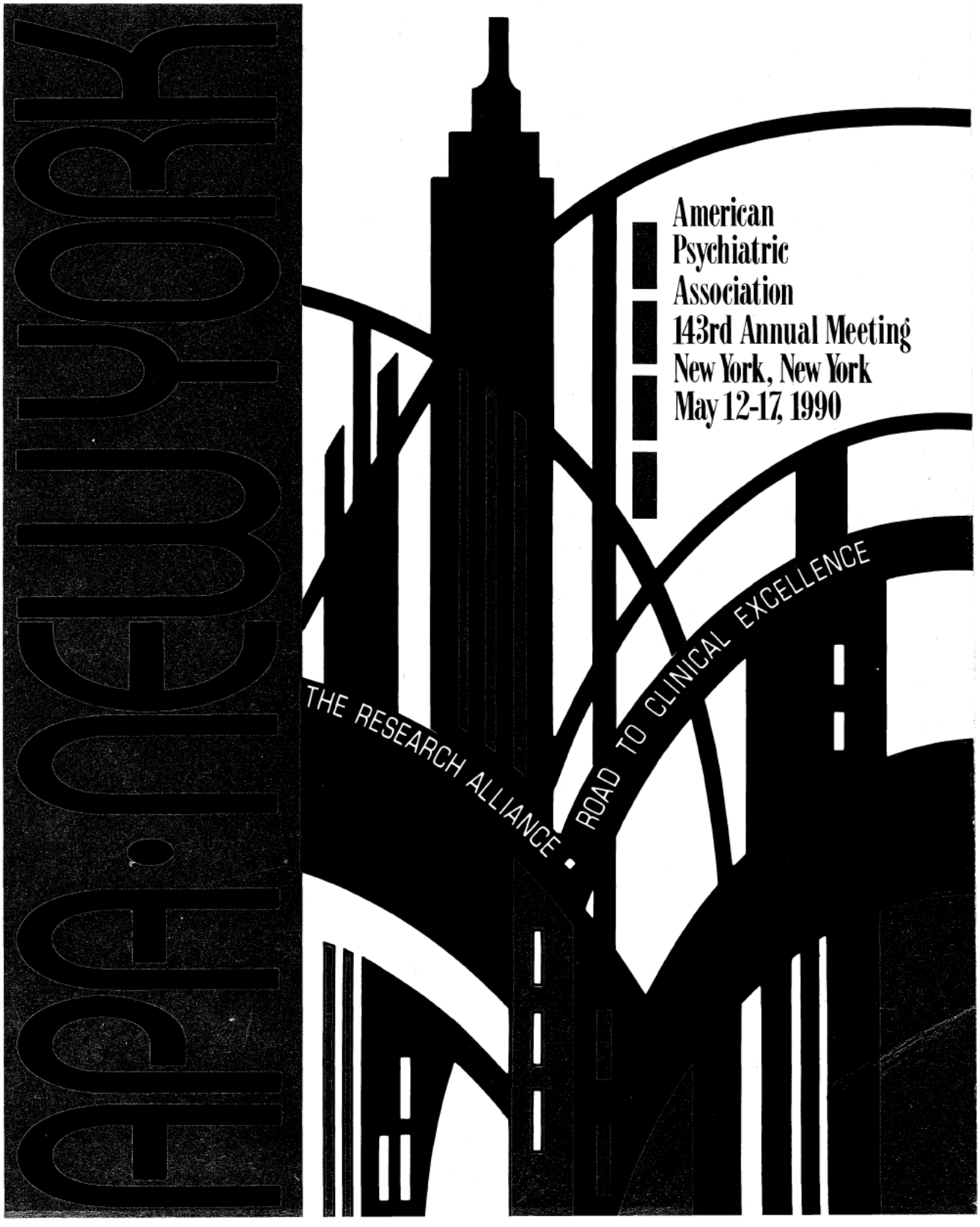
1990
NEW RESEARCH PROGRAM AND ABSTRACTS



PROGRAM
AND
PAPERS ON NEW RESEARCH

IN SUMMARY FORM

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

NEW YORK, NEW YORK
May 12-17, 1990

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

SUBCOMMITTEE ON NEW RESEARCH
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American Psychiatric Association

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

May 12, 1990

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 1990 New Research Program.

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

The program begins Monday, May 14, at 9:00 a.m. with the first of two Young Investigators' Poster Sessions. It continues at 10:30 a.m. with "Research Advances in Psychiatry: An Update for the Clinician," with special emphasis on depression, schizophrenia, Alzheimer's Disease, alcoholism and AIDS. The New Research Science Policy Session will be on Tuesday, May 15, from 10:30 a.m.–12 noon with discussion by a panel of experts on the anatomy of research funding.

The New Research Oral/Slide Sessions will be held Tuesday, May 15, through Thursday, May 17, 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, childhood disorders and AIDS (Thursday). Poster Sessions will be held Tuesday and Wednesday from 12 noon-2:00 p.m. and 3:00 p.m.-5:00 p.m., and on Thursday from 12 noon-2:00 p.m. These sessions will be devoted to schizophrenic and anxiety disorders and biological psychiatry (Tuesday); mood disorders; psychoimmunology; psychopharmacology; personality, substance abuse and eating disorders; and psychotherapy and diagnostic issues (Wednesday); and organic mental disorders, AIDS, childhood disorders, and consultation/liaison psychiatry (Thursday).

The 36 Oral/Slide and over 600 Poster presentations are as diverse and, we believe, is 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. Kaufmann

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

Outside Reviewers for the New Research Program

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Thomas W. Uhde, M.D
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Daniel R. Weinberger, M.D.
George E. Woody, M.D.
Stuart C. Yudofsky, M.D.

NEW RESEARCH

Monday, May 14, l990, 9:00 a.m.-10:30 a.m.

New Research 1—Poster Session—Westside Ballroom North/Center, Fifth Floor, Marriott Marquis

YOUNG INVESTIGATORS' POSTER SESSION

Moderator: Harold Alan Pincus, M.D.

NR1 Neuropsychiatric and Psychosocial Assessment of HIV-Seropositive Soldiers
Louis K. Duchin, M.D., Gregory P. Hollis, Ph.D., Stephen N. Xenakis, M.D., Frederick N. Garland, Ph.D.

NR2 Depression and Support in Army HIV-Seropositive Patients
E. Cameron Ritchie, M.D., Alan O. Radke, M.D., Barbara J. Ross, M.A.

NR3 Immunity, Dimensional Scores and Panic Disorders in Major Depressive Disorders
Antonio V. Andreoli, M.D., Charles J. Taban, M.D., Maya Rabaeus, M.D., Line E. Zaugg, L.EB., G. Garrone

NR4 Alprazolam Sensitivity in Panic Disorder
Gary B. Kaplan, M.D., David J. Greenblatt, M.D., Jill E. Goddard, M.A., Richard I. Shader, M.D.

NR5 Effect of Pregnancy on Pre-Existing Panic Disorder
Virginia A. Villeponteaux, M.D., R. Bruce Lydiard, M.D., Michele T. Laraia, R.N., Gail W. Stuart, Ph.D., James C. Ballenger, M.D.

NR6 Effect of Alprazolam on Mood in Panic Disorder
J. Allen Melvin, M.D., R. Bruce Lydiard, M.D., Michele T. Laraia, R.N., Mark D. Fossey, M.D., James C. Ballenger, M.D.

NR7 Cardiac Status of Panic Patients: With and Without Cardiac Symptoms
Robert R. Jolley, M.D., R. Bruce Lydiard, M.D., Michael E. Assey, M.D., Mark D. Fossey, M.D., James C. Ballenger, M.D.

NR8 The Specificity of the Attentional Bias in Panic Disorder
Cameron S. Carter, M.B., Richard J. Maddock, M.D., Joseph R. Magliozzi, M.D., Kathryn Moriyana, Ph.D.

NR9 Effects of Clonidine Pretreatment of Lactate-Induced Panic
Jeremy D. Coplan, M.D., Michael R. Liebowitz, M.D., Jack M. Gorman, M.D., Abby J. Fyer, M.D., Donald F. Klein, M.D.

NR10 Anxiolytic Effects of Oral Yohimbine in Differentially Reared Nonhuman Primates
Jeremy D. Coplan, M.D., Leonard A. Rosenblum, Ph.D., Steven Friedman, Ph.D., Trina B. Bassoff, M.A., Jack M. Gorman, M.D.

NR11 Chronic Hair Pulling: A Descriptive Study of 62 Subjects
Gary A. Christenson, M.D., Thomas B. Mackenzie, M.D., James E. Mitchell, M.D.

NR12 High Cholesterol in Panic Disorder: Complication or Artifact?
Waheed K. Bajwa, M.D., Gregory M. Asnis, M.D., William C. Sanderson, Ph.D., Naveed Iqbal, M.D., Herman M. van Praag, M.D., Amaro Reyes-Garza, M.D.

NR13 Evidence that an Altitude Challenge Enhances Human Visual Information Processing
Thomas E. Schlaepfer, M.D., Hans-U Fisch, M.D.

NR14 Rat Brain Fluphenazine Level After Electroconvulsive Shock
Iannis M. Zervas, M.D., Lawrence B. Greenberg, M.D., Thomas Cooper, Ph.D., Lina Jandorf, M.A., Max Fink, M.D.

NR15 Lithium Potentiates Insulin's Effect on Skeletal Muscle cAMP
Leslie R. Vogel, M.D., Andrea Giaccari, M.D., Simona Frontoni, M.D., Su B. Choi, M.D.

NR16 Plasma HVA Increases After Metyrapone Administration
Ruth A. Richter, M.D., Richard L. Hauger, M.D., S. Craig Risch, M.D., Kathy Resovsky, R.N., Shahrokh Golshan, Ph.D., J. Christian Gillin, M.D.

NR17 Loss, Affective Illness and HPA Axis Dysfunction
John M. Petitto, M.D., Cort A. Pedersen, M.D., Arch A. Hicks, M.A., Dwight L. Evans, M.D.

NR18 Super Sensitivity to Light in Depression
Harriet L. MacMillian, M.D., Meir Steiner, M.D., Jo Ann L. Seggie, Ph.D.

NR19 Overlap of Avoidant Personality and Social Phobia
Franklin R. Schneier, M.D., Robert L. Spitzer, M.D., Michael R.Liebowitz, M.D., Abby J. Fyer, M.D., Raphael Campeas, M.D., Eric Hollander, M.D.

NR20 Plasma Catecholamine Levels in Patients with the Chronic Fatigue Syndrome
Susan M. Levine, M.D., Robert L. Trestman, M.D., Charlotte Cunningham-Run, M.D., James Halper, M.D.

NR21 Parental Loss as a Risk Factor for Depression: A Meta-Analytic Study
Scott B. Patten, M.D.

NR22 Children's Food and Mood Study: Pilot Results
Vincenzo F. Di Nicola, M.D., Louise Oke, B.A.

NR23 Substance Use and Child Rearing Practices in Boys
Welmoet Van Kammen, Ph.D., Rolf Loeber, Ph.D., Magda Loeber, Ph.D.

NR24 Dimensions of Temperament in Four Adolescent Groups
Richard Shaw, M.D., Hans Steiner, M.D., Ying-Chiao Lee, M.D.

NR25 The Fenfluramine Challenge in Depressed Adolescents
Daniel E. Grosz, M.D., Gregory M. Asnis, M.D., Jill M. Harkavy Friedman, Ph.D., Kausar Shamim, M.D., James K. Zimmerman, Ph.D., Herman M. van Praag, M.D.

NR26 The DST in Depressed Inpatient Versus Outpatient Prepubertal Children
Shahnour Yaylayan, M.D., Elizabeth B. Weller, M.D., Ronald A. Weller, M.D., Mary A. Fristad, Ph.D., Sheldon H. Preskorn, M.D.

NR27 Peripheral Blood Count and the DST in Depressed Children
Shahnour Yaylayan, M.D., Elizabeth B. Weller, M.D., Ronald A. Weller, M.D., Mary A. Fristad, Ph.D., Sheldon H. Preskorn, M.D.

NR28 Amantadine and Behavior in Nursing Home Patients
Adrienne C. Lahti, M.D., Nancy M. Speed, M.D., Alan M. Mellow, M.D., Joseph A. Schwartz, M.D., Thomas L. Brewer, M.S., Jon K. Zubieta, M.D., Stephen M. Aronson, M.D.

NR29 Quality of Life in Liver and Heart Transplant Patients
Anne Marie Riether, M.D

NR30 Psychiatric Consultations in an Emergency Room Setting
Rebecca Johnson, M.D., Michelle Riba, M.D., Mahlon S. Hale, M.D.

NR31 Identifying Risk Factors in Organ Transplantation
Ranjit C. Chacko, M.D., Mark Kunik, M.D., Robert G. Harper, Ph.D.

NR32 Heterogeneity of High Hospital Users Across VA Psychiatry Service Types
Michael S. Neale, M.S., Robert Rosenheck, M.D.

NR33 Legal Offenders in an Urban Community Mental Health Center
Geetha Jayaram, M.D., Margaret Phillips, R.N., Shaila Pai, Ph.D.

NR34 Psychopathology in Vietnamese Refugees
W. Ladson Hinton, M.D., Joseph Chen, M.D., Nang Du, M.D., Carolee Tran, Jeanne Miranda, Ph.D., Francis G. Lu, M.D., Shotsy Faust, M.N.

NR35 A Comparison of Alexithymia Measures
Michael Pierce, M.D., John H. Krystal, M.D., Alice Faryna, M.D., Ronald Markert, Ph.D., Anne Davidson, M.D.

NR36 Serum Vitamin B12, Folate and Psychiatric Illness
Helen L. Miller, M.D., Robert N. Golden, M.D., Terry Brown, D.O., David Ekstrom, M.P.H., Dwight L. Evans, M.D.

NR37 The Development of a Computer Administered Hamilton Anxiety Scale
Kenneth A. Kobak, M.S.W., William M. Reynolds, Ph.D., John H. Greist, M.D.

NR38 How Normal are the Controls? A Prospective Study of a Large Volunteer Group
Paul A. Gaist, B.A., Frederick M. Jacobsen, M.D.

NR39 Diagnosing Late Luteal Phase Dysphoric Disorder with Comorbid Mood Disorders
Kimberly A. Yonkers, M.D., Kerrin White, M.D., Susan L. McElroy, M.D.

NR40 A 4.5 Year Follow-Up Study of Inpatient Bulimics
Brian A. Fallon, M.D., B. Timothy Walsh, M.D., Carla Sadik, M.S.W., Valerie Lukasik, B.A.

NR41 Self-Mutilation and Bulimia
Brian A. Fallon, M.D., Ronald M. Winchel, M.D., B. Timothy Walsh, M.D., Carla Sadik, M.S.W., Valerie Lukasik, B.A.

NR42 Ego Functions in BPD and Eating Disorder Patients
Thomas E. Smith, M.D., Nancy A. Burkey, M.D., John Nawn

NR43 Addictive and Reactive Subtypes of Bulimia
Kristin Levitan, M.D., Hans Steiner, M.D., Susan Smiga, M.D.

NR44 Standardized Report Form for Mental Status Exams
Robert G. Ruegg, M.D., Dwight L. Evans, M.D., Robert N. Golden, M.D.

NR45 Psychiatry Today: Psychology Versus Biology
Ileana Zaharovits, M.D., William Fried, Ph.D.

NR46 A National Survey on Psychiatric Ethics Training
John H. Coverdale, M.D., Patricia G. Isabell, M.D., Timothy L. Bayer, M.D., Steven Moffic, M.D.

NR47 Support Groups for Young Adults with Diabetes
Rose Shalom, M.D., Janice Ryan

NR48 The Right to Refuse Medication: A Clinical Dilemma
Elizabeth Lazaroff, M.D., Rhonda K. Hahn, M.D.

NR49 Recidivism Among Insanity Acquitees
Bill J. Komer, M.D., Donald A. Galbraith, M.D.

NR50 Family History and Course of Schizophrenic Illness
Kenneth L. Subotnik, C.Phil., Keith H. Nuechterlein, Ph.D., Robert Asarnow, Ph.D., David Fogelson, M.D., Michael Goldstein, Ph.D., Sharon A. Talovic, Ph.D.

NR51 Pharmacokinetics of Arecoline in Patients with Dementia of Alzheimer's Type
Pearse Morris, M.D., Timothy T. Soncrant, M.D., Kathleen Raffaele, Ph.D., Heggunje U. Shetty, Ph.D., Harold W. Holloway, B.S., Eileen M. Daly, B.S., Nigel H. Greig, Ph.D., James Haxby, Ph.D., Mark B. Schapiro, M.D., Stanley I. Rappaport, M.D.

NR52 Staff Attitudes Toward Geropsychiatric Consultation
Deborah A. Banazak, D.O., Harry L. Piersma, Ph.D.

NR53 Axis II: Tridimensional Personality Profiles
Ron G. Goldman, M.D., Andrew E. Skodol, M.D., Norman R. Doidge, M.D., H. David Kellman, M.D., Lyle Rosnick, M.D., John M. Oldham, M.D.

NR54 ERP Negative Component in Elderly Subjects at Risk for Dementia
Ma-Li Wong, M.D., Mary Schroder, Ph.D., Allan Blau, Ph.D., Richard B. Lipton, M.D., Walter Ritter, Ph.D., Herbert Vaugham, M.D.

NR55 Mental Health Needs of the Elderly Vary by Setting
Susan Lehmann, M.D., Geetha Jayaram, M.D., Peter V. Rabins, M.D.

NR56 Telephone Utility of Short Portable Mental Status Questionnaire and a Shortened Mini-Mental State Examination
William H. Roccaforte, M.D., William J. Burke, M.D., Barbara Bayer, M.S.N.

NR57 Personality Changes in Dementia
Steven P. Wengel, M.D., William J. Burke, M.D., William H. Roccaforte, M.D., Barbara Bayer, M.S.N.

NR58 Aggression in Psychiatric Hospitalized Geriatric Patients
Jill S. Meyer, M.D., Robert L. Schalock, Werner M. Mendel, M.D., Hannelore Genaidy, M.D.

NR59 Folate, B12 and Cognition in Alzheimer's Disease
Anthony J. Levitt, M.D., Harry Karlinsky, M.D., Jim Kirkland, M.D., D. McLauchlan, M.D.

NR60 Elderly Responders to Unilateral Versus Bilateral ECT
Peter Aupperle, M.D., Donald Johannessen, M.D., Arthur Gabriel, M.D., Brian A. Lawlor, M.D.

NR61 Short-Term Memory Effects of ECT in Elderly Versus Young Depressed Inpatients
Stephen M. Aronson, M.D., Bruno Giordani, Ph.D., Atul C. Pande, M.D., Leon J. Grunhaus, M.D., Carol Lindsay, B.A., Stanley Berent, Ph.D.

NR62 Diminished Caudate Volumes in Major Depression
William M. McDonald, M.D., Mustafa M. Husain, M.D., Murali Doraiswamy, M.D., Gary S. Figiel, M.D., Orest B. Boyko, M.D., Everett H. Ellinwood, Jr., M.D., Charles B. Nemeroff, M.D., K. Ranga R. Krishnan, M.D.

NR63 Predictors of Corpus Callosum Morphology on MRI
Ioanis A. Parashos, M.D., C. Edward Coffey, M.D., Richard D. Weiner, M.D., Mark Webb, M.D.

NR64 Quantitative EEG and Cognitive Potentials in Chronic Obstructive Pulmonary Disease
Camran Adly, M.D., John J. Straumanis, M.D., Frederick A. Struve, Ph.D., Jeffrey Knight, Ph.D., Gloria Patrick, M.S., Yoram Raz, M.A.

NR65 PET, Frontal Lobe Head Injury and Schizophrenia
Stephen Lottenberg, M.D., Brian Stankiewicz, Michelle R. Solano, Ronald M. Ruff, Ph.D., Monte S. Buchsbaum, M.D.

NR66 Proton Magnetic Resonance Spectroscopy of Brain
Rajiv P. Sharma, M.D., P.N.V. Subramanian, Ph.D., Michael Barany, M.D., John M. Davis, M.D.

NR67 Limbic Measures by MRI in Depressives and Controls
Shashidhar M. Shettar, M.D., Atul C. Pande, M.D., Rao Aravapalli, M.D., Roger F. Haskett, M.D., Leon J. Grunhaus, M.D.

NR68 CSF and Plasma Cachectin in Eating Disorder
Julio Licinio, M.D., Ma-Li Wong, M.D., Samuel J. Listwak, B.Sc., Margaret Altemus, M.D., Mark A. Demitrack, M.D., Philip Gold, M.D.

NR69 Complaints of Victimization by Psychotic Women in the Emergency Room
Valerie D. Raskin, M.D., Carole Warshaw, M.D.

NEW RESEARCH

Monday, May 14, 1990, 3:00 p.m.-5:00 p.m.

New Research 2—Poster Session—Westside Ballroom North/Center, Fifth Floor, Marriott Marquis

YOUNG INVESTIGATORS' POSTER SESSION

Moderator: Charles A. Kaufmann, M.D.

NR70 Lorazepam Augmentation of Low-Dose Haloperidol in Mania
James C-Y Chou, M.D., Harlan Kosson, M.D., Jan Volavka, M.D.

NR71 Clinical Trials of Sodium Valproate on Manic Patients
Chuong C. Huang, M.D., Laurens D. Young, M.D., Harold H. Harsch, M.D.

NR72 A Medicinal Herb Combination in the Treatment of Affective Disorders
Osama L.M. Omer, M.D.

NR73 A Naturalistic Study of Winter Depression
Michael S. Easton, M.D., Tarun Israni, M.D., Edward Altman, Psy.D.

NR74 Acute Response to Three Different Doses of Haloperidol
Michael S. Easton, M.D., Philip G. Janicak, Ph.D., Javaid I. Javaid, Ph.D., E. Canelas, M.D., S. Dowd, B.S., John M. Davis, M.D.

NR75 Hippocampal Pathology in Major Depression
Murali Doraiswamy, M.D., Sunjay A. Shah, B.S., Gary S. Figiel, M.D., Mustafa M. Husain, M.D., William M. McDonald, M.D., Orest B. Boyko, M.D., Everett H. Ellinwood, Jr., M.D., Charles B. Nemeroff, M.D., K. Ranga R. Krishnan, M.D.

NR76 SCID-RDC: DSM-III-R and RDC Integrated Interview
Diana O. Perkins, M.D., Julie A. Dickison, M.A., Dwight L. Evans, M.D.

NR77 Plasma Dexamethasone Levels in Treatment-Resistant Depression
Steven I. Altchuler, M.D., Siong-Chi Lin, M.D., Toshihiko Maruta, M.D., Deborah C. Newman, M.D., Jarrett W. Richardson, M.D., Paul A. Fredrickson, M.D., James M. Naessens

NR78 Symptomatic and Seasonal Variations in Depression
Mark N. Mollenhauer, B.S., Sylvia G. Simpson, M.D., John R. Lipsey, M.D., Andrew Feinberg, M.D., J. Raymond DePaulo, Jr., M.D.

NR79 Analysis of Serial DSTs by Random Regression
Rajiv P. Sharma, M.D., Donald Hedeker, Ph.D., Ghanshyam N. Pandey, Ph.D., Philip G. Janicak, M.D., John M. Davis, M.D.

NR80 Associated Psychopathology in Winter Depression
Valerie J. Del Medico, M.D., Amjed Quadri, Steven C. Dilsaver, M.D.

NR81 Stroke and Depression: The Use of a Traumatic Stress Model
Thomas L. Brewer, M.S., Joseph A. Schwartz, M.D., Nancy M. Speed, M.D.

NR82 Bipolar Disorder and Crohn's Disease
Suzanne Holroyd, M.D., J. Raymond DePaulo, Jr., M.D.

NR83 Adrenal Androgen and Cortisol in Major Depression
Hadley C. Osran, M.D., Christopher Reist, M.D., Cheng-Chun Chen, M.D., Lawrence N. Parker, M.D.

NR84 Anosognosia and Depression in Stroke
Sergio E. Starkstein, M.D., John Paul Fedoroff, M.D., Joseph B. Breyer, M.D., Robert G. Robinson, M.D.

NR85 Physiologic Marker of ECT Seizure Generalization
Andrew D. Krystal, M.D., Richard D. Weiner, M.D., Eric Moffet, M.D., C. Edward Coffey, M.D., Pamela Smith, Rebekka Arias

NR86 Verbal Memory Deficits in Schizophrenia and Temporal Lobe Epilepsy
Lyn Harper-Mozley, M.S., Andrew J. Saykin, Psy.D., Ruben C. Gur, Ph.D.
Raquel E. Gur, M.D.

NR87 Sleep Apnea: Permanent Neuropsychologic Deficits
Alexandros N. Vgontzas, M.D., Roger J. Cadieux, M.D., Ralph A.W. Lehman, M.D., Daniel H. Ingram, M.Ed., Elizabeth B. Lange, B.A.

NR88 A Trial of IV Clomipramine in Five Patients with Obsessive Compulsive Disorder
Brian A. Fallon, M.D., Michael R. Liebowitz, M.D., Raphael Campeas, M.D., Franklin R. Schneier, M.D., Eric Hollander, M.D., Julie Hatterer, M.D.

NR89 Basal Ganglia Disturbances in Obsessive Compulsive Disorder
Michael F. Osterheider, M.D., Delia Lettmaier, M.D., Helmut Beckmann, M.D.

NR90 Eye Movement Disorders in Schizophrenia and Obsessive Compulsive Disorder
Donna R. Palumbo, M.A., John A. Sweeney, Ph.D., Richard A. Shapiro, B.A., James Halper, M.D., M. Katherine Shear, M.D.

NR91 Treatment Effects on Eye Movement Abnormalities in Obsessive Compulsive Disorder
Richard A. Shapiro, B.A., Donna R. Palumbo, M.A., John A. Sweeney, Ph.D., M. Katherine Shear, M.D.

NR92 Lithium Plus Fluoxetine Treatment of Obsessive Compulsive Disorder
Robert G. Ruegg, M.D., Dwight L. Evans, M.D., Wilson S. Comer, M.D., Robert N. Golden, M.D.

NR93 A Controlled Trial of Buspirone Augmentation in Obsessive Compulsive Disorder
Francine L'Heureux, M.D., Teresa A. Pigott, M.D., T.H. Yoney, M.D., Gay N. Grover, M.S.N., James L. Hill, Ph.D., Dennis L. Murphy, M.D.

NR94 Lithium Versus Thyroid Augmentation in Obsessive Compulsive Disorder: A Controlled Comparison
Teresa A. Pigott, M.D., Michele T. Pato, M.D., Gay N. Grover, M.S.N., James L. Hill, Ph.D., Suzanne E. Bernstein, B.S., Dennis L. Murphy, M.D.

NR95 OCD, Anorexia Nervosa and BulimiNa Nervosa: A Controlled Comparison of Symptoms
Teresa A. Pigott, M.D., Margaret Altemus, M.D., Francine L'Heureux, M.D., Katalin Bihari, M.D., Philip Gold, M.D., Dennis L. Murphy, M.D.

NR96 Adult Night Terrors and Associated Psychopathology
M. Beatriz Currier, M.D., Maria D. Llorente, M.D., Susan E. Norman, M.S.N., Thomas A. Mellman, M.D.

NR97 Biological Correlates of Impulsivity/Aggression
Timothy L. Lawrence, M.D., Emil F. Coccaro, M.D., David P. Bernstein, Ph.D., Ginny Condello, M.D., Larry J. Siever, M.D.

NR98 Dopaminergic Dysfunction in Schizotypal Personality Disorders
Oren Kalus, M.D., Larry J. Siever, M.D., Emil F. Coccaro, M.D., David P. Bernstein, Ph.D., Theresa Mahon, B.A., Kenneth L. Davis, M.D.

NR99 Type, Severity and Course of Mood Disorder in BPD
H. David Kellman, M.D., Andrew E. Skodol, M.D., Janis L. Cutler, M.D., Alan, M.D., Holly A. Schneier, M.D., Julia L. Winston, M.D.

NR100 Treatment of Lithium-Induced Polyuria with Potassium: A Political Study
Bhaskara R. Tripuraneni, M.D.

NR101 Clozapine and Haloperidol: Receptor Regulation
Clifford Widmark, M.D., Steven J. O'Dell, Ph.D., Gerald J. La Hostle, Ph.D., Raymond M. Shapiro, M.D., Steven G. Potkin, M.D., John F. Marshall, Ph.D.

NR102 ECT and Dopamine: A Brain Microdialysis Study
George G. Nomikos, M.D., Athanasios Zis, M.D., Geert Damsma, Ph.D., Hans C. Fibiger, Ph.D.

NR103 Clozapine Plasma Concentrations and Clinical Response
Delwyn D. Miller, M.D., Paul Perry, Ph.D., Remi J. Cadoret, M.D.

NR104 ECT Seizure Duration: CUFF Versus EEG Versus Quantitative EEG
John H. Gilmore, M.D., Robert N. Golden, M.D., Michael R. Isley, Ph.D., Li Sheng Kong, A.B., Dwight L. Evans, M.D., Enid R. Kafer, M.D.

NR105 Buspirone: Sedative or Stimulant Effect?
Rocco L. Manfredi, M.D., Edward O. Bixler, Ph.D., Charles M. Falcone, B.A., Melda A. Isaac, B.S., Roger J. Cadieux, M.D.

NR106 Tranylcypromine Withdrawal Phenomena
Mark T. Halle, M.D., Steven C. Dilsaver, M.D.

NR107 Management of Mania with Benzodiazepines, Lithium and Anticonvulsants
Mark T. Halle, M.D., Valerie J. Del Medico, M.D., Steven C. Dilsaver, M.D.

NR108 Similarities Between the Dopamine D2 Receptor and Calmodulin
Patrick J. Rogue, M.D., Jean Zwiller, Ph.D., Anant N. Malviya, Ph.D., Guy Vincendon, M.D.

NR109 Characterization of Ethanol-Induced Calcium Release
Patrick J. Rogue, M.D., Anant N. Malviya, Ph.D., Guy Vincendon, M.D.

NR110 Personality Organization in Analytic and Inpatients
Norman R. Doidge, M.D., Andrew E. Skodol, M.D., John M. Oldham, M.D., H. David Kellman, M.D., Lyle Rosnick, M.D., Ron G. Goldman, M.D.

NR111 ECT Therapy with Benzodiazepines
Marc Auriacombe, Denis Grabot, Pierre Marie Lincheneau, Jean Tignol, M.D.

NR112 Psychiatric Markers in Diabetes Control
Cynthia B. Stevens, M.D., Abbey Wellman, M.D., David Reiss, M.D., Robert E. Ratner, M.D.

NR113 Medication Coverage: Prevalence and Attitudes
Richard Goldberg, M.D., Michelle Riba, M.D., Allan Tasman, M.D.

NR114 Cardiovascular Activity and Response in Schizophrenia
Dr. Hans-Peter Volz, Dr. Arthur Mackert, Albert Diefenbacher, M.D., Ingrid Keiler, Dr. Wolfgang Gaebel, Professor Dr. Gunter Stock

NR115 VBR and Neuropsychological Findings in Schizophrenia
John DeQuardo, Rajiv Tandon, M.D., James H. Meador-Woodruff, M.D.

NR116 Assessment of Depression in Schizophrenia
Israel Liberzon, M.D., Rob Goldman, Ph.D., Rajiv Tandon, M.D.

NR117 Effects of Biperiden of Schizophrenia Symptoms
Jon K. Zubieta, M.D., Rajiv Tandon, M.D., Nancy A. Mann, R.N., William H. Eisner, R.N.

NR118 Sleep Onset REM Periods in Schizophrenic Patients
Stephan F. Taylor, M.D., Rajiv Tandon, M.D., James E. Shipley, M.D., Alan S. Eiser, Ph.D., Joann Goodson, B.Sc.

NR119 Clinical Predictors of Outcome in Schizophrenia
Saulo C.M. Ribeiro, M.D., Rajiv Tandon, M.D., Rebecca Ricoy, M.D.

NR120 Clozapine-Induced Weight Gain in the Chronically Mentally Ill
Robert A. Leadbetter, M.D., Diane Pavalonis, M.S.N.

NR121 In Vivo Assessment of Putamen Volume in Depression
Mustafa M. Husain, M.D., William M. McDonald, M.D., Murali Doraiswamy, M.D., Gary S. Figiel, M.D., Orest B. Boyko, M.D., Everett H. Ellinwood, Jr., M.D., Charles B. Nemeroff, M.D., K. Ranga R. Krishnan, M.D.

NR122 Neuroleptic Responsiveness and EPS: Is Less More?
Robert Perovich, M.D., Celeste Johns, M.D., Peter J. Weiden, M.D., Jose Ma. Alvir, D.P.H., Kathleen Frechen, M.D., Gustav Degreef, M.D., John M. Kane, M.D.

NR123 The MCPP Challenge Test in Schizophrenia
Naveed Iqbal, M.D., Gregory M. Asnis, M.D., Herman M. van Praag, M.D., Stanley R. Kay, Ph.D., Shamim Kausar, M.D.

NR124 Effects of SKF-38393 (D-1 Agonist) on Schizophrenia
Nancy A. Breslin, M.D., David G. Daniel, M.D., James M. Gold, Ph.D., Bhaskar S. Kolachana, Ph.D., Joel E. Kleinman, M.D., Daniel R. Weinberger, M.D.

NR125 Neuroleptic Dose Versus Blood Levels in Chronic Patients
Rimal B. Bera, M.D., Jerome F. Costa, M.D.

NR124 SPECT in Schizophrenia with Stimulant Activation
David B. Bresnahan, M.D., Michael Goldstein, Ph.D., John M. Davis, M.D., Rajiv P. Sharma, M.D., Ronald Tikofsky, Ph.D., Robert S. Hellman, M.D.

NR127 Positive and Negative Symptoms: A One-Year Follow-Up
John T. Moranville, M.D., David L. Braff, M.D., Robert K. Heaton, Ph.D., Julia Kuck, M.A., John R. Montague, Ph.D., Ana Maria Andia, M.D., Sidney Zisook, M.D.

NR128 Substance Abuse and Psychosis: Past and Present
John T. Moranville, M.D., John Tsuang, M.D., Sidney Zisook, M.D., Julia Kuck, M.A., David L. Braff, M.D., Robert K. Heaton, Ph.D.

NR129 Expressed Emotion and Positive/Negative Symptoms in Schizophrenia
Ernesto Mujica, M.A., Gretchen L. Haas, Ph.D., Denise Hien, M.S., Dodi Goldman, M.A., Steven Passik, M.S., Glynn Rudich, M.S.W.

NR130 Bizarre Delusions in DSM-III-R Schizophrenia
Denise Hien, M.S., Dodi Goldman, M.A., Gretchen L. Haas, Ph.D., John A. Sweeney, Ph.D., Allen J. Frances, M.D.

NR131 Neurocognitive Deficits as Discriminators in Schizophrenia
Richard S.E. Keefe, M.A., Richard C. Mohs, Ph.D., Larry J. Siever, M.D., Philip D. Harvey, Ph.D., Harold A. Sackeim, Ph.D., Kenneth L. Davis, M.D.

NR132 Principal Components of Negative Symptoms and Formal Thought Disorder in Schizophrenia
Richard S.E. Keefe, M.A., Philip D. Harvey, Ph.D., Lindsey Bergman, B.A., Mark R. Serper, M.A., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

NR133 Immunoblotting to HSV in Schizophrenia
Anthony L. Pelonero, M.D., Daniel H. Conrad, Ph.D., Anand K. Pandurangi, M.D.

NR134 Management of Risk of Relapse in Schizophrenia
William Wirshing, M.D., Thad Eckman, Ph.D., Stephen R. Marder, M.D., Robert P. Liberman, M.D.

NR135 Illness Duration Effects in First Episode Schizophrenia
Antony D. Loebel, M.D., Jeffrey A. Lieberman, M.D., Darlene Jody, M.D., Sally Szymanski, M.D., Jose Ma. Alvir, D.P.H., Michael Borenstein, Ph.D.

NR136 A Trial of L-Dopa and Molindone in Schizophrenia
David G. Daniel, M.D., Nancy A. Breslin, M.D., James Clardy, M.D., James M. Gold, Ph.D., Joel E. Kleinman, M.D., Daniel R. Weinberger, M.D.

NR137 Natural Killer Cell Activity in Schizophrenia and Schizoaffective Disorder
John S. McDaniel, M.D., Samuel C. Risch, M.D., Rita D. Jewart, Ph.D., Mary B. Eccard, M.S.N., William E. Pollard, Ph.D., Jane Caudle, M.S., Mark Stipetic, B.S., Emile D. Risby, M.D., Richard Lewine, Ph.D.

NR138 Cavum Septum Pellucidum in Psychosis
George J. Jurjus, M.D., Stephen C. Olson, M.D., Jeffrey A. Coffman, M.D., Steven B. Schwarzkopf, M.D., Henry A. Nasrallah, M.D.

NR139 Obsessive Compulsive Symptoms in Schizophrenia
Ileana Zaharovits, M.D.

NR140 Striatal D1, D2 Receptors Unchanged by Cortex Lesions
Zafar A. Sharif, M.D., Serge Przedborski, M.D., Jean L. Cadet, M.D.

NR141 Sexual Interest and Menstrual Cycle Phase in Late Luteal Phase Dsyphoric Disorder
Tung-Ping Su, M.D., Kari L. Muller, B.A., David R. Rubinow, M.D.

NR142 Ultrashort Transition from Methadone to Naltrexone
Norbert Loimer, M.D., Kurt Lenz, M.D., Otto Presslich, M.D., R. Schmid, Ph.D.

NR143 Cognition and Depression in Substance Abusers
Mary H. Closser, D.O., Kirk J. Brower, M.D., Frederic C. Blow, Ph.D., Rosalind Fantone, R.N., Thomas P. Beresford, M.D.

NR144 A Substance Use Consultation/Liaison Service: Characteristics of Patients and Pedagogical Potential
Frances Rudnick-Levin, M.D., William W. Weddington, M.D., Charles A. Haertzen, Ph.D., Arthur Cohen, M.A., D.A. McDuff, M.D.

NR145 Taken as Needed Medication use as a Predictor of Alcoholic Recidivism
Nathaniel Marvel, Jr., M.D., Thor Tangvald IV, M.D., Van Silka, M.D.

NR146 Quantitative EEG Correlates of DSM-III-R Crack Cocaine Dependence
Kenneth R. Alper, M.D., Robert J. Chabot, Ph.D., Anthony Kim, M.D., Leslie S. Prichep, Ph.D., E. Roy John, Ph.D.

NR147 Alprazolam Attenuates Effects of MCPP in Normals
Avi Molcho, M.D., Serge Sevy, M.D., Serena-Lynn Brown, M.D., Moshe Kotler, M.D., Robert Plutchik, Ph.D., Herman M. van Praag, M.D.

NR148 Negative and Depressive Symptoms in Suicidal Schizophrenics
Sidney J. Jones, M.D., Barbara Stanley, Ph.D., Jeannine Guiido, M.A., Ronald M. Winchel, M.D., Michael Stanley, Ph.D.

NR149 Family History and Adolescent Suicidality
James K. Zimmerman, Ph.D., Gregory M. Asnis, M.D., Herman M. van Praag, M.D., Laura C. Lemle, Ph.D.

