR LCS Bldg 10, Rm 3B19 9000 Rockville Pike, Bethesda, MD 20892; Debra K. Garnett, M.S.W., Markku Linnoila, M.D.

## Summary:

Recently, Cloninger postulated three genetically independent dimensions underlying personality and behavior (1-3), and constructed the Tridimensional Personality Questionnaire (TPQ) in order to quantify these dimensions: Novelty Seeking (NS), Harm Avoidance (HA), and Reward Dependance (RD). Except for one paper (4) comparing the TPQ scores of medical students with other personality tests, little is known of the psychometric properties of the TPQ. The current study examines the validity of the TPQ by comparing the scores of alcholics to staff ratings on each of the dimensions. Fifty alcoholics (39 males, 11 females) participating in inpatient research at the National Institute on Alcohol Abuse and Alcoholism completed the TPQ after at least three weeks of abstinence. Independent ratings of each dimension of the TPQ were done by the primary nurse, staff psychiatrist, and recreational therapist using a seven point scale (-3 to +3) as defined by Cloninger (5). Raters were blind to TPQ scores and to Cloninger's theory regarding the relationship between personality and Type I and Type II alcoholism. Overall, the alcoholics had the following scores: NS=16.7 ± 5.4, HA=13.9 ± 6.6, RD=19.3 ± 4.2. Pearson correlation coefficients among each of the raters and the TPQ ranged from .26-.64 for NS, .03-.35 for HA, and .22-.33 for RD. Composite scores were computed by combining each rater's score. Pearson correlations for the composite and the TPQ were: NS=.66 (p<.001), HA=.30 (p<.04), RD=.39 (p<.01). The psychometric characteristics of the TPQ and possible abnormalities in alcoholics will be discussed further.

## **NR288**

## MULTIPLE PERSONALITY AND PARTIAL COMPLEX SEIZURES

PUBERTAL TIMING AND DIET PRACTICES IN ADOLESCENCE

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

Colin A. Ross, M.D., Psychiatry, St. Boniface Hospital, 409 Tache Avenue, Winnipeg, MA 00000, Canada R2H2A6; G. Ron Norton, Ph.D., Sharon Heber, R.N., Geri Anderson, R.P.N.

## Summary:

Several reports have suggested a relationship between multiple personality disorder (MPD) and partial complex seizures. To investigate this relationship we administered a valid and reliable structured interview, the Dissociative Disorders Interview Schedule (DDIS), and the Dissociative Experiences Scale, a 28-item valid and reliable self-report instrument to 20 subjects with MPD, 20 with partial complex seizures, and 28 neurological controls. MPD and seizure subjects were matched for age and sex. MPD subjects differed from seizure subjects on all of 17 different items. Seizure subjects differed from controls on only one at p<.05. Items included DSM-III diagnoses of major depressive episode, somatization disorder, borderline personality and all the dissociative disorders as well as history of sexual abuse, physical abuse, sleepwalking, trance states, imaginary playmates, secondary features of MPD, extrasensory experiences, Schneiderian symptoms, and Dissociative Experiences Scale score. There is little phenomenological overlap between MPD and partial complex seizures and no more reason to consider partial complex seizures in the differential diagnosis of MPD than any other neurological disorder.

## NR289

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

Adam Drewnowski, Ph.D., Psychiatry, Univ of Michigan, School of Public Health M-5164, Ann Arbor, MI 48109; Doris K. Yee, M.A., Dean D. Krahn, M.D.

## Summary:

The influence of maturational, familial, and socioeconomic factors on extreme dieting practices among adolescent females was examined in a cross-sectional survey study of 2,030 school girls (ages 11-18) and 1,299 of their mothers. Thirty-six percent of all girls reported dieting at the time of the study. While frequent fasting was widespread (20.8%), the use of diet pills (3.1%), laxatives (1.2%), or vomiting after meals (1.9%) were not. Responses consistent with a probable DSM-III-R diagnosis of bulimia nervosa were obtained from 2.2 percent of the girls. Analyses by age and maturational status showed that following puberty, girls were more dissatisfied with body image, saw themselves as overweight, and were more likely to diet (39.4%) than the pre-pubertal group (19.5%), or to employ bulimic behaviors for weight control. The timing of puberty affected both the onset and the intensity of dieting: early maturers were more likely to diet (43.5%) than late maturers (27.2%), often reporting first dieting by the age of 11. Analyses of familial variables revealed that fully 50 percent of dieting girls, but only 14% of non-dieters, reported being encouraged to diet by their mothers. Higher socioeconomic status was linked to greater concern with weight control and elevated dieting rates among both mothers and daughters; however, prevalence estimates for bulimia nervosa among adolescent girls were unaffected by socioeconomic variables. The present survey study confirms clinical reports that early-maturing girls may be at greater risk for eating disorders, and is the first to explore the role of maternal attitudes and mother-daughter interactions in early dieting and the development of eating disorders in a large sample of adolescent girls.

#### NR290 CHILDREN'S EXPOSURE TO PARENTAL PSYCHOPATHOLOGY

John E. Richters, Ph.D., NIMH Bldg 15K, 9000 Rockville Pike, Bethesda, MD 20892

## Summary:

The relation between timing of children's first exposure to parent psychopathology and their social-emotional adjustment in young-adulthood is examined in a prospectively assessed, longitudinal sample of 263 high-risk offspring. Early first exposure to diagnosed episodes of parent psychopathology was significantly related to more frequent exposure, to exposures of longer duration, and to more severe ratings of parent psychopathology. Early exposure *per se*, however, was not significantly related to offspring adjustment levels. The results instead support a cumulative stress model in which overall levels of exposure to parent psychopathology are related to offspring adjustment. Reports from other investigators concerning the differential effects of early exposure have failed to control for overall exposure levels. The implications of this finding for research, theory, and intervention are discussed.

## NR291

## EXPRESSED EMOTION AND CHILD PSYCHOPATHOLOGY

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

Carl E. Schwartz, M.D., Psychiatry, Harvard Medical School, Mass Mental Hith Fenwood Road, Boston, MA 02115; William R. Beardslee, M.D., David J. Dorer, Ph.D., Philip W. Lavori, Ph.D., Martin B. Keller, M.D.

#### Summary:

Expressed Emotion (EE) refers to a set of emotional aspects of speech for which ratings have been derived. Five independent studies have established that EE is a powerful predictor of relapse in patients with schizophrenia, and two studies have established an association of high EE in a spouse with relapse of depression in his or her mate. There are no previous studies of parental EE as a predictor of child affective disorder or other disorders not in the schizophrenia spectrum.