NR150 Pineal Calcification: Marker of Tardive Dyskinesia
Reuven Sandyk, M.D., Gavin I. Awerbuch, M.D., Stanley R. Kay, Ph.D., J. Daniel Kanofsky, M.D.

NR151 Low Dose Bromocriptine in the Treatment of Tardive Dyskinesia
Lauren B. Marangell, M.D., Stanley R. Kay, Ph.D., Jean-Pierre Lindenmayer, M.D.

NR152 Testing the GABA Hypothesis of Tardive Dyskinesia
Shawn L. Cassady, M.D., Adrian Birt, M.D., Richard Ellsberry, B.A., Gunvant K. Thaker, M.D., Carol A. Tamminga, M.D.

NR153 Diagnosis of Post Traumatic Disorder
Eitan D. Schwarz, M.D., Janice M. Kowalski, Ph.D.

NR154 Serotonin and Victims of Childhood Sexual Abuse
Mark H. Corrigan, M.D., James C. Garbutt, M.D., Gregory M. Gillette, M.D., George Mason, Ph.D., Stanley Carson, Pharm. D., Robert N. Golden, M.D.

NR155 Sensory Modalities of Flashbacks: Post-Trauma
Heidi S. Resnick, Ph.D., Dean G. Kilpatrick, Ph.D., Julie A. Lipovsky, Ph.D., Angelyne Amick, Ph.D., Connie L. Best, Ph.D., Benjamin E. Saunders, Ph.D., Ellie Sturgis, Ph.D.

NR156 The Acute Effects of Aerobic Exercise on Mood in Normal Men
Joshua Simon, Ed.D., Dale A. D'Mello, M.D., Peter C. Douris, Ed.D.

NR157 Premenstrual Syndrome in a Psychiatric Setting
Catherine Hair, M.D., Richard Schramm, M.D., Susan Caruso, Ph.D., Mahlon S. Hale, M.D.

Tuesday, May 15, 1990, 9:00 a.m.-10:30 a.m.

New Research 3—Oral/Slide Session—Rooms D3/D4, Level 1, Javits Center

SCHIZOPHRENIC DISORDERS

Chp.: Robert W. McCarley, M.D.

NR158	Brain Morphology at the Onset of Schizophrenia Lynn E. DeLisi, M.D., Anne L. Hoff, Ph.D., Gail Shields, M.D., Joseph Schwartz, Ph.D., Shree Halthore, M.D., Azad Anand, M.D.	9:00 a.m.
NR159	Auditory Hallucinations and Language Areas of the Brain in Neuroleptic-Free Schizophrenics John M. Cleghorn, M.D., E. Steven Garnett, M.B., Claude Nahmias, Ph.D., Sheryl Franco, R.N., Barbara Szechtman, M.A., Ronald D. Kaplan, Ph.D., Henry Szechtman, Ph.D., Gregory M. Brown, M.D.	9:15 a.m.
NR160	Quantitative Data and the Genetics of Schizophrenia Steven O. Moldin, Ph.D.	9:30 a.m.
NR161	Schizotypy and Sustained Attention Mark F. Lenzenweger, Ph.D., Barbara Cornblatt, Ph.D.	9:45 a.m.
NR162	MCPP Effects in Schizophrenic Patients John H. Krystal, M.D., John P. Seibyl, M.D., Lawrence P. Price, M.D., Scott W. Woods, M.D., George R. Heninger, M.D., Dennis S. Charney, M.D.	10:00 a.m.
NR163	Is Six-Months Criterion Needed for DSM-IV Schizophrenia? Ming T. Tsuang, M.D.	10:15 a.m.

Tuesday, May 15, 1990, 9:00 a.m.-10:30 a.m.

New Research 4—Oral/Slide Session—Rooms D5/D6, Level 1, Javits Center

ANXIETY DISORDERS

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

NR164	Pre-Vietnam Service Medical Records of PTSD Veterans Roger K. Pitman, M.D., Scott P. Orr, Ph.D., Michael Macklin, B.A., Bruce Altman, Psy.D.	9:00 a.m.
NR165	Sleep in Survivors of the Nazi Holocaust Jules Rosen, M.D., Charles F. Reynolds, M.D., Patricia R. Houk, M.S.W., Amy L. Yeager, B.A., Linda F. Hurwitz, M.A.	9:15 a.m.
NR166	Comorbidity of Panic Disorder Seizures: Affinity or Artifact? Richard Neugebauer, Ph.D., Robert Ouellette, M.P.H., Myrna M. Weissman, Ph.D., Jeffrey Markowitz, Ph.D.	9:30 a.m.

NR167 ACTH Response to Pentagastrin in Patients with Panic Disorder and Healthy Control Subjects — 9:45 a.m.
James L. Abelson, M.D., Randolph M. Nesse, M.D., Aaron Vinik, M.D.

NR168 Cognitive Therapy for Panic: Comparative Efficacy — 10:00 a.m.
David M. Clark, D.Phil., Michael Gelder, D.M., Paul Salkovskis, M.Phil., Ann Hackmann, M.Sc., Hugh Middleton, M.D., Pavlos Anastasiades, B.Sc.

NR169 Types of Symptoms and Response to Clomipramine in Obsessive Compulsive Disorder — 10:15 a.m.
Wayne K. Goodman, M.D., Steven A. Rasmussen, M.D., Lawrence H. Price, M.D.

NEW RESEARCH

Tuesday, May 15, 1990, 10:30 a.m.-12 noon

New Research 5—Science Policy Session—Room E19, Level 1, Javits Center

ANATOMY OF RESEARCH FUNDING

Chps.: Charles F. Kaufmann, M.D., and Harold Alan Pincus, M.D.

Participants: Richard Green, M.D., Lewis L. Judd, M.D., Heinz E. Lehmann, M.D., Robert Levy, M.D., Mr. David M. Nee

NEW RESEARCH

Tuesday, May 15, l990, 12:00 noon-2:00 p.m.

New Research 6—Poster Session—Westside Ballroom North/Center, Fifth Floor, Marriott Marquis

SCHIZOPHRENIC DISORDERS AND BIOLOGICAL PSYCHIATRY

Moderator: Charles B. Nemeroff, M.D.

NR170 Triune Brain: Clinical Applications for Psychiatry
Elliot S. Cohen, M.D., Arun V. Hejmadi, Ph.D., Patricia J. Lyall, B.S.

NR171 Etomidate Anesthesia in ECT
Paula T. Trzepacz, M.D., Fred C. Weniger, Jr., M.D., Joel Greenhouse, Ph.D.

NR172 Three Year Community Follow-Up On CT's NGRIs
Robert T.M. Phillips, M.D., Deborah Scott, M.S.W., Martha Lewis, M.S.W.

NR173 Beta-1 Receptor Response in Normals on Desipramine
Robert B. Pohl, M.D., Vikram K. Yeragani, M.D., Richard Balon, M.D., Debra A. Glitz, M.D., Richard Berchou, D.Pharm., C. Ramesh, M.D.

NR174 Depression, BLPH.BE and ACTH in Cushing's Disease
Monica N. Starkman, M.D., David E. Schteingart, M.D.

NR175 Plasmatic Neurotensin and VIP Modifications in Mood and Anxiety Disorders
Jeronimo Saiz-Ruiz, M.D., Jose L. Carrasco, M.D., Angel Hernanz, M.D.

NR176 Enhanced Alpha EEG with Clozapine Response
Steven G. Potkin, M.D., Yi Jin, M.D., C.W. Chris Heh, M.D., Bob Isenhart, Curt Sandman, Ph.D.

NR177 Heart Rate Variability in Major Depression
Gregory W. Dalack, M.D., Steven P. Roose, M.D., Alexander H. Glassman, M.D., Sally Woodring, R.N., J. Thomas Bigger, M.D.

NR178 Imipramine and Paroxetine Binding with Zacopride
John C. Pecknold, M.D., Lorenz Luthe, M.Sc., Linda J. Iny, M.A., Michael J. Meaney, Ph.D.

NR179 Effect of Sleep Deprivation on Mood and Arden Ratios
Christopher Reist, M.D., Kenneth N. Sokolski, M.D., Edward M. Demet, Ph.D.

NR180 Correlates of Plasma Dexamethasone Levels in Depression
Jacqueline A. Samson, Ph.D., Anthony J. Rothschild, M.D., Joseph J. Schildkraut, M.D., Monica Luciana, B.S., Herbert Y. Meltzer, M.D., Alan F. Schatzberg, M.D.

NR181 Catecholamine Output Versus Receptor Function
Fred Grossman, D.O., Emile D. Risby, M.D., Husseini J. Manji, M.D., John K. Hsiao, M.D., William Z. Potter, M.D.

NR182 Sensitivity of TRH Test Versus TSH in Hypothyroidism
Irl L. Extein, M.D., Mark S. Gold, M.D., Paul J. Goodnick, M.D.

NR183 A Primate Model for Evaluating Novel Antipsychotics
R. Francis Schlemmer, Ph.D., John M. Davis, M.D.

NR184 Neuroendocrine Effects of SM3997
Pedro L. Delgado, M.D., Christine Fischette, Ph.D., John P. Seibyl, M.D., Cindy D'Amico, R.N., George R. Heninger, M.D., Dennis S. Charney, M.D.

NR185 Photoaffinity Labeling of the GBR Binding Site
S. Paul Berger, M.D., Russel Martensen, Ph.D., Peter Laing, Ph.D., Steven M. Paul, M.D.

NR186 Membrane Phospholipid Content in Bipolar Disorder
Alan G. Mallinger, M.D., Jeffrey K. Yao, Ph.D., Jonathan M. Himmelhoch, M.D., Michael E. Thase, M.D., Christine S. Dippold, B.S., Marylin O. Frantz, B.Ed.

NR187 Hippocampal Lesions and Brain Dopamine Systems
Barbara K. Lipska, Ph.D., George E. Jaskiw, M.D., Farouk Karoum, Ph.D., Joel E. Kleiman, M.D., Daniel R. Weinberger, M.D.

NR188 Heat Loading in Haloperidol-Treated Schizophrenics
Haggai Hermesh, M.D., Moshe Birger, M.D., Arik Shalev, M.D., Yoram Epstein, Ph.D., Hanan Munitz, M.B., Suzy Floru, M.D.

NR189 Low-Dose Clomipramine for Refractory Akathisia
Haggai Hermesh, M.D., Dov Aizenberg, M.D., Galia Friedberg, M.D., Zvi Zemishlani, M.D., Hanan Munitz, M.B.

NR190 Intergenerational Effects of Postpartum Psychosis
John J. Sigal, Ph.D., Jacqueline Royer, M.D.

NR191 WITHDRAWN

NR192 A Prospective Study of Depression in Nursing Homes
Barry W. Rovner, M.D., Pearl German, Sc.D., Larry Brant, Ph.D.

NR193 Criterion Prevalence of ADHD in a Suburban Town
Kerim Munir, M.D., David Boulifard, B.A., Eva Deykin, D.P.H.

NR194 Correlates of Clinically Diagnosed Dementia
Sophie Auriacombe, M.D., Michele Gagnon, M.A., J. Francois Dartigues, Ph.D., Claude Messier, Ph.D., Benedicte Rigal, M.D., J. Marc Orgogozo, M.D.

NR195 Rates of Psychiatric Disorders in the Medically Ill
George Fulop, M.D., James J. Strain, M.D.

NR196 Risk Factors for the Schizophrenia Syndrome
Allen Y. Tien, M.D., William W. Eaton, Ph.D.

NR197 Schizophrenia Spectrum: Personality and Cognition
Allen Y. Tien, M.D., Gunvant K. Thakar, M.D., Paul T. Costa, Jr., Ph.D., William W. Eaton, Ph.D.

NR198 Tardive Dyskinesia in Asians: Multinational Study
Edmond H. Pi, M.D., Gregory E. Gray, M.D., Dong G. Lee, M.D., Zhongfu Ji, M.D., Yongzhen Weng, M.D., Chang K. Kim, M.D., Yong S. Kim, M.D., Tie M. Leung, M.D., Akira Kishimoto, M.D., Chen-I Wu, M.D.

NR199 Does ECT Change Serotinergic Function?
Matthew V. Rudorfer, M.D., Husseini K. Manji, M.D., John K. Hsiao, M.D., Emile D. Risby, M.D., Ossama T. Osman, M.D., William Z. Potter, M.D.

NR200 Axis II Personality Features in the First Degree Relative of Probands with Schizophrenic Disorder, Affective Disorder and No Disorder (Normal Controls)
Elizabeth Squires-Wheeler, Ph.D., L. Erlenmeyer-Kimling, Ph.D.

NR201 Sixty Percent Concordance for Alzheimer's Disease in Monozygotic Twin Pairs
Kathleen Welsh, Ph.D., John C.S. Breitner, M.D., Kathryn M. Magruder-Habib, Ph.D., Cynthia M. Churchill, M.D., C. Dennis Robinette, Ph.D., Marshal F. Folstein, M.D.

NR202 Timing Prenatal Insult in Schizophrenia: Twin Study
H. Stefan Bracha, M.D., Stephen R. Paige, Ph.D., E. Fuller Torrey, M.D.

NR203 Platelet 5HT Uptake in Sons of Alcoholic Fathers
Jeffrey L. Rausch, M.D., Maristela Monteiro, M.D., Marc A. Schuckit, M.D.

NR204 Genetics of Psychoses in Large Pedigrees of Quebec
Michel Maziade, M.D., Vincent Raymond, M.D., Marc De Braekeleer, M.D., Maria Martinez, Ph.D., Chantal Caron, M.D., Chantal Merette, Ph.D.

NR205 Use of (AC)n Repeat Polymorphisms in Schizophrenia
Mihael H. Polymeropoulos, M.D., Hong Xiao, M.D., Lynn Delisi, M.D., L. James Weber, Ph.D., R. Carl Merril, M.D.

NR206 Mapping Genes for Manic Depression and Schizophrenia
William F. Byerley, M.D., Mark Leppert, Ph.D., John Holik, B.A., Angela M. Lubbers, B.A., Steve Jensen, B.A., Ray White, Ph.D.

NR207 Familial Pedigrees of Paraphilia
Alain Labelle, M.D., Dominique Bourget, M.D., Pierre Tessier, M.D., Martin Alda, M.D., J.M.W. Bradford, M.B.

NR208 Preliminary Analysis of a Large Stuttering Pedigree
Charles D. Mellon, M.D., Sandra Hasstedt, Ph.D., Marvin Hanson, Ph.D., Wendal Walton, Ph.D., Mark Leppert, Ph.D., Ray White, Ph.D.

NR209 Alzheimer's in Hispanics and Their Families
Jacobo Mintzer, M.D., Margarita Lermo, M.D.

NR210 Lithium Induced Polyuria Ameliorated by Potassium
Mahmoud N. Musa, M.D., Bhaskara Tripuraneni, M.D., Demitrios Zikos, M.D., Ramaswamy Lakshmanan, M.D., John Caliendo, M.D.

NR211 Utah Tourette Family Study
William M. McMahon, M.D., Mark Leppert, Ph.D., Francis Filloux, M.D., Ben J.M. Van De Wetering, M.D.

NR212 Ventriculomegaly in Sporadic Schizophrenia
Steven B. Schwarzkopf, M.D., Bernhard Bogerts, M.D., Stephen C. Olson, M.D., Jeffrey A. Coffman, M.D., Henry A. Nasrallah, M.D.

NR213 Low Family History in Schizophrenia Winter Births
Steven B. Schwarzkopf, M.D., Henry A. Nasrallah, M.D., Stephen C. Olson, M.D., Jeffrey A. Coffman, M.D.

NR214 Methodological Bias in the Assessment of Negative Symptoms of Schizophrenia
David H. Strauss, M.D., Xavier F. Amador, Ph.D.

NR215 The Longitudinal Course of Schizophrenic Symptoms
Jean M. Addington, Ph.D., Donald E. Addington, M.D.

NR216 Cognitive Functioning and Schizophrenic Symptoms
Jean M. Addington, Ph.D., Donald E. Addington, M.D.

NR217 Length of Stay and Recidivism in Schizophrenia
Lawrence Appleby, Ph.D., Desai N. Prakash, M.D., Daniel J. Luchins, M.D., Robert D. Gibbions, Ph.D., Donald K. Hedeker, Ph.D., Russel A. Puetz, M.A.

NR218 Negative Schizophrenic Symptoms and EEG Alpha
Edward L. Merrin, M.D., Thomas C. Floyd, M.A.

NR219 Source Derivation EEG Coherence and Schizophrenia
Edward L. Merrin, M.D., Thomas C. Floyd, M.A.

NR220 Saccades in Schizophrenia: More Than a Marker
Frederic Flach, M.D., Melvin Kaplan, O.D., Herbert Bengelsdorf, M.D., Barbara Orlowski, Ph.D., Dennis Carmody, Ph.D.

NR221 Novel Quantitative Psychotherapy Outcome Measures
Dinko Podrug, M.D.

NR222 Cholecystokinin, Dopamine and Schizophrenia
Margery Beinfeld, Ph.D., Jeffrey K. Yao, Ph.D., David L. Garver, M.D.

NR223 MRI Correlates of Negative Symptoms in Schizophrenia
Peter C. Williamson, M.D., David Pelz, M.D., Harold Merskey, D.M., Sandra L. Morrison, M.A., Patrick Conlon, M.D.

NR224 Neurological Signs, VBR and Neuroleptic Response in Schizophrenia
Gyorgy Bartko, M.D., Gyorgy Zador, M.D., Arpad Kulin, M.D., Gaspar Biro, M.D.

NR225 Leukoencephalopathy in Late Onset Schizophrenia
John C.S. Breitner, M.D., Mustafa M. Husain, M.D., K. Ranga R. Krishnan, M.D., Gary S. Figiel, M.D., Orest B. Boyko, M.D.

NR226 Schizophrenia: Brain Stem Cholinergic Nuclei
Craig N. Karson, M.D., Sue W. Griffin, Ph.D., Muhammad Husain, M.D., Robert Mrak, M.D., Jason A. Smith, Edgar Garcia-Rill, M.D.

NR227 Poor Neuroleptic Response: Do We Need Many Drugs?
Arieh Y. Shalev, M.D., Joseph Rothberg, Ph.D., Hanan Munitz, M.B.

NR228 NMR Spectroscopy of Psychotropic Drugs in the Brain
Joseph E.O. Newton, M.D., Richard A. Komoroski, Ph.D., P. Mohanakrishnan, Ph.D., Jay Sprigg, M.S., Dave Cardwell, B.S., Craig N. Karson, M.D.

NR229 Symptom Correlates of Ventricle Size in Schizophrenia
Gustav Degreef, M.D., Manzar Ashtari, Ph.D., Robert M. Bilder, Ph.D., Bernhard Bogerts, M.D., Jeffrey A. Lieberman, M.D.

NR230 Milacemide Treatment of Schizophrenia
Richard B. Rosse, M.D., Barbara L. Schwartz, Ph.D., Michael P. Leighton, B.A., Stephen I. Deutsch, M.D.

NR231 Noradrenergic Function in Chronic Schizophrenia
Alan F. Breier, M.D., Owen M. Wolkowitz, M.D., Alec Roy, M.D., William Z. Potter, M.D., David Pickar, M.D.

NR232 NIMH Longitudinal Study of Chronic Schizophrenia
Alan F. Breier, M.D., Judith L. Schreiber, M.S.W., Janyce Dyer, M.S.N., David Pickar, M.D.

NR233 Longitudinal Plasma HVA in Psychiatric Patients
Javaid I. Javaid, Ph.D., Rajiv P. Sharma, M.D., Philip G. Janicak, M.D., John M. Davis, M.D.

NR234 Haloperidol Plasma Levels: Steady-State Prediction
Javaid I. Javaid, Ph.D., Philip G. Janicak, M.D., Donald K. Hedeker, Ph.D., Michael S. Easton, M.D., Rajiv P. Sharma, M.D., John M. Davis, M.D.

NR235 Serotonergic Responsivity in Schizophrenia
Richard R. Owen, Jr., M.D., Rolando L. Gutierrez, M.D., Kayleen Hadd, M.S.N., Chawki Benkelfat, M.D., Dennis L. Murphy, M.D., David Pickar, M.D.

NR236 Disturbed Water Metabolism in Schizophrenia
William B. Lawson, M.D., Dennis E. Schmidt, Ph.D., Eric Morales, B.S.

NR237 Clozapine Effects on Positive Versus Negative Symptoms
Jean-Pierre Lindenmayer, M.D., Leon Mabugat, M.D., Stanley R. Kay, Ph.D., Lisa Murrill, M.A., Serge Sevy, M.D.

NR238 Visual Selective Attention in Schizophrenia
Paul G. Nestor, Ph.D., Steven F. Faux, Ph.D., Robert W. McCarley, M.D., Virginia Penhune, B.A., Stephen Sands, Ph.D.

NR239 Visual P300 ERPs in Schizophrenia
Steven F. Faux, Ph.D., Paul G. Nestor, Ph.D., Robert W. McCarley, M.D., Martha E. Shenton, Ph.D., Virginia Penhune, B.A., Seth D. Pollak, M.Ed.

NR240 The Entorhinal Cortex in Schizophrenia
Manuel F. Casanova, M.D., Richard Saunders, Ph.D., Lori Altshuler, M.D., Terry E. Goldberg, Ph.D., Este Armstrong, Ph.D., Daniel R. Weinberger, M.D., Joel E. Kleinman, M.D.

NR241 Pathology of Cognitive Impairment in Schizophrenia
Manuel F. Casanova, M.D., Nicholas Carosella, M.D., James M. Gold, Ph.D., Richard E. Powers, M.D., Daniel R. Weinberger, M.D., Joel E. Kleiman, M.D.

NR242 Impact of Clozapine on Cognition in Schizophrenia
Richard Greenberg, M.D., Terry E. Goldberg, Ph.D., Suzanne J. Griffin, M.D.

NR243 A Strategy for Linkage in Typical Schizophrenia
Jeremy M. Silverman, Ph.D., Richard C. Mohs, Ph.D., David A. Greenberg, Ph.D., Larry J. Siever, M.D., William Wallace, Ph.D., Kenneth L. Davis, M.D.

NR244 Platelets, Eosinophils and Psychiatric Symptoms
Murray A. Cowen, M.D., Maurice Green, M.D.

NR245 Alkaline Phosphatase and Psychiatric Symptoms
Murray A. Cowen, M.D., Maurice Green, M.D.

NR246 Family, Cognition and Schizophrenia Outcome
Peter Stastny, M.D., Deborah A. Perlick, Ph.D., Steven Mattis, Ph.D., Jeanne Teresi, Ph.D., Maureen Empfield, M.D.

NR247 Neurocognitive Correlates of Schizophrenia Outcome
Deborah A. Perlick, Ph.D., Peter Stastny, M.D., Steven Mattis, Ph.D., Jeanne Teresi, Ph.D., Ira R. Katz, M.D.

NR248 Schizophrenic Depression: Response to Neuroleptics
Menahem Krakowsky, M.D., Pal Czobar, Ph.D., Jan Volavka, M.D.

NR249 Cognitive Deficits in Early Schizophrenia
Anne L. Hoff, Ph.D., Gail Shields, M.D., Donald O'Donnell, M.A., Lynn E. DeLisi, M.D.

NR250 Prefrontal Cortex and Cognition: A PET Study
Karen Faith Berman, M.D., Christopher Randolph, Ph.D., James M. Gold, Ph.D., Douglas W. Jones, Ph.D., Terry E. Goldberg, Ph.D., Gary W. Berg, M.D., Richard E. Carson, Ph.D., Peter Herscovitch, M.D., Daniel R. Weinberger, M.D.

NR251 Change in Self-Destructiveness of Borderline Patients
Alex N. Sabo, M.D., Deborah Chauncey, A.B., John G. Gunderson, M.D.

NR252 Antipsychotic Drugs: Liability to Affect Seizures
Bruce I. Diamond, Ph.D., Bonnie VanSchooneveld, M.D., Richard L. Borison, M.D.

NR253 Memory in Monozygotic Twins Discordant for Schizophrenia
James M. Gold, Ph.D., Terry E. Goldberg, Ph.D., J. Daniel Ragland, M.A., Richard Coppola, D.Sci., E. Fuller Torrey, M.D., Daniel R. Weinberger, M.D.

NR254 Lithium Response, VBR, Brain Density and Schizophrenia
Surendra Kelwala, M.D., Anil K. Jain, M.D., Ibrahim Youssef, M.D., L.J. Bronn, M.D., Pramila Baddigam, M.D., Suresh Yerasi

NR255 Effect of Domperidone on Plasma HVA in Schizophrenia
P. Eric Konicki, M.D., William Z. Potter, M.D., Richard E. Scott, B.A., David Pickar, M.D.

NR256 Job Club for Psychiatric Patients: Training Job Finding Skills
Robert P. Liberman, M.D., Harvey E. Jacobs, Ph.D., Jim Mintz, Ph.D.

NR257 Schizophrenia, Mania and Attentional Dysfunctions
Barbara Cornblatt, Ph.D., Michael Obuchowski, M.A., Paul Fergeson, B.A., Sukhdeb Mukherjee, M.D.

NR258 Platelet MAO in Schizophrenia and Affective Subtype
Ghanshyam N. Pandey, Ph.D., Philip G. Janicak, M.D., John M. Davis, M.D., Jin Hua, M.D., Ed Atlman, Psy.D., Jim Peterson, B.S.

NR259 Refining the Concept of Negative Symptoms
Janice A. Husted, Ph.D., Morton W. Beiser, M.D.

NR260 Low Amine Metabolite Excretion in Schizophrenia
Jan A. Fawcett, M.D., Javaid I. Javaid, Ph.D., Hector C. Sabelli, M.D., Unb Durai, M.D., Nancy Hein, A.S.

NR261 Sleep in Schizophrenics On and Off Neuroleptics
Daniel P. Van Kammen, M.D., Thomas C. Neylan, M.D., Jeffrey L. Peters, M.D.

NR262 Clozapine Response in Treatment Resistant Patients
John J. Boronow, M.D., Norman Ringel, M.A., Frederick Parente, Ph.D.

NR263 The Effect of Target Characteristics on the Specificity of Smooth Pursuit Eye Tracking Dysfunction
Xavier F. Amador, Ph.D., Harold A. Sackeim, Ph.D., Sukdeb Mukherjee, M.D.

NR264 Cerebral SPECT in Drug Free Schizophrenic Patients
Antonio Vita, M.D., Professor C. Lorenzo Cazzullo, Emilio Sacchetti, M.D., G. Marco Giobbio, M.D., Massimiliano Dieci, M.D., Marco Garbarini, M.D., Giovanna Valvassori, M.D., Professor Giordano Invernizzi, Longostrevi G. Poggi, M.D.

NR265 Tardive Dyskinesia in Neuroleptic-Treated Diabetics
Linda K. Ganzini, M.D., Ronald T. Heintz, M.D., William Hoffman, M.D., Daniel E. Casey, M.D.

NR266 Diagnosis of Dysphagia in Psychiatric Inpatients
Patricia H. Bazemore, M.D., Joseph M. Tonkonogy, M.D., Rajoo R. Ananth, M.S., Jay M. Colby, M.D.

NR267 Diltiazem Suppresses Quinpirole-Induced Stereotypy
Olgierd Pucilowski, Ph.D., Burr S. Eichelman, M.D.

NR268 Do Neuroleptics Cause Pain?
Paolo Decina, M.D., Giovanni Caracci, M.D., Kay Harrison, R.N., Reuven Sandik, M.D.

NR269 High Dose Buspirone in Tardive Dyskinesia
Vernon M. Neppe, M.D.

NR270 Delayed Onset of Hydrophilic B-Blockers in Akathisia
Lenard A. Adler, M.D., Burt Angrist, M.D., John P. Rotrosen, M.D.

NR271 Sensitization to Neuroleptic Treatment
Birte Yding Glenthoj, M.D., Tom G. Bolwig, M.D., Ralf Hemmingsen, M.D.

NR272 Negative Symptoms and Awareness of Dyskinesias
Haranath Parepally, M.D., Sukdeb Mukherjee, M.D., Ravinder Reddy, M.D., David B. Schnur, M.D., Hyacinth Thompson, R.N., Richard Costa, M.A.

NEW RESEARCH

Tuesday, May 15, l990, 3:00 p.m.-5:00 p.m.

New Research 7—Poster Session—Westside Ballroom North/Center, Fifth Floor, Marriott Marquis

ANXIETY DISORDERS AND OTHER PSYCHIATRIC TOPICS

Moderator: Trey Sunderland, M.D.

NR273 Cost of Capitated Care for Chronic Mental Illness
Thomas E. Gift, M.D., Phyllis E. Marshall, M.S.W., Haroutun H. Babigian, M.D., William D. McMainas, M.D., Fred J. Volpe

NR274 Carbamazepine and ACTH/Cortisol Responses to Corticotropin-Releasing Hormone
Mitchel A. Kling, M.D., Joseph R. Calabrese, M.D., Giulia I. Perini, M.D., M. Jennifer Hart, B.A., Robert M. Post, M.D., Philip W. Gold, M.D.

NR275 PTSD: Risks for Event Exposure and Syndrome
Naomi Breslau, Ph.D., Glenn C. Davis, M.D., Patricia Andreski, M.A.

NR276 Generalized Anxiety Disorder and Dysthymia: The Detroit Epidemiologic Study
Naomi Breslau, Ph.D., Glenn C. Davis, M.D.

NR277 DSM-III-R Generalized Anxiety Disorder: The Detroit Epidemiologic Study
Naomi Breslau, Ph.D., Glenn C. Davis, M.D.

NR278 Follow-Up of Soft-Signs and Anxiety into Adulthood
Eric Hollander, M.D., Concetta DeCaria, M.S., Bonnie Aronowitz, M.A., Michael R. Liebowitz, M.D., Donald F. Klein, M.D., David Shaffer, M.D.

NR279 Panic Acuity Affects Anxiogenic Vulnerability
Steven D. Targum, M.D.

NR280 Prevalence of Panic Attacks in Adolescents
Jean-Philippe Boulenger, M.D., Francoise Chastang, M.D.

NR281 Comorbidity of Social Phobia with Psychiatric Illness
Michael van Ameringen, M.D., Catherine Mancini, M.D.

NR282 CCK-4 Versus CO2 Panic Attacks in Panic Disorder
Jacques Bradwejn, M.D., Diana Koszycki, M.A., Christian L. Shriqui, M.D.

NR283 Cholecystokinin Panic: Panic Disorder Versus Agoraphobia
Jacques Bradwejn, M.D., Diana Koszycki, M.A., Christian L. Shriqui, M.D.

NR284 Dose-Ranging Study of CCK-4 in Healthy Volunteers
Jacques Bradwejn, M.D., Diana Koszycki, M.A., Christian L. Shriqui, M.D.

NR285 Psychological Correlates of Response to Inhalation of Thirty-Five Percent CO2
Diana Koszycki, M.A., Jacques Bradwejn, M.D., James Campbell, M.D.

NR286 Platelet Alpha2-Receptor Binding in PTSD, Generalized Anxiety Disorder and Major Depressive Disorder
Rachel Yehuda, Ph.D., Bruce D. Perry, M.D., Steven M. Southwick, M.D., Earl L. Giller, Jr., M.D.

NR287 CSF Opioid Activity in Panic Patients and Controls
R. Bruce Lydiard, M.D., Kathleen T. Brady, M.D., James C. Ballenger, M.D., Michele T. Laraia, R.N., Jenny Shook, Ph.D., Mark D. Fossey, M.D.

NR288 CSF Monoamine Metabolites in Obsessive Compulsive Disorder
R. Bruce Lydiard, M.D., James C. Ballenger, M.D., Everett H. Ellinwood, Jr., M.D., Michele T. Laraia, R.N., Linda S. Austin, M.D., Mark D. Fossey, M.D.

NR289 Noradrenergic Function in Panic: New CSF Findings
R. Bruce Lydiard, M.D., James C. Ballenger, M.D., Michele T. Laraia, R.N., Mark D. Fossey, M.D.

NR290 Imipramine Binding Predicts Response in Panic Disorder
John C. Pecknold, M.D., Lorenz Luthe, M.Sc.

NR291 Panic Disorder Comparing Drug and Psychotherapy
M. Katherine Shear, M.D., Andy Leon, Ph.D., Laura Portera, B.A., Gerald L. Klerman, M.D.

NR292 Trichotillomania and Obsessive Compulsive Disorder
Melinda A. Stanley, Ph.D., Theron C. Bowers, M.D., Alan C. Swann, M.D.

NR293 Plasma Vasopressin Elevated by Stressful Interview
James L. Meyerhoff, M.D., Marvin Oleshansky, M.D., K. Kalogeras, M.D., Edward H. Mougey, M.D., George P. Chrousos, M.D., Larry Granger

NR294 Effect of IV Procaine on Alcoholics with Panic
David T. George, M.D., David J. Nutt, M.D., Markku I. Linnoila, M.D.

NR295 A Pilot Study of Fluoxetine for Trichotillomania
Ronald M. Winchel, M.D., Barbara Stanley, Ph.D., Jeannine Guido, M.A., J. Sidney Jones, M.D., Kelly Posner, B.A., Michael Stanley, Ph.D.

NR296 Early Onset Phobias and Later Major Depression
Alan F. Schatzberg, M.D., Jacqueline A. Samson, Ph.D., Anthony J. Rothschild, M.D., Rachel Bruno, B.A., Monica Luciana, B.S., Sandra Cole, M.S.

NR297 Lymphocyte Beta-Adrenoreceptors in Panic Disorder
Richard J. Maddock, M.D., Cameron S. Carter, M.B., Joseph R. Magliozzi, M.D., Dorothy Gietzen, Ph.D.

NR298 Effects of Fluvoxamine on Yohimbine Anxiety
Andrew W. Goddard, M.D., Dennis S. Charney, M.D., George R. Heninger, M.D., Scott W. Woods, M.D.

NR299 Postpartum Onset of Panic Disorder
Diane E. Sholomskas, Ph.D., Scott W. Woods, M.D., Lisa Dogolo, B.A., Deborah W. O'Brien, R.N.

NR300 Drug/Behavior Treatment of Panic: Study Design
Diane E. Sholomskas, Ph.D., David H. Barlow, Ph.D., Jacob Cohen, Ph.D., Jack M. Gorman, M.D., Karla Moras, Ph.D., Laszlo A. Papp, M.D., M. Katherine Shear, M.D., Scott W. Woods, M.D.

NR301 An Open Trial of Fluoxetine in PTSD
Christopher J. McDougle, M.D., Steven M. Southwick, M.D., Ronald L. St. James, A.C.S.W., Dennis S. Charney, M.D.

NR302 Lithium Augmentation in Fluvoxamine Refractory Obsessive Compulsive Disorder
Christopher J. McDougle, M.D., Lawrence H. Price, M.D., Wayne K. Goodman, M.D., Dennis S. Charney, M.D., George R. Heninger, M.D.

NR303 On the Agoraphobia/Simple Phobia Boundary
George C. Curtis, M.D., Joseph A. Himle, M.S.W., Julie A. Lewis, B.A., Yue-Joe Lee, M.D.

NR304 Maintenance Drug Therapy of Panic Disorder
George C. Curtis, M.D., Juan Massana, M.D., Claudio Udina, M.D., Jose L. Ayuso-Gutierrez, M.D.

NR305 Comorbidity of Anxiety Disorders in Obsessive Compulsive Disorder Patients
Linda S. Austin, M.D., R. Bruce Lydiard, M.D., Mark D. Fossey, M.D., Michele T. Laraia, R.N., James C. Ballenger, M.D.

NR306 Diagnosis of Anxiety Disorder: Insights from SCL-90
Cary L. Hamlin, M.D.

NR307 Post-Earthquake Fears in Girls with Panic Attacks
Chris R. Hayward, M.D., Joel D. Killen, Ph.D., Ruthven D. Patrick, M.A., C. Barr Taylor, M.D.

NR308 Urine pH in Panic: A Simple Screening Device
Laszlo A. Papp, M.D., Jack M. Gorman, M.D., Jeremy D. Coplan, M.D., Eric Hollander, M.D., Donald F. Klein, M.D.

NR309 CRF and TRH in the CSF of Panic Patients
Mark D. Fossey, M.D., R. Bruce Lydiard, M.D., Michele T. Laraia, R.N., Garth Bissette, Ph.D., Charles B. Nemeroff, M.D., James C. Ballenger, M.D.

NR310 Experiments with the Buspirone Metabolite 1-PP
Marc L. Leavitt, Ph.D., Trevor R.P. Price, M.D., Joseph C. Maroon, M.D.

NR311 Verticality Perception in Agoraphobic Patients
Jean-Claude Bisserbe, M.D., Jean-Philippe Boulenger, M.D., Bernadette Laverdure, Edouard Zarifian, M.D.

NR312 A Placebo-Controlled Study of Valproate in Mania
Susan L. McElroy, M.D., Harrison G. Pope, Jr., M.D., Paul E. Keck, Jr., M.D., James I. Hudson, M.D.

NR313 Mode of Onset Simple Phobia Subtypes
Joseph A. Himle, M.S.W., David Crystal, M.S.W., George C. Curtis, M.D., Thomas E. Fluent, M.D.

NR314 Panic Anxiety: Diazepam/Clompramine Comparison
Sergio Gloger, M.D., Francisco O'Ryan, M.D., Danica Gladic, Alexei Franulic, M.D., Mario Barahona, R.N.

NR315 Seasonal Bias in the Onset of First Panic Attack
J-P Lepine, M.D., J-M Chignon, M.D., M. Teherani, Ph.D.

NR316 Efficacy of Short-Term Inpatient Treatment: A 6 to 18 Month Follow-Up Study
Jeffrey M. Jonas, M.D., Jeff Eagle, Ph.D., Allyson McClave, B.S., Nancy Smith, M.S., Alice Zimmerman, Med.

NR317 Reduction in Maternal Depressive Symptoms Following Miscarriage: The Effect of Research Interviews
Richard Neugebauer, Ph.D., Jennie Kline, Ph.D., Patricia O'Connor, Ph.D., Pat Shrout, Ph.D., Jim Johnson, Ph.D., Andrew E. Skodol, M.D., Judith Wicks, B.A., Mervyn Susser, B.Ch.

NR318 Psychiatric Symptoms and the Capacity for Work
Robert P. Liberman, M.D., Jim Mintz, Ph.D., Mary Jane Arruda, M.S., H. Keith Massell, Ph.D., Harvey E. Jacobs, Ph.D., Carol Giannini, M.S.

NR319 Reducing Disability in SSDI Applicants
Samuel O. Okpaku, M.D., Leonard Bickman, Ph.D., Kathryn H. Anderson, Ph.D., J.S. Butler, Ph.D.

NR320 Evaluation of Psychiatric Problems Among Iranian Immigrants in Canada
Aghdas A. Bagheri, M.D.

NR321 Behavior Therapy for Immigrant Hispanic Families
Cynthia A. Telles, Ph.D., Steven R. Lopez, Ph.D., Rosario H. Mendrano, M.S.W., Gloria de la Cruz, M.S.W.

NR322 Religious Variables in Drug and Alcohol Outpatients
Shimon Waldfogel, M.D., Paul R. Wolpe, Ph.D., Ronald Serota, M.D., Brenda Byrne, Ph.D.

NR323 The Determinants of Disability
Bruce M. Smoller, M.D., Virginia Leone, C.R.C.

NR324 Managed Mental Health Care and Medical Cost Offset
Bernard S. Rappaport, M.D., Michael S. Pallak, Ph.D., Nicholas A. Cummings, Ph.D.

NR325 Effects of Involuntary Patients' Right to Refuse Psychotropics
Yvette I. Sheline, M.D., Martha C. Beattie, Ph.D.

NR326 Recent Nonverbal Memory Deficit in Obsessive Compulsive Disorder
Kathy J. Christensen, Ph.D., Suck-Won Kim, M.D., Maurice W. Dysken, M.D., Kathy T. Maxwell, B.A.

NR327 Trichotillomania Syndrome and Fluoxetine Response
Cesar L. Benarroche, M.D.

NR328 Serotonergic, Alpha2-Adrenergic Treatment Comparison in Obsessive Compulsive Disorder
William A. Hewlett, Ph.D., Sophia Vinogradov, M.D., W. Stuart Agras, M.D.

NR329 SPECT and MRI in Obsessive Compulsive Disorder
Steven R. Machlin, M.D., Gordon J. Harris, M.S., Godfrey D. Pearlson, M.D., Rudolf Hoehn-Saric, M.D., Edwaldo E. Camargo, M.D., Jonathan M. Links, Ph.D.

NR330 CSF Arginine Vasopressin and Oxytocin in Obsessive Compulsive and Eating Disorders
Margaret Altemus, M.D., Teresa A. Pigott, M.D., Mark A. Demitrack, M.D., Samuel J. Listwak, B.Sc., Dennis L. Murphy, M.D., Philip W. Gold, M.D.

NR331 Imbalance Between the Cerebral Hemispheres in Obsessive Compulsive Disorder
Bruce E. Wexler, M.D., Wayne K. Goodman, M.D.

NR332 WITHDRAWN

NR333 Sex Offender Treated with Fluoxetine: Preliminary Results
Kenneth Kashkin, M.D., David D'Amora, M.A., Ronald Anderson, Ph.D.

NR334 Neuroanatomical Abnormalities in Obsessive Compulsive Disorder
Frederick G. Moeller, M.D., Renee M. Dupont, M.D., Terry L. Jernigan, Ph.D., Nelson Butters, Ph.D., J. Christian Gillin, M.D., Stephen M. Stahl, M.D.

NR335 Significant Issues of the Second Sexual Revolution
Samuel S. Janus, Ph.D., Cynthia Janus, M.D.

NR336 Are Mental Hospital Episode Rates Going Up or Down?
Alex Richman, M.D., Rodney Riley, B.A.

NR337 A Causal Model of Community Tenure
Suzanne King, Ph.D., Celine Mercier, Ph.D.

NR338 Stress Symptoms and Epinephrine
Oliver G. Cameron, M.D., Sharon Gunsher, B.S., M. Hariharan, Ph.D.

NR339 Emotion and Physical Activity in Healthy Women
Thomas F. Flynn, M.D., Grant D. Miller, M.D., Lisa A. Hill, B.S., Barbara J. Scott, M.P.H., Sachiko T. St. Jeor, Ph.D.

NR340 Treatment of Type-A Behavior in Cardiac Patients with Buspirone
Andrew B. Littman, M.D., Maurizio Fava, M.D., Stefania Lamon-Fava, M.D., Kathleen McKool, R.N.

NR341 The Long-Term Effects of Childhood Sexual Abuse
Geoffrey M. Margo, M.D., Elvera M. Weld, M.A.

NR342 PTSD in Alsatian World War II Veterans
Marc-Antoine Crocq, M.D., Jean-Paul Macher, M.D., Fabrice Duval, M.D., Jorge Barros-Beck, M.D., John C. Kluznik, M.D., Stewart J. Rosenberg, M.D.

NR343 Combat Stress Among Homeless Vietnam Veterans
Robert Rosenheck, M.D., Peggy Gallup, M.P.H., Catherine A. Leda, M.P.H.

NR344 Cyclic AMP Signal Transduction in PTSD
Bernard Lerer, M.D., Avraham Bleich, M.D., Richard P. Ebstein, Ph.D.

NR345 Animal Models for PTSD
Bruce I. Diamond, Ph.D., Mark B. Hamner, M.D., Thomas L. Chalker, B.S., Richard L. Borison, M.D.

NR346 Elevated Plasma Dopamine Levels in PTSD
Mark B. Hamner, M.D., Bruce I. Diamond, Ph.D.

NR347 Alexithymia Predicts PTSD Treatment Response
Thomas R. Kosten, M.D., Earl L. Giller, Jr., M.D., Julia B. Frank, M.D., Elisheva Dan, P.A., John H. Krystal, M.D.

NR348 Dissociative Reactions to the Bay Area Earthquake
David Spiegel, M.D., Etzel Cardena, Ph.D.

NR349 Subtypes of Sexually Abused Women
Nicholas G. Ward, M.D., Albert S. Carlin, Ph.D.

NR350 REM Sleep Disturbance as the Hallmark of PTSD
Richard J. Ross, M.D., William A. Ball, M.D., David F. Dinges, Ph.D., Nancy B. Kribbs, Ph.D., Adrian R. Morrison, D.V.M., Steven M. Silver, Ph.D.

NR351 Childhood Abuse and Personality Disorders
Stanley W. Raczek, M.D.

NR352 Psychopathological Sequelae of Childhood Trauma
Stanley W. Raczek, M.D.

NR353 Psychiatrists Injured by Patient Attacks
Harold A. Carmel, M.D., Mel Hunter, M.P.A.

NR354 Caffeine Ingestion: Diagnosis and Violence
Harold A. Carmel, M.D., Mel Hunter, M.P.A.

NR355 Patient Census and Patient Aggression
Harold A. Carmel, M.D., Mel Hunter, M.P.A.

NR356 Violence Toward Psychiatric Residents
Marian Fireman, M.D., Joseph D. Bloom, M.D., Larry R. Faulkner, M.D.

NR357 Buspirone Response in PMS and Platelet 5-HT Uptake
Candace S. Brown, Pharm.D., Carolyn M. Chesney, M.D., Frank W. Ling, M.D., Barbara G. Wells, Pharm. D., Abbas E. Kitabchi, M.D.

NEW RESEARCH

Wednesday, May 16, l990, 9:00 a.m.-10:30 a.m.

New Research 8—Oral/Slide Session—Rooms D3/D4, Level 1, Javits Center

MOOD DISORDERS

Chp.: Frederic M. Quitkin, M.D.

NR358 Depressive Symptoms in the Six Months Following Miscarriage — 9:00 a.m.
Richard Neugebauer, Ph.D., Jeannie Kline, Ph.D., Patricia O'Connor, Ph.D., Pat Shrout, Ph.D., Jim Johnson, Ph.D., Andrew E. Skodol, M.D., Judith Wicks, B.A., Mervyn Susser, B.Ch.

NR359 Sleep Abnormalities in Remitted Depressives — 9:15 a.m.
Michael E. Thase, M.D., Anne D. Simons, Ph.D.

NR360 Linkage Strategies for Bipolar Affective Disorder — 9:30 a.m.
Sylvia G. Simpson, M.D., Susan E. Folstein, M.D., J. Raymond DePaulo, Jr., M.D.

NR361 Quantitative SPECT Changes with Treatment of Depression — 9:45 a.m.
Anand Kumar, M.D., P. David Mozley, M.D., Michel V. Velchik, M.D., Chris Dunham, M.D., John Reilley, C.N.M.T., Abass Alavi, M.D.

NR362 Lithium-7 Nuclear Magnetic Resonance Spectroscopy of the Human Brain — 10:00 a.m.
Laszlo Gyulai, M.D., Steven W. Wicklund, B.S., Robert Greenstein, M.D., Mark S. Bauer, M.D., Patrick Ciccione, M.D., Peter Whybrow, M.D.

NR363 Imipramine is Effective Treatment for Cognitive Therapy Nonresponders — 10:15 a.m.
Jonathan W. Stewart, M.D., Frederic M. Quitkin, M.D., Mary Ann Mercier, Ph.D.

NEW RESEARCH

Wednesday, May 16, l990, 9:00 a.m.-10:30 a.m.

New Research 9—Oral/Slide Session—Rooms D5/D6, Level 1, Javits Center

PERSONALITY, SUBSTANCE ABUSE AND EATING DISORDERS

Chp.: Katherine A. Halmi, M.D.

NR364 Personality Disorder Structure in Two Samples — 9:00 a.m.
W. John Livesley, M.D., Marsha L. Schroeder, Ph.D.

NR365 Eye Movement Dysfunction in Schizotypal Personality Disorder — 9:15 a.m.
David P. Bernstein, Ph.D., Richard S.E. Keefe, M.A., Emil F. Coccaro, M.D., Jeremy M. Silverman, Ph.D., Richard C. Mohs, Ph.D., Larry J. Siever, M.D.

NR366 Testing a Scale for Outcome Prediction in BPD — 9:30 a.m.
Jonathan R. Aronoff, Ph.D., Eric M. Plakun, M.D., Thomas H. McGlashan, M.D., George S. Patrick, M.D.

NR367 A New Look at Therapeutic Alliance and Outcome — 9:45 a.m.
Marianne Kardos, M.D., J. Christopher Perry, M.D., Jon Perry, Ph.D.

NR368 Bromocriptine and Reactivity to Cocaine Cues — 10:00 a.m.
Henry R. Kranzler, M.D., Lance Bauer, Ph.D.

NR369 Long-Term Mortality of Anorexia Nervosa — 10:15 a.m.
L.K. George Hsu, M.D., Arthur H. Crisp, M.D., John S. Callender, M.B., Walter H. Kaye, M.D

NEW RESEARCH

Wednesday, May 16, l990, 12:00 noon-2:00 p.m.

New Research 10—Poster Session—Westside Ballroom North/Center, Fifth Floor, Marriott Marquis

MOOD DISORDERS, PSYCHOPHARMACOLOGY AND PSYCHOIMMUNOLOGY

Moderator: Ellen Leinbenluft, M.D.

NR370 The Role of Quantitative EEG in Neuropsychiatric Lupus
Robert J. Chabot, Ph.D., Chris T. Ritchlin, M., Kenneth Alper, M.D.

NR371 Kindling: Somatostatin and Enkephalin Immunoreactivity
Tom G. Bolwig, M.D., Benedikte Wanscher, M.D., Jorn Kragh, M.D., David I. Barry, B.Sci., Jens Zimmer, M.D.

NR372 Decreased Cholesterol in Mania
Conrad M. Swartz, M.D.

NR373 Combined Buspirone-Fluoxetine in Severe Depression
Louis F. Fabre, M.D.

NR374 Pure Versus Compounded Depression: Outcome at 12 Months
Gabor I. Keitner, M.D., Christine Ryan, Ph.D., Ivan W. Miller, Ph.D.

NR375 Recovery and Major Depression
Gabor I. Keitner, M.D., Christine Ryan, Ph.D., Ivan W. Miller, Ph.D., William H. Norman, Ph.D.

NR376 The Comorbidity of Anxiety and Depression in Daily Life
Marten W. de Vries, M.D., Philippe A. Delespaul, Ph.C., Chantal I. Dijkman-Caes, Ph.C.

NR377 Life Events and Severe Mood Disorders
Netta Horesh, Ph.D., Elie Lepkifker, M.D., Suzy Floru, M.D., Noah Milgram, Ph.D.

NR378 Endocrine Effects of SDZ HDC-912 in Schizophrenia
Fabrice Duval, M.D., M-Claude Mokrani, Ph.D., Jean-Paul Macher, M.D., Jean-Marc Moeglen, B.Psych, Paul Bailey, M.B.

NR379 TRH-TSH Test, DST and Antidepressant Treatment
Fabrice Duval, M.D., Jean-Paul Marcher, M.D., M-Claude Mokrani, Ph.D., Jaurez Oliveira Castro, M.D., Marc-Antoine Crocq, M.D.

NR380 PRL Responses to TRH and Apomorphine in Depression
Fabrice Duval, M.D., M-Claude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Oliveira Castro Juarez, M.D., Jean-Paul Macher, M.D.

NR381 Circadian Variations in Response to TRH Challenge
Fabrice Duval, M.D., M-Claude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Jaurez Oliveira Castro, M.D., Jean-Paul Macher, M.D.

NR382 Refractory Depression: A Controlled Clinical Trial
Patrick J. McGrath, M.D., Jonathan W. Stewart, M.D., Wilma Harrison, M.D., Edward V. Nunes, M.D., Steven Wager, M.D., Frederic M. Quitkin, M.D.

NR383 Chronic Depressive Disorder (Dysthymia) Responds to a 5HT2 Receptor Antogonist, Ritanserin
Declan Murphy, M.D., Stuart A. Checkley, M.D.

NR384 The Importance of the Plasma Dexamethasone Window: A Dose Response Study in Depressed Patients
Gordon F. Johnson, M.B., Brendan T. Osullivan, M.B., Glenn E. Hunt, MS.c.

NR385 Effects of Lithium on Neutrophil Function in Vivo
Michael H. Kronig, M.D., Susan A. Moak, M.S., Robert A. Greenwald, M.D.

NR386 Paradoxical Effects of Reward in Depression
Paul A. Newhouse, M.D., Judy Lewis, M.D., June Corwin, Ph.D.

NR387 Catechol-Cortisol Correlations: Fact or Artifact?
Jacqueline A. Samson, Ph.D., Russell G. Vasile, M.D., Kerry L. Bloomingdale, M.D., John J. Mooney, M.D., Edison Miyawaki, M.D., Joseph J. Schildkraut, M.D.

NR388 Depression in Combat PTSD
Steven M. Southwick, M.D., Rachel Yehuda, Ph.D., Earl L. Giller, Jr., M.D.

NR389 Cardiovascular Effects of Bupropion
Steven P. Roose, M.D., Gregory W. Dalack, M.D., Alexander H. Glassman, M.D., Sally Woodring, R.N., B. Timothy Walsh, M.D., Elsa G.V. Giardina, M.D.

NR390 Is Doxepin a Safer Tricyclic for the Heart?
Steven P. Roose, M.D., Alexander H. Glassman, M.D., Sally Woodring, R.N., Jeffrey K. Halpern, M.D., Elsa G.V. Giardina, M.D.

NR391 Implicit Memory is Impaired in Major Depression
Carolyn M. Szostak, Ph.D., Mitchel A. Kling, M.D., Philip W. Gold, M.D., Robert M. Post, M.D., Herbert Weingartner, Ph.D.

NR392 Acute Stimulant Responses Predict Trazadone Effect
Karley Y. Little, M.D., Tamara L. Gay, M.D.

NR393 Valproate in Mania: A Double-Blind Study
Thomas W. Freeman, M.D., Jeffrey L. Clothier, M.D., Peggy Pazzaglia, M.D., Michael D. Lesem, M.D., Alan C. Swann, M.D., Ann Roache, Pharm.D.

NR394 Decreased Natural Killer Cells in Major Depression
Dwight L. Evans, M.D., James D. Folds, Ph.D., Cort A. Pedersen, M.D., Robert N. Golden, M.D., John J. Haggarty, Jr., M.D., Mark H.N. Corrigan, M.D., Howard Ozer, M.D.

NR395 Number of REM Periods and Weight Change in Major Depression
Timothy Hsu, M.D., James E. Shipley, M.D., Alan S. Eiser, Ph.D., Roger F. Haskett, M.D., Leon J. Grunhaus, M.D., Atul C. Pande, M.D.

NR396 Alexithymia in Diverse Patient Groups
Phillip Epstein, M.D., Bonnie E. Litowitz, Ph.D., Linda Neidelkoff

NR397 Imipramine for Alcoholics with Depression or Panic
Edward V. Nunes, M.D., Jonathan W. Stewart, M.D., Patrick J. McGrath, M.D., Frederic M. Quitkin, M.D., Wilma Harrison, M.D., Steven Wager, M.D.

NR398 Lithium for Bipolar Spectrum Cocaine Abusers
Edward V. Nunes, M.D., Patrick J. McGrath, M.D., Steven Wager, M.D., Frederic M. Quitkin, M.D.

NR399 The Sex Chromosomes and Psychological Development
Bruce G. Bender, Ph.D., Arthur Robinson, M.D., Mary G. Linden, M.S.

NR400 Language and Memory Deficits in Pseudodementia
V. Olga Emery, Ph.D., Charles Solow, M.D.

NR401 Effects of Light on Mood After Simulated Jet Lag
Margaret L. Moline, Ph.D., Charles P. Pollak, M.D., Daniel R. Wagner, M.D., Steven M. Zendell, Laurie S. Lester, Ph.D., Charles A. Salter, Ph.D., Edward Hirsch, Ph.D.

NR402 Acoustic Analysis in Major Depression and Parkinson's Disease
Alastair J. Flint, M.D., Sandra E. Black, M.D., Irene Campbell-Taylor, Ph.D., Gillian F. Gailey, MHSc, Irene Tamas, MHSc

NR403 EEG and Evoked Potentials in Depression
Stephen L. Stern, M.D., Michael W. Torello, Ph.D., Jeffrey A. Coffman, M.D.

NR404 Serotonergic Function in Depression
Robert N. Golden, M.D., Robert G. Ruegg, M.D., Mark H. Corrigan, M.D., John H. Gilmore, M.D., Helen L. Miller, M.D., Stanley W. Carson, Pharm.D.

NR405 WITHDRAWN

NR406 Recognition of Dysthymia in a Psychiatric Setting
Deborah B. Marin, M.D., James H. Kocsis, M.D., Winifred Lloyds, John C. Markowitz, M.D., Allen J. Frances, M.D., Gerald L. Klerman, M.D.

NR407 The Effect of Medical Ovariectomy on LLPDD
Stephanie D. Jofe, M.D., Edwin H. Cassem, M.D., David A. Schoenfeld, Ph.D., William F. Crowley, Jr., M.D.

NR408 Proposed Research Criteria for LLPDD
Stephanie D. Jofe, M.D., Edwin H. Cassem, M.D., David A. Schoenfeld, Ph.D., William F. Crowley, Jr., M.D.

NR409 Cortisol and Outcome in Depression
Anthony J. Rothschild, M.D., Alan F. Schatzberg, M.D., Jacqueline A. Samson, Ph.D., Joseph J. Schildkraut, M.D., Monica Luciana, Maureen Letson

NR410 IMP SPECT Brain Imaging in Bipolar Disorder
Laszlo Gyulai, M.D., Abass Alavi, M.D., P. David Mozley, M.D., John Reilley, CNMT, Mark S. Bauer, M.D., William A. Ball, M.D.

NR411 Noradrenergic/HPA Dysregulation in Depression
Robert L. Trestman, M.D., Martin H. Teicher, M.D., Emil F. Coccaro, M.D., David P. Bernstein, Ph.D., Steven Gabriel, Ph.D., Larry J. Siever, M.D.

NR412 Tryptophan Depletion Alters Mood in Depression
Pedro L. Delgado, M.D., Dennis S. Charney, M.D., Lawrence H. Price, M.D., George K. Aghajanian, M.D., George R. Heninger, M.D.

NR413 Serotonergic Responsivity in Major Depression
Baruch Shapira, M.D., Bernard Lerer, M.D., Pesach Lichtenberg, M.D., Seth Kindler, M.D., Avraham Calev, Ph.D.

NR414 Physiological Aspects of Emotion in Depression
Bruce E. Wexler, M.D., Lawrence H. Price, M.D., Lawrence Levenson, M.D., Stephen Warrenburg, Ph.D.

NR415 Intravenous Versus Intramuscular Atropine in ECT
Barry A. Kramer, M.D., Anoshiravan Afrasiabi, M.D., Vickie E. Pollock, Ph.D.

NR416 Demoralization Predicts Nonresponse to Cognitive Therapy
Jonathan W. Stewart, M.D., Frederic M. Quitkin, M.D., Mary Ann Mercier, Ph.D.

NR417 Phototherapy, Spectral EEG and Activity in SAD
Martin H. Teicher, M.D., Carol A. Glod, M.S., David Harper, B.S., Eleanor Magnus, B.S., Arlene F. Frank, Ph.D., Gregory Benson, B.A.

NR418 Effects of L-dopa on Mood and Eye Function in SAD
Dan A. Oren, M.D., Douglas E. Moul, M.D., Norman E. Rosenthal, M.D.

NR419 Dopaminergic Function, Oestrogen Withdrawal and Bipolar Relapse in Recently Delivered Mothers
Dr. Angelika Wieck, A.D. Hirst, M.N. Marks, T.C. Campbell, S.A. Checkley, R. Kumar,

NR420 Plasma Tranylcypromine Levels and Acute Mood Actions
Alan G. Mallinger, M.D., Michael E. Thase, M.D., Jonathan M. Himmelhoch, M.D., David J. Edwards, Ph.D., Edward Smith, M.D.

NR421 Deprenyl-Phenylalanine: Fast Relief for Depression
Hector C. Sabelli, M.D.

NR422 Speaking Rate Predicts Antidepressant Response
Samuel W. Anderson, Ph.D., Joseph Jaffe, M.D.

NR423 Platelet (3H)-Imipramine Binding in Fibromyalgia
Douglas H. Finestone, M.D., David L. Knight, B.S., Charles B. Nemeroff, M.D.

NR424 Hidden Factors in Emergency Department Chest Pain: Panic Disorder and Depression
Lawson R. Wulsin, M.D., Kevin Ying Ling, M.D., Lesley Mussio, M.D., Greg Rouan, M.D.

NR425 Sympathoadrenal Function in Mixed and Pure Mania
Alan C. Swann, M.D., Steven K. Secunda, M.D., Charles L. Bowden, M.D., Peter E. Stokes, M.D., Stephen H. Koslow, Ph.D., John M. Davis, M.D.

NR426 Side Effects in Acute Treatment of Affective Psychosis
Vincenzo R. Sanguneti, M.D., Marjorie O. Brooks, Ph.D., Neftal I. Ortiz, M.D.

NR427 Adolescent Bereavement: Post-Parental Death
Elizabeth B. Weller, M.D., Mary A. Fristad, Ph.D., Ronald A. Weller, M.D.

NR428 DST and Suicidality in Children
Ronald A. Weller, M.D., Elizabeth B. Weller, M.D., Mary A. Fristad, Ph.D., J. Hittner, B.A., Sheldon H. Preskorn, M.D.

NR429 Childhood Antecedents of Adult Depression
Richard C. Shelton, M.D., Scot E. Purdon, B.S.

NR430 Sleep Deprivation Augmentation of Antidepressants
Richard C. Shelton, M.D., Peter T. Loosen, M.D.

NR431 Old Age Depressive Pseudodementia: Three-to-Four-Year Outcome
Elisse Kramer, Ph.D., Blaine S. Greenwald, M.D.

NR432 Idazoxan in Treatment-Resistant Bipolar Depression
Ossama T. Osman, M.D., Matthew V. Rudorfer, M.D., Husseini K. Manji, M.D., Fred Grossman, D.O., William Z. Potter, M.D.

NR433 Life Events and Familial Subtypes of Depression
Jose L. Ayuso-Gutierrez, M.D., Rosa Yanez, M.D., Jose Delgado, M.D., Elena Ezquiaga, M.D., Jose L. Ayuso Mateos, M.D.

NR434 Fluoxetine Test Versus (3H)-Imipramine Binding in Depression
Jose L. Ayuso-Gutierrez, M.D., Olga Borrego, M.D., Jose V. Baeza, M.D., Ana Barabash, M.D., Jose A. Cabranes, M.D., Maribel B. Cebeira

NR435 Predictors of Response to ECT in Manic Patients
David B. Schnur, M.D., Sukdeb Mukherjee, M.D., Carl Lee, M.D., Steven Roth, M.D., Harold A. Sackeim, Ph.D., Haranath Parepally, M.D.

NR436 CSF Somatostatin CRH and ACTH in Alcoholics
Alec Roy, M.D., Bryon Adinoff, M.D., Philip W. Gold, M.D., Judith DeJong, Ph.D., David R. Rubinow, M.D., Markku I. Linnoila, M.D.

NR437 Etomidate Versus Methohexital for Anesthesia in ECT
Anthony L. Kovac, M.D., Manuel P. Pardo, M.D., Maryanne Butterfield, M.D.

NR438 Diagnosis, Treatment and Outcome in Refractory Depression
Arnold L. Lieber, M.D., Nancy D. Newbury, M.S.N.

NR439 Treatment of Psychotic Depression Subtypes
Raymond F. Anton, M.D., Earl A. Burch, M.D.

NR440 GH Response to Clonidine and Insulin in Depression
Jay D. Amsterdam, M.D., Greg Maislin, M.S., Jennifer Phillips, B.S., Andrew Winokur, M.D.

NR441 Effect of Labetalol on Hemodynamics and Seizure Duration During ECT
Vaughn W. McCall, M.D., Frank E. Shelp, M.D., Richard D. Weiner, M.D., Shirley Austin, R.N., Audrey Harril, R.N., Eric Moffet, M.D.

NR442 Buspirone Augmentation of Antidepressant Response
Frederick M. Jacobsen, M.D.

NR443 Combined Thyroid Hormone and ECT Treatment
Robert A. Stern, Ph.D., Charles T. Nevels, M.D., Mark E. Shelhourse, M.D., Mark L. Prohaska, Arthur J. Prange, Jr., M.D.

NR444 Antidepressants for Mild Depressives
Frederic M. Quitkin, M.D., Jonathan W. Stewart, M.D., Wilma Harrison, M.D., Edward V. Nunes, M.D., Steven Wager, M.D., Patrick J. McGrath, M.D.

NR445 Neuroleptic Adjuncts in the Emergency Treatment of Schizophrenia
James G. Barbee, M.D., Donna M. Mancuso, M.D., Charles R. Freed, M.D.

NR446 Genetic Study of Lithium Response: Analysis of the Mode of Inheritance
Martin Alda, M.D., Paul Grof, M.D., Eva Grof, M.D., Peter Zvolsky, M.D., Mary Walsh, M.S.W.

NR447 Oral S-Adenosylmethionine Versus DMI in Depression
Kate M. Bell, M.D., Steven G. Potkin, M.D.

NR448 Nicotine Potentiates Haloperidol in Tourette Cases
Brian J. McConville, M.D., Andrew B. Norman, Ph.D., Harold M. Fogelson, M.D., W.M. Klykylo, M.D., P.Z. Manderscheid, P.R. Sandberg, Ph.D.

NR449 WITHDRAWN

NR450 Coexistence of Neuroleptic-Induced Parkinsonism and Acute Dystonic Reaction
Patricia I. Rosebush, M.D., Michael Mazurek, M.D., Wendy Hiscox, R.N.

NR451 Alprazolam Versus Clonazepam: Interdose Rebound?
Anthony Kales, M.D., Joyce D. Kales, M.D., Eric C. Fee, B.A., Claudia F. Baldassano, B.A., Kathy L. Tyson, B.S., Errol M. Aksu, M.D.

NR452 Winter Depression Response to Tranylcypromine
Steven C. Dilsaver, M.D.

NR453 Optimising ECT Schedule: A Double Blind Study
Bernard Lerer, M.D., Baruch Shapira, M.D., Avraham Calev, Ph.D., Seth Kindler, M.D., Pesach Lichtenberg, M.D., Heinz Drexler, M.D.

NR454 Rapid Antidepressant Effect of Desipramine Plus Fluoxtine
J. Craig Nelson, M.D., Carolyn M. Mazure, Ph.D., Malcolm B. Bowers, M.D., Peter I. Jatlow, M.D.

NR455 Estazolam Treatment of Insomnia with Anxiety
John E. Crowder, M.D., Gary L. Post, M.D., John P. Houston, M.D., James M. Ferguson, M.D., Vincent S. Shu, Ph.D., Mark W. Pierce, M.D.

NR456 Placebo Side Effects in Depression and OCD
Hugh Johnston, M.D., Kenneth A. Kobak, M.S.W., John H. Greist, M.D.

NR457 Use of Carbamazepine in a State Hospital
Paul Barreira, M.D., Bruce Gaulin, M.S., Joseph Tonkonogy, M.D., Paul Sorgi, M.D.

NR458 Drug Responsive Symptoms in Acute Psychosis
Carolyn M. Mazure, Ph.D., J. Craig Nelson, M.D., Peter I. Jatlow, M.D., Malcolm B. Bowers, Jr., M.D.

NR459 Effect of Chronic Neuroleptic Treatment on Dopamine D2 Receptor MRNA and Binding
Patrick J. Rogue, M.D., Jean Zwiller, Ph.D., Emiliana Sassone-Corsi, Ph.D., Andre Hanauer, M.D., Jean-Louis Mandel, M.D., Guy Vincendon, M.D.

NR460 Pindolol to Treat Aggression in the Mentally Retarded
Karen J. Lindem, B.S., James Fletcher, M.D., Miriam Blumenkrantz, John J. Ratey, M.D.

NR461 Buspirone for Aggression in the Mentally Retarded
John J. Ratey, M.D., Robert Sovner, M.D., Kristen L. Rogentine, Karen J. Lindem, B.S.

NR462 Risk Factors for Anabolic Steroid Use in Men
Kirk J. Brower, M.D., Frederic C. Blow, Ph.D., Elizabeth Hill, Ph.D.

NR463 Incidence of Neuroleptic Malignant Syndrome
Haggai Hermesh, M.D., Dov Aizenberb, M.D., Catherine Mayor, M.D., Hanan Munitz, M.B.

NR464 Prospective Long-Term Follow-Up of Depressives with and without Suicide Attempts
Thomas Bronisch, M.D.

NR465 Serotonin S2 Receptors in Schizophrenia
Joel E. Kleinman, M.D., Marc Laruelle, M.D., Manuel F. Casanova, M.D., Daniel R. Weinberger, M.D., Susan Camparini, M.D., Rosanne Toti

NR466 Prediction of Suicide in 1,906 Psychiatric Inpatients
Donald W. Black, M.D., Rise Goldstein, M.S.W., Amelia Nasrallah, M.A., George Winokur, M.D.

NR467 Disturbed Serotonergic Lateralization in Suicide
Mihaly Arato, M.D., Kornelia Tekes, Ph.D., Ede Frecska, M.D., Laszlo Tothfalusi, Ph.D., Miklos Palkovits, M.D., Duncan MacCrimmon, M.D.

NR468 Serotonin-2 Receptors in Depression and Suicide
Ghanshyam N. Pandey, Ph.D., Subash Pandey, Ph.D., Philip G. Janicak, M.D., Robert Marks, M.D., John M. Davis, M.D.

NR469 Causes of Repetition of Suicide Attempts
Isaac Sakinofsky, M.D., Robin S. Roberts, M.Tech., Yvonne Brown, M.A., Carmen Cumming, B.A., Patricia James, M.A.

NR470 Aggressive and Self-Destructive Behavior
Harold A. Carmel, M.D., Mel Hunter, M.P.A.

NR471 Personality Disorders and Suicidal Behavior in the U.S. Navy Servicemen
Stanley W. Raczek, M.D.

NR472 Clinical Correlates of Suicidality in Schizophrenia
Gretchen L. Haas, Ph.D., John A. Sweeney, Ph.D., Denise A. Hien, M.S., Dodi Goldman, M.A., J. John Mann, M.D.

NR473 Brain 3H-Paroxetine Binding in Depressed Suicides
Cornelius L. Katona, M.B., Kevin M. Lawrence, M.Sc., Freddy De Paermentier, Ph.D., Sharon C. Cheetham, Ph.D., Rufus M. Crompton, M.D., Roger W. Horton, Ph.D.

NR474 Suicide and Diagnostic Practice in Hungary
Cornelius L. Katona, M.B., Toltan Rihmer, M.D., Judit Barsi, M.D., Katlin Veg, M.D.

NR475 Suicidality and Fluoxetine: Is There A Relationship?
Maurizio Fava, M.D., Jerrold F. Rosenbaum, M.D.

NEW RESEARCH

Wednesday, May 16, 1990, 3:00 p.m.-5:00 p.m.

New Research 11—Poster Session—Westside Ballroom North/Center, Fifth Floor, Marriott Marquis

PERSONALITY, SUBSTANCE ABUSE AND EATING DISORDERS, AND PSYCHOTHERAPY AND DIAGNOSTIC ISSUES

Moderator: James W. Thompson, M.D.

NR476 ECT Emergence Agitation and Succinylcholine Dose
Conrad M. Swartz, M.D.

NR477 Post-Traumatic Distress Among Burn Victims
Robert P. Roca, M.D., Linda Rice, Ph.D., Elizabeth Eaton

NR478 Yohimbine in PTSD
Steven M. Southwick, M.D., John H. Krystal, M.D., Dennis S. Charney, M.D.

NR479 Antidepressant Treatment of PTSD: A Meta-Analysis
Steven M. Southwick, M.D., Rachel Yehuda, Ph.D., Earl L. Giller, Jr., M.D., Dennis S. Charney, M.D.

NR480 DSM-III and DSM-III-R: Who is Using Them and Why?
V. Chowdary Jampala, M.B., Mark Zimmerman, B.A., Frederick Sierles, M.D., Michael A. Taylor, M.D.

NR481 DSM-IV: A Nosology Sold Before Its Time?
Mark Zimmerman, B.A., V. Choudary Jampala, M.D., Frederick Sierles, M.D., Michael A. Taylor, M.D.

NR482 Two-Tier Diagnostic System for Psychotic Disorders
Stanley R. Kay, Ph.D., Abraham Fiszbein, M.D., Amy Gorelick, M.D., Lewis A. Opler, M.D., Robert L. Spitzer, M.D., Janet B.W. Williams, D.S.W., Miriam Gibbon, M.S.W., Michael B. First, M.D.

NR483 An Artificial Intelligence Emotion Profiler
David A. S. Garfield, M.D., Charles Rapp, M.A., Martha Evens, Ph.D.

NR484 Speech Analysis in Turkish Speaking Subjects
Levent Mete, M.D., Paula P. Schnurr, Ph.D., Thomas E. Oxman, M.D., Stanley D. Rosenberg, Ph.D., Inci Doganer, M.D., Soli Sorias, M.D.

NR485 One-Thousand Borderlines: A Study in Comorbidity
Armand W. Loranger, Ph.D.

NR486 Detecting Dissociative Disorders: A Comparison of a Screening Instrument and a Structured Diagnostic Interview
Marlene Steinberg, M.D., Bruce J. Rounsaville, M.D., Domenic V. Cicchetti, Ph.D.

NR487 Antisocial Diagnosis: Relation to Adult Behavior
Robert K. Brooner, Ph.D., George E. Bigelow, Ph.D., Chester W. Schmidt, Jr., M.D.

NR488 Course of Illness and Multiaxial Diagnosis
Miguel R. Jorge, M.D., Juan E. Mezzich, M.D.

NR489 Subtyping Aggression in Mental Retardation
Joyce E. Mauk, M.D., David Behar, M.D.

NR490 Assessing the Elements of Psychosocial Functioning
Richard E. Gordon, M.D., Katherine Gordon, M.A.

NR491 Depression Masquerading as Partial Complex Seisure
Rajesh Sachdeo, M.D., Sudhansu Chokroverty, M.D.

NR492 Psychiatric Comorbidity in Eating Disorders
Victor Fornari, M.D., David E. Sandberg, Ph.D., Michael Matthews, C.S.W., Gerardo Montero, M.D., Myra Kaplan, M.A., Jack L. Katz, M.D.

NR493 Seasonal Mood Patterns in Bulimia and SAD
Raymond W. Lam, M.D., Leslie Solyom, M.D., Arlene Tompkins, M.S.C.

NR494 CSF Beta-Endorphin Decreased in Abstinent Bulimics
Harry E. Gwirtsman, M.D., Walter H. Kaye, M.D., Wade H. Berrettini, M.D., David T. George, M.D., David C. Jimerson, M.D., Philip W. Gold, M.D.

NR495 Bulimia Nervosa Treatment and Borderline Symptoms
Richard L. Pyle, M.D., James E. Mitchell, M.D.

NR496 Increased 5-HT-1A Receptors in the Hippocampus of Obese Zucker Rats: Possible Significance to Feeding Behavior
Susan Delanty, A.B.D., Serge Przedborski, M.D., Robin Marks-Kaufman, Ph.D., Jean L. Cadet, M.D.

NR497 Fluoxetine Improves Outcome in Anorexia Nervosa
Theodore E. Weltzin, M.D., Walter H. Kaye, M.D., L.K. George Hsu, M.D., Theresa Sobkiewicz, M.S.W.

NR498 Caloric Needs and Metabolism in Eating Disorders
Theodore E. Weltzin, M.D., Walter H. Kaye, M.D., Madelyn H. Ferstrom, Ph.D., Donna Hansen, M.A., Claire McConaha, R.N.

NR499 New Evidence Links Anorexia Nervosa to OCD
Walter H. Kaye, M.D., Theodore E. Weltzin, M.D., L.K. George Hsu, M.D., Theresa Sobkiewicz, M.S.W.

NR500 Prediction of Treatment Noncompletion in Bulimia
Allan S. Kaplan, M.D., Marion P. Olmsted, Ph.D., D. Blake Woodside, M.D., Sarah Maddocks, Ph.D.

NR501 Psychopathology and Outcome Prediction in Anorexia
Edward J. Schork, Ph.D., Katherine A. Halmi, M.D., Elke D. Eckert, M.D.

NR502 Obesity: Clinical and Sleep Lab Correlates
Tjiauw-Ling Tan, M.D., Joyce D. Kales, M.D., Kelly Slaybaugh, M.D., Thomas P. Kobylski, M.D., Duane D. Shubert, M.D., Donald P. Masey, M.S.

NR503 Serotonergic Responsivity in Anorexia Nervosa
P. Anne McBride, M.D., George M. Anderson, Jodi Marinacci, B.A., Shelley Berger-Mitnick, B.A., Katherine A. Halmi, M.D.

NR504 Low CSF Immunoreactive-TRH Levels in Anorexia
Michael D. Lesem, M.D., Walter H. Kaye, M.D., Garth Bissette, M.D., David C. Jimerson, M.D., Charles B. Nemeroff, M.D.

NR505 CSF Quinolinic Acid Levels in Anorexia Nervosa
Mark A. Demitrack, M.D., Melvyn P. Heyes, Ph.D., Margaret Altemus, M.D., Teresa A. Pigott, M.D., Dean D. Krahn, M.D., Blake A. Gosnell, Ph.D., Philip W. Gold, M.D.

NR506 Psychotherapy Operations as Predictors of Outcome
Dan A. Giacomo, M.D., Mona S. Weissmark, Ph.D.

NR507 Somatization and Patterning of Family Behavior
James L. Griffith, M.D., Edward Meydrech, M.D., Melissa E. Griffith, M.S.N.

NR508 Family Satisfaction and Abnormal Illness Behavior
James L. Griffith, M.D., Janette Seville, M.A., Edward Meydrech, M.D., Melissa E. Griffith, M.S.N.

NR509 Nonmedical Management of Premenstrual Syndrome
Teri Pearlstein, M.D., Ellen Frank, Ph.D., Ana Rivera-Tovar, Ph.D.