In this study we investigated the relationship between the level of maternal EE and the incidence of affective disorder (major depression, mania or dysthymia), substance abuse, or conduct disorder in 275 children. We found that high levels of maternal EE were associated with a three-fold increase in risk for either depression or dysthymia, substance abuse, or conduct disorder. This increased risk was independent of the increased risk associated with parental affective illness. Research and clinical implications are discussed.

#### NR292 ADULT CHILDREN OF PROBLEM DRINKERS IN THE COMMUNITY

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

Nady El-Guebaly, M.D., Univ of Calgary Psychiatry, School of Medicine, 1403 29th Street NW, Calgary AB, Canada T2N2T9; John R. Walker, Ph.D., Colin A. Ross, M.D., Raymond F. Currie, Ph.D.

#### Summary:

The problems in adulthood of children of problem drinkers (ACPB) and alcoholics (ACOA) have been publicized. In a midsize urban community, a random sample of 581 households was reached by telephone and then in person in case of refusal. One respondent per household had to be 18 years or older. One hundred twenty-nine respondents (22.6%) thought "that one or both of their parents had a drinking problem for at least 2 weeks." The biological father was involved in 81.4% of cases and biological mother in 14.7% of cases. Among these ACPB's, 70% were ACOA's defined as reporting parents who experienced two or more problems with alcoholism. Compared to the rest of the sample, the ACPB responders were a younger group but with the same sex distribution. Controlling for age, ACPB's left home at an earlier age. Like their parents, they were more likely to have experienced a marital breakdown but did not differ in socioeconomic status. The ACPB's as a group reported a higher amount of substance use and scored higher on the CAGE, mostly due to a larger number of heavy drinkers in their midst. The possibility that ACPB's experience a more negative affect as a group was not supported using the Bradburn Affect Balance Scale in this community sample. However, ACPB's sought help significantly more frequently from professionals, groups or literature to cope with stress and anxiety, to deal with their parents or own substance abuse but not for their parenting skills.

## NR293 WEIGHT LOSS, OPIATE FUNCTION AND EATING BEHAVIOR

Arlene P. Hegg, M.D., DIRP/LCS/SBP, NIMH Bldg 10 3S231, 9000 Rockville Pike, Bethesda, MD 20892; Michael D. Lesem, M.D., Harry A. Brandt, M.D., David C. Jimerson, M.D.

## Summary:

There is current interest in the effects of diet on eating behavior. This has been studied with respect to neuroendocrine, catecholamine, and serotonin systems. The endogenous opiate system (EOS) may also modulate eating behavior and thus, alterations in central opiate function could play a role in anorexia nervosa or bulimia. This is supported by a report of reduced central  $\beta$ -endorphin in low weight anorexic patients. Since anorexic and many bulimic patients are at reduced weight, this study was designed to evaluate the effects of mild weight loss on the EOS. We studied four healthy, medication free, female volunteers within 10% of normal weight. Using a randomized double-blind design, a single dose of naloxone (0.5 mg/kg i.v.) or placebo was infused on separate test days, followed by a test meal. Subjects then followed a reduced calorie diet, resulting in weight loss of approximately one kilogram per week for three-four weeks. After weight loss, the naloxone challenge was repeated.

At baseline weight, subjects ate significantly fewer calories following naloxone  $(434 \pm 97 \text{ (SE) kcal})$  vs placebo ( $829 \pm 131 \text{ kcal}$ , p<.02). Caloric intake on placebo days did not change significantly after weight loss. However, following weight loss, naloxone produced no significant decrease in caloric intake compared to placebo. Thus, the naloxone induced decrement in eating after weight loss ( $21 \pm 8 \text{ kcal}$ ) was significantly less than at baseline weight ( $395 \pm 81 \text{ kcal}$ , p<.02). These preliminary results indicate that weight loss may modify the role of the EOS on eating. Hence, weight loss observed in anorexic and bulimic patients may alter central neuromodulators contributing to the perpetuation of these eating behaviors.

#### NR294 COMPULSIVE PERSONALITY DISORDER IN THE COMMUNITY

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

Gerald Nestadt, M.D., Psychiatry, Johns Hopkins Day Hosp, 600 N Wolfe St Myr2-228, Baltimore, MD 21205; Alan J. Romanoski, M.D., Marshal F. Folstein, M.D., Ernest M. Gruenberg, M.D., Paul R. McHugh, M.D.

#### Summary:

The compulsive personality disorder has a well-established clinical tradition. The publication of *DSM-III* criteria and the development of several clinical instruments to define this disorder have encouraged further research. This paper presents data on this disorder in the community.

Eight hundred and ten community-residing subjects in Baltimore were examined in the second stage of a two-stage morbidity survey as part of the Epidemiologic Catchment Area Program (ECA). Each subject was examined using the Standardized Psychiatric Examination (SPE) by one of four psychiatrists. Evidence for each of the compulsive traits was recorded. An acceptable level of inter-rater agreement was attained.

The prevalence of this disorder is estimated at 1.7% in the general population. It appears to have a distinct demographic distribution. There is a strong relationship to birth order. A high frequency of both affective and anxiety disorders was noted.

The interaction between compulsive traits and preceding life events with respect to the presence of anxiety disorders will be presented.

These data suggest that this disorder has identifiable risk factors, distinct demographic distribution and consequences which include a propensity to develop anxiety disorders in the context of life changes.
### NR295 PERSONALITY DISORDER IN BALTIMORE'S HOMELESS

Gerald Nestadt, M.D., Psychiatry, Johns Hopkins Day Hosp, 600 N Wolfe St Myr2-228, Baltimore, MD 21205; William R. Breakey, M.D., ALan J. Romanoski, M.D., Pamela J. Fisher, Ph.D.

# Summary:

Estimates of the distribution of psychiatric conditions within the "homeless" population is valuable for reasons of service provision, policy decision, and the demonstration of the nature, course, and disability incurred by various disorders.

This presentation will focus on the distribution of DSM-III Personality Disorders diagnosed in this population.

Two hundred and five subjects in shelters for the homeless and in the Baltimore City Jail were randomly selected and participated in the second stage of a two stage survey.

Each subject was examined by one of three research psychiatrists employing the Standardized Psychiatric Examination (S.P.E.). In addition parts of the Structured Clinical Interview for *DSM-III* (S.C.I.D.) and the Eysenck Personality Inventory were employed.

Over 40% of this population were diagnosed to have an Axis II disorder. There was a substantial prevalence of paranoid and schizoid disorders in this group. The examining psychiatrists recommended treatment for most of these subjects.

These findings are discussed from several vantage points.

Do these disorders interact with Axis I conditions to provoke this most severe disability?

Are these disorders the psychological expression of the vulnerability that leads to the disaffiliation evident in this group? Is "homelessness" an extreme result of the impairment and disability certain of these disorder engender?

### NR296

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

# STUDIES OF BASAL METABOLISM IN BULIMIA

Michael J. Devlin, M.D., NYS Psych Inst Box 116, 722 West 168th Street, New York, NY 10032; B. Timothy Walsh, M.D., Steven B. Heymsfield, M.D., Sondra Dantzic, B.A., Linda Wong, B.A.

# Summary:

A relationship between bulimia and semistarvation has been suggested by clinical observations of preoccupation with food and binge eating behavior in bulimic patients, epidemiologic studies reporting frequent onset of bulimia during periods of dieting, and biological studies of abnormal neuroendrocrine function in bulimia. In order to further test the hypothesis that bulimic women of statistically normal weight are physiologically in a state resembling semistarvation, we studied resting metabolic rate (RMR), a known index of energy conservation in semistarved states, in a sample of 17 normal weight women with bulimia and nine matched controls. Expressing RMR as percent deviation from predicted values, there was a strong trend toward lower RMR in the bulimic sample (-13.2 percent vs. -5.1 percent, p=.076). Both bulimic and control groups were of normal weight (94 percent of ideal body weight vs. 965 percent of ideal body weight). These findings provide preliminary support for the idea that bulimic patients are in an energy conserving state similar to that seen in semistarvation and suggest that appetitive abnormalities seen in bulimia and semistarvation may be mediated by related physiological mechanisms.

#### NR297 INFLUENCE OF PERCEIVED CONTROL ON CARBON DIOXIDE PANIC

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

William S. Sanderson, Ph.D., CSAD, 1535 Western Avenue, Albany, NY 12203; Ronald M. Rapee, Ph.D., David H. Barlow, Ph.D.

# Summary:

The current study tested the notion that a sense of control can mitigate anxiety and panic attacks caused by the inhalation of 5.5% CO<sub>2</sub> enriched air. Twenty Panic Disorder patients inhaled a mixture of 5.5% CO<sub>2</sub> enriched air for 15 minutes. All patients were instructed that illumination of a light directly in front of them would signal that they could decrease the amount of CO<sub>2</sub> they were receiving, if desired, by turning a dial attached to their chair. For ten patients the light was illuminated during the entire administration of CO<sub>2</sub>. For the remaining ten patients the light was never illuminated. In fact all patients experienced the full CO<sub>2</sub> mixture and the dial was ineffective.

When compared to patients who believed they had control, patients who believed they could *not* control the CO<sub>2</sub>: 1) Reported a greater number of *DSM-III-R* panic attack symptoms, 2) rated the symptoms as more intense, 3) reported greater subjective anxiety, 4) reported a greater number of catastrophic cognitions, 5) reported a greater resemblance of the overall inhalation experience to a naturally occurring panic attack, and 6) were significantly more likely to report panic attacks. These data illustrate the contribution of psychological factors to laboratory induction of panic attacks via inhalation of 5.5% CO<sub>2</sub> enriched air.

#### NR298 HABITUATION OF STARTLE IN PTSD

William A. Ball, M.D., Psychiatry, Univ of Pennsylvania, Walnut St Mellon Bank Building, Philadelphia, PA 19104; Michelle E. Cohen, Ph.D., Steven M. Silver, Ph.D., Adrian R. Morrison, D.V.M., Richard J. Ross, M.D.

#### Summary:

Exaggerated startle to various stimuli is typically described (1) in posttraumatic stress disorder (PTSD). We hypothesized that exaggerated startle in PTSD patients may reflect an inability to habituate readily to repeated stimuli.

Subjects included eight inpatient Vietnam combat veterans (age 35-46 years) free of substances or psychotropic medications for at least one month. All met *DSM-III-R* criteria for current PTSD, and seven reported heightened startle. They received counterbalanced sets of 150 glabellar taps (20 msec each) and 150 tones (100 db, 1000Hz, 50msec each) at interstimulus intervals of 4 sec in both conditions. Taps were delivered via solenoid-activated plunger, and tones were presented binaurally through headphones. The eyeblink component of the startle reflex was measured as the output of an infrared densitometer recorded on a strip chart. Contrary to expectations, repeated taps and tones both produced a significant decline in eyeblink amplitude across blocks of five trials (F (19, 159)=12.79 and F (19, 114)=16.14, respectively, p<.01). The subjects averaged more than a 50% drop in eyeblink amplitude within 10 trials in both conditions, a rate at least as rapid as that described for normal acoustic startle (2).

Thus, PTSD patients exhibit rapid *habituation* of startle to affectively neutral tactile or acoustic stimuli. Reports of exaggerated startle in PTSD (1) probably reflect either the effects of stimulus conditions not reproduced here or the existence of a behavior qualitatively different from startle, such as conditioned avoidance. (We thank Dr. H. Hoffman for the use of his equipment.)

#### NR299

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

SELF-REPORT VERSUS DST IN ASSESSING DEPRESSED CHILDREN Mary A. Fristad, Ph.D., Psychiatry, Ohio State University, 473 W. Twelfth Ave Upham Hall, Columbus, OH 43210; Elizabeth

B. Weller, M.D., Ronald A. Weller, M.D., Marijo Teare, B.S., Sheldon H. Preskorn, M.D.

#### Summary:

With the recent recognition of depression in children, research on its proper assessment has increased. As in adults, both self-reports and biological markers have been utilized. Most common of these are the Children's Depression Inventory (CDI) and the Dexamethasone Suppression Test (DST). To date, however, no published study has compared the sensitivity and specificity of these two assessment techniques. The purpose of this study was to compare sensitivity and specificity of the DST and CDI utilizing three groups of prepubertal children: 1) 63 depressed (*DSM-III* criteria) inpatients; 2) 14 nondepressed inpatient psychiatric controls; and 3) 21 normal community sample controls. Parent and child forms of the CDI and plasma cortisol levels at 8 a.m. and 4 p.m. were used. Results suggest the CDI provides a good screening instrument (sensitivity, CDI-C=44%; CDI-P=75%, CDI-C &/or CDI-P=89%). It clearly demarcated the two hospitalized groups from the normal control group (p<.05) but scores did not differ between the depressed group and nondepressed psychiatric controls. Specificity was high for the DST (DST-8=97%; DST-4=94%; DST-8 &/or DST-4=91%). The DST clearly differentiated the depressed group from the psychiatric and normal control groups (p<.05). If the DST is administered to all children with elevated CDI scores, diagnostic confidence is 97.5%. Cautions and recommendations for use of the CDI and DST are made.