NR510 Expressed Emotion in Families of Dementia Patients
Daniel J. Luchins, M.D., Patricia L. Hanrahan, M.A., Mary Mathews, B.A., Sant Singh, M.A.

NR511 Validity of the Categorical Structure and Clustering of DSM-III-R Personality Disorders
Wim van den Brink, M.D., Cor J.A. De Jong, M.D.

NR512 Psychotherapy and Buspirone in Borderline Patients
Michael Wolf, M.D., Thomas Grayden, M.D., Danilo Carreon, M.D., Martin Cosgro, M.A., Donald Summers, M.D., Ron Leino, M.D., Jay Goldstein, M.D., Steven G. Potkin, M.D.

NR513 Axis II Psychopathology in Combat PTSD
Rachel Yehuda, Ph.D., Steven M. Southwick, M.D., Earl L. Giller, Jr., M.D.

NR514 BPD/NPD Comorbidity: Longitudinal Course and Outcome
Eric M. Plakun, M.D.

NR515 Axis II Comorbidity of Borderline Personality Disorder
H. George Nurnberg, M.D., Philip E. Levine, M.D., Marjorie Raskin, M.D., Ozzie Siegel, Ph.D., Robert Prince, Ph.D., Simcha Pollack, Ph.D.

NR516 Antisocial Personality and Event Related Potentials
Sean J. O'Connor, M.D., Victor Hesselbrock, Ph.D., Allan Tasman, M.D.

NR517 Platelet MAO Activity in Personality Disorders
Christopher Reist, M.D., Richard J. Haier, Ph.D., Edward DeMet, Ph.D., Aleksandra Chicz-DeMet, Ph.D.

NR518 Treatment of Panic: The Role of Personality
Eve D. Richer, Ph.D., Laszlo A. Papp, M.D., Charolette Zitrin, M.D., Evelyn Abeshouse, M.A., Jack M. Gorman, M.D.

NR519 Premature Termination in Working with Borderlines
Renate Forssmann-Falck, M.D.

NR520 Cognitive Therapy with Depressed Inpatients
Michael E. Thase, M.D.

NR521 Dopamine, HVA and Early Neuroleptic Response
David L. Garver, M.D., Jeffrey K. Yao, Ph.D., Daniel P. Van Kammen, M.D.

NR522 Group Intervention and Self-Esteem: Women's Issues
Robert A. Prehn, Ph.D., Patricia Thomas, R.N.

NR523 WITHDRAWN

NR524 Factors Influencing Adoption of a Skills Training Program for the Mentally Ill
Sally J. MacKain, Ph.D., Charles J. Wallace, Ph.D.

NR525 Inpatient Treatment of Mentally Ill College Students
Xavior Mastrianni, M.D., Frances L. Hoffman, Ph.D.

NR526 Effects of Brief Hospitalization on Several Dimensions of Patient Functioning
Paul B. Lieberman, M.D., Elise Egerter, M.D., Susan Von Rehn, A.N.C., Ellen Dickie, B.A., Binette Elliott, B.A., Peter Mills, Ph.D., Paul Compton, M.D.

NR527 Length of Stay in Private Psychiatric Hospitals
Stephen B. Shanfield, M.D.

NR528 Brain Edema After Electrically Induced Seizures
Tom G. Bolwig, M.D., Annette Gjerris, M.D., Henning Laursen, M.D., David I. Barry, B.Sc.

NR529 Acute Abstinence Syndrome in Male Cocaine Addicts
William W. Weddington, M.D., Barry S. Brown, Ph.D., Charles A. Haertzen, Ph.D., Edward J. Cone, Ph.D., Elizabeth M. Dax, M.D., Ronald I. Herning, Ph.D.

NR530 Affect Disorders in Substance Abusing Adolescents
David L. Pogge, Ph.D., John Stokes, Ph.D., Sheila A. Cooperman, M.D., Philip D. Harvey, Ph.D.

NR531 Prenatal Cocaine Alters u-Opiate Receptor Binding
Ronald P. Hammer, Jr., Ph.D., Daniel W. Clow, Ph.D., Linda P. Spear, Ph.D., Cheryl L. Kirstein, Ph.D.

NR532 Fluoxetine in Cocaine Abuse: Drug and Psychiatric Outcome
Steven L. Batki, M.D., Luisa B. Manfredi, B.A., James Sorensen, Ph.D., Roland Dumontet, Reese T. Jones, M.D.

NR533 Prediction of Alcohol Detoxification Outcome
James A. Wilcox, D.O.

NR534 Carbamazepine for Benzodiazepine Withdrawal
Richard K. Ries, M.D.

NR535 Diagnosing Alcoholism in Psychiatric Patients
Burns Woodward, M.D., Jeffrey Fortgang, Ph.D., Maureen Sullivan-Trainor, E.D.M., Helen Stojanov, Steve M. Mirin, M.D.

NR536 Persistent Cognitive Effects of Prolonged Cocaine Use
Michael Sherer, M.D., Louis M. French, M.A., Allan F. Mirsky, Ph.D.

NR537 Management of Problematic Benzodiazepine Use
Joy M. Schmitz, Ph.D., Eileen McGorry, R.N., Melinda A. Stanley, Ph.D., Daniel L. Creson, M.D., John Grabowski, Ph.D.

NR538 Axis II and Substance Abuse in Eating Disorders
Michael Newman, M.D., Michele Lemaire, M.D., Mark S. Gold, M.D.

NR539 The 1990 Crack User: Consequences of Daily Crack
Mark S. Gold, M.D.

NR540 Drug Testing False Negative Rate by NIDA Criteria
Magnus Lakovics, M.D., David Martin, Ph.D.

NR541 A 5-HT1A Treatment of Comorbid Anxiety and Alcoholism
Gary D. Tollefson, M.D., Jon Montague-Clouse, M.S., Sherrie L. Lancaster, R.N.

NR542 Serotonergic Abnormality in Alcoholism
Myung A. Lee, M.D., Herbert Y. Meltzer, M.D.

NR543 The Case Study: 2. When is an Alcoholic an Alcoholic?
Thomas P. Beresford, M.D., Frederic C. Blow, Ph.D., Elizabeth Hill, Ph.D., Kathleen M. Singer, R.N.

NR544 Benzodiazepine Selection by Substance Abusers
Robert J. Malcolm, M.D., Amanda Johnston, Ph.D., Kathleen T. Brady, M.D., Malcolm Cunningham, M.D.

NR545 Smoking Cessation on an in Patient Unit
Jeffrey M. Jonas, M.D., Jeff Eagle, Ph.D., Allyson McClave, B.S., Nancy Smith, M.S., Alice Zimmerman, M.Ed.

NR546 Nicotine Dependence, Nicotine Gum and Brief Treatment
Michael G. Goldstein, M.D., Raymond S. Niaura, Ph.D., David B. Abrams, Ph.D., Cheryl A. Eaton, B.A.

NR547 Smoking Cessation, Nicotine Dependence and Clonidine
Lirio S. Covey, Ph.D., Alexander H. Glassman, M.D., Fay Stetner, M.S., Gregory W. Dalack, M.D.

NR548 Interaction of Alcohol with Immune Cells
Mariano V. Tolentino, Jr., M.D., Martha Sarasua, M.D., Suio-Ling Chen, Ph.D.

NR549 Profiles of Hospitalized Benzodiazepine Abusers
Kathleen T. Brady, M.D., Amanda Johnston, Ph.D., Robert J. Malcolm, M.D., Malcolm Cunningham, M.D.

NR550 Discriminant Function EEG Analyses of THC Abusers
John J. Straumanis, M.D., Frederick A. Struve, Ph.D., Yoram Raz, M.A., Gloria Patrick, M.S.

NR551 Clinical Neurobiology of Cocaine Withdrawal
Christopher J. McDougle, M.D., Lawrence H. Price, M.D., Joseph Palumbo, M.D., Thomas R. Kosten, M.D., Herbert D. Kleber, M.D., George R. Heninger, M.D.

NR552 Naloxone-Precipitated Opioid Withdrawal
Philip D. Kanof, M.D., Leonard Handelsman, M.D., Marvin J. Aronson, Ph.D., Robert C. Ness, Ph.D., Karen J. Rubinstein, M.A., Kenneth J. Cochrane, Ph.D.

NR553 Seasonal Change of Melatonin Rhythm in Alcoholics
Anil K. Jain, M.D., Surendra Kelwala, M.D., Jan Campbell, M.D., Barbara Powell, Ph.D., Sailaja Yerasi, M.D., Sleman Khoury, M.D.

NR554 Effect of Combined Substance Use on Laboratory Markers of Alcoholism
Michael Chang, M.D., Jungwha Kwon, M.D., Roger S. Hamada, Ph.D., Paul Yahiku, Ph.D.

NR555 Automated Group Therapy Scores as a Predictor of Alcoholism Treatment Attendance
Michael Chang, M.D.

NR556 Amantadine Treatment of Cocaine Withdrawal
Marian P. Droba, M.D., Arthur I. Alterman, Ph.D., Charles P. O'Brien, M.D., Karen A. Sweeney, PA.C

NR557 Neurobiological Response to Alcohol and Alcohol Consumption in Socially Separated Rhesus Monkeys
Gary W. Kraemer, Ph.D., Michael H. Ebert, M.D., Dennis E. Schmidt, Ph.D.

NR558 Who Completes Residential Addictions Programs?
Lionel P. Solursh, M.D., Robert C. Ness, Ph.D., William Nolan, Ph.D., Lois Cecil, M.A., Mary A. Forney, Ed.D.

NR559 Cocaine and Hospital Course in Schizophrenia
John P. Seibyl, M.D., Sally Satel, M.D., Dominic Anthony, M.S.W, Steven M. Southwick, M.D., Rajani Nadkarni, M.D., William Giakas, M.D., Robert Malison, M.D., Dennis S. Charney, M.D., John H. Krystal, M.D.

NR560 Excitatory Amino Acid Antagonist for Opiate Withdrawal
John H. Krystal, M.D., Kurt R. Rasmussen, Ph.D., George K. Aghajanian, M.D.

NR561 Cocaine Abuse: Changes in Axis II with Treatment
Helen M. Pettinati, Ph.D., Bradley D. Evans, M.D., Jacqueline Jensen, M.A., Kathleen Meyers, M.S., Veronique Valliere, B.A., Ayshe B. Ergin, M.S.

NR562 Troubled Doctors: A New Survey of Medical Board Actions
Norma Josef, M.D., R. John Kinkel, Ph.D.

NR563 Effects of Withdrawal Stress on Tricyclic Therapy
Joseph A. Kwentus, M.D., William A. Kehoe, Pharm.D., Arthur F. Harralson, Pharm.D., William B. Sheffel, M.A.

NR564 Treatment Needs of Psychiatrically Ill Alcoholics
Barbara J. Mason, Ph.D., James H. Kocsis, M.D.

NR565 Neurolectric Changes in Acute Cocaine Intoxication
Allan Tasman, M.D., Sean J. O'Connor, M.D., Nancy Kluck, M.S.

Thursday, May 17, 1990, 9:00 a.m.-10:30 a.m.

New Research 12—Oral/Slide Session—Rooms D3/D4, Level 1, Javits Center

ORGANIC MENTAL DISORDERS AND AIDS

Chp.: Marvin Stein, M.D.

NR566 HIV Seroprevalence and Risk in Psychiatric Patients — 9:00 a.m.
Michael H. Sacks, M.D., Helen Dermatis, Ph.D., Salome Looser-Ott, M.A., Samuel W. Perry III, M.D.

NR567 Cognitive Impairment in HIV Infected Hemophiliacs — 9:15 a.m.
Netta Horesh, Ph.D., Elie Lepkifker, M.D., Sigmond Sancovici, M.D., David Varon, M.D., Suzy Floru, M.D., Uri Martinowitz, M.D.

NR568 Analysis of P3 Latencies in AIDS Dementia — 9:30 a.m.
Leonard Handelsman, M.D., Marvin J. Aronson, Ph.D., Thomas B. Horvath, M.D., Ann Peterson, M.S., Jeffrey Jacobson, M.D., Robert Ness, Ph.D.

NR569 SPECT Brain Imaging of HIV Patients with HMPAO — 9:45 a.m.
Scott W. Woods, M.D., Stephanie O'Malley, Ph.D., Lawrence H. Price, M.D., Christopher J. McDougle, M.D., Paul B. Hoffer, M.D., Thomas R. Kosten, M.D.

NR570 Neuroanatomical Abnormalities in Late Onset Depression — 10:00 a.m.
Anand Kumar, M.D., David Yousem, M.D., Gary Gottlieb, M.D.

NR571 Postural Hypotension and Cholinergic Therapy in Alzheimer's Disease — 10:15 a.m.
Nunzio Pomara, M.D., Dennis Deptula, Ph.D., Rajkumar R. Singh, Philip A. De Simone, Ph.D.

Thursday, May 17, 1990, 9:00 a.m.-10:30 a.m.

New Research 13—Oral/Slide Session—Rooms D5/D6, Level 1, Javits Center

CHILDHOOD DISORDERS

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

NR572 Increasing Rate of Depression in Youth — 9:00 a.m.
Neal D. Ryan, M.D., Douglas Williamson, B.S., Joaquim Puig-Antich, M.D., Satish Iyengar, Ph.D.

NR573 Children's Grief During First Year Post-Parental Death — 9:15 a.m.
Elizabeth B. Weller, M.D., Beth Grosshans, M.A., Mary A. Fristad, Ph.D., Ronald A. Weller, M.D.

NR574 Children's Responses to the Challenger Disaster — 9:30 a.m.
Lenore C. Terr, M.D., Daniel Bloch, Ph.D., Michael Beat, M.D., John Reinhart, Ph.D., Suzanne Matayer

NR575 Psychosis and Suicidal Behavior in Children — 9:45 a.m.
Richard Livingston, M.D.

NR576 Specificity of a Biological Marker for Temperament 10:00 a.m.
Michel Maziade, M.D., Louise Theriault, Ph.D., Robert Cote, Ph.D., Chantal Merette, Ph.D., Hughues Bernier, M.Ss., Georges LeBlond, Ph.D.

NR577 Sub-Cortical Abnormalities in Autism 10:15 a.m.
Jacques Thivierge, M.D., Robert Cote, Ph.D., Michel Maziade, M.D.

NEW RESEARCH

Thursday, May 17, 1990, 12:00 noon-2:00 p.m.

New Research 14—Poster Session—Westside Ballroom North/Center, Fifth Floor, Marriott Marquis

ORGANIC MENTAL DISORDERS, AIDS, CHILDHOOD DISORDERS AND CONSULTATION/LIAISON PSYCHIATRY

Moderator: Fred R. Volkmar, M.D.

NR578 Noncompliance of Patients Hospitalized with AIDS
Michael Blumenfield, M.D., Jane Milazzo, R.N., Gary Wormser, M.D.

NR579 Reactions by Cocaine Addicts to HIV-Serostatus
William W. Weddington, M.D., Charles A. Haertzen, Ph.D., Judith M. Hess, M.A., Barry S. Brown, Ph.D.

NR580 Buspirone Treatment for Anxiety in HIV Infection
Dan Alan Hirsch, Ph.D., Joanne Fishman, Ph.D., William Breitbart, M.D., Maurice Emery, D.Pharm., Jeffrey Schwimmer, M.D.

NR581 Fluoxetine Treatment for AIDS Related Depression
Daniel L. Creson, M.D., Eileen McGorry, R.N., John D. Roache, Ph.D., Melinda A. Stanley, Ph.D., Germaine B. Welch, M.A.

NR582 Effect of Psychoeducation After HIV Testing
Baruch Fishman, Ph.D.

NR583 Effect of HIV Testing on Homosexual Risk Behaviors
Lawrence B. Jacobsberg, M.D.

NR584 Psychosoical Variables and CD 4 Cells in HIV + Adults
Samuel W. Perry III, M.D.

NR585 Depressive Symptoms After HIV Antibody Testing
Allen J. Frances, M.D.

NR586 Neuroleptic-Induced EPS in Patients with AIDS Encephalopathy
Emmanuel Hriso, M.D., Thomas Kuhn, M.D., Joseph C. Masdeu, M.D., Michael Grundman, M.D.

NR587 Incidence of Psychiatric Disorder in HIV Infection
J. Hampton Atkinson, M.D., Igor Grant, M.D., Rosben L. Gutierrez, M.D., Stephen J. Brown, M.D., Pamela Pace, M.S., James R. Weinrich, Ph.D.

NR588 Quantitative SPECT in AIDS Dementia
Gordon J. Harris, M.S., Godfrey D. Pearlson, M.D., Frederick Schaerf, M.D., Justin C. McArthur, M.D., Edwaldo E. Camargo, M.D., Jonathan M. Links, Ph.D., Norman D. LaFrance, M.D.

NR589 P3 as a Marker of Cognitive Change in HIV Dementia
Leonard Handelsman, M.D., Marvin J. Aronson, Ph.D., Thomas B. Horvath, M.D., Ann Peterson, M.S., Karen Holloway, M.D., Jill Wiener, M.D.

NR590 Male Prostitutes as a Vector for HIV to Heterosexuals
Paul M. Balson, M.D., Howard J. Ossofsky, M.D., Edward V. Morse, Ph.D., Patricia M. Simon, M.S.W.

NR591 Which Role Plays Drug Use on the Mental State of HIV Patients?
Georg Pakesch, M.D., Norbert Loimer, M.D., Dorothea Pfersmann, M.D., Josef Grunberger, M.D., Klaus Guggenberger, M.D.

NR592 HIV Risk and Cocaine Use in Alcoholic Inpatients
John C. Mahler, M.D., Donna Yi, M.D., Helen Dermatis, Ph.D., Michael H. Sacks, M.D.

NR593 Dementia and Mood Disorder in HIV+ Gay Men
Robert A. Bornstein, Ph.D., Henry A. Nasrallah, M.D., Patricia Rosenberger, Ph.D., Michael Para, M.D., Robert Fass, M.D.

NR594 Self-Defeating Pattern Analysis in Focused Therapy
Jody Lanard, M.D., J. Christopher Perry, M.D.

NR595 Psychiatric Morbidity in AIDS Medical Inpatients
Stephen Snyder, M.D., Andrew Reyner, M.D., Eileen Bogursky, Henry Gomez, James J. Strain, M.D.

NR596 SCID Diagnosis in Psychogenic Seizure Patients
Stephen Snyder, M.D., James Rowan, M.D., David Rosenbaum, M.D., Daniel Luciano, M.D., Robin Fein, M.S.W.

NR597 PTSD and HIV Infection
Brian J. Kelly, M.D., Beverley Raphael, M.D., Anna Zournazi, B.Sc., Michael Dunne, B.Sc.

NR598 WITHDRAWN

NR599 Methylphenidate Therapy of Aggressive Adolescents
Stuart L. Kaplan, M.D., Joan Busner, Ph.D., Samuel Kupietz, Ph.D., Evelyn Wasserman, M.D., Boris Segal, M.D.

NR600 The Empirical Study of Defense and Coping in Preschoolers
Michael P. Bond, M.D., Margaret Schibuk, M.D., Rachelle Bouffard, M.D.

NR601 Effectiveness of Day Treatment for Children
Natalie Grizenko, M.D., Liliane Sayegh, M.Ed.

NR602 Interpersonal Problems in Adult Children of Divorce
Robert A. Bolgar, M.D., Hallie Frank, Ph.D., Joel Paris, M.D.

NR603 Borderline Personality Disorder in Adolescence
William L. Grapentine, M.D., C. Picariello

NR604 Cross-Cultural Adjustment of Japanese Children
Hisako M. Koizumi, M.D., Jennifer Farkas, Ph.D., Tetsunori Koizumi, Ph.D.

NR605 Quality of Care Problems in an OCHAMPUS Project
William Sonis, M.D., Jeffrey Berlant, M.D., Cynthia Tudor, Ph.D., Margaret Keyes, M.A.

NR606 Adolescent AIDS Risk: A Hospital Survey
Dewleen G. Baker, M.D., Douglas Mossman, M.D.

NR607 Childhood Psychiatric Status and Criminality
Michael S. Lundy, M.D., Bruce M. Pfohl, M.D., Samuel Kuberman, M.D.

NR608 Panic Attacks in Sixth and Seventh Grade Girls
Chris R. Hayward, M.D., Joel D. Killen, Ph.D., C. Barr Taylor, M.D., Larry Hammer, M.D., Iris Litt, M.D., Darrell Wilson, M.D.

NR609 Consultation/Liaison Psychiatry: Concordance with Recommendations
Graeme C. Smith, M.D., Louise N. Seward, M.D., Geoffrey W. Stuart, Ph.D.

NR610 Dual Diagnosis in Somatoform Pain Disorder
Peter B. Polatin, M.D., Regina K. Kinney, B.A., Robert J. Gatchel, Ph.D.

NR611 Depression and Recent Diagnosis of Leprosy
Mitchell G. Weiss, M.D., Dinsha R. Doongaji, M.D., Ashit Sheth, M.D., Ruis Fernandes, M.D., Sanjay Siddharth, M.B., My Acharekar, M.D.

NR612 Psychological Comorbidity and Increased Length of Stay
Stephen M. Saravay, M.D., Barbara Weinschel, Ph.D., Simcha Pollack, Ph.D., Nancy Alovis, Ph.D., Robert A. Stern, M.D., Robin Horwitz, M.D.

NR613 Stress, Heart Rate Variability and Heart Transplantation
Richard P. Sloan, Ph.D., Peter A. Shapiro, M.D., Jack M. Gorman, M.D., Jerome B. Korten, M.S., Michael M. Myers, Ph.D.

NR614 Substance Use Disorders in Chronic Fatigue Patients
Henry R. Kranzler, M.D., Victor Hesselbrock, Ph.D., Peter Manu, M.D., Thomas J. Lane, M.D., Dale A. Matthews, M.D.

NR615 The Effects of Deferral Legislation Upon Treatment Acceptance
Dale A. D'Mello, M.D., Michael Bowden, A.C.S.W., Beverly Anderson, Msibi Bhekumusa, B.A., Kevin R. Bowman, B.S.

NR616 Delirum During Intraaortic Balloon Pump Therapy: Incidence and Management
Kathy M. Sanders, M.D., Theodore A. Stern, M.D., Patrick T. O'Gara, M.D., Terry S. Field, M.P.H., Scott L. Rauch, M.D., Rachel E. Lipson, M.D., Kim A. Eagle, M.D.

NR617 Neural Networks in Psychiatric Decisionmaking
Eugene C. Somoza, M.D., John Somoza, B.S.

NR618 The Violent Psychiatric Emergency
Kimberly A. White, M.D., James C. Beck, M.D., Bruce C. Gage, M.D.

NR619 More on ECT and Parkinson's Disease: Clinical Effects
Richard Douyon, M.D., Michael Serby, M.D., Bruce Klutchko, M.D., John P. Rotrosen, M.D.

NR620 Homocysteine, B12 and Folate in Geriatric Depression
Iris R. Bell, M.D., Joel S. Edman, M.S., Jacob Selhub, Ph.D., Frank D. Morrow, Ph.D., David W. Marby, B.S., Douglas C. Shepard, M.S.

NR621 MRI Abnormalities in Elderly Depressives
Peter V. Rabins, M.D., Godfrey D. Pearlson, M.D., Elizabeth H. Aylward, Ph.D., Ashok J. Kuman, M.D.

NR622 Inpatient Psychiatric Treatment of Dementia
Peter V. Rabins, M.D., Chris Nicholson, R.N.C.

NR623 EEG Correlates of Cognitive Decline in Normal Elderly
Peter C. Williamson, M.D., Harold Merskey, D.M., Sandra L. Morrison, M.A., Kiran Rabheru, M.D., Kim Wands, B.SC., Vladimir Hachinski, M.D.

NR624 Risk of Institutionalization in Alzheimer's Disease
Cynthia D. Steele, M.P.H., Barry W. Rovner, M.D., Marshal F. Folstein, M.D., Gary A. Chase, Ph.D.

NR625 Disturbed Behavior in Dementia: N-of-1 Treatment Trials
Lawrence R. Herz, M.D., Ladislav Volicer, M.D., Virginia Ross, M.A.P., Yvette Rheaume, R.N.

NR626 Meta-Analysis of Neuroleptic Efficacy in Dementia
Lon S. Schneider, M.D., Vicki E. Pollock, Ph.D., Scott A. Lyness, M.A.

NR627 Hydroxynortriptyline Kinetics in the Elderly
Lon S. Schneider, M.D., Julie Dopheide, PharmD, Ray Suckow, Ph.D., Thomas B. Cooper, M.A., Ruby Palmer, R.N., R. Bruce Sloane, M.D.

NR628 Challenge Studies in Alzheimer's Disease
Linda M. Bierer, M.D., Michael Davidson, M.D., Rami Kaminsky, M.D., Peter J. Knott, Ph.D., James Schmeidler, Ph.D., Kenneth L. Kavis, M.D.

NR629 Clinical Correlates of HPA Axis Function in Alzheimer's Disease
Brian A. Lawlor, M.D., Richard C. Mohs, M.D., Gabriel K. Tsuboyama, M.D., Moshen Aryan, M.D., Bonnie M. Davis, M.D., Michael Davidson, M.D., Kenneth L. Davis, M.D.

NR630 Acute Effect of Buspirone and Lorazepam on Memory
Brian A. Lawlor, M.D., Jeanne L. Radcliffe, M.P.H., Trey Sunderland, M.D., Susan E. Molchan, M.D., Rick A. Martinez, M.D., Dennis L. Murphy, M.D.

NR631 Aging and the Relationship Between Mood and Memory
Dennis Deptula, Ph.D., Rajkumar R. Singh, M.D., Nunzio Pomara, M.D.

NR632 Cognition in Early Versus Late-Onset Alzheimer's Disease
Steven Sevush, M.D., Nancy Leve, M.A., Andrew Brickman, Ph.D., Robert Morgan, Ph.D.

NR633 Psychiatric Disorders and Medical DRGs: Type and Length of Hospital Stay
George Fulop, M.D., James J. Strain, M.D.

NR634 A Follow-Up Study of Dementia in Beijing
Ge Li, Ph.D., Yu-Cun Shen, M.D., Cuang-Hui Chen, M.D., Yo-Wen Zou, M.D., Su-Ran Li, M.D., Mian Lu

NR635 Quantitative MRI and SPECT in Alzheimer's Disease
Godfrey D. Pearlson, M.D., Gordon J. Harris, M.S., Richard E. Powers, M.D., Patrick E. Barta, M.D., Edwaldo E. Camargo, M.D., John A.O. Besson, M.D., Jonathan A. Links, Ph.D., Larry E Tune, M.D.

NR636 Somatization in Older Panic Disorder Patients
Javaid I. Sheikh, M.D., Gregory R. Bail, B.A.

NR637 A Comparison of Late-Onset Paranoia and Paraphrenia
Alastair J. Flint, M.D., Sandra L. Rifat, M.S.C., M. Robin Eastwood, M.D.

NR638 Circadian Temperature and Activity Rhythms in Alzheimer's Disease
Andrew Satlin, M.D., Martin H. Teicher, M.D., Harris Lieberman, Ph.D., Ladislav Volicer, M.D., Yvette Rheaume, R.N.

NR639 Life Review in Older Adulthood: A Comparative Study
Rhoda Frankel, M.A., William Borden, Ph.D., Benedict Gierl, M.D., Alice Ras, B.A.

NR640 Aggressive/Disruptive Behaviors in Nursing Homes
Blaine S. Greenwald, M.D., Elisse Kramer, Ph.D., Jacob Reingold, M.S., Elaine B. Jacks, R.N., Steven Staum, C.S.W., Conn Foley, M.D.

NR641 Incessant Screaming in Advanced Dementia
Blaine S. Greenwald, M.D., Elisse Kramer, Ph.D.

NR642 Cost Offset: Psychiatric Intervention in Surgery
James J. Strain, M.D., John Lyons, M.D., Marianne Fahs, Ph.D., Jeffrey S. Hammer, M.D., A. Lebovits, Ph.D.

NR643 RDC Evaluation of Cancer Patients During Treatment
James J. Strain, M.D., A. Lebovits, Ph.D., Steven J. Schleifer, M.D., Jeff Tanaka, Ph.D.

NR644 Quantitative Evoked Potential Correlates of Cognitive Impairment in Aging
E. Roy John, Ph.D., Leslie S. Prichep, Ph.D.

NR645 A Prospective EEG Study of Delirium in the Elderly
Ira R. Katz, M.D., Jana Mossey, Ph.D., Sharon M. Curlik, D.O., Richard N. Harner, M.D., Neal M. Sussman, M.D., Kathryn A. Knott, R.N.

NR646 Mental Competency Testing of Demented Elderly
Benedict Gierl, M.D., Alice Ras, B.A.

NR647 Quantitative I-123 Labeled Iofetamine SPECT Analysis in Depression
P. David Mozley, M.D., Abass Alavi, M.D., Jay D. Amsterdam, M.D.

NR648 Increased Blink Rates in Drug-Naive Schizophrenics
Dr. Arthur Mackert, Klaus-Malte Flechtner, M.D., Johannes Kasper, M.D., Dr. Hans-Peter Volz, Charles Woyth, M.D.

NR649 Clinical Neuroimaging in Traumatic Brain Injury
Jeffrey L. Clothier, M.D., Thomas W. Freeman, M.D., John Cassidy, M.D., Kenneth Bonnet, Ph.D.

NR650 Fragile X Adults: Neuropsychology, Brain Metabolism and Anatomy
Declan Murphy, M.D., Mark B. Shapiro, M.D., James Haxby, Ph.D., Randi J. Hagerman, M.D., Stanley I. Rappaport, M.D.

NR651 MRI Abnormalities in Late-Onset Schizophrenia
Terry L. Jernigan, Ph.D., Dilip V. Jeste, M.D., Jackuelyn M. Harris, M.D., David Salmon, M.D.

NR652 MRI in Schizophrenia: Computer Aided Measures of Brain and CSF
Martha E. Shenton, Ph.D., Ron Kikinis, M.D., Robert W. McCarley, M.D., Tamas Sandor, D.P., David Metcalf, B.S., Ferenc Jolesz, M.D.

NR653 Morphometry of Brain Structures in Schizophrenia
Manuel F. Casanova, M.D., Dennis Atkinson, M.D., Terry Goldberg, Ph.D., Mark Zito, M.S., E. Fuller Torrey, M.D., Daniel R. Weinberger, M.D.

NR654 MRI of Superior Temporal Gyrus and Hallucinations
Patrick E. Barta, M.D., Godfrey D. Pearlson, M.D., Richard E. Powers, M.D., Stephanie Richards, B.S., Larry E. Tune, M.D.

NR655 Quantitative EEG Correlates of Cognitive Deterioration in the Elderly
Leslie S. Prichep, Ph.D., E. Roy John, Ph.D., Barry Reisberg, M.D., Steven Ferris, Ph.D., Kenneth Alper, M.D., Robert Cancro, M.D.

NR656 The Brain: Asymmetries, Non-Linear Dynamics and Behavior
Peter F. Andrus, M.D.

NR657 Temporal Lobe Structure by Magnetic Resonance in Bipolar Affective Disorders and Schizophrenia
Alessandro Rossi, M.D., Paolo Stratta, M.D., Vittorio Dimichele, M.D., Massimo Gallucci, M.D., Alessandra Splendiani, M.D., Massimo Casacchia, M.D.

NR658 Brain Dopamine Imaging by Single Photon Tomography
Robert M. Kessler, M.D., John R. Votaw, Ph.D., Tomas de Paulis, Ph.D., Dennis E. Schmidt, Ph.D., Jeffrey A. Clanton, M.S., Mohammed S. Ansari, B.S., K.P. Holdeman, M.D., Rhonda Pfeffer, B.S., Ronald G. Manning, Ph.D., Michael H. Ebert, M.D.

NR659 Contrast Enhanced MRI Study of ECT
Raymond A. Faber, M.D., Dolores Sands, Ph.D., J. Neal Rutledge, M.D., Roger McCary, M.D., Jean Swinney, M.A., Heather Becker, Ph.D.

NR660 Reduced Cerebral Volume in Schizophrenia
Jeffrey A. Coffman, M.D., Stephen C. Olson, M.D., Steven B. Schwarzkopf, M.D., Henry A. Nasrallah, M.D.

NR661 Correlates of Hippocampus Hypoplasia Schizophrenia
Henry A. Nasrallah, M.D., Bernhard Bogerts, M.D., Stephen C. Olson, M.D., Steven B. Schwarzkopf, M.D., Jeffrey A. Coffman, M.D.

NR662 Functional and Physiological Markers in Patients at Risk for Dementia of the Alzheimer's Type
Richard J. White, Michael W. Torello, Ph.D., Robert A. Bornstein, Ph.D., Jeffrey A. Coffman, M.D., Henry A. Nasrallah, M.D., Elizabeth Burns, Ph.D.

NR663 Drug Conditioning of Dopamine Metabolism
Jorge Perez-Cruet, M.D.

NR664 Neurofibrillary Degeneration in Alzheimer's Disease
William Bondareff, M.D., Claude M. Wischik, M.D., Martin Roth, M.D.

NR665 Lithium Effects on EEG Power and Coherence
Edward L. Merrin, M.D., Thomas C. Floyd, M.A.

NR666 Brain Dysfunction as a Predictor of Outcome
Marshall L. Silverstein, Ph.D., Martin Harrow, Ph.D., Louis Fogg, Ph.D.

NR667 Major Depression and Personality Disorder
Mark Zimmerman, B.A., Bruce M. Pfohl, M.D., William Coryell, M.D., Caryn Corenthal, M.A., Dalene Stangl, M.A.

NR668 Psychiatric Aspects of CNS Myelinolysis
Barbara P.I. Karp, M.D., Robert Laureno, M.D.

NR669 Violence and Temporal Lesion, CT Scan, MRI Data
Joseph M. Tonkonogy, M.D.

NR670 Physiological Evidence of Exaggerated Startle Response in PTSD
Robert W. Butler, Ph.D., Melissa A. Jenkins, B.A., David L. Braff, M.D., Jeffrey L. Rausch, M.D., Mark A. Geyer, Ph.D.

NR671 Chronic MK801 Treatments in a Neuropsychiatric Model
Andrew B. Norman, Ph.D., Lisa M. Ford, M.D., Magda Giordano, M.S., P.R. Sanberg, Ph.D.

NR672 More About SPECT Scans in Neuropsychiatry
Ben Zimmer, M.D., Robert Fields, Ph.D., Christopher Starratt, Ph.D., Mustafa Adatepe, M.D., Trevor R.P. Price, M.D.

NR673 Comparison of Computer and Manual Wisconsin Card Sort Test
Allen Y. Tien, M.D., Tara V. Spevack, Douglas W. Jones, Ph.D., Godfrey D. Pearlson, M.D., Milton E. Strauss, Ph.D.

NR674 Hemispheric Asymmetry in Emotional Awareness
Richard D. Lane, M.D., Lowell Kivley, S., Marion A. Dubois, Padmini Shama, M.D., Gary E. Schwartz, Ph.D.

NR675 The SCID-Epilepsy
Jeffrey I. Victoroff, M.D.

NR676 Treatment of Emotional Incontinence with Fluoxetine
Andrew Hornstein, M.D., James Flax, M.D., Glenn Seliger, M.D., Joseph Herbert, M.D., Karl Schroeder, M.D.

NR677 Platelet Markers in Anxiety, Depression and Stress
Linda J. Iny, M.A., John C. Pecknold, M.D., N.P.V. Nair, M.D., Barbara Suranyi-Cadotte, M.D., Lorenz Luthe, M.Sc., Michael J. Meaney, Ph.D.

NR678 Serotonergic Function in Borderline Personality
Eric Hollander, M.D., David Kellman, M.D., Concetta DeCaria, M.A., Daniel Stein, M.D., Michael R. Liebowtiz, M.D., Lyle E. Rosnick, M.D.

NR679 Dopamine Sensitivity and Cocaine Abuse
Eric Hollander, M.D., Edward V. Nunes, M.D., Concetta DeCaria, M.A., Frederic M. Quitkin, M.D., Thomas B. Cooper, M.A., Donald F. Klein, M.D.

NR680 Four-Factor Model of Schizophrenia
Stanley R. Kay, Ph.D.

NR1 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

NEUROPSYCHIATRIC AND PSYCHOSOCIAL ASSESSMENT OF HIV-SEROPOSITIVE SOLDIERS

Louis K. Duchin, M.D., Psychiatry, Eisenhower Medical Center, Fort Gordon, GA 30905; Gregory P. Hollis, Ph.D., Stephen N. Xenakis, M.D., Frederick N. Garland, Ph.D.

Summary:

This study examined the effects of human immunodeficiency virus seroposivity on mood and mentation in asymptomatic individuals. Fifty-three HIV-seropositive soldiers and 25 HIV-seronegative controls matched for age, sex, and level of education underwent a standardized neuropsychological test battery, and completed a psychosocial assessment questionnaire, as well as self-report instruments of mood. A neuropsychological impairment index, based on nine measures of cognitive functions, was prepared. The HIV-seropositive soldiers showed decreased coping skills, higher anxiety, and a relative increase in depression. There were significant differences in six of the ten scales of the MMPI across groups; the Schizophrenia Scale was clinically elevated within the HIV-seropositive group. The HIV-seropositive soldiers performed in the borderline impaired range on the Stroop Test, and exhibited poorer visual memory than controls. The Impairment Index was significantly higher in the HIV-seropositive group and fell within the borderline-impaired range. There was no correlation between neuropsychological/mood variables and time since seroconversion, stage, or CD4 count. Neuropsychological score differences could not be accounted for by measures of depression or anxiety, suggesting that these differences reflect an organically-based compromise of neurobehavioral functioning.

NR2 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

DEPRESSION AND SUPPORT IN ARMY HIV-SEROPOSITIVE PATIENTS

E. Cameron Ritchie, M.D., Psychiatry, Walter Reed Army, Medical Center, Washington, DC 20307; Alan O. Radke, M.D., Barbara J. Ross, M.A.

Summary:

Psychiatric interviews were conducted with 57 male, HIV + patients, who were either on active duty in the Army or medically retired for HIV. Seventy-nine percent were in the very early stages of the disease at the time of diagnosis. Sixty-eight percent had Axis I diagnoses of a depressive disorder. Forty-two percent reported feeling depressed at the time of the interview. Fifty-two percent had a history of suicidal thoughts. Twelve percent had a history of a suicide attempt. Sixty-eight percent said that they followed a more healthy life-style since their diagnosis. Seventy-five percent described the military as being important to them; of these 39% were depressed. The relationship of depression to their support systems was assessed. Perceived lack of support, from either family, work or the military was associated with depressive symptoms.