NR300 WITHDRAWN Thursday, May 12, 12 noon-2:00 p.m.

# NR301 CORTISOL FUNCTIONING IN BEREAVED CHILDREN

FAMILY PSYCHOPATHOLOGY IN DEPRESSED CHILDREN

Elizabeth B. Weller, M.D., Psychiatry, Ohio State University, 473 W. Twelfth Ave Upham Hall, Columbus, OH 43210; Ronald A. Weller, M.D., Mary A. Fristad, Ph.D., Jennifer M. Bowes, B.A.

### Summary:

Abnormalities of the hypothalamic pituitary adrenal (HPA) axis have been observed in depressed adults and children. As many bereaved individuals develop depressive symptoms, their HPA axis function is of interest. Elevated cortisol levels have been noted in bereaved adults, but have not been studied in children. In this study, the HPA axis of bereaved children was assessed utilizing the Dexamethasone Suppression Test (DST). Participating families were recruited through obituaries, and no family member had received psychiatric treatment in the past two years. Subjects were 18 children (eight prepubertal, 10 pubertal, ages 7-18 ( $M\pm$ SD=13.1 $\pm$ 3.2). None had physical conditions that might affect DST results. Subjects were administered the Diagnostic Interview for Children and Adolescents to assess psychiatric status 4 weeks post-parental death. They were also given Dexamethasone at 11 pm (dose=0.5 mg., prepubertal; 1.0 mg, pubertal). Cortisol samples were drawn at 4 pm the next day, and levels were determined by radioimmunoassay. Overall, 50% of prepubertal children and 29% of pubertal children failed to suppress cortisol secretion. Nonsuppression was defined as a 4 pm post-Dexamethasone cortisol level

5 mg/dl. No differences between suppressors and nonsuppressors were found on any *DSM-III* symptom of depression or on total number of depressive symptoms present. Further studies are necessary to determine if there is a biological link between depressive illness and depression occurring during bereavement.

# NR302

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

Ronald A. Weller, M.D., Psychiatry, Ohio State University, 473 W. Twelfth Ave Upham Hall, Columbus, OH 43210; Elizabeth B. Weller, M.D., Mary A. Fristad, Ph.D., Loribeth Cohn, B.S., Sheldon H. Preskorn, M.D.

### Summary:

Family history studies utilizing adult probands have provided useful information regarding the familial nature of affective disorders. Unfortunately, similar studies with prepubertal depressed probands are lacking. This study obtained family psychiatric histories for 100 inpatient prepubertal children who met *DSM-III* criteria for major depression. Family psychiatric history was determined from standard structured diagnostic interviews and clinical interviews of parent (Psychiatric Diagnostic Interview—PDI) and child (Diagnostic Interview for Children and Adolescents—DICA-C, DICA-P). Psychiatric disorders were more prevalent among adult relatives of depressed children than among the general adult population. Using Weissman's data for comparison, major affective disorders in these depressed probands' parents were 6.5 times more frequent, 3.5 times more frequent among 2° relatives, and 4.6 times more frequent among 3° relatives. Of 100 probands, 44 had 1° relative with affective disorders; 32 had both 1° *and* 2° relatives with affective disorders; and 8 had 2° relatives with affective disorders, and somatization disorder also occurred at higher rates among 1°, 2°, and 3° relatives. Thus, occurence of affective disorders, in families of prepubertal probands is markedly increased. There is also evidence of increased rates of other psychopathology in their families.

# NR303 PERSONALITY PROFILES IN ANOREXIA AT TEN-YEAR FOLLOW-UP

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

Edward J. Schork, Ph.D., Psychiatry, Cornell Univ Med Coll, 21 Bloomingdale Road, White Plains, NY 10605; Katherine A. Halmi, M.D., Elke D. Eckert, M.D., Aline L. Bisgaier, B.A.

# Summary:

Fifty-eight individuals completed a standardized objective test of psychopathology, the MMPI, in a follow-up study conducted 10 years after they had been hospitalized for anorexia nervosa. Using *DSM-III-R* criteria, nine (15%) had *Anorexia Nervosa without bulimia* at followup, eight (14%) had *Anorexia Nervosa with bulimia*, 11 (19%) had *Bulimia Nervosa*, 12 (21%) had *Eating Disorder NOS*, and 18 (31%) had *no diagnosable eating disorder*. The non-diagnosed and NOS groups displayed significantly less psychopathology on the MMPI than the three anorectic or bulimic groups. The former two groups showed little pathology, while the currently anorectic or bulimic individuals showed clinically significant levels of depression, anxiety, somatization, obsessionality, ideosyncratic thinking, or characterological problems. The two anorectic groups did not differ, but each differed from the bulimia nervosa group, contrary to previous reports of greater similarity of bulimic-anorectics to normal weight bulimics than to other anorectics. Regression analysis showed that four of the MMPI scales together explained 29% of the variance in body weight; persons weighed more who were less paranoid, less socially withdrawn, less defensive, and more open about their problems. The results: a) underscore the chronicity and diversity of outcome in anorexia nervosa; b) demonstrate an enduring association between psychopathology and eating disorder symptoms; c) support the validity of the *DSM-III-R* diagnostic categories.

### NR304 DYSREGULATION OF 5-HT FUNCTION IN BULIMIA NERVOSA

Timothy D. Brewerton, M.D., Psychiatry, MUSC, 171 Ashley Avenue, Charleston, SC 29425; Edward A. Mueller, M.D., Harry A. Brandt, M.D., Michael D. Lesem, M.D., Dennis L. Murphy, M.D., David C. Jimerson, M.D.

### Summary:

Evidence supporting dysregulated serotonin (5-HT) function in bulimia nervosa is reviewed. Data from controlled studies are presented on tests of 5-HT function in patients with bulimia nervosa challenged with L-tryptophan (L-TRP), the dietary precursor of 5-HT, and m-chlorophenylpiperazine (m-CPP), a post-synaptic 5-HT agonist. Patients with bulimia nervosa (n=36), regardless of weight or mood, have blunted prolactin (PRL) responses to m-CPP in comparison to healthy controls (n=15), but only those with concurrent anorexia nervosa or major depression show blunting to L-TRP. Notably, PRL responses to m-CPP are negatively correlated with baseline cortisol (rho= -0.45, p -0.007). Temperature elevations following m-CPP are significantly greater in patients than controls, whereas the hypothermia produced by L-TRP is equivalent across diagnostic groups. Both increased and decreased 5-HT receptor sensitivity in the same subjects is consistent with current notions dysregulated neurochemical systems. The reasons for the discrepancies in the response measures following m-CPP and L-TRP may relate to differential involvement of pre- and post-synaptic 5-HT receptor sensitivity is altered in bulimia nervosa. Similar alterations in 5-HT receptors at or above the level of the hypothalamus may contribute to binge eating and other behavioral symptoms.

#### NR305 P300 AUGMENTATION IN POST-TRAUMATIC STRESS DISORDERS

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

Ron K. Wolner, M.D., Psychiatry, VA Medical Center, 113 Holland Avenue, Albany, NY 12208; Lawrence C. Kolb, M.D, Venkat Ramani, M.D.

### Summary:

A cardinal feature of the posttraumatic stress disorders (PTSD) is an exaggerated response to loud threatening noises. The late cognitive evoked potential, P3b, was measured in response to 90 dB tones and to 60 dB tones, in four patients with severe PTSD, four healthy normals, and three combat veterans with minimal to no PTSD. The severity of PTSD symptomology was determined by a 40 question symptom self-report scale. Subjects with severe PTSD had significant elevations of P3b amplitude, expressed as a ratio of evoked response at 90 dB to response at 60dB. The augmentation ratio for the severe PTSD group (average 2.56) was significantly greater than the ratio for the combined normals and combat veteran group (average .91) as evaluated by the Mann Whitney U test (one tailed significance .021). These findings are consistent with reports of increased autonomic responsivity in PTSD and suggest that severe PTSD patients may have an altered involuntary processing of noxious stimulus.

### NR306

# A CLINICAL AND DEMOGRAPHIC STUDY OF HYPERACTIVE ADULTS

Thursday, May 12, 12 noon–2:00 p.m.

Walid O. Shekim, M.D., Child Psychiatry, UCLA Neuropsych Inst, 760 Westwood Plaza, Los Angeles, CA 90024; Robert Asarnow, Ph.D., Esther Hess, M.A., Ruth Chao, M.A., Noel Wheeler, Ph.D.

### Summary:

It is becoming increasingly recognized that 1/3 to 1/2 of children diagnosed as having attention deficit/hyperactivity disorder (ADHD) continue to exhibit symptoms of the disorder into adulthood. The nature of the clinical picture is not well understood by a substantial number of clinicians. The purpose of this study is to report on the demographic and clinical profile of 49 adults, ages 20-65 (42 males, 7 females) who present with adult ADHA and meet *DSM-III-R* criteria for the disorder. Patients underwent a diagnostic work-up consisting of medical and psychiatric evaluation, a structured interview (SADS-L), the SCL-90R, Conners ADDH scale, structured interview for ADHD and, when available, information from parents was obtained. 88% of our sample met the Utah Criteria for adult ADHD (Wender et al, 1981). The majority of the sample had additional *DSM-III-R* diagnoses and only 7 had ADHD diagnosis alone. 45% of the sample met the criteria for Generalized Anxiety disorder, 28% alcohol abuse or dependence, 26% drug abuse, 20% dysthymic disorder, 20% cyclothymic disorder. These findings were similar to those reported in the literature. These findings as well as other correlations between SADS-L diagnosis and SCL-90R factor scores will be discussed. Future reports should include attention tests and treatment outcome measure.

# NR307 INTER-RATER AGREEMENT IN PSYCHOTHERAPY RESEARCH

Gordon D. Strauss, M.D., Psychiatry, UCLA, 760 Westwood Plaza, Los Angeles, CA 90024; Marcia K. Goin, M.D., Robert S. Martin, M.D.

### Summary:

Outcome research for longterm psychodynamic psychotherapy (i.e. lasting one year or more) has not progressed as readily as research focussing on briefer treatment. Open-ended therapy for chronic dysphoric states or for character pathology doesn't lend itself to treatment manuals and outcome measures focussed on symptoms are inadequate for a process which seeks to achieve intrapsychic change. The semi structured interview developed by McGlashan for the Chestnut Lodge Follow-Up Study has promise as a possible outcome measure for longterm psychotherapy. However, studies of inter-rate *agreement* (in contrast to *reliability*) have not been published for this 33-item instrument. Eight patient interviews with this instrument were taped and independently scored. Inter-rater agreement was examined two ways: by patient (how much agreement on 33 items?) and by item (how much agreement on eight patients?) Using the Tinsley-Weiss index of inter-rater agreement, average agreement by patient was .68 (p<.01) and by item was .71 (P<.05). Two patients were re-interviewed after one year of psychotherapy, and inter-rater agreement was .67 and .87 (both p<.001). These results, added to McGlashan's estimates of inter-rater reliability, suggest this semi-structured interview may be useful as an outcome measure for research on longterm psychotherapy.

#### NR308 CLINICAL CORRELATES OF BRAIN METABOLISM IN BULIMIA

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

Jennifer Hagman, M.D., Psychiatry, Univ of Calif Irvine, 400 Newport Ctr Dr. #706, Newport Beach, CA 92660; Barton J. Blinder, M.D., Joseph C. Wu, M.D., Monte S. Buchsbaum, M.D., Melissa Derfler, M.D.

### Summary:

Eight patients with *DSM-III-R* diagnoses of Bulimia Nervosa underwent Positron Emission Tomography (PET) scans using the 18-fluro-2-deoxyglucose method.<sup>1</sup> Prior to PET scanning each subject completed the Eating Attitudes Test (EAT) and a standardized interview to evaluate binge/purge frequency and the presence of depression as rated on the Hamilton Depression Inventory and by clinical assessment. These scores were then correlated with brain metabolic activity as measured by PET scan. EAT score was negatively correlated with left parietal cortex, left mid-thalamus, and left posterior thalamus. Binge frequency was negatively correlated with left frontal cortex and right posterior thalamus. Frequency of vomiting episodes was positively correlated with right caudate and right posterior thalamus. Depression ratings were negatively correlated with right striatum, left and right parietal cortex, and positively correlated with left striatum. All correlations reported were significant at P 0.05 for N=8. These results are presented suggesting exploratory hypotheses. Some may have occurred by chance given the large number of correlations. However, these results suggest that specific brain regions may be involved in the development of Bulimia Nervosa and the affective and behavioral components of the disorder.

# NR309

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

Roger L. Cambor, M.D., Payne Whitney Clinic, 525 East 68th Street, New York, NY 10021; M. Katherine Shear, M.D., Lisa A. Spielman, B.S., John A. Bargh, Ph.D., John A. Sweeney, Ph.D.