NR3 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

IMMUNITY, DIMENSIONAL SCORES AND PANIC DISORDERS IN MAJOR DEPRESSIVE DISORDERS

Antonio V. Andreoli, M.D., Psychiatry, Univ of Geneva, Rue Des Vollandes, Geneva, GE 01207, Switzerland; Charles J. Taban, M.D., Maya Rabaeus, M.D., Line E. Zaugg, L.EB., G. Garrone

Summary:

Significance: Since evidence of altered immunity was found in selected subgroups of depressive patients (Shleifer, 1989), and simultaneous depression and panic were addressed as a distinct nosographic entity (Uhde, 1985), we designed a study aimed to investigate cell mediated immunity - dimensional scores and panic disorder comorbidity relationships in *DSM-III-R* major depressive disorders (MDE). *Methods*: 28 reliably assessed (PDE, SCID, I-OP, HAS, HDRS, SCL-90, GAS, GAF) untreated, otherwise healthy *DSM-III-R* MDE outpatients and 29 pair-matched controls were studied comparing a wide range of immunological parameters. *Results:* We found slightly increased mitogen induced lymphocyte stimulation ($p < .05$) in depressive outpatients vs pair-matched controls. Mitogen stimulation ($p < .01$ to $< .001$), T helper subset size ($p < .01$) and TAC receptors ($p < .01$) were, therefore, strongly increased in subjects with MDE + panic disorder ($n = 15$) vs subjects with MDE only ($n = 13$). The effect of subjective anxiety and panic had positive ($p < .05$ to $p < .01$) and the effect of severity - hopelessness - global distress had negative ($p < .05$ to $p < .025$) partial correlation to mitogen stimulation and T helper subset size. *Comment*: Our results suggest that both dimension scores and common morbidity may be associated to specific immune correlates in MDE bringing new evidence of simultaneous MDE and panic as an autonomous nosographic entity. Comment is provided.

NR4 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

ALPRAZOLAM SENSITIVITY IN PANIC DISORDER

Gary B. Kaplan, M.D, Psychiatry, New England Medical Ctr., 750 Washington St. Box 1007, Boston, MA 02111; David J. Greenblatt, M.D., Jill E. Goddard, M.A., Richard I. Shader, M.D.

Summary:

Alprazolam, a triazolobenzodiazepine derivative, has been found effective and well-tolerated in patients with panic disorder. We employed a double-blind, single-dose (1 mg), placebo-controlled design to better delineate the effects and kinetics of alprazolam in panic patients and normal volunteers. Subjective responses, as measured by visual analogue scales (VAS), and blood samples were obtained at various times before and after treatment. Alprazolam concentrations were measured in plasma by gas chromatography. Comparisons were then made between eight panic patients, and eight age- and sex-matched controls. At baseline, panic patients had significantly greater VAS anxiety measures, Hamilton Anxiety scores (23.3 vs 3.0) and Hamilton Depression scores (24.3 vs 3.8). After alprazolam treatment, patients felt more "contented," "friendly," "pleasant," and "at ease," while controls became more "sedated and fatigued" ($p < 0.05$). There were no placebo-induced change with these measures; however, after placebo treatment, panic patients felt more "calm," "peaceful," and "relaxed." Kinetic parameters for panic subjects were: time at maximum concentration = 1.2 hr, maximum concentration = 22.8 ng/ml, half-life 15.1 hr. Kinetic parameters were not significantly different between groups. In conclusion, panic patients were intrinsically more sensitive to the anxiolytic effects of alprazolam and placebo treatment.

NR5 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

EFFECT OF PREGNANCY ON PRE-EXISTING PANIC DISORDER

Virginia A. Villeponteaux, M.d., Psychiatry, M.U.S.C., 171 Ashley Avenue, Charleston, SC 29425; R. Bruce Lydiard, M.D., Michele T. Laraia, R.N., Gail W. Stuart, Ph.D., James C. Ballenger, M.D.

Summary:

Clinical experience and very limited published data suggest that pregnancy may reduce the severity of symptoms in women with pre-existing panic disorder. In order to discern whether this is in fact a common phenomenon, we surveyed a group of female patients with panic disorder with or without agoraphobia who had been seen in our anxiety disorders program over the past several years. Questionnaires were mailed to all female patients with panic disorder who may have experienced pregnancy; follow-up phone calls were made in some cases. One hundred and fifty patients were included in the survey. Seventy patients completed the questionnaire. Of these, 32 had onset of panic attacks prior to experiencing at least one pregnancy. Preliminary data suggest that the majority did experience reduction in panic severity and anxiety, while others noted no effect, and some indicated a worsening of their symptoms. In addition, survey data regarding the effects of the menstrual cycle and the post-partum state on panic symptoms will also be presented.

NR6 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

EFFECT OF ALPRAZOLAM ON MOOD IN PANIC DISORDER

J. Allen Melvin, M.D., Psychiatry, M.U.S.C., 171 Ashley Avenue, Charleston, SC 29425; R. Bruce Lydiard, M.D., Michele T. Laraia, R.N., Mark D. Fossey, M.D., James C. Ballenger, M.D.

Summary:

There have been conflicting reports regarding the emergence of depressive symptoms during treatment of panic disorder with benzodiazepines. We report the effects of two fixed doses of alprazolam or placebo on Hamilton Depression Rating Scale (Ham-D) scores in panic disorder patients.

METHOD: Thirty-one patients, ages 18-65, with panic disorder with or without agoraphobia were randomly assigned to six weeks double-blind treatment with either 2 mg (N=10) or 6 mgs (N=10) alprazolam or placebo (N-11) after a one-week washout. Patients with major depression were excluded unless depression occurred after the onset of panic disorder and was not clinically predominant. Ham-D ratings were obtained prior to and after six weeks of treatment.

RESULTS: The three groups were comparable in age, sex, and baseline Ham-D ratings. No significant differences were found in the change in Ham-D ratings between the three groups. However, one patient in each group had a marked increase in Ham-D ratings. An additional patient was dropped from the alprazolam 2 mgs group after a suicide attempt. While no group differences emerged during the course of this short-term study, individual differences were apparent. Practical and theoretical implications of these findings will be discussed.

NR7 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

CARDIAC STATUS OF PANIC PATIENTS: WITH AND WITHOUT CARDIAC SYMPTOMS

Robert R. Jolley, M.D., Psychiatry, M.U.S.C., 171 Ashley Avenue, Charleston, SC 29425; R. Bruce Lydiard, M.D., Michael E. Assey, M.D., Mark D. Fossey, M.D., James C. Ballenger, M.D.

Summary:

In order to determine if patients with panic disorder with prominent cardiac symptoms actually have more cardiac abnormalities than panic disorder patients without prominent cardiac symptoms, we conducted a pilot study to assess the cardiovascular status of these patient groups. Ten patients who met *DSM-III-R* criteria for panic disorder with or without agoraphobia as their primary psychiatric diagnosis, were free of other primary AXIS I disorders, were in good physical health, had no history of significant neurological or medical illness and had sought medical care for cardiac symptoms associated with their panic attacks (cardiac symptom positive) were studied. Ten, age and sex matched panic disorder patients meeting the same criteria, but lacking a history of specifically seeking care for their cardiac symptoms as part of their anxiety (cardiac symptom negative) were also studied. Both groups of patients were evaluated by a cardiologist who was blind to their care seeking histories. The evaluations included a physical examination, EKG, echocardiogram, 24-hour Holter monitor, and treadmill stress test. RESULTS: There were no statistically significant differences between the two groups on any of the tests administered. Surprisingly, mitral valve prolapse was found primarily in the cardiac symptom negative group. Patients who experienced panic attacks during Holter monitoring showed no pathological EKG changes. Two patients with cardiac symptom positive histories had ST segment changes during treadmill stress testing. One of these subsequently had a normal stress thalium evaluation, cardiac symptoms resolved in both patients with treatment of their panic disorder.

NR8 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

THE SPECIFICITY OF THE ATTENTIONAL BIAS IN PANIC DISORDER

Cameron S. Carter, M.B., Psychiatry, UC Davis, 4430 V. Street, Sacramento, CA 95817; Richard J. Maddock, M.D., Joseph R. Magliozzi, M.D. Kathryn Moriyana, Ph.D.

Summary:

Studies showing interference with color naming threat related words in patients with anxiety disorders may reflect an attentional bias toward threatening material in these patients. We assessed the specificity of this finding by administering Stroop cards with a variety of emotional stimuli to 24 panic disorder patients with no history of depression, 29 depressed patients with no history of panic, and 25 controls with no history of an Axis I disorder.

The Stroop cards contained stimuli referent to physical threat, panic symptoms, depressive symptoms, and neutral themes, respectively. As predicted in the panic group Stroop interference was found for physical threat words ($p < 0.05$ 1-tailed), panic words ($p < .02$ 1-tailed) and unexpectedly, interference was also seen with depression words ($p < .05$ 2-tailed). In the depressed group only the depression words tended to produce interference ($p < .06$ 1-tailed).

These findings suggest that abnormal attentional processes in panic disorder may be characterized by a more general bias toward processing emotional stimuli that previously thought. They also suggest that this more general attentional vulnerability may illustrate a difference in the kind of abnormality in information processing present in panic disorder as opposed to major depression.

NR9 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

EFFECTS OF CLONIDINE PRETREATMENT OF LACTATE-INDUCED PANIC

Jeremy D. Coplan, M.D., Psychiatry, NYS Psych Inst., 722 W. 168th Street, New York, NY 10032; Michael R. Liebowitz, M.D., Jack M. Gorman, M.D., Abby J. Fyer, M.D., Donald F. Klein, M.D.

Summary:

Ten patients with panic disorder who panicked during sodium-lactate infusion underwent repeat lactate challenge following pretreatment with intravenous clonidine. Clonidine pretreatment failed to block panic in six patients on repeat lactate challenge. Although clonidine pretreatment significantly lowered baseline systolic blood pressure, it did not significantly lower baseline anxiety levels. Clonidine pretreatment did, however, significantly attenuate the rate of development of Acute Panic Inventory (API) items during the lactate infusion. This effect was most prominent for the API items of a cognitive/affective nature. The effect of clonidine on lactate-induced panic supports the previously acknowledged acute anxiolytic properties of clonidine. The study suggests that increased activity of central nervous system noradrenergic pathways comprises a component of lactate-induced panic. The noradrenergic hypothesis of panic disorder, however, cannot fully account for the observed results. Implications regarding the neurobiology of panic will be discussed.

NR10 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

ANXIOLYTIC EFFECTS OF ORAL YOHIMBINE IN DIFFERENTIALLY REARED NONHUMAN PRIMATES

Jeremy D. Coplan, M.D., Psychiatry, NYS Psych Inst., 722 W. 168th Street, New York, NY 10032; Leonard A. Rosenblum, Ph.D., Steven Friedman, Ph.D., Trina B. Bassoff, M.A., Jack M. Gorman, M.D.

Summary:

The behavioral responses of eight unrestrained, adult, female bonnet macaques were observed for two hours following either two doses of oral yohimbine (0.2 mg/kg and 2.0 mg/kg) or placebo administration. Four of the subjects were normally reared, and four of the subjects were nursery-reared and had undergone early maternal and peer-deprivation with subsequent resocialization. In the normally reared subjects, yohimbine was associated with significant increases of tension behaviors, but also caused significant increases in enervation scores and significant reductions in species-typical normal behaviors, such as autogrooming and social or object explorations. In contrast, the deprived subjects showed reductions in tension and enervative behaviors, and increases on scores reflecting "normal" behaviors on yohimbine. A significant group by treatment interaction was noted on each of these behaviors. The study suggests that early emotional deprivation significantly alters the behavioral response to yohimbine, an effect possibly related to abnormal development or noradrenergic presynaptic alpha-2 autoreceptors. The study fails to support the view that oral yohimbine response in normally reared nonhuman primates is unequivocally anxiogenic, particularly since marked enervative responses were prominent. The study thus reflects the critical role of experiential factors in determining patterns of affective response to putative anxiogenic agents.

NR11 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

CHRONIC HAIR PULLING: A DESCRIPTIVE STUDY OF 62 SUBJECTS

Gary A. Christenson, M.D., Psychiatry, University of Minn, Box 393 420 Delaware Street SE, Minneapolis, MN 55455; Thomas B. Mackenzie, M.D., James E. Mitchell, M.D.

Summary:

Trichotillomania, considered by some as a variant of obsessive compulsive disorder (OCD), appears to be more common than previously suspected. Detailed studies of this disturbance have been confined to the nonpsychiatric literature. This report describes 62 chronic hair pullers, 56 of whom were evaluated in the past year with semi-structured interview using DSM-III-R criteria. The average patient was a 32-year-old female who had been pulling scalp hair from at least two sites continuously for 20 years. All subjects described either tension before or relief after pulling from the primary site. Spread to other sites occurred often without tension/relief phenomena. The majority qualified for the following additional past or current diagnoses: affective disorders 60%; anxiety disorders 50% (OCD 15%); substance use disorders 42%; and eating disorders 19%. This series, the largest reported in the psychiatric literature, indicates that trichotillomania is a chronic, stable disorder affecting mainly women with a high lifetime prevalence of other disorders. Although a majority of patients recognized either tension or relief as important in the maintenance of their disorder, DSM-III-R's insistence that both be present may be unduly restrictive.

NR12 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

HIGH CHOLESTEROL IN PANIC DISORDER: COMPLICATION OR ARTIFACT?

Waheed K. Bajwa, M.D., Psychiatry, Montefiore Medical Center, 111 East 210th Street, Bronx, NY 10467; Gregory M. Asnis, M.D., William C. Sanderson, Ph.D., Naveed Iqbal, M.D., Herman M. van Praag, M.D., Amaro Reyes-Garza, M.D.

Summary:

Long-term follow-up studies of panic disorder suggest increased cardiovascular mortality. In a recent study a significantly higher than expected number of female subjects with panic disorder had cholesterol levels that exceeded the 75th percentile of national reference values. We studied 30 subjects (mean $\pm$ SD age, 37.7 $\pm$ 10.6 years), who met DSM-III-R criteria for panic disorder and compared them with a group of 30 age- and sex-matched patients who met DSM-III-R criteria for major depressive episode and 30 normal controls. Serum cholesterol levels were assessed as part of routine screening on admission. Cholesterol levels were repeated for the panic disorder group at the end of eight weeks of double-blind fluvoxamine treatment. Pre-treatment mean cholesterol level of panic disorder patients (225.76 mg) was significantly greater than that of major depression patients (186.10 mg, T=4.3, df=58, P <.000) and the normal control group (183.5 mg, T=4.0, df=57, P <.000). Cholesterol measurements at the end of successful double-blind fluvoxamine treatment are compared to baseline. Comparison of mean body index and relationship of gender to cholesterol in three groups will be presented.

NR13 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

EVIDENCE THAT AN ALTITUDE CHALLENGE ENHANCES HUMAN VISUAL INFORMATION PROCESSING

Thomas E. Schlaepfer, M.D., Psychiatry, University of Berne, Murtenstr 21, 3010 Berne, Switzerland; Hans-U Fisch, M.D.

Summary:

High altitude (>7000m) is known to have a detrimental effect upon brain function; little, however, is known about the effects of acute hypoxia at lower altitudes despite the possibly greater importance.

Backward masking (BM), reliable marker of visual information processing was used to assess cognitive performance at 550m and 3450m. A target letter (T) was presented tachistoscopically followed by a mask (M) composed of chopped letters. The temporal interval between the onset of T and M (Stimulus Onset Asynchrony = SOA) was the independent variable. Criterion was the percentage of correctly identified letters at each SOA. Athletic subjects (n=10, mean age 23.1 $\pm$ SD 0.7 years) were trained at 550m altitude (test-retest correlation for repeated BM curves r=0.97). After rapid (10 min) helicopter transport to the High Altitude Research Station on the Jungfraujoch (3450m), critical target duration for perception of unmasked T was reduced by 33 percent and the number of correctly identified T increased tenfold at SOA 20ms. ANOVA: SOA x Altitude ($F(5,45) = 7.9$, $p<0.0001$), indicating an increase of performance above normal functioning.

One explanation may be an increase in cerebral blood flow to compensate for the mild hypoxia. These findings indicate the impact of environmental variables on cognitive performance.

NR14 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

RAT BRAIN FLUPHENAZINE LEVEL AFTER ELECTROCONVULSIVE SHOCK

Iannis M. Zervas, M.D., Psychiatry, Suny at Stony Brook, Health Sciences Center T-10, Stony Brook, NY 11794; Lawrence B. Greenberg, M.D., Thomas Cooper, Ph.D., Lina Jandorf, M.A., Max Fink, M.D.

Summary:

The combination of electroconvulsive therapy (ECT) and neuroleptic medications has been found to have increased antipsychotic efficacy in treatment resistant psychosis. It has been hypothesized (Friedel, 1986) that ECT induces greater permeability of the blood brain barrier (BBB) which increased brain levels of the neuroleptic. To test this hypothesis we measured the brain concentration of fluphenazine in two groups of male Sprague Dawley rats (n=12 in each group), one treated with fluphenazine decanoate and electroconvulsive shock (ECS), and the other with fluphenazine decanoate only. No difference in brain neuroleptic concentration was found between the two groups. The experiment was replicated with a larger number of rats (n=24 in each group) and the same result was obtained. Even though technical aspects and parameters not controlled for (blood pressure increase, drypocapnia, hyperglycemia, and rate of exit of fluphenazine from the CNS) may account for the result, it is our conclusion that ECS does not increase BBB permeability to neuroleptics. An alternate hypothesis needs to be considered to account for the clinical observation.

NR15 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

LITHIUM POTENTIATES INSULIN'S EFFECT ON SKELETAL MUSCLE CAMP

Leslie R. Vogel, M.D., Psychiatry, Univ Texas San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78284; Andrea Giaccari, M.D., Simona Frontoni, M.D., Su B. Choi, M.D.

Summary:

We have shown previously that lithium improves *in vivo* insulin action in diabetic and non-diabetic rats. One theory behind lithium's anti-manic action is its inhibition of adrenergically activated adenylate cyclase activity, through its interaction with a G-protein. To determine whether such effects extend to insulin-sensitive peripheral tissues, we now examine the relationship between insulin-stimulated skeletal muscle glycogen synthesis (MGS) and a cyclic AMP (cAMP) concentrations under identical conditions of euglycemia/hyperinsulinemia (plasma insulin conc=~450 μU/ml) in CONtrol and DIABetic (90 percent pancreatectomized) rats. CON and DIAB conscious rats (n=8/group) treated for three weeks with lithium (plasma conc.=1 meq/L) or placebo, underwent an insulin clamp study. In CON total glucose uptake (GU) was 34$\pm$1 mg/kgmin and MGS was 12.8$\pm$1.1 mg/kgmin. Skeletal muscle cAMP concentration decreased from 1.34$\pm$.10 nmol/g ww (basal) to 0.93$\pm$.10 ($p<0.01$) during the insulin infusion. In DIAB, GU (25$\pm$1) and MGS (4.7$\pm$.9) were severely impaired during the insulin clamp, while muscle cAMP levels were similar to CON (1.04$\pm$.11). Lithium treatment caused a decrease in muscle cAMP concentrations in both CON (0.67$\pm$.06; $p<0.01$) and DIAB (0.62$\pm$.04; $p<0.01$), while stimulating GU (CON=41$\pm$1 and DIAB 37$\pm$1) and MGS (CON=19$\pm$1 and DIAB=17$\pm$1). The lithium-induced increase in GU/MGS was closely correlated with the decline in muscle cAMP conc (r=0.68 and 0.79, $p< 0.01$). These results suggest that lithium's effect on adenylate cyclase extends to skeletal muscle and is responsible for the cation's insulin-mimetic property.

NR16 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

PLASMA HVA INCREASES AFTER METYRAPONE ADMINISTRATION

Ruth A. Richter, M.D., Psychiatry, CRC UC San Diego, M-003, La Jolla, CA 92093; Richard L. Hauger, M.D., S. Craig Risch, M.D., Kathy Resovsky, R.N., Shahrokh Golshan, Ph.D., J. Christian Gillin, M.D.

Summary:

Recent studies have suggested that dexamethasone administration increases plasma homovanillic acid (HVA) concentrations in human controls. In the first part of this study we examined the effects of metyrapone, a selective 18-hydroxylase inhibitor of adrenal cortisol formation, as well as the effects of dexamethasone on both HVA and 3-methoxy-4-hydroxyphenylglycol (MHPG) plasma levels. After a 4 p.m. baseline blood sample, an oral dose of 3 grams of metyrapone was given to normal male controls at 11 p.m. followed by two additional doses of 750 mg PO at 8 a.m. and 12 noon the next day. Blood samples were taken hourly from 8 a.m. to 4 p.m. On a separate day, this protocol was repeated following an 11 p.m. oral dose of 2 mg of dexamethasone. At each time point, plasma concentrations of ACTH, cortisol, 11-deoxycortisol, prolactin, HVA, and MHPG were measured. After metyrapone administration, plasma ACTH increased significantly and cortisol was reduced. There was a transient increase in prolactin secretion in the early morning, as well as an increase in HVA followed by a gradual return to baseline by 4 p.m. MHPG was not significantly changed. Following dexamethasone administration, ACTH, cortisol and 11-deoxycortisol were suppressed, there was no significant change in prolactin secretion and, in contrast to previous studies plasma HVA decreased at 4 p.m. and MHPG was unchanged. We have chosen to extend the study to include a placebo day to confirm the postdexamethasone HVA findings and to look at possible circadian influences postmetyrapone. We have observed that inhibition of adrenal steroid formation results in significant increases in plasma HVA, ACTH, and prolactin. Consequently, ACTH or other adrenocorticosteriods secreted in metyrapone-treated subjects may have a role in regulating plasma HVA levels.

NR17 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

LOSS, AFFECTIVE ILLNESS AND HPA AXIS DYSFUNCTION

John M. Petitto, M.D., Psychiatry, Univ of North Carolina, CB– 7160 Med. Sch. Wing B, Chapel Hill, NC 27599; Cort A. Pedersen, M.D., Arch A. Hicks, M.A., Dwight L. Evans, M.D.

Summary:

We previously noted that a considerable percentage of mixed manic patients admitted to our inpatient unit who were dexamethasone (DEX) nonsuppressors had a history of object loss. Several lines of evidence suggest that genetic predisposition and early attachment-bond disruption may be two important factors that influence HPA axis regulation. Therefore, we studied retrospectively 50 patients with major affective illness and loss history, hypothesizing that in addition to diagnostic subtype, childhood loss of a parent would predict cortisol nonsuppression following DEX challenge. Using a stepwise discriminant function analysis, diagnostic subtypes were found to be significant predictors of the variance in DST category, and 4 p.m. and 11 p.m. cortisol concentrations (p.05). Moreover, two additional variables were found to predict post-DEX cortisol levels. Greater number of losses before age 20 were associated with lower post-DEX cortisol levels. Non-parent first loss was associated with higher post-DEX cortisol levels. Although the age of first loss among these patients spanned all developmental stages, the mean age of first loss was 22. Thus, loss of a sibling or child at this age may have greater psychobiologic significance than that of a parent. These findings suggest that the type and timing of loss may have varied influences on HPA axis activity.

NR18 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

SUPER SENSITIVITY TO LIGHT IN DEPRESSION

Harriet L. MacMillian, M.D., Psychiatric Unit, McMaster University, St. Joseph's Hospital, Hamilton Ontario, Canada L8N 4A6; Meir Steiner, M.D., Jo Ann L. Seggie, Ph.D.

Summary:

The EOG was used to measure standing electrical potentials of the retinal pigmented epithelium in response to dark and light in healthy controls (N = 20) and depressed patients (N = 21). Subjects were ophthalmologically screened and mood was assessed. They were then light adapted (in a dimly lit room) for 30 minutes prior to testing during which time their pupils were dilated and electrodes were attached and checked for impedance. The EOG was performed between 1000-1500 hours. When age, sex, and time of day were controlled, there was no difference between the Arden Ratio (Light Peak/Dark Trough) of the control group (mean $\pm$ S.D.: 2.17 $\pm$ .42) compared with the depressed group (2.25 + .72). However when the actual electrical potentials were examined, the depressed group reached significantly ($p < .01$) lower potentials (400-450 μ volts) compared with the control group (650-700 μ volts) during 8-12 minutes of darkness. Following exposure to light there were no significant differences between the groups. We conclude that the Arden Ratio, which has high variability due to the influence of age, sex, response to dark vs light, and time of day, is not a useful index in depression. Nevertheless, the abnormal response of depressed patients to darkness in comparison to a matched control group may indicate a state of "supersensitivity" to light and deserves further study with appropriate methodologies.

(Supported by the Canadian Psychiatric Research Foundation, Ontario Mental Health Foundation, and St. Joseph's Hospital Foundation).

NR19 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

OVERLAP OF AVOIDANT PERSONALITY AND SOCIAL PHOBIA

Franklin R. Schneier, M.D., Therapeutics, NY State Psych Inst., Box 13, 722 West 168th Street, New York, NY 10032; Robert L. Spitzer, M.D., Michael R. Liebowitz, M.D., Abby J. Fyer, M.D., Raphael Campeas, M.D., Eric Hollander, M.D.

Summary:

The DSM-III-R criteria for avoidant personality disorder (APD) and social phobia (SP) overlap extensively, although the co-occurrence of these diagnoses in patients and its implications for treatment have not been examined thoroughly.

Patients (n = 50) diagnosed as social phobic by DSM-III-R were assessed for APD using SCID II. APD was present in 89% of patients with the generalized subtype of SP, and 21% of patients with the discrete (non-generalized) subtype of SP.

A second group of patients (n = 47) meeting DSM-III social phobia criteria (without the criterion excluding APD) were assessed for APD traits before and after eight weeks of treatment with placebo or phenelzine using a checklist of DSM-III criteria. Rates of three APD traits and mean number of traits decreased for patients on phenelzine compared with placebo. Presence or absence of APD did not influence SP response to phenelzine.

The overlap of diagnoses of SP and APD raises the theoretical issue of whether this psychopathology is better described by Axis I or Axis II, and the practical issue of whether these diagnoses as currently defined here are clinically informative or too redundant.

NR20 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

PLASMA CATECHOLAMINE LEVELS IN PATIENTS WITH THE CHRONIC FATIGUE SYNDROME

Susan M. Levine, M.D., Private Practice, 2 West 86 Street, New York, NY 10024; Robert L. Trestman, M.D., Charlotte Cunningham-Run, M.D., James Halper, M.D.

Summary:

Patients with Chronic Fatigue Syndrome (CFS) often report palpitations, flushing, and sweats, symptoms suggestive of an activated sympathetic nervous system. We measured basal and standing plasma norepinephrine (NE) levels in 20 CFS patients and in 12 age-matched normal controls. All of the CFS patients had significantly higher mean basal (337 +/− 146.11 pg/ml vs. 175.33 +/− 43.64 pg/ml, $p < 0.0001$) and standing (541 +/− 197.83 pg/ml vs. 276 +/− 58.9 pg/ml, $p < 0.0001$) plasma NE levels when compared with normal controls. For plasma epinephrine levels there was no significant difference between the two groups. Standing pulse rate was significantly higher in CFS patients when compared with normal controls (18.3 +/− 1.34 beats/minute (bpm) vs. 16.9 +/− 1.64 bpm, $p < 0.016$), while no significant difference in Mean Arterial Pressure was found. In addition, we found a significant correlation between both basal ($R = 0.72$, $p < 0.0003$) and standing ($R = 0.45$, $p < 0.05$) plasma NE levels and duration of illness. Patients with CFS had a mean total score of 14 +/− 6.95 on the Beck Depression Inventory and 13.95 +/− 3.1 on the Hamilton Depression Rating Scale, both of which were consistent with mild depressive symptoms; neither correlated with plasma NE levels. These preliminary data suggest that patients with CFS have a dysregulated adrenergic system, a potentially unifying theory that could relate diverse clinical manifestations of this illness.

NR21 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

PARENTAL LOSS AS A RISK FACTOR FOR DEPRESSION: A META-ANALYTIC STUDY

Scott B. Patten, M.D., Psychiatry, Univ of Calgary, 1403 19th Street NW, Calgary Alberta, Canada T2N 2T9

Summary:

A knowledge of the risk factors predisposing to an illness is of critical importance for understanding the illness as well as for planning preventative programs. The loss of a parent during childhood has been described as a risk factor for depressive illness. However, the literature examining the relationship between parental loss and depression has been contradictory. In this study, the technique of meta-analysis was applied to the data available in this literature. A strong statistical association was found between the loss of a mother before the age of eleven and the occurrence of depression (p .0001). The pooled odds ratio was 2.56 (95 percent confidence interval: 1.99 - 3.31). The best estimate of attributable risk, based on an odds ratio of 2.56, was 61 percent. Population attributable risk percent was estimated as 6.3 percent - 12 percent.

NR22 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

CHILDREN'S FOOD AND MOOD STUDY: PILOT RESULTS

Vincenzo F. Di Nicola, M.D., Child Psychiatry, Royal Ottawa Hospital, 1145 Carling Avenue, Ottawa Ontario, Canada K1Z 7K4; Louise Oke, B.A.

Summary:

Recent research on eating disorders in young children challenges the pubertal model of anorexia nervosa as too narrow. Our developmental model of eating and mood disorders is based on two factors: (1) Relationship between age of onset and precipitants (adolescent cases are triggered by more normative psychosocial events; prepubertal cases are in more pathologic family and social situations). (2) Age of onset of eating disorders and their relationship to mood disorders (older cases have more clearly differentiated eating and mood disorders; younger cases show less differentiation). We are conducting a two-stage community survey of grade school children (both sexes, ages 9-14, n = 4,000). In Stage 1, children answer three measures: Children's Eating Attitudes Test, Children's Depression Inventory, Children's Stress Inventories, and height and weight are recorded. The Parent Questionnaire includes: items on demographics, family eating behavior and weight concerns, and child's menstrual history; General Functioning Subscale of the Family Assessment Device; Family Stress Events Checklist; and Child Behavior Checklist. In Stage 2, at-risk children are offered a clinical interview to establish *DSM-III-R* diagnoses to validate the self-report measures and interventions as indicated. Preliminary results of a pilot study (n = 300) will be used to evaluate our developmental model of eating and mood disorders.

NR23 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

SUBSTANCE USE AND CHILD REARING PRACTICES IN BOYS

Welmoet Van Kammen, Ph.D., Psychiatry, University of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213; Rolf Loeber, Ph.D., Magda Loeber, Ph.D.

Summary:

Based on the developmental model of Kandel (1975), a group of 506 boys (mean age 13.37 $\pm$ .86) were ranked from 0 to 5 according to their lifetime report of substance use. Subjects who had never smoked or used alcohol or drugs received a score of 0, while boys who had used hard drugs such as heroin or cocaine, were given a score of 5. Subjects and their primary caretaker were also interviewed about child-rearing. Lower child-parent communication scores, a greater permissiveness towards drugs, less persistent disciplining and decreased supervision outside the home were significantly related to higher scores on the substance use scale. When the group was divided into boys who were reared by a single-parent and boys who had two caretakers, the relationship between the child-rearing variables and substance use was stronger in the single parent group compared with the intact families; this could not be explained by difference in substance use. Implications of the relationship of substance use to child-rearing practices, family functioning, peer relationships and family composition will be discussed.

NR24 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

DIMENSIONS OF TEMPERAMENT IN FOUR ADOLESCENT GROUPS

Richard Shaw, M.D., Child Psychiatry, Stanford University, 520 Sand Hill Road Box 17, Palo Alto, CA 94304; Hans Steiner, M.D., Ying-Chiao Lee, M.D.

Summary:

Previous studies have suggested an association between temperament and psychopathology (Windle, 1989). The aim of this study is to differentiate girls with anorexia (N = 23), bulimia (N = 25), and depression (N = 25) on the basis of temperament. Patients were divided into three groups on the basis of their primary DSM-III-R diagnosis. Groups were matched for SES, sex, and age (mean = 15.3, $\pm$ 1.3 years). Subjects completed the DOTS-R questionnaire, a self-rating instrument (Windle and Lerner, 1986) that identifies temperament across nine subscales in the course of their psychiatric evaluation.

Analysis by MANOVA shows that it is possible to distinguish the three groups from a normal population and from each other (Wilk's Lambda = 0.57, F(18/124) = 2.25, p = 0.005). Anorexic and bulimic girls differ significantly from a normal population on the subscales Rhythmicity of Eating, Rhythmicity of Daily Habits, and Mood. These two groups can be distinguished from each other on the subscales Approach, Task Orientation, and Rhythmicity of Eating. Depressed girls differ from a normal population on the subscales Approach, Flexibility, Mood, and Rhythmicity of Daily Habits and these subscales also distinguish them from the eating disorder group.

These results suggest: 1) Temperament contributes to the typology of psychiatric syndromes which are otherwise closely related. 2) Premorbid temperament characteristics could identify populations at risk for anorexia, bulimia, and depression.

NR25 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

THE FENFLURAMINE CHALLENGE IN DEPRESSED ADOLESCENTS

Daniel E. Grosz, M.D., Psychiatry, Montefiore Medical Center, 111 E. 210th Street, Bronx, NY 10467; Gregory M. Asnis, M.D., Jill M. Harkavy Friedman, Ph.D., Kausar Shamim, M.D., James K. Zimmerman, Ph.D., Herman M. van Praag, M.D.

Summary:

Fenfluramine (FEN), a 5-HT indirect agonist, is a widely used yet controversial 5-HT probe. We studied the fenfluramine challenge test with particular attention to adolescents seeking treatment in a depression suicide clinic. Three groups participated in a 60 mg oral FEN challenge (I: 15 adults with MDD, mean age 49.5 $\pm$ 15.2; II: 10 normal adult controls, mean age 39.6 $\pm$ 13.5; and III: seven depressed adolescent patients, mean age 15.3 $\pm$ 0.76). Prolactin (PRL) and cortisol were measured in 30-minute intervals for five hours. Group III also received a separate challenge with placebo. The three groups were compared using ANCOVA. The dependent variables were peak-baseline changes in cortisol and PRL. The independent variable was group and the covariate was age. The groups did not differ significantly. Age was a significant covariate for PRL ($p < .03$) but not for cortisol. For the adolescents, active and placebo challenge tests were compared using repeated measures ANOVA. There was a significant difference between FEN and placebo challenges for PRL ($F = 25.71$, $df = 1,6$, $p = .002$) but not for cortisol. While a control group is needed, this study highlights several methodological issues such as the effects of age and the differential effects on specific hormones. Implications for future research will be discussed.

NR26 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

THE DST IN DEPRESSED INPATIENT VERSUS OUTPATIENT PREPUBERTAL CHILDREN

Shahnour Yaylayan, M.D., Psychiatry, The Ohio State Univ, 473 W. 12th Avenue, Columbus, OH 43210; Elizabeth B. Weller, M.D., Ronald A. Weller, M.D., Mary A. Fristad, Ph.D., Sheldon H. Preskorn, M.D.

Summary:

Most reports on the dexamethasone suppression test (DST) have focused on either inpatients or outpatients, but not both. Thus comparison between two groups have been infrequent. The DST was studied in two groups of prepubertal children with moderate to severe major depression (DSM-III) criteria): 63 inpatients and 14 outpatients. The Diagnostic Interview for Children and Adolescents was used to establish criteria-based diagnoses. Baseline cortisol levels were measured at 8 a.m. and 4 p.m. At 11 p.m., a 0.5 mg oral dose of dexamethasone was given. Cortisol levels were measured utilizing radioimmunoassay the next day at 8 a.m. and 4 p.m. At 8 a.m., 45% of inpatients and 42% of outpatients had positive DSTs (serum cortisol level $\geq$ 5 mg/dl). Sensitivity at 4 p.m. was 54% for inpatients and 50% for outpatients. Sensitivity for the DST-Either (DST positive at 8 a.m. and/or 4 p.m.) was 67% for inpatients and 75% outpatients. Sensitivity for DST-Both (DST positive at 8 a.m. *and* 4 p.m.) was 32%, inpatients and 8%, outpatients ($X^2 = 3.48$, $p < .07$). Post-dexamethasone cortisol levels were higher for inpatients at 8 a.m. (7.2 $\pm$ 8.2 vs 4.8 $\pm$ 5.0; $t = 1.42$; $p < .08$) and 4 p.m. (6.7 $\pm$ 5.5 vs. 4.1 $\pm$ 3.3; $t = 2.32$; $p < .03$). Thus, the DST results were comparable in moderately to severely depressed prepubertal children regardless of hospitalization status, although higher post-dexamethasone cortisol levels were more typical of inpatients.

NR27 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

PERIPHERAL BLOOD COUNT AND THE DST IN DEPRESSED CHILDREN

Shahnour Yaylayan, M.D., Psychiatry, The Ohio State Univ, 473 W. 12th Avenue, Columbus, OH 43210; Elizabeth B. Weller, M.D., Ronald A. Weller, M.D., Mary A. Fristad, Ph.D., Sheldon H. Preskorn, M.D.

Summary:

Abnormally high cortisol levels may influence the distribution of different types of white cells in the blood. We studied the immune system in three groups of prepubertal inpatients: 35 with major depressive disorder (MDD:DSM-III criteria) who were DST positive (MDD/+), 25 with MDD who were DST negative (MDD/–) and 50 psychiatric controls (disruptive behavior disorders without a diagnosis of depression). A 0.5 mg oral dose of dexamethasone was given at 11 p.m. and cortisol levels were measured by radioimmunoassay at 8 a.m. and 4 p.m. the next day. Red blood cell (RBC) count, white blood cell (WBC) count, and total number and relative percent of neutrophils, lymphocytes, monocytes, eosinophils and basophils in the WBC were assessed. Groups were compared using analysis of variance. Overall, differences on these measures were significant between groups only for RBC (F = 5.23, $p < .007$) and for total lymphocyte count (F = 3.45, $p < .04$). Pairwise comparisons to clarify which specific groups differed from one another were made using contrast analyses. The MDD/+ group had significantly higher RBC levels than the psychiatric controls ($M + SD$ = 4.95 $\pm$ 0.34 10^6/ml vs. 4.75 $\pm$ 0.32 10^6 /ml; F = 7.63; $p < .007$). The MDD/+ group also had a significantly higher mean total lymphocyte count than did the psychiatric controls ($M \pm SD$ = 2.44 + 0.74 k/ml vs. 2.03 $\pm$ 0.63 k/ml; F = 6.40, $p < .01$). These results differ from those reported in adults, in which lymphopenia and neutrophilia are found.

NR28 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

AMANTADINE AND BEHAVIOR IN NURSING HOME PATIENTS

Adrienne C. Lahti, M.D., Psychiatry, Univ of Michigan UH-9D, 1500 E Med Ctr Dr Box 0718, Ann Arbor, MI 48109; Nancy M. Speed, M.D., Alan M. Mellow, M.D., Joseph A. Schwartz, M.D., Thomas L. Brewer, M.S., John K. Zubieta, M.D., Stephen M. Aronson, M.D.

Summary:

Amantadine, an agent with both antiviral and antiparkinsonian properties, has been used in the prophylaxis and treatment of influenza A. Because of its dopaminergic activity, it has been associated with adverse behavioral effects, including agitation, induction of mania and exacerbation of schizophrenia. It has been suggested that the elderly may be more susceptible to this toxicity. We have examined the behavioral effects of amantadine during a recent influenza A epidemic at our VA nursing home. Twenty-six patients (mean age 66.0 $\pm$ 11.0, mean $\pm$ S.D.) were evaluated with the Mini Mental State Exam (MMSE) and Brief Psychiatric Rating Scale (BPRS) at two week intervals before, during, and after a 14 day course of amantadine, 100 mg/day. An additional 24 patients (mean age 65.1 $\pm$ 12.5) who did not receive amantadine were also evaluated with serial MMSE and BPRS ratings. Ratings were performed by investigators blind to drug status (receiving or not receiving amantadine). MMSE scores did not differ significantly between treated and untreated groups either at baseline or during subsequent ratings (treated: 24.3 $\pm$ 6.2, untreated: 23.4 $\pm$ 6.1; F=1.44, p=0.236). Likewise, BPRS scores did not differ at baseline or over time (treated 28.9 $\pm$ 6.4, untreated: 27.9 $\pm$ 7.8; F=0.003, p=0.95). No new cases of influenza developed during the treatment period. Amantadine, in a low-dose regiment for influenza prophylaxis, appears to be free of behavioral toxicity in a nursing home population. Additional data will be presented to help clarify whether certain subgroups of elderly patients may be at risk for such side effects.