### Summary:

ATTENTIONAL BIAS IN PANIC DISORDER

Background and Aims: Recent work by British researchers suggests that abnormal cognitive processing is a feature of anxiety. Data from studies of GAD patients indicate that the abnormalities in cognition are attentional. The Stroop Color-Naming Task is a sensitive and specific instrument for testing attentional processes. Subjects are asked to respond to the color of a word stimulus as rapidly as possible, regardless of the semantic content of the stimulus. Differences in reaction time to specific words, or between groups of subjects, indicate the presence of attentional interference, or bias toward semantic processing of the stimulus. Attentional bias is involuntary and, among anxious subjects, selective of threat-related information. Using a modification of the Stroop paradigm, we tested attentional processes in 12 patients meeting *DSM-III-R* criteria for Panic Disorder, and 12 matched controls.

Methods and Results: Subjects were asked to respond to the location of single words presented above or below a fixation point on the visual display unit of a microcomputer. Words were either neutral or threatening (bodily arousal, bodily damage, or socially undesirable) in content. Analysis of reaction times showed patients to be slower than controls on threat, but not neutral words ( $\underline{F}$ =(1,19) 5.16; ( $\underline{p}$ =.035). Patients, but not controls, had slower times for threat versus neutral words ( $\underline{F}$ =(1, 19) 4.84: p=.04).

Discussion: Our results suggest that patients with Panic Disorder have selective attentional bias for threat information. Such bias could be involved in the etiology or maintenance of panic attacks.

### Thursday, May 12, 12 noon-2:00 p.m. DEPRESSION AS AN EATING DISORDER: NUTRITION, BEHAVIOR AND NEUROENDOCRINOLOGY

Manfred M. Fichter, M.D., Psychiatry, Nussbaumstr F., Munich, West Germany; K.M. Pirke, M.D.

### Summary:

In a series of studies 1. in patients with anorexia nervosa gaining weight, 2. normal weight patients with bulimia with and without previous restricted food intake and 3. in healthy subjects during experimental conditions of starvation, we assessed behavior mood and endocrinology. Dexamethasone suppression tests (DST's), TRH-tests, and clonidine-tests were performed and nocturnal 30-minute blood samples were taken. Reduced caloric intake was associated with elevated plasma cortisol. insufficient suppression in the DST, blunted TSH-response to TRH, and diminished HGH-response to clonidine. Irrespective of diagnosis the "nutritional hypothesis," which states that neuroendocrine disfunctions can be a result of reduced nutritional intake, was confirmed. "Poor appetite or significant weight loss when not dieting" (DSM-III) are considered common symptoms of depression. Very similar neuroendocrine disturbances as in anorexic bulimic eating disorders and fasting healthy subjects have been found in depression. They appear to be specific for a state of reduced nutritional intake, largely independent of body weight. Our data point to the importance of assessing nutritional intake in depression, which has been widely neglected.

# **NR311**

# CORRELATES OF AXIS II COMORBIDITY IN BULIMIA

PSYCHIATRIC EXAMINATIONS OF HOMELESS MEN AND WOMEN

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

William R. Yates, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; Bruce Sieleni, M.D.

#### Summary:

We evaluated a series of 30 normal-weight DSM-III-R females with bulimia nervosa using the Diagnostic Interview Schedule, Personality Diagnosis Questionnaire, Eating Disorders Inventory (EDI), Eating Attitudes Test (EAT), and the Shipley Institute of Living Cognitive Scale (SILS). Fourteen bulimic patients meeting criteria for an Axis II personality disorder (PD) were compared to bulimics without a personality disorder (no PD).

Personality disorder bulimic patients scored significantly higher (more severe) on the total EDI score (91.8 vs. 23.9, t=2.29, .05). The EDI subscales Drive for Thinness, Body Dissatisfaction, Ineffectiveness, and Personal Distress were significantly elevated for the PD group, while subscales measuring Interoceptive Awareness, Bulimia, Perfectionism, and Maturity Fears were not different for PD compared to no PD bulimics. PD bulimics had significantly lower abstraction scores on the SILS abstraction scale (31.7 vs. 36.7, t=2.63, p < .05) and were more likely to have a lifetime diagnosis of depression (79% vs. 38%). chi square=5.2, p < .05) and a history of a suicide attempt (31% vs. 0%, chi square=5.1, p < .05). These findings support personality disorder comorbidity in bulimics as an indicator of increased psychological severity, impaired abstraction, and increased affective disorder and suicide attempt risk.

### **NR312**

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

William R. Breakey, M.B., Psychiatry, Johns Hopkins University, 600 North Wolfe Street, Baltimore, MD 21205; Alan J. Romanoski, M.D., Gerald Nestadt, M.D., Pamela J. Fischer, Ph.D., Alan Ross, Ph.D.

### Summary:

As part of a larger survey of 500 homeless people in Baltimore, psychiatric examinations were performed on 205 subjects. The subjects were randomly selected from among the residents of the various shelter programs in the city and from the residents at Baltimore City Jail who were homeless at time of arrest. Examinations were performed using a standard protocol which included the Standardized Psychiatric Examination and additional items and scales focussing on substance abuse and personality disorders. Women were over-sampled to permit male:female comparisons to be made with maximum power. The prevalence of psychiatric disorder was found to be very high. 39% of subjects were found to have a major mental disorder, with higher rates for women than for men. Alcohol use disorders, either active or in remission, were found in two thirds of men and in one third of women. Other substance abuse disorders were diagnosed in 20%. Symptoms of worry, depression, and anxiety were very frequent. Phobias were diagnosed in 24% and personality disorders in 44%. The implication for mental health service providers is that they must be prepared to provide a wide variety of treatment, support, and assistance services to homeless people.

### HPA AXIS FUNCTION AND CSF PEPTIDES IN ALCOHOLICS

Bryon Adinoff, M.D., NIAAA Bldg 10 3B19, 9000 Rockville Pike, Bethesda, MD 20850; Peter R. Martin, M.D., Michael J. Eckardt, Ph.D., George H.A. Bone, M.D., Markku I. Linnoila, M.D., Philip W. Gold, M.D.

### Summary:

Plasma adrenocorticotropin (ACTH) and cortisol response to ovine corticotropin-releasing hormone (oCRH) were assessed in long-term abstinent (>6 months) alcoholics (n=9), abstinent (>3 weeks) alcoholics with alcohol amnestic syndrome (AAS) (Korsakoff's syndrome) (n=10), and healthy controls (n=15). CSF concentrations of CRH and ACTH were also measured. Mean plasma integrated ACTH and cortisol response to oCRH and CSF levels of ACTH and CRH were similar in the three groups. In controls, a significant negative correlation was found between baseline plasma cortisol and the cortisol response to oCRH )r=0.8, p<0.001), indicating intact glucocorticoid feedback upon the pituitary. Neither the abstinent alcoholic group nor the AAS patients demonstrated a similar correlation (r=0.14 and r=0.08, respectively). There was a high correlation between CSF CRH and ACTH in the controls (r=0.69, p=0.01) and the abstinent alcoholics (r=0.83, p=0.01) that was not apparent in the AAS patients (r=0.19). These findings suggest that systems involved in stress-response are altered in alcoholics, progressing from impaired pituitary responsiveness in abstinent alcoholics to CSF neuropeptide dysregulation in AAS. Elevations in corticosteroid levels, which have been demonstrated during the ethanol withdrawal syndrome, have been associated with central nervous system structural and physiologic changes. As patients with alcohol dependence often experience repeated episodes of withdrawal, we suggest that multiple episodes of cortisol hypersecretion may result in HPA axis dysfunction and alcohol-induced organic brain syndrome.

#### NR314 CHILDHOOD TRAUMA IN BORDERLINE PERSONALITY DISORDER

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

Judith L. Herman, M.D., Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139; J. Christopher Perry, M.D., Bessel van der Kolk, M.D.

### Summary:

The hypothesis that childhood trauma is specifically associated with borderline personality disorder was tested by comparing subjects with Borderline Personality Disorder (BPD) (N=21), subjects with borderline trait (N=11) and subjects with the "near-neighbor" diagnoses of schizotypal personality disorder, antisocial personality disorder, and bipolar II affective disorder (N=23). Diagnostic interviews were conducted by one of the principal investigators (JCP). Trauma histories were obtained by in-depth interviews conducted by the two other principal investigators, who were blind to the subjects' diagnoses.

The great majority (86%) of subjects with definite BPD gave histories of major childhood trauma. Seventy-one percent had been physically abused, 68% had been sexually abused, and 62% had witnessed domestic violence. Abuse histories were less common in patients with borderline trait and least common in the subjects with no borderline diagnosis (p=0.001). Histories of trauma in early childhood (ages 0-6) were found almost exclusively in borderline subjects (p=0.001). The positive association between a borderline diagnosis and a history of childhood trauma was sustained after controlling for the effects of gender differences. These results demonstrate a strong association between a diagnosis of borderline personality disorder and a history of abuse in childhood.

### NR315 PERSONALITY DISORDER IN OBSESSIVE COMPULSIVES

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

Donald W. Black, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; WIlliam R. Yates, M.D., Russell Noyes, Jr., M.D., Bruce Pfohl, M.D., James H. Reich, M.D.

#### Summary:

Twenty-one patients (six men, 15 women) with obsessive-compulsive disorder (OCD) were evaluated using the Schedule for Affective Disorders in Schizophrenia (SADS) and the Personality Diagnostic Questionnaire (PDQ). The prevalence and pattern of *DSM-III* personality disorder among obsessive-compulsives was compared to an age- and sex-matched group of controls selected from a community based survey using the PDQ, a well validated self-report instrument. Each case was compared with two community controls. Seven (33.3%) obsessive-compulsive patients met criteria for at least one *DSM-III* personality disorder compared with five (11.9%) community controls. Obsessive-compulsive patients were significantly more likely than controls to manifest cluster B—histrionic, borderline, narcissistic, and antisocial—personality disorders or traits (odds ratio=10, p<.05). Mean PDQ scores for cluster B and cluster C personality traits were significantly higher for obsessive-compulsive patients than for community controls. Obsessive-compulsives also had a significantly higher level of impairment, as measured by the PDQ (p=.0001). This study supports previous reports of increased prevalence of personality disorder among obsessive-compulsive patients, but not *DSM-III* compulsive personality.

#### NR316 PERSONALITY DISORDER IN MORBIDLY OBESE PATIENTS

Donald W. Black, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; William R. Yates, M.D., Sue Bell, R.N., Edward E. Mason, M.D., Rise B. Goldstein, M.S.W., James H. Reich, M.D.

### Summary:

Thirty-eight patients (30 women, eight men) with morbid obsesity who presented for vertical banded gastroplasty (VBG) at a bariatric clinic were each compared with two age- and sex-matched controls from the community for *DSM-III* personality disorder. Patients and controls were assessed with the Personality Diagnostic questionnaire (PDQ), a well-validated self-report instrument. Patients enrolled in this study were at least twice their desirable weight, or at least 100 pounds over desirable weight, according to actuarial tables. Fifteen (39.5%) morbidly obese patients and 10 (13.2%) control subjects met criteria for at least one *DSM-III* personality disorder (odds ratio=5.8, p<.001). Morbidly obese patients were significantly more likely than control subjects to display cluster A—paranoid, schizoid, schizotypal—and cluster B—histrionic, antisocial, narcissistic, borderline—personality disorders, particularly borderline personality. This study demonstrates that a significant minority of morbidly obese patients have *DSM-III* personality disorders when compared with age- and sex-matched community controls. This finding may have important clinical implications, including possible problems with treatment compliance, appointment scheduling, and weight loss after surgery.

#### NR317 AS NEEDED TREATMENT OF PANIC DISORDER WITH RO 16-6028

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

Heinz Katschnig, M.D., Univ Vienna, Psychiatric Clinic, Waehringer Guertel 18-20, Vienna, Austria A1090; Walter A. Merz, M.D., Detlev O. Nutzinger, M.D.

### Summary:

Ro 16-6028, a partial benzodiazepine agonist, is a short acting anxiolytic compound with a mean elimination half-life of 2, 3 hours, which is rapidly absorbed after oral administration and exerts its anxiolytic effect already after a few minutes. This rapid onset of action suggests that Ro 16-6028 may be used as a p.r.n., discontinuous treatment of panic attacks. This p.r.n. treatment strategy (one dose per attack) was explored in a double-blind placebo controlled parallel group study of 24 patients suffering from panic disorder according to DSM-III-R criteria. Patients were instructed to take one dose of the trial drug either when they realized that a panic attack was developing or when they entered a situation where they would normally expect a panic attack to occur. Dose titration was performed in the range from 0.5 to 1.5 mg (i.e. one to three tablets per impending attack). In the treatment phase the optimum dose was then to be used in 12 successive attacks; the procedure could be repeated once. Inefficacy related dropouts or exclusions from treatment occurred in 8 of 12 placebo patients and only in one of 12 patients on Ro 16-6028 (p<.01). The efficacy of Ro 16-6028 is also reflected in parameters such as decrease of the frequency (p<.05) and intensity (p<.01) of panic attacks. These results suggest that targeted p.r.n. treatment of panic attacks with Ro 16-6028 may prove a promising alternative strategy for the treatment of panic disorder.