NR29 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

QUALITY OF LIFE IN LIVER AND HEART TRANSPLANT PATIENTS

Anne Marie Riether, M.D., Psychiatry, Emory University, 1365 Clifton Road, Atlanta, GA 30322

Summary:

Quality of life variables, cognitive function, anxiety, and depression were studied in patients both before and at three-month intervals for up to one year after heart and liver transplant surgery. To test our hypothesis that after transplantation, quality of life improves, and that anxiety, sickness related dysfunction, and depressive symptomatology decrease, we used the Wisconsin Card Sort Test (WCST), Trailmaking Tests A & B (TMT), the Auditory Verbal Learning Test (AVLT), Mini-Mental State (MMS), Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI), and the Sickness Impact Profile (SIP). Interpersonal style and flexibility was rated using the Impact Message Profile (IMI). Preliminary analysis of 10 percent of the 95 patients tested so far shows no statistical difference over time within and between groups on MMS, TMT, SIP or STAI, although mean scores did improve. There was a statistically significant decrease ($p < .05$) for the BDI and AVLT long delay free recall ($p < .02$) for both groups combined. If these trends continue, we predict statistical significance will occur for other quality of life variables and interpersonal styles between and within groups when the entire sample is analyzed.

NR30 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

PSYCHIATRIC CONSULTATIONS IN AN EMERGENCY ROOM SETTING

Rebecca Johnson, M.D., Psychiatry, Univ of Conn Health Ctr, 263 Farmington Avenue, Farmington, CT 06032; Michelle Riba, M.D., Mahlon S. Hale, M.D.

Summary:

Methods of evaluation and record-keeping in emergency room evaluations of psychiatric patients have received scant attention. As emergency room evaluations of psychiatric patients are often performed by health care workers of varied backgrounds, variabilities in assessment inevitably lead to variability in disposition and outcome.

To study the current practice of emergency room evaluations in an 1100-bed general hospital, we conducted a chart review of 100 emergency visits during a two-month period using a 60-item checklist. Our findings showed inconsistent documentation of past psychiatric histories (60 percent), previous violence (90 percent), past suicide attempts (82 percent), components of the mental status examination, and all types of medical histories.

There exists no standardized form for evaluation of patients in the emergency room setting. Based on commonly encountered psychiatric problems, we propose a structured form to be utilized as a guide regardless of discipline. This form permits more thorough documentation of data that have a high likelihood of determining diagnosis, treatment, and disposition. It should also increase communication among colleagues, allow data to be codified for research purposes and perhaps serve as an impetus to change the structure of psychiatric emergency room services currently offered by general hospitals.

NR31 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

IDENTIFYING RISK FACTORS IN ORGAN TRANSPLANTATION

Ranjit C. Chacko, M.D., Psychiatry, Baylor College of Med., 6560 Fannin Ste 832, Houston, TX 77030; Mark Kunik, M.D., Robert G. Harper, Ph.D.

Summary:

Pretransplant selection and outcome process variables were studied in a transplant population (23 heart, 12 kidney, two liver, one heart/lung), utilizing psychiatric interview and psychometric measures of personality, coping and psychosocial adjustment, employing the Millon Health Behavior Inventory (MBHI) and Psychosocial Adjustment to Illness Scale (PAIS). Possible psychiatric complications identified included history of drug abuse (six cases), history or current excessive alcohol use (18 cases), and prior or current medical compliance problems (19 cases). Twenty-nine patients received an Axis I diagnosis, and 12 qualified for Axis II diagnoses. Half the patients had four or more of the 20 MHBI scales elevated at a level of clinical significance; 62% had one or more PAIS scales elevated. The MBHI sensitive personality-coping style and PAIS Extended Family Support measures were significantly associated with compliance problems. These variables classified 83% of patients for compliance/noncompliance. The sensitive coping style was also correlated with measures of emotional distress, negative orientation to health care, emotional vulnerability, cardiac reactivity, and life-threat reactivity. Findings support conjoint use of psychiatric interview and these psychometric measures of health behavior/social and support factors in transplant candidate selection and treatment.

NR32 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

HETEROGENEITY OF HIGH HOSPITAL USERS ACROSS VA PSYCHIATRY SERVICE TYPES

Michael S. Neale, M.S., West Haven VA Medical Ctr, 950 Campbell Avenue, West Haven, CT 06516; Robert Rosenheck, M.D.

Summary:

Introduction/Methods: In 1986, the Department of Veterans Affairs established the Region I Mental Health Initiatives (MHI), an 11-site demonstration project of community-based intensive case management for veterans with chronic mental illness. Entry criteria included: 1) current inpatient status, 2) primary psychiatric diagnosis, and 3) attainment of local thresholds for "recent high hospital use." Baseline characteristics of 1,062 participants in a randomized outcome study of MHI programs were examined for differences across three psychiatric facility types.

Findings: Demonstration sites were categorized into three psychiatric services types (PSTs) on the basis of ADC and ALOS: PST1 = 10-50 beds, 20 days; PST2 = 50-150 beds, 21-40 days; PST3 = >150 beds, >41 days. MHI high hospital users formed a continuum across the three PSTs. On average, PST3 veterans were significantly older and more functionally disabled, with longer hospital histories and fewer supports, and with fewer subjective symptoms, than the other two groups. PST 1 veterans were younger, more often married and employed, and more acutely symptomatic than other participants. PST 2 veterans fell between those from the other two groups.

Conclusion: Heterogeneity among "chronic", "high-use" patients, across facility types, may have profound implications for patterns of service delivery and effectiveness of intensive case management services. These differences cannot be fully addressed in single-site studies.

NR33 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

LEGAL OFFENDERS IN AN URBAN COMMUNITY MENTAL HEALTH CENTER

Geetha Jayaram, M.D., Meyer 144, Johns Hopkins Hospital, 600 North Wolfe Street, Baltimore, MD 21205; Margaret Phillips, R.N., Shaila Pai, Ph.D.

Summary:

The authors compared a group of 38 patients with a positive legal history at intake who were registered consecutively at an urban CMHC, with 30 others who did not have a legal history. Data were collected by chart review and therapist interviews. Data included socio-demographic variables, background history of child abuse, head injury, history of medical disorders, aspects of patients' current diagnoses and treatment, medications prescribed and compliance. Therapists' opinions regarding treatment outcome after six months and factors associated with it were gathered. Non-parametric tests were applied to assess significance of noted differences in the two groups. They revealed significant differences in some demographic variables such as sex, education, employment, type of housing, etc. Significant differences were also found in background variables such as previous psychiatric treatment, history of head injury and neurological disorders, mini-mental state score and psychiatric diagnoses. Implications of findings for treatment planning are discussed, and specific interventions that may be useful are outlined. Further reviews are in progress.

NR34 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

PSYCHOPATHOLOGY IN VIETNAMESE REFUGEES

W. Ladson Hinton, M.D., RWJ Clin. Scholars Prog, 350 Parnassus Ave, Room 407, San Francisco, CA 94117; Joseph Chen, M.D., Nang Du, M.D., Carolee Tran, Jeanne Miranda, Ph.D., Francis G. Lu, M.D., Shotsy Faust, M.N.

Summary:

The prevalence of major psychiatric disorders in the Vietnamese refugee community is unknown. To determine this prevalence in recently arrived Vietnamese refugees, a native Vietnamese-speaking psychiatrist using a written Vietnamese translation of the SCID (Structured Clinical Interview for DSM-III-R) evaluated 135 consecutive (90% participation rate) adult Vietnamese refugees undergoing mandatory health screening. Subjects were predominantly ethnic Chinese-Vietnamese. Current prevalence of major psychiatric disorders was

Disorder	Percentage
Adjustment disorder	6.7
Major depression	5.2
Generalized anxiety disorder	2.2
Psychotic disorder	1.5
Post-traumatic stress disorder	0.7

Overall, 13% met criteria for one or more DSM-III-R disorders. Presence of a disorder was associated with being married, low English proficiency (both $p < .01$), and longer time in the U.S. ($p < .06$).

The prevalence of major psychiatric disorders reported is lower than might be expected based on previous community surveys of Vietnamese refugees using psychiatric symptom checklists. Characteristics of this sample (especially length of time in the U.S.) may explain the discrepancy. Use of the SCID in cross-cultural psychiatric assessment and epidemiological research will be presented.

NR35 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

A COMPARISON OF ALEXITHYMIA MEASURES

Michael Pierce, M.D., Psychiatry, University Hospital, 2074 Abington Road, Cleveland, OH 44106; John H. Krystal, M.D., Alice Faryna, M.D., Ronald Markert, Ph.D., Anne Davidson, M.D.

Summary:

Alexithymia (Greek: "no words for feelings") is a cognitive-affective trait described in patients with diagnoses including somatic illness, substance abuse, and post-traumatic stress disorder. Although clinically linked to psychotherapy response, the study of alexithymia has been hampered by the absence of reliable and valid measures. This study compares three recently introduced measures for alexithymia and a dichotomous global alexithymia assessment in an attempt to evaluate the convergent validity of these scales. *Methods*: 60 volunteers from a chronic pain treatment center were evaluated using two self-rated measures, the Toronto Alexithymia Scale (TAS) and the Analog Alexithymia Scale (AAS), and a structured interview, the Alexithymia Provoked Response Questionnaire (APRQ). In addition, tapes of the APRQ interviews were rated globally for the presence of alexithymia. *Results*: The APRQ showed a modest but significant correlation with the AAS ($r=.30$, $p=.02$), and no correlation with the TAS ($r=.08$, $p=.28$). The AAS correlated well with the TAS ($r=.55$, $p=.001$). Patients dichotomously rated as alexithymic had lower APRQ scores (mean: 8 ± 3 [SD] vs. 12 ± 3, $T=4.88$, $p=.001$) whereas neither self-report scale reliably distinguished these patients. Inter-rater reliability of APRQ scores was good ($r=.85$). The self-report scale factors failed to correlate significantly with the APRQ, which is a clinician-rated instrument with face validity for several of the characteristics thought to be defined by these factors. *Comment*: The APRQ, which measures verbal expression of affect, appears to reliably assess a characteristic clinically identified as alexithymia. These data suggest that the self-rating measures for alexithymia may be measuring related but distinct constructs.

NR36 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

SERUM VITAMIN B12, FOLATE AND PSYCHIATRIC ILLNESS

Helen L. Miller, M.D., Psychiatry, Univ of North Carolina, CB 7160, Chapel Hill, NC 27599; Robert N. Golden, M.D., Terry Brown, D.O., David Ekstrom, M.P.H., Dwight L. Evans, M.D.

Summary:

The recent development of more accurate assays for serum concentrations of vitamin B_{12} and folate has stimulated renewed interest in the relationship between deficiencies of these compounds and psychiatric illness. We have reported previously neuropsychiatric illness in patients with low serum vitamin B_{12} levels and normal hematological parameters. To further characterize the patients with low and marginal levels of these nutrients, we studied retrospectively 862 and 855 consecutive serum B_{12} and folate determinations that were obtained routinely from patients admitted to our adult psychiatric service over a 24-month period. Ten patients (1.2%) had folate levels lower than the laboratory norm (1.9 ng/ml); 21 patients (2.4%) had B_{12} levels that were below the norm (200 pg/ml). A retrospective chart review compared patients with low vitamin B_{12} and folate to patients with marginal deficiencies and to psychiatric controls with normal levels. Diagnoses and other clinical data, including neuropsychiatric assessments, were compared among the groups. Only one of the vitamin B_{12} deficient patients had macrocytic anemia; over half of the deficient patients had normal hematological indices. Thus, these B_{12} deficient patients would not have been identified without serum B_{12} testing. Moreover, we found no relationship between low or marginal B_{12} levels and psychiatric diagnoses. The clinical use of B_{12} testing and its implications for treatment will be discussed. The findings for folate deficiencies will also be presented.

NR37 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

THE DEVELOPMENT OF A COMPUTER ADMINISTERED HAMILTON ANXIETY SCALE

Kenneth A. Kobak, M.S.W., Psychiatry, Univ of Wisconsin, 600 Highland Avenue, Madison, WI 53792; William M. Reynolds, Ph.D., John H. Greist, M.D.

Summary:

The recent renewed interest in the anxiety disorders and their assessment has led to a renewed interest in the Hamilton Anxiety Scale (HAS). The use of a computer administered version has a number of potential benefits, including: 1) increased reliability from standardization of administration, 2) ease of administration, 3) constant availability and low cost, 4) collection of data in computer processable form, and 5) saved clinician time through administration by nonprofessional personnel.

A computer administered form of the Hamilton Anxiety Scale was developed to provide a high degree of correspondence with the clinician version. Both forms were administered pre and post treatment in a counterbalanced design to 95 subjects participating in several clinical drug trials. Total sample included 26 outpatients with a diagnosed anxiety disorder (panic, generalized anxiety or obsessive-compulsive disorder), 26 outpatients with an affective disorder (major depression or dysthymia) and 39 controls (no current diagnosis). The computer-administered HAS demonstrated high internal consistency reliability (.93) and correlated highly with the clinician version (.95). The mean score differences between versions was small (1.35 points) but significant ($t = 3.64$, $p < .001$). Mean score differences between versions in patients with anxiety disorders was not significant. Ninety-two percent reported feeling comfortable taking the computer version, and 51.5% said they had no preference between the two forms.

NR38 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

HOW NORMAL ARE THE CONTROLS? A PROSPECTIVE STUDY OF A LARGE VOLUNTEER GROUP

Paul A. Gaist, B.A., Clin. Psychbio., NIMH/ADAMHA, RM12C-22 5600 Fisher Lane, Rockville, MD 5600 Fisher Lane, Rockville, MD 20857; Frederick M. Jacobsen, M.D.

Summary:

Objective: Although a control group is frequently considered critical in psychiatric research, few studies have investigated the characteristics of persons volunteering to be controls.

Methods: A prospective study using a newspaper recruitment screening questionnaire for "healthy normal volunteers" (without psychiatric, drug/alcohol, or neurological history) was conduced over a two-year period, and respondents were subsequently tracked through the research system.

Results: Of 466 respondents to the questionnaire, 98 (21%) were immediately disqualified by "abnormal" responses. In subsequent telephone interviews, 20% of the remaining 368 respondents admitted previous psychiatric treatment, 5% admitted current depression, 6% reported significant sleep problems, 2% reported significant head injuries, and 14% reported psychiatric illness in a first-degree relative. Of 131 subjects who entered studies as controls after passing psychiatric, physical, and laboratory examinations, two subjects later admitted past psychiatric treatment.

Conclusion: These findings raise questions regarding the selection of "normal volunteers." Further analysis of the subjects' data is provided, and recommendations are advanced concerning the selection and monitoring of controls for clinical research.

NR39 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

DIAGNOSING LATE LUTEAL PHASE DYSPHORIC DISORDER WITH COMORBID MOOD DISORDERS

Kimberly A. Yonkers, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02135; Kerrin White, M.D., Susan L. McElroy, M.D.

Summary:

Late luteal phase dysphoric disorder (LLPDD), as described in the appendix of DSM-III-R, requires premenstrual symptom changes severe enough to impair social and/or work relationships which are not merely an exacerbation of another Axis I disorder. Overlap of criteria for LLPDD and depressive disorders makes it difficult to diagnose LLPDD in the setting of a mood disorder.

We are conducting a longitudinal, naturalistic study on women with complaints of severe premenstrual changes. Patients with comorbid mood disturbances obscuring the LLPDD have had their diagnoses made clearer when we have followed them past the offset of major depression.

Fifteen women between the ages of 20 and 49 have been entered to date. All report severe premenstrual changes and are free of psychotic disorders, organic disorders or concurrent substance abuse disorders.

A screening questionnaire for LLPDD provides a medical and gynecological history. Patients are instructed in keeping a daily menstrual calendar, the Daily Rating Form. After a second interview involving a Structured Clinical Interview for diagnosis, they continue daily ratings and receive a Longitudinal Interval Follow-up Evaluation at six months.

Patients depressed at intake did not meet LLPDD criteria, but did so after remission of their depression. For women who met criteria for LLPDD and then became depressed, premenstrual symptom variation diminished during the depressive episode.

NR40 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

A 4.5 YEAR FOLLOW-UP STUDY OF INPATIENT BULIMICS

Brian A. Fallon, M.D., Therapeutics, NYS Psychiatric Inst., 722 West 168th Street Box 13, New York, NY 10032; B. Timothy Walsh, M.D., Carla Sadik, M.S.W., Valerie Lukasik, B.A.

Summary:

A 4.5 year follow-up study of 52 consecutively admitted inpatients with bulimia was conducted using self-report measures and semi-structured and clinical interviews to ascertain the course of bulimia and factors related to outcome. Variables assessed at follow-up included lifetime *DSM-III-R* Axis I diagnoses, current personality diagnoses, impulsive behaviors, eating behaviors, duration of bulimia prior to admission, characteristics of the early family environment, family psychopathology, history of child abuse, and Global Assessment of Functioning Scores. 37.8 percent of the 45 women interviewed had recovered fully from bulimia. A preliminary analysis reveals that factors associated with poor outcome included a history of childhood physical abuse, no laxative abuse, and an early family environment characterized by poor interpersonal cohesion, increased control, and increased interpersonal conflict.

NR41 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

SELF-MUTILATION AND BULIMIA

Brian A. Fallon, M.D., Therapeutics, NYS Psychiatric Inst., 722 West 168th Street Box 13, New York, NY 10032; Ronald M. Winchel, M.D., B. Timothy Walsh, M.D., Carla Sadik, M.S.W., Valerie Lukasik, B.A.

Summary:

Semi-structured interviews were used to assess the lifetime prevalence of self-mutilation, *DSM-III-R* Axis I and Axis II Disorders, impulsiveness, eating behaviors, and history of child abuse among 45 women with a previous hospitalization for bulimia. 37.8 percent of these women had a history of self-mutilation. The self-mutilators were more likely than the non-self-mutilators to report childhood sexual abuse, impulsive behaviors, and lifetime obsessive compulsive disorder and panic disorder. These findings indicate a high frequency of self-mutilation in bulimic women. Further, the results suggest that an anxiety disorder may underlie the urge to self-mutilate in a subgroup of bulimic patients.

NR42 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

EGO FUNCTIONS IN BPD AND EATING DISORDER PATIENTS

Thomas E. Smith, M.D., Psychiatry, New York Hospital, 21 Bloomingdale Road, White Plains, NY 10605; Nancy A. Burkey, M.D., John Nawn

Summary:

In a study of co-morbidity between eating disorder (ED) and borderline personality disorder (BPD) diagnostic groups, 10 ED and seven BPD patients were compared using demographic, descriptive/behavioral, and ego function rating scales on admission to an inpatient unit. DSM-III-R diagnoses were assigned by trained interviewers; although most patients in both groups had secondary mood disorder diagnoses, there was no overlap between ED and BPD diagnoses. Analysis of demographic data showed the BPD group to have a more extensive history of psychiatric treatment. The ED group had a significantly higher mean GAS score, whereas the BPD group demonstrated a greater incidence of self-destructive and violent behaviors. Other descriptive measures of behavior and level of function, including BPRS, employment, and social contact scores, did not distinguish the two groups. Bellak's ego function assessment (EFA) profiles were used to compare intrapsychic functioning. The mean EFA profile for the ED group showed consistently higher (healthier) ego functioning, except for five ego functions that fell down into the "borderline" range. The data suggest that ED and BPD patients share a cluster of ego deficits having to do with impulse/affect regulation and identify diffusion, but have otherwise easily distinguishable ego function profiles.

NR43 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

ADDICTIVE AND REACTIVE SUBTYPES OF BULIMIA

Kristin Levitan, M.D., Child Psychiatry, Stanford University, 520 Sand Hill Road Box 17, Palo Alto, CA 94304; Hans Steiner, M.D., Susan Smiga, M.D.

Summary:

Literature and clinical experience suggest the existence of distinct sub-populations of bulimic patients—those with binge/purge patterns reactive to stressors and those with patterns that are habitual and autonomous. The latter may share characteristics of substance abusers. Based upon clinical experience and literature, we chose several features characteristic of substance abusers for examining bulimics (Wurmser, 1977, and Treece and Khantzian, 1986). We studied 31 adolescent girls with a primary diagnosis of either bulimia or anorexia nervosa with bulimic features. A senior clinician divided them into Stress-Reactive (STR) (N = 16) and Habitual (HAB) (N = 15) groups matched for age, SES, and distribution of primary diagnosis. Two raters, blind to initial grouping, assessed patients for characteristics judged indicative of substance abusers (eating behavior, affect surrounding habitual behavior, social/vocational functioning, and family history). HAB's were significantly more socially isolated and more likely to be involved with drugs, truancy, and stealing. HAB's also had more frequent binge/purge episodes and hospitalizations and more preoccupation with diet. They exhibited more compulsivity, suicidality, grandiosity, splitting, externalization, "emptiness," and disturbances of identity and boundaries. Their families were more abusive and indirect in communication. All P's <0.05. Results suggest that HAB's and other addictive illnesses share important features.

NR44 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

STANDARDIZED REPORT FORM FOR MENTAL STATUS EXAMS

Robert G. Ruegg, M.D., Psychiatry, Univ of North Carolina, CB 7160, Chapel Hill, NC 27599; Dwight L. Evans, M.D., Robert N. Golden, M.D.

Summary:

We have examined the mental status examination (MSE) performance of psychiatrists-in-training before and after the introduction of a standardized report form. Previous work by others has shown that important MSE data are often not documented by fully trained psychiatrists, and that a standardized report form improves this reporting.

Eighty-four charts from consecutive admissions before and 87 from six months after the introduction of a standardized form were retrieved and evaluated by comparison with a list of elements generally accepted as important to an adequate MSE.

We found use of the form to be associated with a 40% increase in the completeness of the reports. However, an important item not on the form was less likely to be recorded than with an unstructured record of the MSE. The most improvement occurred for the MSE items "unusual movements," "flight of ideas," "speech clarity" and "spontaneous motor activity."

The form makes the data more accessible, it serves as a teaching aid, cueing trainees with a broader range of the observations and tests that they might make, and it greatly improves the quality of the MSE in the record. Therefore, we recommend that some version of a comprehensive, structured MSE form be adopted for use on adult inpatient psychiatry units where residents are being trained.

NR45 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

PSYCHIATRY TODAY: PSYCHOLOGY VERSUS BIOLOGY

Ileana Zaharovits, M.D., Psychiatry, Maimonides Hospital, 950 49 Street #10G, Brooklyn, NY 11219; William Fried, Ph.D.

Summary:

Recently a lot has been written about psychiatry being at a crossroad with a switch from a psychological approach toward a biological emphasis. While some authors have expressed their concern about this biological tendency to the detriment of the psychological approaches, others, however, are confident that biological progress is in perfect accord with the progress of psychiatry. There is no study that shows the distribution of biological and psychological tendencies among psychiatrists in the United States. The present study serves this purpose.

A 19-item questionnaire was sent nationwide to approximately 6000 APA member psychiatrists, selected randomly. The response rate was of 31%. The results were analyzed for two groups: one comprises psychiatrists in practice for at least 15 years, and another group in practice for less than 15 years or in training. Although the younger group is slightly more biological in orientation, overall there is no significant correlation between the period of training and the biology vs. psychology orientation. A significant difference of preference and orientation was noticed among psychiatrists depending on their type of practice: e.g., there is a greater biological orientation among the members in academia compared with private practitioners. The study also presents information about psychiatrists' views regarding the importance of psychotherapy and its role in the future of psychiatry, and about the way psychiatrists perceive themselves among other medical specialists.

NR46 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

A NATIONAL SURVEY ON PSYCHIATRIC ETHICS TRAINING

John H. Coverdale, M.D., Psychiatry, Baylor Col of Medicine, One Baylor Plaza, Houston, TX 77030; Patricia G. Isabell, M.D., Timothy L. Bayer, M.D., Steven Moffic, M.D.

Summary:

Introduction: Information is not available on how ethics is taught to psychiatric residents, yet psychiatric ethics are currently the focus of national attention. *Method:* Ninety-seven chief residents, (81 percent of the total sample surveyed), responded to a mailed out and structured questionnaire). *Results:* Eighty-six percent (N = 83) reported that ethics teaching was of high critical importance and 92 percent (N = 89) thought that this should be part of the core curriculum. However, only 34 percent (N = 33) reported that ethics was taught by formal seminar series, while the most frequent reasons given for this lack were its relative unimportance (N = 30), and that it is learned in supervision (N = 15). Issues cited as worthy of formal attention included therapist-patient sex (N = 30), confidentiality (N = 30), and the right to refuse treatment (N = 20). However, each of these topics was covered by less than half of those programs which offered a formal course. Both resident and faculty interest in ethics was rated as being moderate to high with no significant difference between groups ($t = 1.426$, d.f. = 192, $p > 0.05$). *Implications:* This gap between what residents believe is important to learn and what is actually taught illustrates a need for increased attention to ethics training.

NR47 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

SUPPORT GROUPS FOR YOUNG ADULTS WITH DIABETES

Rose Shalom, M.D., Psychiatry, Duke, Box 3812 DUMC, Durham, NC 27710; Janice Ryan

Summary:

Young adults with type 1 diabetes often have difficulties dealing with their diabetes. These difficulties may manifest themselves as a depressive state, an anxiety state, or as persistent noncompliance with medical regimens. These individuals are often reluctant to pursue individual psychotherapy. In view of the difficulty in helping these very distressed patients, this study was undertaken. Its goal was to investigate the role of a peer support group in a college campus as a means of improving how young adults with diabetes deal with their illness.

Three closed-membership groups, with a total of 20 participants, were held. Each group met for 10 weekly sessions, co-led by a medical and by a psychiatric professional. Hemoglobin AIC (HgbAIC, a measure of blood sugar control) determinations prior to participation in the group ranged from 4.0 to 11.7, with a mean of 8.6. (HgbAIC for a non-diabetic person ranges from 4.0-6.0). After participation in the group, the HgbAIC levels of group members improved to a mean of 6.10, $P < 0.01$, by paired T test analysis. This improvement was stable for a 12 month follow-up period.

Twenty-three students with diabetes who did not participate in the group, who had analogous baseline HgbAIC levels than the group participants, and who were followed regularly by the medical co-leader of the group for their diabetes, served as the control population. Their HgbAIC levels in a one-year follow-up period showed no statistically significant change.

These data suggest that a peer support group co-led by a medical and a psychiatric professional may provide a means of helping individuals with a chronic illness cope better with the physical and the psychological ramifications of their disease.

NR48 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

THE RIGHT TO REFUSE MEDICATION: A CLINICAL DILEMMA

Elizabeth Lazaroff, M.D., Psychiatry, UCI Medical Center, 101 City Dr., So. Bldg 2 Rt 88, Orange, CA 92668; Rhonda K. Hahn, M.D.

Summary:

In June of 1989, the California Supreme court let stand an appellate court decision granting an involuntary psychiatric patient the right to refuse medication. The court contended that, absent an emergency, an involuntary patient could not be administered antipsychotic medication against their will without a judicial determination of incompetency to make a treatment decision. Although the intent of this case law was to preserve patients' rights, its potential impact on clinical management appeared great and prompted this study to objectively explore those issues. The medical records of the first 32 involuntary patients who required judicial review for competency to refuse treatment were examined. Information regarding diagnosis, length of stay, use of seclusion and restraint, and need for forcible administration of medication was obtained. For comparison, the previous involuntary admissions of the same patients prior to the implementation of adjudication procedures for refusing treatment were also reviewed. This allowed 24 patients to serve as their own controls. The results were significant for longer length of stay, increased use of seclusion and restraint, and increased involuntary administration of medication. These findings suggest that displacing judgment from physician to courtroom may not appropriately address a patient's right to refuse treatment.

NR49 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

RECIDIVISM AMONG INSANITY ACQUITTEES

Bill J. Komer, M.D., St. Thomas Psych Hosp, P.O. Box 2004, St. Thomas Ontario 00000, Canada N5P 3VP; Donald A. Galbraith, M.D.

Summary:

There has been much recent discussion about recidivism of individuals detained on a Warrant of the Lieutenant Governor (individuals found not guilty by reason of insanity or unfit to stand trial), which has questioned the effectiveness of treatment programs. This paper reports the findings of a follow-up study of WLG's who had community placement (N = 32). The results show that the recidivism rate in this select population is low, and that except for a few individuals, this group has functioned well in the community.

NR50 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

FAMILY HISTORY AND COURSE OF SCHIZOPHRENIC ILLNESS

Kenneth L. Subotnik, C.Phil., Psychiatry, Univ of California, 760 Westwood Plaza Box 18, Los Angeles, CA 90024; Keith H. Nuechterlein, Ph.D., Robert Asarnow, Ph.D., David Fogelson, M.D., Michael Goldstein, Ph.D., Sharon A. Talovic, Ph.D.

Summary:

Affective and schizophrenic disorders among first- and second-degree relatives of 43 schizophrenic patients were examined in association with the presence of both depressive and negative symptoms in these probands. Both family-study and family-history methods were used to assess psychiatric illness in 192 first-degree relatives, and family-history information was obtained on 407 second-degree relatives. It was hypothesized that affective symptoms in the schizophrenic probands would be associated with the presence of affective illness in their relatives, and that negative symptoms would be associated with familial schizophrenic disorders in the relatives.

The findings confirmed the hypothesis that there is an association between depression in schizophrenic patients and a family history of affective illness. Some evidence was found for an association between manic features in the schizophrenic probands while they were outpatients and a family history of bipolar affective disorder. Contrary to our hypothesis, there was no evidence that negative symptoms in the schizophrenic probands were related to family history of schizophrenic disorder. The finding that familial affective illness was associated with depressive but not negative symptoms in the probands was taken as partial validation of the independence of these two symptom constructs. The findings are consistent with a model where affective liability is viewed as exerting a modifying influence on the symptoms shown by schizophrenic patients.

NR51 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

PHARMACOKINETICS OF ARECOLINE IN PATIENTS WITH DEMENTIA OF ALZHEIMER'S TYPE

Pearse Morris, M.D., Natl. Inst. on Aging, Bldg 10 Rm 6C414, Natl. Inst., Bethesda, MD 20892; Timothy T. Soncrant, M.D., Kathleen Raffaele, Ph.D., Heggunje U. Shetty, Ph.D., Harold W. Holloway, B.S., Eileen M. Daly, B.S., Nigel H. Greig, Ph.D., James Haxby, Ph.D., Mark B. Schapiro, M.D., Stanley I. Rappaport, M.D.

Summary:

Therapeutic trials of cholinergic agonists in subjects with DAT have been largely negative. A problem with most studies has been failure to account for drug pharmacokinetics. As part of a therapeutic trial of the muscarinic cholinergic agonists, arecoline, in DAT, pharmacokinetic studies were conducted in 11 subjects with either mild or moderate DAT. Subjects were 8 male, 65.4 $\pm$ 10.7 yr (mean age $\pm$ SD), and 3 female, 60.3 $\pm$ 10.0 yr. Arecoline 5 mg was infused intravenously over 30 minutes after methscopolamine 2.5 mg was given orally to reduce peripheral side effects. Serial blood samples were taken before, during and after the drug infusion. Subsequent assay of plasma arecoline concentrations with a gas-chromatographic-mass-spectrometric technique demonstrated that steady state levels of arecoline were achieved during the infusion. After cessation of drug administration, arecoline disappeared from plasma with a half-life of less than 5 minutes. To ensure adequate and steady-state arecoline brain concentrations during outcome measurements, subjects then received a two-week, continuous intravenous infusion of arecoline in doses starting at 0.2 mg and escalating to 40 mg per 24 hr. Repeated cognitive testing was used to identify the optimal dose of arecoline, which was then given in a double-blind placebo-controlled crossover phase. The short half-life of arecoline is typical of many cholinergic agents. Pharmacokinetics need to be considered in the design of studies and in the choice of mode and timing of drug administration.

NR52 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

STAFF ATTITUDES TOWARD GEROPSYCHIATRIC CONSULTATION

Deborah A. Banazak, D.O., Pine Rest Christian Hosp., 300 68th St. SE P.O. Box 165, Grand Rapids, MI 49509; Harry L. Piersma, Ph.D.

Summary:

While clinical opinion suggests that psychiatric consultation is valuable for older adults living in extended care facilities, the elderly have typically been underserved by the psychiatric community. Most previous work in this area has focused upon physician reluctance to provide consultation services to the elderly. This study examined staff perception of influential factors in the provision of consultation services. To do this, a survey (Staff Attitude Survey) was developed to assess staff members' beliefs and attitudes toward psychiatric consultation. The survey was administered to 56 individuals at two residential facilities for the elderly in the Midwest. Most staff members were direct care provides (i.e., RNs, LPNs, and nursing aides), working on assisted living units, or basic/skilled nursing care units. There were several interesting findings. Almost half of the staff felt that patient resistance prevented consultation while almost a third of staff believed that family resistance was a major factor in consultation failure. Staff members believed that they more often initiated psychiatric consultation than did the attending physician. Future research would best focus upon the specific reasons for patient and staff resistance to consultation.

NR53 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

AXIS II: TRIDIMENSIONAL PERSONALITY PROFILES

Ron G. Goldman, M.D., Psychiatry, Columbia University, Box 99, 722 W. 168th Street, New York, NY 10032; Andrew E. Skodol, M.D., Norman R. Doidge, M.D., H. David Kellman, M.d., Lyle Rosnick, M.D., John M. Oldham, M.D.

Summary:

Cloninger's system for describing personality variants is based on three hypothesized personality dimensions: novelty seeking (NS), harm avoidance (HA), and reward dependence (RD). The purpose of this study was to measure the relationship between *DSM-III-R* personality disorders and these dimensions in patients with a range of personality pathology. We studied 52 patients, applying to a psychoanalytic clinic (n=25) or for admission to a long-term inpatient unit for treatment of severe personality disorders (n=27). Subjects underwent a structured diagnostic interview (SCID) and completed the Tri-dimensional Personality Questionnaire (TPQ). The sample had a mean age of 29.9; 98 percent were Caucasian, 40 percent male, 81 percent never married, 58 percent college graduates, 46 percent were employed at the time of initial assessment.

We found that patients who met criteria for borderline personality disorder (which has no predicted tri-dimensional profile) had significantly higher NS ($T=2.33$, $p<.025$), but did not differ in other dimensions. NS was strongly correlated ($p<.01$) to total number of Cluster B traits, inversely to number of avoidant traits; HA to number of avoidant, obsessive-compulsive, and total Cluster C traits; RD inversely to number of schizotypal traits. Concurrent mood or anxiety disorders appeared to be as strongly associated with NS and HA as were Axis II disorders.

NR54 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

ERP NEGATIVE COMPONENT IN ELDER SUBJECTS AT RISK FOR DEMENTIA

Ma-Li Wong, M.D., CNE, NIMH Bldg 10 Rm 3S231, 9000 Rockville Pike, Bethesda, MD 20982; Mary Schroder, Ph.D., Allan Blau, Ph.D., Richard B. Lipton, M.D., Walter Ritter, Ph.D., Herbert Vaugham, M.D.

Summary:

Goal: Evaluate whether cognitive event-related-potentials (ERPs) (1) can differentiate elderly subjects at high and low risk for dementia.

Subjects: Two groups of elderly patients were examined: a group of 24 subjects at low risk for dementia or normals (Blessed score of 0-4), mean age of 82.57 $\pm$ 3.46; and a group of 14 subjects at high risk for dementia (Blessed score of 5-8), mean age of 84.20 $\pm$ 2.45. The two groups consisted of individuals participating in the Bronx Aging Study.

Methods: Electrophysiological recordings and averaging were done with a Nicolet med-80 computer with a 16 channel Grass EEG polygraph. A Nicolet Pathfinder computer was used to obtain area measurements under the ERP waves. The subjects were submitted to an auditory odd ball paradigm. ERP activities associated with frequent and infrequent stimuli were averaged separately. The subjects were also submitted to neurophysiological testing.

Results: Grand means of the ERP waves were obtained at the midline, and a negative component appeared at Cz when the grand means of the waveform for the infrequent stimuli of the two groups were compared. Area measurements under the ERP waves were then performed and indeed were found to be statistically significant at Cz for time beans 300-400ms (423.5 $\pm$ 107.1, and 6.0 $\pm$ 116.9, normal and high risk subjects respectively; $p<0.01$) (mean $\pm$ SE), and 400-500ms (549.9 $\pm$ 138.5, and -7.3 $\pm$ 172.5; $p<0.02$). This negative component showed strong correlation to neurophysiological variables that were altered in subjects with mild cognitive changes.

Discussion: We describe a negative component only present in the ERPs of our subjects at high risk for dementia. This component was found in the waveform for the infrequent stimuli at Cz and lasted from 300-500ms. This negative component might be a marker for cognitive dysfunction.

NR55 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

MENTAL HEALTH NEEDS OF THE ELDERLY VARY BY SETTING

Susan Lehmann, M.D., Psychiatry, Johns Hopkins, Meyer 279 600 N Wolfe Street, Baltimore, MD 21205; Geetha Jayaram, M.D., Peter V. Rabins, M.D.

Summary:

To determine if outpatient psychiatric needs of the elderly vary by setting in which care is offered, we compared the charts of 75 patients over age 60 in an inner city community mental health center (CMHC), 43 patients in a hospital based psychogeriatric clinic (PC) and 26 patients in a geriatric outreach program (GOP) in northwest Baltimore County. While all groups had a 3:1 female to male ratio, the CMHC population had a much greater percentage of black ($p<.001$) and unmarried ($p<.001$) patients. The majority of CMHC patients experienced onset of psychiatric illness before age 55 (76 percent), unlike the PC patients (48 percent) or the GOP patients (23 percent) ($p<.001$). Additionally, schizophrenia was the most common diagnosis among CMHC patients (43 percent), while affective disorder was most common among PC patients (65 percent) and GOP patients (50 percent) ($p<.001$). In all three settings adjustment disorders and family therapy were needed more often for patients with late life onset psychiatric disorders. Over 84 percent of CMHC and PC patients were treated with psychotropic medication compared to 54 percent of GOP patients ($p=.001$).

We conclude that differences in diagnoses, chronicity of illness, and family support systems exist among elderly psychiatric patients in different outpatient settings. Refinement of geriatric mental health care must involve tailoring services to the targeted population.

NR56 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

TELEPHONE UTILITY OF SHORT PORTABLE MENTAL STATUS QUESTIONNAIRE AND A SHORTENED MINI-MENTAL STATE EXAMINATION

William H. Roccaforte, M.D., Psychiatry, Univ of NE Med. Center, 600 South 42nd Street, Omaha, NE 68198; William J. Burke, M.D., Barbara Bayer, M.S.N.

Summary:

The Mini-Mental State Examination (MMSE) and the Short Portable Mental Status Questionnaire (SPMSQ) are widely used screening measures of cognitive function. Phone versions of these were tested as part of an extensive telephone screening instrument for dementia, the Adult Lifestyle and Function Interview (ALFI).

One hundred subjects undergoing geriatric assessment were interviewed by phone with the ALFI an average of 8.7 days prior to their clinic visit. Twenty-two of the 30 MMSE and all ten of the SPMSQ items were suitable for phone administration. Phone and clinic results were compared. The mean MMSE scores of 21.4 ($\pm$ 5.6) for the 30-item test and 14.6 ($\pm$ 4.8) for the phone version were highly correlated ($r = .85$, $p = .0001$), as were the phone and clinic mean scores of the SPMSQ ($r = 0.82$, $p < .0001$).

Interrater reliability for the presence of cognitive impairment was assessed using kappa. Cutoffs of 24 for the full MMSE, 17 for the abbreviated test (proportionate to the 24 MMSE cutoff) and 8 for the SPMSQ yielded kappas of .61 and .56, respectively.

We believe that phone versions of the MMSE and SPMSQ are reliable relative to face-to-face administration and may be useful when only phone contact is possible. The shortened MMSE is limited by lack of information concerning the cognitive domains tested by deleted portions.

NR57 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

PERSONALITY CHANGES IN DEMENTIA

Steven P. Wengel, M.D., Psychiatry, Univ of NE Med. Center, 600 South 42nd Street, Omaha, NE 68198; William J. Burke, M.D., William H. Roccaforte, M.D., Barbara Bayer, M.S.N.

Summary:

Investigations of personality change in dementia have been surprisingly sparse. Influential in the existing reports are the open-ended "Changes in personality, interests, and drives" items from the Blessed Dementia Scale. These 11 items have been operationalized into a series of 30 questions as one part of an extensive telephone screening instrument for dementia (ALFI)*. We report our experience in asking these items of patients and their collateral sources (CS) scheduled to undergo comprehensive geriatric assessment.

One hundred patients were interviewed, 19 of whom were cognitively intact and 65 were mildly to moderately demented. No difference was found in symptom frequency reported by the CS of subjects with dementia of the Alzheimer type and subjects with other dementias. The mean number of symptoms reported by the CS of the demented subjects was significantly greater than for the intact subjects ($t = 3.37$, $p < .001$). The CS's of demented patients endorsed six items significantly more often than their counterparts: 1) concern only about one's own problems; 2) less concern about others' feelings; 3) decreased emotional responsiveness; 4) difficulty starting activities; 5: allowing others to make decisions; and 6) motor restlessness.

These results help expand and clarify our understanding of personality change in dementia. The availability of operationalized items should facilitate detection and allow greater reliability in the assessment of such changes.

NR58 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

AGGRESSION IN PSYCHIATRIC HOSPITALIZED GERIATRIC PATIENTS

Jill S. Meyer, M.D., Psychiatry, Hastings Regional Center, Box 579, Hastings, NE 68902; Robert L. Schalock, Werner M. Mendel, M.D., Hannelore Genaidy, M.D.

Summary:

Data are presented that summarize the antecedents-behaviors-consequences (ABC) of aggressive episodes (defined as threats to or actually inflicting harm to self or others) among geriatric (60+) patients. This group represents 15.8 percent of the daily census, but exhibited only 4.1 percent of the aggressive episodes during the last three years. Numbers in parentheses are for 1,901 non-geriatric patients within the same facility during the same time period; asterisks represent statistically significant differences ($p < .01$).

Antecedents (What Preceeded)

Asked to do something:	32.9%	(41.1%)
Approached by patient:	11.0	(6.3)*
Approached by staff:	6.8	(18.4)*
Sitting:	9.6	(4.7)*
Standing:	8.2	(3.2)*
Walking:	15.1	(13.2)
Not Sure:	16.4	(13.2)

Behavior

Other Directed:	86.7	(70.1)
Staff	59.5	(86.2)*
Patient	40.5	(13.8)*
Self Directed:	4.8	(14.3)*
Object Directed:	8.4	(15.5)*

Preceding Intervention

Verbal:	65.8	(66.8)
Time Out:	10.5	(18.4)*
Chemical (PRN):	23.7	(14.7)*

Type of Physical Intervention

Restraint:	30.9	(40.2)
Seclusion:	61.7	(46.2)*
Mechanical Support:	7.4	(13.7)

Diagnosis

Substance Abuse:	3.8	(6.0)
Schizophrenia:	46.8	(29.8)*
Organic Mental Disorder:	41.8	(28.9)*
Major Affective:	7.6	(4.0)

NR59 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

FOLATE, B12 AND COGNITION IN ALZHEIMER'S DISEASE

Anthony J. Levitt, M.D., Psychiatry, Toronto General Hospital, 200 Elizabeth Street, Toronto ON, Canada M5G 2C4; Harry Karlinsky, M.D., Jim Kirkland, M.D., D. McLauchlan, M.D.

Summary:

Both folate and B_{12} are involved in important metabolic pathways in the CNS and may influence cognition. Recent studies have demonstrated a positive correlation between folate and scores on the Mini-Mental Status Exam (MMSE) in patients with dementia. However, it is not known whether this relationship is specific to AD. We therefore examined the relationship between folate, B_{12} and severity of cognitive impairment in patients with AD as compared with other disorders associated with cognitive impairment. Patients were 66 consecutive referrals to an AD clinic. Using NINCDS-ADRDA criteria, 25 patients had either possible or probable AD, 23 had other dementias (OD) and 18 had cognitive impairment but did meet criteria for dementia (CI). Patients were administered the MMSE, and within 24 hours blood was drawn for serum, red cell folate and B_{12}, as well as other biochemical indicators of nutrition. In the AD group, MMSE scores were significantly correlated with red cell folate ($r = .53$, p.005) and with B_{12} ($r = .40$, p.05) but not with serum folate or other biochemical indicators of nutrition. Regression analysis demonstrated that only B_{12} contributed significantly to variance in MMSE ($R^2 = .39$, p.01). There were no significant correlations between MMSE and folate or B_{12} in the OD or CI group. These findings suggest the possibility of a specific relationship between B_{12} and cognitive functioning in patients with AD.

NR60 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

ELDERLY RESPONDERS TO UNILATERAL VERSUS BILATERAL ECT

Peter Aupperle, M.D., Mount Sinai School of Med., One Gustave Levy Place Bx 1230, New York, NY 10029; Donald Johannessen, M.D., Arthur Gabriel, M.D., Brian A. Lawlor, M.D.

Summary

In the elderly, unilateral ECT is generally recommended over bilateral because of the increased memory loss produced by bilateral treatments. However, a proportion of patients do not respond to unilateral treatment and still require bilateral ECT. This study was undertaken to determine if there were clinical or demographic variables that might indicate why some patients fail to respond to unilateral ECT. Data were collected from the charts of patients meeting the DSM-III-R criteria for major depression who had undergone ECT on an inpatient unit during 1988-1989. Nine patients (mean age 73.7 $\pm$ 5.7 SD, six females, three males) who had received unilateral ECT, and 16 patients (mean age 77.3 $\pm$ 5.4 Sd, 10 females, six males) who had received unilateral followed by bilateral treatment after failure to respond to unilateral ECT were identified. Demographic and clinical variables, including outcome measures, were compared between these two groups of patients and were analyzed by ANOVA. There were no significant differences between the groups in age, sex, co-morbidity, length of stay, frequency and number of treatments, initial Hamilton Depression Rating Scale (HDRS) or decrease in HDRS following treatment. Interestingly, those patients who received bilateral ECT following failed unilateral ECT showed no difference in MMS score at the completion of treatment compared to those treated with unilateral ECT only. In this pilot study, no clinical or demographic variables could be identified that distinguished unilateral responders from nonresponders. Further prospectively designed studies examining these and other clinical biological variables may help identify which elderly depressed patients will require bilateral rather than unilateral treatment.

NR61 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

SHORT-TERM MEMORY EFFECTS OF ECT IN ELDERLY VERSUS YOUNG DEPRESSED INPATIENTS

Stephen M. Aronson, M.D., Psychiatry, Univ of Michigan, CFOB Box 0704, Ann Arbor, MI 48109; Bruno Giordani, Ph.D., Atul C. Pande, M.D., Leon J. Grunhaus, M.D., Carol Lindsay, B.A., Stanley Berent, Ph.D.

Summary:

The effects of ECT on memory in the elderly have not been adequately studied. We have been examining neuropsychological test performance in patients with Major Depressive Episodes (MDE) who undergo ECT to study pre-ECT and post-ECT cognitive function, with special emphasis on the elderly. In the present study we report a pre- and post-ECT comparison between two groups of patients, a younger (age <45, $n=15$) and an older group (age <64, $n=15$), on the Wechsler Memory Scale (WMS, alternate forms). All patients met DSM-III-R criteria for MDE. There were no significant differences found between groups on education, Full-Scale IQ, initial MMPI-Depression scale, seizure duration, and days between WMS administrations ($M=5$ days). Older patients had longer ECT courses (10.4 ± 2.6 vs 8 ± 3, $p<.05$). Comparisons of WMS performance were analyzed using repeated measures ANOVA. With treatment, both groups demonstrated significant improvement in depression ($p<.004$) and a general psychopathology rating ($p<.0002$). No significant pre- to post-ECT differences were found on WMS subtests reflecting personal information, orientation, and attention/concentration. Following ECT, both groups improved in immediate recall of visual stimuli ($p<.0008$) and information from verbal passages ($p<.002$), though the younger patients demonstrated greater improvement on the verbal measure ($p<.04$). Both groups, however, declined equally in their learning of lists of verbal paired associations ($p<.002$). When delayed (30 min.) recall was measured, both groups declined in verbal passage learning ($p<.007$), though no decline was noted for visual recall. Our findings suggest that older, as compared with younger patients, are not generally at greater risk for neuropsychological impairment following ECT. Factors that will be discussed with reference to our findings include ECT factors such as number of treatments, laterality, severity of depression, and time course in response to treatment, as well as the level of difficulty and the immediacy of recall for the learning tasks.

NR62 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

DIMINISHED CAUDATE VOLUMES IN MAJOR DEPRESSION

William M. McDonald, M.D., Psychiatry, Duke University, Box 3215, Durham, NC, 27710; Mustafa M. Husain, M.D., Murali Doraiswamy, M.D., Gary S. Figiel, M.D., Orest B. Boyko, M.D., Everett H. Ellinwood, Jr., M.D., Charles B. Nemeroff, M.D., K. Ranga R. Krishnan, M.D.

Summary:

Serial axial (T1, intermediate and T2 weighted) brain magnetic resonance images (MRI) were used to measure the volume of the caudate nucleus in 39 patients who met *DSM-III* criteria for major depression (mean age ± SD, 54 ± 19 yrs, 15 males) in comparison with 39 normals (54 ± 19 yrs, 18 males) free of major neurologic and psychiatric disorders. Depressed patients had significantly smaller caudate volumes (5.7 ± 2.5 ml) when compared to controls (9.4 ± 3.6 ml) ($t = 5.11$, $df = 67.5$, $p = 0.0001$, two tailed t-test). Age was negatively correlated with caudate volume in depressed patients ($r = -0.69$, $p = 0.0001$) as well as in controls ($r = -.069$, $p = .0001$). There were no significant sex differences in both groups. These results are the *first* demonstration of diminished caudate volumes in depression and support a role for the caudate nucleus in the etiopathogenesis of major depression. Supported by NIMH MH-44716, MH-40159, MH-17632 and MH-42088.

NR63 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

PREDICTORS OF CORPUS CALLOSUM MORPHOLOGY ON MRI

Ioanis A. Parashos, M.D., Psychiatry, Duke University, P.O. Box 3812, Durham, NC 27710; C. Edward Coffey, M.D., Richard D. Weiner, M.D., Mark Webb, M.D.

Summary:

Studies in normal and psychiatric populations suggest that the morphology of the corpus callosum on MRI may be related to a number of factors, including age, sex, height, handedness, and possibly a diagnosis of schizophrenia. Relatively little data are available, however, on the relationship of these variables to corpus callosum morphology in patients with depression.

METHOD: Brain MRI (GE 1.5 Tesla Signa system) was performed on 48 normal subjects and on 41 patients with *DSM-III-R* major depression. All subjects were right-handed and age, height, and sex distribution were similar in the two groups. The total area of the corpus callosum and the area of its five subdivisions (anterior to posterior) were measured blindly using computer-assisted technology on the MRI console.

RESULTS: Although there were no differences between the normal and depressed subjects on any of the measures of corpus callosum size, the two groups differed on the relationship of these measures to other subject variables. Thus, in the *normal population* 1) age was significantly related to the total area and to the areas of the second, third, and fourth region, but not to those of the genu and splenium; 2) sex was significantly related to the area of the fourth region only; and 3) height, IQ, and SES were not related to any measures. In the *depressed population* 1) age was significantly related to the area of the third region only; 2) IQ was related to the total area and the areas of the second, third and fourth regions; and 3) height and sex were not predictive of any measures. These findings indicate that several variables need to be considered in studies of the morphology of the corpus callosum in normal and psychiatric populations.

NR64 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

QUANTITATIVE EEG AND COGNITIVE POTENTIALS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Camran Adly, M.D., Psychiatry, LSU. Med. Center, P.O. Box 33932, Shreveport, LA 71130; John J. Straumanis, M.D., Frederick A. Struve, Ph.D., Jeffrey Knight, Ph.D., Gloria Patrick, M.S., Yoram Raz, M.A.

Summary:

Chronic hypoxemia often occurs in patients with chronic advanced COPD. This pilot study examines the hypothesis that chronic hypoxemia in COPD patients may lead to neurophysiological or cognitive dysfunction. Topographic quantitative EEG, cognitive evoked potentials, and psychometric cognitive testing were employed with nine COPD patients and nine non-COPD psychiatric comparison subjects. The nine COPD patients were screened for presence of hypoxemia and lack of significant hypercapnia or acidosis. They had no medical or neurological disorder which could affect study results. Comparison psychiatric patients were selected based upon approximate age compatibility and absence of medical or organic brain disorders.

Results: The mean auditory P-300 cognitive potential for latency for the COPD patients was 396.9 ms, and 370.4 ms for the control subjects. The difference is statistically significant at $P \leq -028$ (Median Test). Study subjects' mean age was 65.6 and 59.4 for control. There were no significant differences in quantitative EEG results between the COPD subjects and controls. Psychometric cognitive testing showed some degree of impairment (mild to severe) in all COPD patients. However, there did not seem to be any over all relationship between these tests and the EEG variables or P300 latency. Subtest correlations are currently being analyzed.

NR65 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

PET, FRONTAL LOBE HEAD INJURY AND SCHIZOPHRENIA

Stephen Lottenberg, M.D., Psychiatry, Univ of Calif. Irvine, Brain Imaging Center RM 164, Irvine, CA 92717; Brian Stankiewicz, Michelle R. Solano, Ronald M. Ruff, Ph.D., Monte S. Buchsbaum, M.D.

Summary:

We studied 18 never-medicated patients with schizophrenia (18 men, mean age 29) and 18 patients with closed head injury (15 men and 3 women, mean age 47) who had at least one cortical area which was 2 standard deviations below the mean of 2 SD asymmetrical in comparison to 24 normal controls. All subjects performed the Continuous Performance Test (CPT) during uptake of 18F-deoxyglucose. Scans were transformed to glucose metabolic rate and a computer algorithm used to identify 16 cortical areas in each hemisphere. Patients with schizophrenia were assessed as in previous reports with an index of relative frontal function, the right inferior frontal gyrus/occipital ratio. This ratio was 1.07 in the controls and 1.01 in the patients with schizophrenia ($p<0.05$, t-test) and was lowest for the inferior frontal gyrus. In our group of head injury patients, we identified a group with significantly diminished function in the inferior frontal gyrus (7 patients) and contrasted them with 11 patients with a significant abnormality in other brain regions. The CPT showed the inferior frontal group (mean = 0.743, SD-1.195) significantly lower than the remainder of the sample (mean = 2.591, SD = 1.316), ($t = 3.07$, $p<0.005$). Bilateral inferior frontal injury was the most frequent abnormality in the head injury group. Taken together, these results indicate the importance of the inferior frontal lobe for visual vigilance deficits in schizophrenia.

NR66 **Monday, May 14, 9:00 a.m.-10:30 a.m.**

PROTON MAGENTIC RESONANCE SPECTROSCOPY OF BRAIN

Rajiv P. Sharma, M.D., Research, Ill. State Psych. Inst., 1601 West Taylor Street, Chicago, IL 6061r; P.N.V. Subramanian, Ph.D., Michael Barany, M.D., John M. Davis, M.D.

Summary:

Magnetic resonance (MR) spectroscopy provides a safe and noninvasive method to study brain chemistry. We have used the modified STEAM pulse (Frahm et al) sequence to examine localized water suppressed MR proton spectra from two brain regions of normal volunteers ($n = 9$) and patients (schizophrenia $n = 4$, affective disorders $n = 5$). These regions were a) the structures surrounding the anterior horn of the lateral ventricle (including the caudate nucleus), and b) the occipital cortex. N-acetylaspartate (NAA), phosphocreatine-creatine (PCr), choline (CHO) and inositol (INO) resonances were seen in both regions. Ratios of metabolite peak integrals to PCr peak integral were calculated for each spectrum. Patients had a significant increase in the NAA/PCr ratio of the anterior horn region when compared to the corresponding anterior horn region of normals (2.13 vs 1.38 $n = 6$, $t = 2.3$ $p = 0.03$). Five patients were treated with neuroleptics and four bipolar affective patients were treated with lithium. The NAA/PCr ratio of the anterior horn region in the bipolar/lithium treated patients was clearly greater than in the neuroleptic treated patients (2.59 vs 1.68 $t = 1.85$, $p = 0.1$). This study suggests that elevated N–acetylaspartate in the anterior horn region may be associated with either the diagnosis of bipolar affective disorder, and/or with lithium treatment.

NR67 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

LIMBIC MEASURES BY MRI IN DEPRESSIVES AND CONTROLS

Shashidhar M. Shettar, M.D., Psychiatry, VA Medical Center, 2215 Fuller Road, Ann Arbor, MI 48105; Atul C. Pande, M.D., Rao Aravapalli, M.D., Roger F. Haskett, M.D., Leon J. Grunhaus, M.D.

Summary:

Limbic pathology has been proposed in various psychiatric disorders, but few studies have quantified changes in the morphology of limbic structures. Since the temporal lobes are integral to limbic function we compared the width of the temporal lobes as seen on MRI brain scans of patients with Major Depressive Disorder ($N = 20$) versus age- and sex-matched "medical" controls who had clinically "normal" MRI scans on record. MRI measurements were made by a neuroradiologist blind to the diagnosis. Maximum widths of both temporal lobes, medial to the temporal horns perpendicular to their long axes consisting predominantly of hippocampal and other limbic system structures (parahippocampal, dentate gyrus, subiculum fornix and other structures) were manually measured on axial T1 and/or T2 weighted images at the anterior margin of the mid brain. Unpaired two tailed t-tests were used to compare the two groups. There were no significant differences in the left and right limbic lobe measurements between the two groups. The problem of using "medical" controls for comparison will be discussed.

NR68 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

CSF AND PLASMA CACHECTIN IN EATING DISORDER

Julio Licinio, M.D, CNE, NIMH Bldg 10 Rm 3S231, 9000 Rockville Pike, Bethesda, MD 20892; Ma-Li Wong, M.D., Samuel J. Listwak, B.Sc., Margaret Altemus, M.D., Mark A. Demitrack, M.D., Philip Gold, M.D.

Summary:

Goal: Cachectin is a recently-discovered cytokine that causes weight loss in inflammatory and neoplastic diseases (1). This study was conducted to determine whether cachectin mediates abnormalities in ingestive behavior and regulation of body weight in eating disorders.

Subjects: Patients were medication-free for one month prior to admission and throughout the study. Anorexia nervosa patients (AN) were studied on admission (AN low-wt), on short-term weight recovery (AN nl-wt), and four weeks after maintaining normal weight (AN 4-weeks) (n = 8). Normal-weight bulimia nervosa (BN) patients (n = 14) were studied on admission (BN-admission) and after 4-6 weeks of abstinence of binge-purge behavior (BN-abstinent). Sex- and age-matched normal controls were studied (n = 9).

Methods: Blood and CSF samples were collected at 09:00 a.m. from all subjects. Because cortisol, known to be higher in the morning, inhibits cachectin production, we also collected blood samples hourly for 24 hours in 6 AN before and after weight gain, 8 BN (admission and abstinent), and 4 NC. Samples were assayed in our lab, using an immunoradiometric assay, limit of detection = 15 pg/ml.

Results: Cachectin was not detected in plasma, at any of our time points. Cachectin was present in CSF at the following levels: AN low-wt = 48.28 ± 2.38 pg/ml (mean ± SEM); AN nl-wt = 45.05 ± 2.19 pg/ml; AN 4-weeks = 45.71 ± 2.52 pg/ml; BN-admission = 47.65 ± 2.62 pg/ml; BN-abstinent = 47.53 ± 2.07 pg/ml; NC = 44.64 ± 3.98 pg/ml. There were no statistical differences among groups.

Discussion: Cachectin has profound anorexigenic effects in vivo (2). In our population we could not detect cachectin in plasma either at baseline or in the 24-hour samples. However, cachectin was detected at the same concentration in CSF in normals and in eating disorder patients. In conclusion, central or peripheral cachectin does not seem to mediate eating behavior and regulation of body weight in eating disorders. Central cachectin is present in humans; further studies are needed to elucidate the physiological role of central cachectin.

NR69 **Monday, May 14, 9:00 a.m. - 10:30 a.m.**

COMPLAINTS OF VICTIMIZATION BY PSYCHOTIC WOMEN IN THE EMERGENCY ROOM

Valerie D. Raskin, M.D., Psychiatry, Michael Reese Hospital, Wexler Pavilion Lakeshore 31st, Chicago, IL 60616; Carole Warshaw, M.D.

Summary:

High prevalence rates of abuse are seen in female psychiatric patients, with markedly higher rates detected by direct inquiry, leading to the presumption that the clinical issue underlying underdetection of interpersonal violence is the failure to ask. However, investigators working with torture victims and emergency medical physicians have described a "reluctance to know" in which overt histories of victimization are ignored. We reviewed 472 emergency charts from a one year period to investigate how information about victimization was described by psychiatry residents examining psychotic women. Of the 69 cases of psychotic women, 14 (20 percent) had explicit complaints of victimization (n = 10) or delusions suggestive of victimization (n = 4); interrater agreement = 97 percent. In 13/14 (93 percent), the examining resident ignored or attributed the complaint of victimization to psychosis; in one case the psychosis was attributed to victimization. Of the 13 cases in which complaints of victimization were attributed to psychosis, 11 of the examining residents were female (84.6 percent vs. 55.4 percent for other psychotic women, $x^2 = 3.79$,, df = 1, p = .052). Psychotic women were significantly less likely than nonpsychotic women to have any information about a significant other recorded (15.9 percent vs. 42.4 percent, $x^2 = 12.806$, df = 1, p = .0003). The countertransference problems suggested by the data will be discussed in relation to the emergency assessment of complaints of victimization in psychotic women.

NR70 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

LORAZEPAM AUGMENTATION OF LOW-DOSE HALOPERIDOL IN MANIA

James C-Y Chou, M.D., Building 35, Nathan Kline Institute, Orangeburg, NY 10962; Harlan Kosson, M.D., Jan Volavka, M.D.

Summary:

Lithium and neuroleptics are the main treatment used for mania with psychotic features, and haloperidol is used often. The reported daily doses of haloperidol in this combination vary widely and range from 17 mg/day to 90 mg/day. Treating patients with lower doses of neuroleptic may decrease the risk of side effects. Mood disorder patients in particular, since they are more vulnerable than schizophrenic patients to tardive dyskinesia, should have their neuroleptic exposure minimized.

Lorazepam and clonazepam alone have been shown to be effective in mania, but sometimes behavioral control of psychotic manic patients requires very high doses. Some patients cannot be managed even with very high doses of benzodiazepines alone (up to lorazepam 40mg/day or more).

In this open study 8 psychotic manic patients with BPRS scores exceeding 40 were treated with lithium and a fixed dose of *haloperidol 10 mg./day* for 2 weeks. Lorazepam was available as a prn medication and was added as a scheduled medication if needed. Mean BPRS scores improved from a baseline of 49.1 ($\pm$ 5.96) to a final of 28.25 ($\pm$ 7.40). *Lorazepam* dose ranged from *0 to 4 mg/day.* Even severely agitated and combative patients were well controlled. Lorazepam side effects were minimal, and no withdrawal could be detected. Benzodiazepine augmentation of low dose neuroleptics may minimize risk of neuroleptic side effects without compromising efficacy or requiring excessive doses of either drug.

NR71 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

CLINICAL TRIALS OF SODIUM VALPROATE ON MANIC PATIENTS

Chuong C. Huang, M.D., Psychiatry, Med. Col. of Wisconsin, 9455 Watertown Plank Road, Milwaukee, WI 53226; Laurens D. Young, M.D., Harold H. Harsch, M.D.

Summary:

Sodium valproate was used in open trial to treat 15 acutely psychotic patients with manic symptoms, aged 21 to 56, 10 F & 5 M (12 bipolar manic, two schizoaffective manic, and one borderline personality with manic behavior). Peterson manic scale and Global Assessment of Functioning Scale (GAS) were used to evaluate the patient's manic symptoms. All patients received repeat SGOT tests. Eleven patients had CT scans and eight patients had EEG examinations. SGOT were all within normal range. No significant abnormal EEG or CT scan were found. Valproate blood level ranged from 25.6 to 96.1 mg/l and on doses of 500 to 2000 mg every day. Valproate was found to be effective in treating bipolar and schizoaffective disorder patients but not effective in treating the borderline personality patient. The mean Peterson scale change is from 21.0 to 11.4, and mean GAS change from 34.0 to 59.3. Twelve patients showed improvement in one to seven days after administration of valproate which is faster than the lithium treatment. Three patients became depressed. Six patients' manic symptoms reoccurred after the medications were discontinued due to the noncompliance with the outpatient treatment. It appears that sodium valproate is a rapidly acting antimanic agent and may be a specific agent for the treatment of manic symptoms. Its mechanism of action might be GABAergic or direct effect on neuronal membrane. Minimal side effects were found.

NR72 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

A MEDICINAL HERB COMBINATION IN THE TREATMENT OF AFFECTIVE DISORDERS

Osama L.M. Omer, M.D., Medicine, Clinic Rheinfelden, Stelleacker 18, Rheinfelden, 07888, West Germany

Summary:

The study describes the effect of a unique combination of medicinal herbs consisting of absinth (absinthium vulgaris), buds of roses (flores rosae damascena), cardamom (fructus elettaria cardamomum), resin of mastiche (resin pistacia lenticus), milky bark of bambus (resin bambusa arundinaceae) and flowers of Kaozuban (flores onosma brateatum), in the treatment of affective disorders. One hundred twenty-five patients selected on the basis of *DSM-III* criteria of affective disorders were treated for four weeks with a dried mixture of plants (2-3 gm/day). As indicated by Hamilton's Scale of depression and several self-rating scales, 92 (73 percent) patients responded to the treatment. In the fifth week the responders were divided into two groups randomly and blindly. One group ($n = 47$) continued to receive the active treatment with the medicinal herbs for another month, in the second group ($n = 45$) the active treatment was replaced with placebo. The psychic symptoms deteriorated significantly ($p = 0.05$ in Hamiltons scale total score) of the group switched over to placebo. The active treatment continued in 20 patients for 18 months without signs of relapse. No side effects or any changes in blood chemistry were observed. No concomitant psychotropic medication was given. The study provides strong evidence of the efficacy of the medicinal herb combination. The study also suggests that phytopharmacological treatment is a possible alternative to the classical tricyclic antidepressant therapy.

NR73 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

A NATURALISTIC STUDY OF WINTER DEPRESSION

Michael S. Easton, M.D., Research, Ill. State Psych Inst., 1601 West Taylor, Chicago, IL 60612; Tarun Israni, M.D., Edward Altman, Psy.D.

Summary:

The validity of winter depression as a distinct diagnostic entity continues to be questioned. To further examine this, we reviewed all non-geriatric unipolar and bipolar depressed pts admitted to our inpatient unit for research between 1982 and 1989 (N = 97). All pts had received DSMIII/RDC dx and a 24-item HDRS. Pts had their charts evaluated by two separate reviewers, for presence of atypical symptoms (hypersomnia and hyperphagia). Admission dates and, in atypicals, months of onset were recorded. Seven (7.2 percent) patients definitely and one possibly, had atypical symptoms with an average age of 33.2 ± 8.2 yrs. (range 22-44), average HDRS of 21.3 ± 8.8 & M:F::3:5. In evaluating month of onset, 6 of 8 pts had a fall/winter onset (F:W::3:3), one was in August and one was unknown. This small sample correlates with other data on winter depression in terms of onset, age, and HDRS scores. 89 pts had typical symptoms with an average age of 40 ± 12.6 yrs, average HDRS 27.8 ± 9.1 and M:F::39:50. There was no discernible pattern to their admissions with an equal distribution over the season (F = 29, W = 26, Sp = 20, Sum = 24). this naturalistic review adds support to the concept of a distinct fall/winter onset depression. Larger prospective studies need to further cross-validate the specificity of this diagnostic subtype.

NR74 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

ACUTE RESPONSE TO THREE DIFFERENT DOSES OF HALOPERIDOL

Michael S. Easton, M.D., Psychiatry, Ill. State Psych Inst., 1601 West Taylor, Chicago, IL 60612; Philip G. Janicak, Ph.D, Javaid I. Javaid, Ph.d., E. Canelas, M.D., S. Dowd, B.S., John M. Davis, M.D.

Summary:

We examined the neuroleptic dose response issue in 31 acutely psychotic inpatients in an ongoing targeted haloperidol plasma level project. Following a 5-14 day washout, pts were randomly assigned to 2mg (Low (L) group), 5mg (Medium (M) group), or 10 mg (High (H) group) PO BID for 5 days (wk1). If necessary doses were then titrated to specific plasma levels by wk 2 (L = 4 mg ± 0, M = 25.6 mg ± 15 and H = 52.9 mg ± 16.1 /d). Using 30 percent improvement on the total BPRS, 22.6 percent of the sample of wk 1 and 44.4 percent at wk 2 were responders. An ANCOVA, with the BPRS baseline score as covariate, demonstrated no significant differences in change scores among the 3 groups at wk 1 (f = 1.19, df = 2/27, ns; covariate adjusted means: L = 10.1, M = 5, H = 8.2); or, wk 2 (F = .08, df = 2/23, ns; covariate adjusted means: L = 12.7, M = 11.8, H = 11.0). An ANCOVA of the thought disorder subscale (items 4,5,8,11,12) found similar results at wk 1 (f = 1.93, df = 2/27, ns; covariate adjusted means: L = 5.6, M = 2.8, H = 6.1); and, wk 2 (f = 0.3, df = 2/23, ns; covariate adjusted means: L = 7, M = 5.4, H = 6.7). An ANCOVA for side effects (Simpson-Angus) again demonstrated no significant difference among groups at wks 1 or 2. Agitation scores (items 6 and 17) were generally low (mean = 4.7 ± 2.2 out of 14). Pts on 4 mg/d did as well as those on doses up to 70 mg/d. Low dosing strategies will be discussed.

NR75 **Monday, May 14, 3:00 - 5:00 p.m.**

HIPPOCAMPAL PATHOLOGY IN MAJOR DEPRESSION

Murali Doraiswamy, M.D., Psychiatry, Duke University, P.O. Box 3215, Durham, NC 27710; Sunjay A. Shah, B.S., Gary S. Figiel, M.D., Mustafa M. Husain, M.D., William M. McDonald, M.D., Orest B. Boyko, M.D., Everett H. Ellinwood, Jr., M.D., Charles B. Nemeroff, M.D., K. Ranga R. Krishnan, M.D.

Summary:

Proton relaxation time (T1) as measured by MRI has been found to correlate well with the water content of most tissues, including brain (Foster 1984). Recent MRI studies have reported altered brain T1 values in neuropsychiatric disorders such as Alzheimer's disease and multi-infarct dementia. Using a 1.5 Tesla MRI, we calculated *T1* values, on coronal single slice, multi TR/TE images, for the following brain regions (frontal grey, hippocampus, temporal and frontal white matter) in a group of 19 patients (mean age 49 ± 19 yrs) who met *DSM-III-R* criteria for major depression, in comparison with 28 normal controls of statistically similar age. Depressed patients had significantly lower T1 values for the hippocampus (t=2.2, df=45, p=0.03, two tailed t-test) when compared to controls. Age was significantly correlated with T1 in the hippocampus (r=0.44, p=0.018), temporal white matter (r=0.53, p=0.004) and in the frontal white matter (r=0.79, p=0.0001), in controls, but not in depressed patients. Decreased T1 values have been attributed to dehydration, reduced levels of potassium, sodium, glycogen, or protein content as well as decreased tissue growth rate (Bottomley 1987). Our findings of a reduced T1 in the hippocampus suggests that pathological alterations in this region may contribute to the etiopathogenesis of major depression. Supported by MH-44716, MH-40159 and MH-42088.

NR76 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

SCID-RDC: DSM-III-R and RDC INTEGRATED INTERVIEW

Diana O. Perkins, M.D., Psychiatry, Univ. of North Carolina, South Wing CB 7160, Chapel Hill, NC 27599; Julie A Dickison, M.A., Dwight L. Evans, M.D.

Summary:

The Schedule for the Assessment of Depression and Schizophrenia (SADS) determines Research Diagnostic Criteria (RDC) diagnoses. The recently introduced Structured Clinical Interview for *DSM-III-R* (SCID) determines Diagnostic and Statistical Manual III-Revised (*DSM-III-R*) diagnoses. Neither interview provides both RDC and *DSM-III-R* diagnoses, and sequential administration is time consuming, and unacceptably repetitious given the considerable overlap between diagnostic systems. We have developed a hybrid interview providing for simultaneous determination of RDC and *DSM-III-R* diagnoses. The hybrid interview consists of the complete SCID, modified with additional items needed to make RDC diagnoses. All RDC diagnoses derived from the SADS were included. For each RDC diagnostic criteria the corresponding SCID item was determined. When an RDC item was not adequately assessed by the SCID, additional SADS-based questions and corresponding RDC criteria were added into the text of the SCID. This hybrid clinical interview, the Structured Clinical Interview for *DSM-III-R* and RDC (SCID-RDC), provides both RDC and *DSM-III-R* diagnoses efficiently, lengthening the SCID administration time by only 15 minutes. We conclude that the SCID-RDC is a time efficient, comprehensive research diagnostic interview, which is appropriate when *DSM-III-R* diagnosis are preferable, but comparability with previous research using RDC-based diagnoses are also desirable.

NR77 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

PLASMA DEXAMETHASONE LEVELS IN TREATMENT-RESISTANT DEPRESSION

Steven I. Altchuler, M.D., Psychiatry, Mayo Clinic, 200 First Street SW, Rochester, MN, 55905; Siong-Chi Lin, M.D., Toshihiko Maruta, M.D., Deborah C. Newman, M.D., Jarrett W. Richardson, M.D., Paul A. Fredrickson, M.D., James M. Naessens

Summary:

Forty-three patients previously diagnosed with treatment-resistant major depression were admitted to an inpatient psychiatric unit for clarification of diagnosis and treatment. All patients were managed with a standard protocol which required them to be medication-free for at least two weeks and to undergo evaluation with an extensive battery, including self-reporting instruments, clinical interviews, and biological evaluation, followed by a team review of their case. Biological markers included dexamethasone suppression test (DST), plasma ACTH, and plasma dexamethasone levels. The data on other markers collected are still being analyzed. Data were analyzed by non-parametric rank sum analysis and Spearman (rank) correlation matrices. Results indicate patients with a positive DST had significantly higher baseline cortisol levels (both morning and afternoon); higher ACTH levels following dexamethasone; and lower plasma dexamethasone levels. They also had significantly higher Hamilton Depression Ratings. These results raise once again the question of whether positive DST results occur from an endogenous change, or whether non-suppression in a DST is a result from lower plasma dexamethasone levels due to a secondary change.

NR78 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

SYMPTOMATIC AND SEASONAL VARIATIONS IN DEPRESSION

Mark N. Mollenhauer, B.S., Psychiatry, Johns Hopkins University, Merey 4-181 Johns Hopkins Hosp, Baltimore, MD 21205; Sylvia G. Simpson, M.D., John R. Lipsey, M.D., Andrew Feinberg, M.D., J. Raymond DePaulo, Jr., M.D.

Summary:

The records of 293 consecutive patients referred to an affective disorders clinic were reviewed. Comparisons were made based on clinical interviews conducted by the four faculty psychiatrists evaluating the patients. Symptom comparisons were limited to the current or most recent episode of depression. Bipolar II patients had an earlier age of onset than unipolar patients but they did not differ significantly from bipolar I patients' age of onset. Bipolar II patients more often had increased appetite when depressed than unipolars, but did not have significantly different patterns of sleep change. Bipolar I patients reported significantly fewer changes in concentration and interest when depressed than bipolar II and unipolar patients. Finally, nearly 40 percent of the bipolar II patients had a seasonal pattern of mood changes, whereas unipolar and bipolar I patients had a rate of only ten percent. The criterion for calling a patient seasonal corresponded to criterion A of the *DSM-III-R*. While most patients with seasonal affective disorder are bipolar II (Rosenthal et al, 1984) and bipolar II patients are more likely than others to be seasonal, most patients with bipolar II are not seasonal. The implications of this for the classification of affective disorders will be discussed.

NR79 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

ANALYSIS OF SERIAL DST'S BY RANDOM REGRESSION

Rajiv P. Sharma, M.D., Research, Ill. State Psych. Inst., 1601 West Taylor Street, Chicago, IL 6061r; Donald Hedeker, Ph.D., Ghanshyam N. Pandey, Ph.D., Philip G. Janicak, M.D., John M. Davis, M.D.

Summary:

We report the effects of clinical treatment on cortisol values from serial DST's in 37 depressed inpatients. Measurements for the DST and the Hamilton Depression Rating Scale (HDRS) were obtained after a washout of 18.4 (SD = 8.3) days, and then repeated periodically through eight weeks of somatic treatments for a total of nine weekly time points. There were five cortisol values for each DST (predexamethasone [pre-dex] cortisol at 8 a.m. and 11 p.m., postdexamethasone [post-dex] cortisol at 8 a.m., 4 p.m. and 11 p.m.). All patients had at least three or more measurements on the DST and the HDRS. We then utilized the random regression (RR) model to assess the association between pre-dex and post-dex cortisol values (Hedeker et al 1989). The RR model is particularly useful in longitudinal data designs where individual subjects have been measured at different time points. Specifically, we found a significant effect of the maximum pre-dex cortisol value ($p < 0.02$) as well as the average pre-dex cortisol value ($p < 0.005$) on the HDRS across time points. Furthermore, the average post-dex cortisol value ($p < 0.04$), but not the maximum post-dex cortisol value (P = ns), were related to HDRS scores. These results suggest that improvement of depression as measured by decreases in the HDRS is as strongly associated with decreases in pre-dex cortisol values, as with the post-dex cortisol values.