# NR318

# ANTIDEPRESSANTS AND NICOTINE WITHDRAWAL SYMPTOMS

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

Neil B. Edwards, M.D., Psychiatry, Univ Tennesse, 66 North Pauline Street, Memphis, TN 38105; Jospeh K. Murphy, Ph.D., Anna D. Downs, Ph.D., Bette J. Ackerman, Ph.D.

### Summary:

Cigarette smoking, perhaps the major health concern in this country, has remained resistant to psychopharmacologic intervention. Despite diagnostic similarities (*DSM-III* and *III-R*) between depression and nicotine withdrawal, the use of antidepressants as an aid to the amelioration of withdrawal symptoms has not received systematic attention. In the present study, 21 adults, recruited for a smoking cessation study, received in a double blind manner either active (doxepin HC1) or inert (placebo) medication. Subjects received one (days one-three), two (days four-six), or three (days seven up to 56) capsules (50 mg of doxepin) to be taken at bedtime. Medication was provided at weekly appointments. Each day, 10 withdrawal symptoms were self-monitored for intensity on a scale from 1 (definitely absent) to 6 (definitely present) at 9 a.m., 3 p.m., and 9 p.m. On the 22nd day, subjects were instructed to stop smoking while continuing to monitor symptoms. Results indicated that the greater abstinence of doxepin subjects (p<.05) may have been mediated by attenuation of withdrawal symptom severity. In particular, doxepin subjects' cessation symptoms were comparable to precessation (baseline) levels while placebo subjects experienced a significant (p<.05) increase in symptom severity during the two weeks following cessation. While biochemical mechanisms remain to be elucidated, these preliminary results suggest that antidepressants can enhance the short-term cessation of cigarette smoking.

EPIDEMIOLOGIC ANALYSIS OF ALCOHOL AND DRUG USE AS RISK FACTORS FOR THE INCIDENCE OF SELF-REPORTED DELUSIONS AND HALLUCINATIONS

Allen Y. Tien, M.D., Mental Hygiene, Johns Hopkins Sch of Hyg, Baltimore, MD 21205; James C. Anthony, Ph.D.

#### Summary:

Clinical and laboratory research implicates use of alcohol and other psychoactive drugs as causes of psychoses. However, because of possible biases and confounding, such studies do not directly address questions on the frequency and risk for drug-takers to experience psychoses under ordinary conditions. These questions require an epidemiologic approach, and are addressed in this paper with data from the NIMH Epidemiologic Catchment Area Program. Based on conditional logistic regression analyses, adjusting for confounding sociodemographic and psychopathologic factors, we observed daily use of marijuana among adults aged 18-49 to be associated with a doubling of risk for self-reported delusions or hallucinations. Alcohol disorder in men was associated with over sevenfold risk, and in women a nearly threefold risk. There was a tendency for daily cocaine use to be associated with increased risk. Being separated or divorced was one of several social role and sociodemographic risk factors identified by these analyses. In addition, Diagnostic Interview Schedule determined manic episodes, depressive episodes, and agoraphobia helped predict subject's later reports of delusions or hallucinations. Although subject to several potentially important limitations, these results substantiate prior findings and speculation about hazards faced by drug-takers; they also provide new epidemiologic data on sociodemographic, social, and psychopatholgic risk factors for delusions.

#### NR320

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

K. Roy Mackenzie, M.D., Psychiatry, University of Texas, Box 20708, Houston, TX 77225

METHODS FOR ESTABLISHING A FOCUS FOR PSYCHOTHERAPY

#### 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. Through a case example, this presentation demonstrates several methods being used for the assessment of patients in a 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 semi-structured 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.

The presentation will demonstrate how each method captures different aspects of the same clinical material, and how this information from varied sources can be combined to develop an interpersonal focus of value both for research purposes and for enhancing clinical judgment.

#### NR321 FAMILY HISTORY OF CONTROLS WHO PANIC WITH LACTATE

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

Richard Balon, M.D., Psychiatry, Wayne University, Lafayette Clin 951 E Lafayette, Detroit, MI 48207; Margaret Jordan, Robert Pohl, M.D., Vikram K. Yeragani, M.D., Wendy Jankowski, B.S.

### Summary:

Sporadic panic attacks (SPA) have been reported in the "normal" population. We reported that ten (22%) of our controls panicked during the sodium lactate infusion under double blind conditions. Individuals with SPA or a panic attack triggered by provocative agents may represent a population with a vulnerability for panic disorder. It would be useful to find out if this vulnerability is also associated with a family history of anxiety disorders.

Eight panicking and 26 nonpanicking controls were interviewed by an investigator who was blind to the outcome of the infusion study. The interviewer used the "Family Informant Schedule and Criteria" to obtain family history for 45 relatives of panickers and 115 relatives of nonpanickers. There was no age difference between the living relatives of panickers and nonpanickers.

There was an increased prevalence of anxiety disorders among the relatives of panickers (chi square=8.2, p < 0.01). There was no significant difference in prevalence of mood disorders and substance abuse between panickers and nonpanickers. Our results suggest that individuals with a family history of anxiety disorders may be vulnerable to lactate induced panic.

### AN EMPIRICAL CLASSIFICATION OF PERSONALITY DISORDER

W. John Livesley, M.D., Psychiatry, University of BC, 2255 Wesbrook Mall, Vancouver, BC, Canada V6T2A1

#### Summary:

In previous studies content analysis of the clinical literature and clinicians' judgments were used to identify the basic personality dimensions that delineate the domain of personality pathology. This presentation will report on the relationships between these dimensions observed in a sample of 110 subjects. Scales of behavioral items were developed to assess each dimension. These scales were refined using responses obtained from samples of normal subjects (N=3256). Scales were edited to achieve satisfactory desirability. The result was a set of 1923 behavioral items to assess the 102 dimensions. These items were administered to 110 subjects. The internal consistency of these shorter scales was satisfactory. Multivariate procedures were used to examine the relationship between scales. The results of the Screen test and examination of pattern matrices obtained from different factorial solutions resulted in the decision to adopt a 16-factor oblique solution which accounted for 81.4% of the variance. The factors identified will be described in detail and related to *DSM-III-R* Axis II diagnoses. The results of this study were also used to reduce the number of behavioral items to assess each dimension. The modified sets of items were administered to further samples of subjects to examine the stability of the factor structure across different samples.

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