NR80 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

ASSOCIATED PSYCHOPATHOLOGY IN WINTER DEPRESSION

Valerie J. Del Medico, M.D., Psychiatry, Ohio State University, 473 W. 12th Avenue, Columbus, OH 43210; Amjed Quadri, Steven C. Dilsayer, M.D.

Summary:

Twenty-one (21) women and six men ranging in age from 24 to 57 years and one 12-year-old boy who met either NIMH or DSM-III-R criteria for winter depression were evaluated by clinical and structured (SCID) interview. The diversity of pathology was surprising. Three patients (including the adolescent) had bipolar disorder. Nearly 90 percent of the subjects met the DSM-III-R criteria for melancholia. Thirteen reported unremitting wintertime pain. Seven had headaches, three gastrointestinal pain alone for which they sought treatment, one gastrointestinal and chest pain, one chronic back and knee pain, one arthralgias, one myalgias. Chronic pain remitted with treatment with bright light or antidepressants in all cases. Seven or more patients had recurrent panic attacks. Two patients exhibited seasonal bulimic behavior. A majority of the subjects met the DSM-III-R criteria for social phobia. These observations imply that winter depression is associated with forms of psychopathology not previously linked to it in the literature. The demographic data of these patients and responses to treatment with bright light, desipramine, bupropion or tranylcypromine will be presented.

NR81 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

STROKE AND DEPRESSION: THE USE OF A TRAUMATIC STRESS MODEL

Thomas L. Brewer, M.S., Psychiatry, Univ. of Michigan, 1500 E. Medical Center Drive, Ann Arbor, MI 48109; Joseph A. Schwartz, M.D., Nancy M. Speed, M.D.

Summary:

Depression is a common complication of stroke. While recent studies suggest that specific stroke lesions are associated with depression, the role of psychological factors has not been examined systematically. Using a traumatic stress model, we have assessed the psychological impact of the stroke event on a group of patients at the Ann Arbor Veteran's Hospital. In this pilot study we evaluated 25 consecutively admitted male veterans who came into the hospital for stroke rehabilitation with the Impact of Event Scale (IES), the General Health Questionnaire (GHQ), and the Hamilton Depression Rating Scale (HAM).

We found that the perception of the stroke as a psychological trauma, as measured by the IES, was highly correlated [r=.709 df=23 p=.000] with the severity of depression, as measured by the HAM. The IES also correlated well with distress, as measured by the GHQ [r=.547 df=23 p=.005].

NR82 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

BIPOLAR DISORDER AND CROHN'S DISEASE

Suzanne Holroyd, M.D., Psychiatry, Johns Hopkins Hospital, 600 N. Wolfe St. Meyer 143, Baltimore, MD 21205; J Raymond DePaulo, Jr., M.D.

Summary

Despite an extensive literature examining the relationship between Crohn's disease and psychiatric illness, there is only one published report of mania in a patient with Crohn's disease. We report seven patients, six males and one female, with both manic-depressive illness and Crohn's disease. The ages of onset of both affective disorder and mania were highly correlated with age onset of Crohn's disease. Correlation coefficients were 0.89 and 0.79, respectively, with p values of 0.016 and 0.06, respectively. Four were treated with steroids for Crohn's coincidentally with onset of first mania, but three went on to have further manic episodes not associated with steroid use. The relationship of the two illnesses including possible common provoking factors, the possible role of steroids, and the genetics of the disorders, including the possible relationship to the HLA region, is discussed.

NR83 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

ADRENAL ANDROGEN AND CORTISOL IN MAJOR DEPRESSION

Hadley C. Osran, M.D., Psychiatry, Long Beach VAMC, 5901 East Seventh Street, Long Beach, CA 90822; Christopher Reist, M.D., Cheng-Chun Chen, M.D., Lawrence N. Parker, M.D.

Summary:

Adrenal androgen and cortisol production have been thought to be regulated through the H-P-A axis by ACTH. Previous studies have demonstrated a dissociation of cortisol and adrenal androgen production during psychological stress and chronic medical illness, with hypercortisolemia and decreased dehydroepiandosterone (DHA) levels. This study investigated changes in adrenal androgen and cortisol metabolism in major depression. Ten medication-free male subjects with DSM-III major depression (HAM-D X = 25.9 $\pm$ 3.9) and nine age- and sex-matched normal controls completed the study. Serum cortisol and DHA were measured at 8:00 and 16:00. A 24-hour urine collection was obtained for DHA metabolites and cortisol assay. On day 2, one milligram of dexamethasone was administered at 23:00 with repeat blood collections the following day. The depressed subjects exhibited significantly elevated 8:00 and 16:00 cortisol levels, and 67 percent were DST non-suppressors. DHA levels did not differ between groups at 8:00 and 16:00, but in the depressed group a significant loss of diurnal variation was reflected by mean delta DHA values. These findings will be presented and discussed in detail.

NR84 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

ANOSOGNOSIA AND DEPRESSION IN STROKE

Sergio E. Starkstein, M.D., Psychiatry, Johns Hopkins Univ., 600 N. Wolfe St. Meyer 4-119, Baltimore, MD 21205; John Paul Fedoroff, M.D., Joseph B. Breyer, M.D., Robert G. Robinson, M.D.

Summary:

Although there has been general agreement that depression occurs in 30% to 50% of patients who can be interviewed following stroke, some investigators have suggested that the diagnosis of depression in patients with right hemisphere lesions may be hampered by the presence of anawareness (anosognosia) not only for the motor deficits, but for the presence of a depressive mood as well. Thus, according to this hypothesis, anosognosia and depression should not coexist. We have examined two patients with a negative family and personal history of psychiatric disorders who immediately after a right hemisphere cerebrovascular lesion showed both anosognosia *and* major depression. In one of them, anosognosia cleared within two months after the stroke, while the major depression subsided several months later. In the other patients, the depression improved after she was started on nortriptyline, but the anosognosia persisted until much later. These findings demonstrate that post-stroke depression cannot be construed as a mere reaction to physical deficits, and that anosognosia does not preclude the patient's recognition of emotional impairment.

NR85 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

PHYSIOLOGIC MARKER OF ECT SEIZURE GENERALIZATION

Andrew D. Krystal, M.D., Psychiatry, Duke University, Duke Univ. Med. Ctr. Box 3812, Durham, NC 27710; Richard D. Weiner, M.D., Eric Moffet, M.D., C. Edward Coffey, M.D., Pamela Smith, Rebekka Arias

Summary:

ECT seizure adequacy was believed to be reflected by seizure duration, but recent data suggest that other factors may be involved. Since many investigators believe unilaterally and bilaterally induced seizures differ in efficacy we studied whether potential electrophysiologic markers separate these two groups. Visual ratings of ictal EEG amplitude and regularity and several computer spectral and seizure envelope measures were studied. The study population included 13 subjects with unipolar major depression referred for ECT. Left and right front-mastoid EEG's were recorded on paper and on magnetic tape for computer analysis. Compared to unilateral ECT, bilaterally induced seizures had higher amplitude ictal activity ($p < 0.003$) and lower amplitude post-ictal slowing ($p < 0.01$). Trends were also present for bilaterally induced seizures to have more regular ictal morphology and to display larger ictal and smaller post-ictal interhemispheric coherences than unilaterally induced seizures. These observations all support the hypothesis that bilateral ECT seizures are more fully generalized than those with unilateral ECT. These same markers also suggest a trend toward decreasing seizure generalization over the treatment course, consistent with the known increase in seizure threshold. Potential relationships between this effect and therapeutic outcome will be discussed.

NR86 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

VERBAL MEMORY DEFICITS IN SCHIZOPHRENIA AND TEMPORAL LOBE EPILEPSY

Lyn Harper-Mozley, M.S., Psychiatry, Univ. of Penn., 200 Pier Sol Bldg. HUP, Philadelphia, PA 19104; Andrew J. Saykin, Psy. D., Ruben C. Gur, Ph.D, Raquel E. Gur, M.D.

Summary:

Verbal memory was assessed in unmedicated patients with schizophrenia (SCH) (n=25), and left focus (LTLE) (n=25) and right focus (n=25) temporal lobe epilepsy and compared to normal controls (n=25). A supplemental scoring system for the Wechsler Memory Scale (WMS) was used to score thematic sequencing (organization) and content distortions. The California Verbal Learning Test (CVLT) was also given as a measure of concurrent validity.

All three patient groups had significantly lower WMS organization scores than controls ($p < .0001$). No differences were found in the frequency of WMS content distortions. WMS verbal recall deficits in SCH were as severe as those in patients with LTLE. Patients with RTLE showed higher recall than patients with SCH on the CVLT.

These findings suggest that patients with schizophrenia suffer from significant verbal memory deficits, a function most closely associated with the left temporal-hippocampal system. Many psychiatric treatment modalities depend on a patients' ability to remember their verbal interactions with their mental health care providers as a step towards learning new coping skills. While the pathophysiology of verbal memory deficits in schizophrenia is uncertain, these deficits may have implications for the treatment of patients with schizophrenia.

NR87 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

SLEEP APNEA: PERMANENT NEUROPSYCHOLOGIC DEFICITS

Alexandros N. Vgontzas, M.D., Psychiatry, Penn State University, 500 University Drive, Hershey, PA 17033; Roger J. Cadieux, M.D., Ralph A.W. Lehman, M.D., Daniel H. Ingram, M.Ed., Elizabeth B. Lange, B.A.

Summary:

This study, which links severe obstructive sleep apnea with dementia, examined the degree of mental impairment and possible associated brain damage in 25 patients who had obstructive sleep apnea of sufficient severity to warrant recommendation for tracheostomy. Measurements included the WAIS-R and Halstead-Reitan immediately before and six months after tracheostomy. Patients' premorbid intelligence was estimated with a demographical index for WAIS-R. The group was divided into mild, moderate and severe subgroups based on the severity of clinical symptoms, sleep apnea index and minimum oxygen desaturation. Comparisons (premorbid estimate, pretreatment, and six months after treatment) were made both within and among subgroups. The severe subgroup performed significantly worse at pretreatment than the mild subgroup on a number of items such as Full Scale IQ (FSIQ), Verbal IQ (VIQ), Halstead Impairment Index, Category test and other tests measuring language skills and academic achievement. Further, six months after tracheostomy, the severe subgroup's performance was still significantly worse than the mild group in these measures, and some indices of higher-level cognitive function, such as verbal IQ showed no improvement. Most importantly, the two groups were not different in estimated premorbid FSIQ and VIQ. In addition, the verbal IQ of the severe group as measured with the WAIS-R both presurgically and six months after was significantly lower than their estimated premorbid verbal IQ. The deficits found correlate with brain damage primarily in the left temporal, parietal and frontal areas, suggesting permanent irreversible impairment of higher-level cognitive functions associated with severe sleep apnea.

NR88 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

A TRIAL OF IV CLOMIPRAMINE IN FIVE PATIENTS WITH OBSESSIVE COMPULSIVE DISORDER

Brian A. Fallon, M.D., Therapeutics, NYS Psychiatric Inst., 722 West 168th Street Box 13, New York, NY 10032; Michael R. Liebowitz, M.D., Raphael Campeas, M.D., Franklin R. Schneier, M.D., Eric Hollander, M.D., Julie Hatterer, M.D.

Summary:

Case reports indicate that clomipramine (CMI) when administered intravenously is better tolerated and results in improvement even if past trials with oral CMI have failed. As a preliminary trial, we openly treated 5 OCD patients with 14 IV CMI infusions each. Ratings consisted of the Global NIMH OCD Scale, the YBOCS, the Ham-D, and the Global Improvement Scores.

Three of the 5 patients were rated as much improved after 14 infusions. Of the responders, one was a past complete nonresponder to oral CMI. Another was a past partial responder to oral CMI who showed even more improvement with the IV form. The third responder had responded to oral CMI in the past but experienced an intolerable 50 lb weight gain. Of the two CMI nonresponders, one hadn't been able to tolerate a trial of oral CMI beyond 200 mg; although he tolerated the IV form well, he showed no response. The other nonresponder had never had oral CMI because his obsessions focused on the CMI capsule; although he improved enough to accept oral CMI, he was rated a nonresponder because of other obsessions.

These results suggest that IV CMI may be efficacious when oral CMI has failed or been only partially successful.

NR89 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

BASAL GANGLIA DISTURBANCES IN OBSESSIVE COMPULSIVE DISORDER

Michael F. Osterheider, M.D., Psychiatry, State University, Fuechslein Street 15, Wuerzburg 08700, FRG Germany; Delia Lettmaier, M.D., Helmut Beckmann, M.D.

Summary:

The history and development of the basis, theory, and therapy of obsessions and compulsions are characterised by a multitude of different theories and the abundance of therapeutic approaches. OCD can, for example, occasionally begin after a brain injury. Symptoms are refractory to psychotherapy and often respond dramatically to specific drugs, suggesting that underlying biologic dysfunction may be at the root of the disorder.

Recently, serotonin has been implicated in OCD.

PET scans have indicated abnormalities in the frontal lobes and basal ganglia in some cases. Also sometimes CT and MRI have shown similar results. This combination of findings could suggest a neurologic basis for OCD. New results from an *ongoing* study (on the efficacy of Fluoxetine (FLU) in the treatment of OCD) will be given with focus on some neuropsychological, neurological, and psychopathological findings in OCD-patients and their relatives.

CT and brain mapping (BM) findings in some patients will also be presented and conclusion will be drawn on the basal ganglia hypothesis on OCD.

Patients' outcome on FLU-treatment will be discussed in relation to preexisting neurological and psychopathological symptoms and abnormal findings in CT and EEG for example.

Finally an outlook on further research strategies in OCD will be given.

NR90 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

EYE MOVEMENT DISORDERS IN SCHIZOPHRENIA AND OBSESSIVE COMPULSIVE DISORDER

Donna R. Palumbo, M.A., Psychiatry, New York Hospital, 525 E. 68th Street, New York, NY 10021; John A. Sweeney, Ph.D., Richard A Shapiro, B.A., James Halper, M.D., M. Katherine Shear, M.D.

Summary:

Slow pursuit eye movements are a promising biological marker for schizophrenia, but the specificity of this disorder is not yet well established. Several abnormalities observed in OCD suggest that eye movements may be abnormal in this disorder as well, including frequent motor systems abnormalities, basal ganglia/frontal cortex dysfunction, and problems with attention. METHOD: We compared visual pursuit in 26 unmedicated patients with OCD to age and sex matched groups of unmedicated schizophrenic patients (23) and normal controls (44). All subject performed pursuit eye tracking tasks. Infrared (IR) recordings of eye movements were digitized at 250 Hz. "Gain" of pursuit eye movement (match between target and eye velocity) and frequency of reversal and intrusive saccadic eye movements were determined. RESULTS: Eye tracking performance was significantly impaired in both diagnostic groups. However, while schizophrenic patients demonstrated slow pursuit, patients with OCD demonstrated an abnormality of high-gain or fast pursuit eye movements, with frequent compensatory reversal saccades ($p < .050$). Intrusive square wave jerks, which occurred at approximately the same rate for patients with OCD and normals, were less frequent in the schizophrenic group ($p < .050$). DISCUSSION: These data add support for the specificity of slow pursuit to schizophrenia within psychiatric disorders. Because the high gain pursuit is such an unusual neuro-opthamologic abnormality, it may be a promising and highly specific biological marker for OCD.

NR91 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

TREATMENT EFFECTS ON EYE MOVEMENT ABNORMALITIES IN OBSESSIVE COMPULSIVE DISORDER

Richard A. Shapiro, B.A., Psychiatry, Cornell Univ. Med., 427 East 69th St. #3F Box 11, New York, NY 10021; Donna R. Palumbo, M.A., John A. Sweeney, Ph.D., M. Katherine Shear, M.D.

Summary:

Our previous studies of eye tracking in patients with obsessive compulsive disorder (OCD) revealed an unusual abnormality characterized by high-pursuit gain and reversal saccadic movements. The purpose of this study was to evaluate the effect of medication treatment on this abnormality. *Methods*: 26 patients who participated in double blind studies with either clomipramine or fluoxetine underwent post treatment eye tracking. At the time of tracking 9 patients were taking placebo, 5 clomipramine, and 12 fluoxetine. Patients visually tracked a target oscillating in a horizontal plane at 16 degrees/sec. Eye movements were recorded using an infrared reflecting technique digitalized at 250 Hz. *Results*: The observed oculomotor abnormalities were highly correlated ($r = 0.51$) with severity of OCD symptoms in the overall group. OCD patients treated with fluoxetine showed a normalization of eye movement abnormalities. Patients on placebo had no improvement while the clomipramine treated patients had a slight worsening in eye movement. *Discussion*: Findings suggest high-pursuit gain may be a state dependent abnormality in OCD. Normalization of eye movement with fluoxetine suggests that the abnormality may be mediated by a dysfunction in the serotonergic system.

NR92 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

LITHIUM PLUS FLUOXETINE TREATMENT OF OBSESSIVE COMPULSIVE DISORDER

Robert G. Ruegg, M.D., Psychiatry, Univ. of North Carolina, CB 7160, Chapel Hill, NC 27599; Dwight L. Evans, M.D., Wilson S. Comer, M.D., Robert N. Golden, M.D.

Summary:

We report a series of four cases in which the addition of lithium potentiated the therapeutic effect of fluoxetine treatment of obsessive-compulsive disorder. Three of the four patients responded to this potentiation with an improvement they rated as about 25 percent to 50 percent overall. This improvement began to be apparent within a week of starting lithium. The fourth patient had an augmented antidepressant response but no improvement in obsessive-compulsive disorder symptoms. This patient experienced a serotonin toxic syndrome, which subsided with fluoxetine dosage adjustment and the passage of time. Concordant with the concurrent indoleamine theory of obsessive-compulsive disorder, this case series suggests that the addition of lithium to fluoxetine treatment of obsessive-compulsive disorder can potentiate clinical efficacy.

NR93 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

A CONTROLLED TRIAL OF BUSPIRONE AUGMENTATION IN OBSESSIVE COMPULSIVE DISORDER

Francine L'Heureux, M.D., SCN, LCS, NIMH Bldg 10 Room 3D41, 9000 Rockville Pike, Bethesda, MD 20892; Teresa A. Pigott, M.D., T.H. Yoney, M.D., Gay N. Grover, M.S.N., James L. Hill, Ph.D., Dennis L. Murphy, M.D.

Summary:

A number of psychotropic agents including lithium, fenfluramine, and buspirone have been utilized in obsessive-compulsive disorder (OCD) concomitantly with serotonin-uptake inhibitors [clomipramine (CMI), fluoxetine (FLX)], as potential adjunctive treatments. It has been postulated that such augmentating agents might optimize the antiobsessive effects of the uptake-inhibitors via enhancement of serotonergic (5-HT) pathways felt to be critical for therapeutic efficacy in OCD. Our group (1) has previously reported that buspirone, a 5-HT-1 agonist, was as effective as CMI in a controlled trial in OCD patients. In an open trial, Markowitz et al. (2) reported that buspirone enhanced fluoxetine's effects in OCD. Therefore, in order to assess buspirone's effects as an adjunctive agent when combined with either CMI or FLX in a controlled fashion, eight patients with OCD (six during long-term CMI and two during long-term FLX treatment) were administered buspirone (30 mg/day) under double-blind conditions for 10 weeks after a two-week placebo period. All patients were maintained on the same dose of CMI (mean dose = 183.3 $\pm$ 20.1 mg/day) or FLX (mean dose = 80.0 $\pm$ 0.0 mg/day) throughout the buspirone trial. The patients were rated every two weeks by raters blind to the treatment condition utilizing several standardized depression and O-C scales including the Hamilton Depression Scale, the Yale Brown O-C Scale, the NIMH O-C Rating Scale, and the NIMH Global O-C Scale. After the controlled trial was completed, the patients remained on buspirone on an open basis for an additional month (buspirone dose = 60 mg/day) in order to investigate potential benefits from prolonged treatment and/or higher dosages of adjunctive buspirone. The results from this ongoing controlled trial, as well as results from open, extended treatment with adjunctive buspirone will be presented.

NR94 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

LITHIUM VERSUS THYROID AUGMENTATION IN OBSESSIVE COMPULSIVE DISORDER: A CONTROLLED COMPARISON

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

Summary:

Lithium carbonate (L) and thyroid (L-triiodothyronine or LT-3) have both been reported to enhance the efficacy of tricyclics in the treatment of depressed patients, and lithium has been reported in open studies to be a useful adjunct to clomipramine (CMI) or fluoxetine in the treatment of obsessive-compulsive disorder (OCD). In order to evaluate lithium (L) and thyroid (T) adjunctive treatment in a controlled fashion, patients meeting DSM-II-R criteria for OCD and on a stable dose of CMI for at least 14 weeks were entered into a randomized, double-blind, crossover protocol consisting of four weeks of the first adjunctive medication (L or T) followed by four weeks of the second medication (L or T). The patients were rated every two weeks by experienced blind raters utilizing the Yale-Brown Obsessive-Compulsive Disorder Scale (YBOCS), NIMH Obsessive-Compulsive Scale (NIMH OCR), NIMH Global O-C Scale, and the Hamilton Depression Rating Scale (HDRS). All of the patients entered were partial responders to CMI treatment, and all remained on the same dose of CMI throughout the trial. Analyses of data from the first nine patients (age = 36.3 ± 2.5 SEM, yrs., duration of illness = 16.1 ± 1.6 yrs.) on a stable dose of CMI (172.2 ± 16.4 mg/day, duration of CMI treatment, 9.3 ± 1.7 mo.) who completed the eight-week trail (dosage, L, 1068 ± 53 mg/day; T, 0.25 mg; serum lithium, 0.51 ± .06 mEq/L) using repeated measures ANOVA revealed no significant interactions or evidence of an order effect; more importantly, there was no significant drug or time effect on any of the O-C scales (YBOCS-0.22 ± 1.2 mean max. delta ± SEM on L, and 1.78 ± 1.40 on T; NIMH-OCR, -0.44 ± 1.02 on L and -1.89 ± 1.59 on T; and Global O-C, 0.00 ± 0.24 on L and 0.44 ± 0.29 on T) or the depression scale (HDRS, 1.11 ± 1.21 on L and 0.89 ± 1.37 on T). The lack of significant change and/or improvement in this preliminary group of OCD patients suggests: (1) the addition of lithium or thyroid to the pharmacologic treatment of OCD patients who are partial responders to CMI does not lead to significant, measurable improvement on OCD or depressive measures, and (2) OCD symptoms may not respond to adjunctive agents that often improve depressive symptoms. These data also lend further support to the idea that OCD represents a disorder with characteristics distinct from the affective disorders.

NR95 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

OCD, ANOREXIA NERVOSA AND BULIMIA NERVOSA: A CONTROLLED COMPARISON OF SYMPTOMS

Teresa A. Pigott, M.D., SCN, LCS, NIMH Bldg 10 Room 3D41, 9000 Rockville Pike, Bethesda, MD 20892; Margaret Altemus, M.D., Francine L'Heureux, M.D., Katalin Bihari, M.D., Philip Gold, M.D., Dennis L. Murphy, M.D.

Summary:

Investigations of possible associations between obsessive-compulsive disorder (OCD) and anorexia nervosa (AN) and bulimia nervosa (BN) appear indicated due to the similar clinical features of the disorders including obsessional preoccupations with specific behaviors, as well as the increasing evidence for the shared therapeutic efficacy of serotonin-uptake inhibiting antidepressants (fluoxetine, clomipramine, etc.) in these disorders. A number of reports have suggested an association, but none to our knowledge have simultaneously compared all three of these groups to a control population. Therefore, to systematically assess potential associations between these disorders, we administered a battery of tests including the Maudsley O-C Scale (MOC), the Symptom Checklist-90-Revised (SCL-90-R), and the Eating Disorder Inventory (EDI), to three groups of patients meeting DSM-III-R criteria for: OCD, AN, or BN. The results were then statistically compared to those for a group of healthy controls who had been administered the same rating scales. Preliminary analysis of the data utilizing ANOVA with post-hoc Bonferroni's t-tests reveals that: (1) patients with BN (N = 16 females) or OCD (N = 16 females, N = 20 males) have significantly increased scores on MOC in comparison to age- and sex-matched controls (N = 16 females, N = 16 males) [$F(4,76) = 30.25$, $P < .001$], (2) patients with AN (N = 10) did not differ from controls (N = 10) on the MOC, (3) patients with BN (N = 31) have significantly increased scores on the O-C subscale of the SCL-90-R in comparison to age- and sex-matched controls (N = 24) [$F(1,52) = 30.30$, P .001] and patients with AN (N = 10) have significantly elevated scores on the O-C subscale of the SCL-90 in comparison to age- and sex-matched controls (N = 10) [$F(1,18) = 30.52$, $P < .001$], and (4) female patients with BN (N = 21) scored significantly higher than OCD patients and controls (N = 24) on all eight subscales of the EDI ($P < .05$), yet a distinctive gender difference was found in the OCD patients. Male patients with OCD (N = 20) scored significantly higher ($P < .05$) than controls (N = 16) on six of the eight subscales on the EDI in contradistinction to female patients with OCD (N = 21) who scored higher ($P < .05$) on only three of the eight subscales of the EDI. These results suggest that patients with BN and OCD, compared with patients with AN and controls, have significant O-C symptom overlap and that patients with OCD, particularly males, have some evidence of eating disorder symptoms. This suggests a potential association between OCD and eating disorders and demonstrates the need for careful investigation and assessment of potential co-morbidity in these disorders.

NR96 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

ADULT NIGHT TERRORS AND ASSOCIATED PSYCHOPATHOLOGY

M. Beatriz Currier, M.D., Psychiatry, Jackson Memorial Hospital, 1500 NW 12th Ave. Suite 1026, Miami, FL 33136; Maria D. Llorente, M.D., Susan E. Norman, M.S.N., Thomas A. Mellman, M.D.

Summary:

Night terrors have primarily been characterized in children. Less is known about night terrors in adulthood. Previous studies have suggested that adult night terrors (ANT) are associated with psychopathology. The specific nature of this relationship, however, remains unclear, including whether or not ANT are distinct from sleep attacks in panic disorders.

To date, ten consecutive adult patients referred to a medically affiliated sleep lab whose clinical histories suggested night terrors have been evaluated. Nine of these patients received polysomnography. Five were available for further evaluation with SCID and other structured inquiry regarding course and phenomonology of night terrors.

All patients' episodes featured confusion, fear, vocalizations, and motor movements, which in seven have resulted in injury. Polysomnography confirmed events associated with delta wave sleep. All patients reported other parasomnias. Five reported adult onset. Exacerbation with stressful life events was common, though ANT were often dissociated from psychiatric episodes. All patients had complaints of anxiety and/or depression. SCID derived diagnoses included depressive disorders ($N = 4$), substance abuse ($N = 2$) and anxiety disorders ($N = 1$).

These findings suggest that ANT are phenomenologically similar to night terrors in children and distinct from sleep panic attacks. Although preliminary, our data support an association of ANT with histories of affective disorders.

NR97 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

BIOLOGICAL CORRELATES OF IMPULSIVITY/AGGRESSION

Timothy L. Lawrence, M.D. Psychiatry, Bronx VA Med Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Emil F. Coccaro, M.D., David P. Bernstein, Ph.D., Ginny Condello, M.D., Larry J. Siever, M.D.

Summary:

Previous studies have suggested a relationship between noradrenergic (NE) function and impulsive/aggressive behavior. In order to explore this relationship inpatients with PD, the GH responses to clonidine (IV) were examined in patients with *DSM-III* personality disorder. Those responses were positively correlated with self-rated measures of impulsivity and aggression in 20 PD patients: (Buss-Durkee Hostility Inventory-Total: $r = 0.42$, $p < 0.07$; BDHI-Indirect: $r = 0.46$, $p < 0.05$); BDHI-Irritability: $r = 0.43$, $p < 0.06$). The mean GH response for the PD patients was comparable to that seen in a group of normal volunteers and was greater than that observed for a group of acutely depressed (MDD) patients (Siever, et al, AGP, in review). Thus, these findings suggest that central NE function may be intact or even hyperactive in PD patients with a propensity for impulsivity/aggression. These findings will be discussed in light of findings of an inverse relation between serotonergic (5-HT) function and impulsivity/aggression in a similar population (Coccaro, et al. AGP, 1989). Reduced 5-HT function is associated with both suicidal behavior and with impulsivity/aggression in PD patients, but only with suicidal behavior in MDD patients, suggesting the possibility of an interaction of the two systems in the control of impulsivity/aggression whether directed at self or others. The NE system may then have a modulating effect on the 5-HT system in determining the direction of expressed aggression.

NR98 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

DOPAMINERGIC DYSFUNCTION IN SCHIZOTYPAL PERSONALITY DISORDERS

Oren Kalus, M.D., Psychiatry, Bronx VA Med Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Larry J. Siever, M.D., Emil F. Coccaro, M.D., David P. Bernstein, Ph.D., Theresa Mahon, B.A., Kenneth L. Davis, M.D.

Summary:

The association between plasma levels of the dopamine metabolite homovanillic acid (pHVA) and psychotic symptoms reported in schizophrenia has not been extensively investigated in the genetically and phenomenologically related schizophrenic spectrum disorders. To test the hypothesis that pHVA levels will differ and correlate with psychotic symptoms in schizotypal personality disorder (SPD) as compared to normal controls (NC) and non-schizotypal personality disorders (NSPD), we compared pHVA levels in SPD ($n = 10$), NSPD ($n = 7$) and NCs ($n = 6$). Subjects diagnosed with SIDP, were medication free for a minimum of two weeks on a low monoamine diet for three days. Mean 10am pHVA levels were significantly different in the three groups ($F = 4.63$, $p < .05$), and were significantly higher in the SPD group as compared to the normals ($p < .05$, by Tukey test). As in schizophrenia, pHVA levels significantly correlated with the sum of positive symptoms ($p < .05$), and with two individual positive psychotic symptoms (magical thinking and recurrent illusions; ($p < .05$), but not with the sum of negative symptoms. The results suggest that dopaminergic dysfunction extends beyond schizophrenia to include the schizophrenic spectrum disorders and is associated with positive like psychotic symptoms in SPD.

NR99 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

TYPE, SEVERITY AND COURSE OF MOOD DISORDER IN BPD

H. David Kellman, M.D., Psychiatry, New York State Psych Inst, 722 West 168th Street, New York, NY 10032; Andrew E. Skodol, M.D., Janis L. Cutler, M.D., Alan Felix, M.D., Holly A. Schneier, M.D., Julia L. Winston, M.D.

Summary:

This study characterized the type, severity, and course of depressive syndromes experienced by borderline patients in long-term inpatient treatment.

Hamilton Depression and Atypical Depression scales were given biweekly to 18 patients admitted for treatment of severe personality disorder. Each subject met DSM-III-R criteria for borderline personality disorder according to structured interview assessment and had a current DSM-III-R depressive syndrome at admission. Twelve had major depression; six had other affective disorders, including bipolar, atypical bipolar, schizoaffective, and organic mood disorders. Thirty-three percent had the full syndrome of atypical depression; 61% had reactive mood; 94% had at least one atypical feature.

HAM-D scores on admission were significantly higher for the mood disorders group than for the major depression group (29 v 18; $t = 3.18$; $p < .01$). Patients with other mood disorders improved significantly by 15 weeks (HAM-D: 20; $t = 3.60$; $p < .02$), while those with major depression were unchanged. Atypical features (mood reactivity, reverse vegetative signs) were persistent; 81% of patients presenting with such symptoms still had them at 15 weeks.

These results indicate that the depressive syndromes of borderline patients are heterogeneous, persistent and severe. They underscore the need for careful differential diagnosis and syndrome-specific treatment.

NR100 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

TREATMENT OF LITHIUM-INDUCED POLYURIA WITH POTASSIUM: A POLITICAL STUDY

Bhaskara R. Tripuraneni, M.D., Psychiatry, Chicago Med School, 3333 Green Bay Road, North Chicago, IL 60064;

Summary:

Nephrogenic diabetes insipidus is a common side effect of lithium treatment in bipolar patients up to 20-70 percent. Established treatments have been thiazide diuretics and amiloride whose effects are partial and lead to Li toxicity due to increased proximal reabsorbtion of lithium. Experiments in rats show that potassium administration was effective in treating as well as preventing Li induced polyuria by blunting the Li induced effect on anti-diuretic hormone without affecting Li levels or extracellular volume.

We studied the effects of oral potassium chloride supplementation [20 M.Eq/day] in four sequentially selected patients with Li induced polyuria in this pilot project. Potassium supplementation resulted in statistically significant [Paired t test] reduction in 24 hour urine volume [$t=6.84$, $df=3$, $P=0.0064$] and increase in urinary osmolality [$t=3.60$, $df=3$, $P=0.0368$] without any changes in Li levels, and very little change in potassium levels. There was also significant decrease in subjectively reported thirst, polyuria, and polydypsia.

We conclude that potassium is effective in treating Li induced polyuria, and is a safer and easily available treatment, than currently used diuretics. This is the first clinically reported study in humans using potassium in treating Li induced polyuria, and recommends future controlled studies.

NR101 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

CLOZAPINE AND HALOPERIDOL: RECEPTOR REGULATION

Clifford Widmark, M.D., Psychiatry, UCI Medical Center, 101 City Dr. So. Bldg 2 Rt 88, Orange, CA 92668; Steven J. O'Dell, Ph.D., Gerald J. La Hostle, Ph.D., Raymond M. Shapiro, M.D., Steven G. Potkin, M.D., John F. Marshall, Ph.D.

Summary:

The atypical neuroleptic clozapine (CLZ) is often effective in treating schizophrenics who respond poorly to typical antipsychotics such as haloperidol (HAL), and CLZ is relatively free of the extrapyramidal side effects (EPS) associated with typical neuroleptics. To investigate the neural mechanisms of the differing CNS activities of these drugs, we used quantitative autoradiography to measure changes in dopamine and serotonin receptors in rats after injection with CLZ or HAL for 21 days at clinically relevant dose rations. Levels of D1, D2 and 5-HT2 receptors were determined in frontal cortex, caudate-putamen, and nucleus accumbens. Rats receiving CLZ showed CNS receptor changes markedly different from those in HAL treated animals. Rats treated with HAL showed enhanced D2 binding, while those treated with CLZ did not. In contrast, CLZ induced enhanced D1 binding, whereas these sites were unchanged in HAL treated rats. Also CLZ treatment decreased 5-HT2 binding, while HAL had no significant effects. Further experiments using receptor binding assays, done after acute CLZ treatment followed by EEDQ (receptor alkylating agent), showed CLZ bound to approximately equal numbers of D1 and D2 sites, possibly indicating preferential D1 regulation with chronic treatment. CLZ binding to D1 and D2 receptors appeared reversible over a two-hour period, but occupation of 5-HT2 sites continued. The differential effects of CLZ and HAL on D1, D2 and 5-HT2 receptors may be relevant to the clinical efficacy and side effect profiles.

NR102 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

ECT AND DOPAMINE: A BRAIN MICRODIALYSIS STUDY

George G. Nomikos, M.D., Psychiatry, Univ of BC, 2255 Wesbrook Mall, Vancouver BC, Canada V6T2A1; Athanasios Zis, M.D., Geert Damsma, Ph.D., Hans C. Fibiger, Ph.D.

Summary:

Electroconvulsive treatment (ECT) remains an effective and useful treatment for patients with psychotic depression, catatonia, and mania. A recent editorial in the *American Journal of Psychiatry* (November 1989) had focused attention on the remarkable and rapid motor improvement observed after ECT in Parkinson's patients. In view of the effectiveness of this treatment in Parkinson's disease and the purported role of dopamine (DA) in the pathophysiology of the psychotic depression the effect of ECT on DA transmission is of considerable interest. Behavioral studies in animals have provided evidence that electroconvulsive shock (ECS) produces either an increase in postsynaptic DA receptor sensitivity or a subsensitivity of DA autoreceptors. To date, however, neurochemical studies have failed to find acute effects of ECS on dopaminergic indices. We report here the effects of ECS on interstitial concentrations of DA and its metabolites DOPAC and HVA, the serotonin metabolite 5-H1AA and the purine metabolite uric acid, in the rat striatum using on-line microdialysis in freely moving animals. The mean DA increase was 13.8 fold ($n = 9$) when the ECS was given 24 hours after the implantation of the dialysis probe. A second ECS given to the same animals 24 hours later produced a 5 fold increase. In a separate experiment ECS was given 48 hours after surgery and the mean DA increase was 2.3 fold ($n = 8$). A second ECS given to these animals two hours after the first produced a 1.3 fold increase. The ECS-induced increase in DA was derived from a neuronal $Ca++$ sensitive pool since perfusion of a modified solution in which $Ca++$ had been replaced with $Mg++$ blocked this effect. Increases were also observed in the levels of the metabolites DOPAC, HVA, 5-H1AA and uric acid. By comparison to the changes in DA release these increases were smaller and stable across experimental conditions. The observed differences in interstitial DA release indicate that both the time interval between dialysis probe implantation and ECS as well as repeated exposure to ECS affect the magnitude of DA release. The implications of these observations for the mechanism of action of ECT in psychotic depression and Parkinsonism will be discussed.

NR103 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

CLOZAPINE PLASMA CONCENTRATIONS AND CLINICAL RESPONSE

Delwyn D. Miller, M.D., Psychiatry, Univ of Iowa Hospital, 500 Newton Road, Iowa City, IA 52242; Paul Perry, Ph.D., Remi J. Cadoret, M.D.

Summary:

We studied the relationship between clozapine plasma concentrations and clinical response in 30 treatment-resistant schizophrenics (no response to three six-week trials of at least two chemically dissimilar antipsychotics at dosage equivalent $\geq$ 750 mg. of chlorpromazine/day) on a fixed dose of clozapine for four weeks. Twenty-five patients (83%) received 400 mg./day, four received 300 mg./day, and one received 250 mg./day. Eleven of the 30 patients (37%) were classified as responders by predetermined criteria ($\geq$ 25% reduction in BPRS from baseline to week 4 *and* a post-treatment BPRS of $<$ 40 *or* CGI of $<$ 3). There was no statistical difference between responders and nonresponders for: age, sex, duration of illness, baseline BPRS, or mean steady-state clozapine concentrations. There was no statistically significant correlation when baseline BPRS and mean clozapine concentrations were regressed against week 4 BPRS. However, eight out of 11 patients (73%) with steady-state clozapine plasma concentrations of $\geq$ 325 ng./ml. were responders, and only three out of 19 patients (16%) with steady-state clozapine plasma concentrations of $<$ 325 ng./ml. responded. A chi-square analysis found this to be a statistically significant difference ($X^2 = 9.7$, $p < 0.01$).

NR104 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

ECT SEIZURE DURATION: CUFF VERSUS EEG VERSUS QUANTITATIVE EEG

John H. Gilmore, M.D., Psychiatry, Univ of North Carolina, CB# 7160 Med. Sch. Wing B, Chapel Hill, NC 27599; Robert N. Golden, M.D., Michael R. Isley, Ph.D., Li Sheng Kong, A.B., Dwight L. Evans, M.D., Enid R. Kafer, M.D.

Summary:

We compared the seizure duration in 114 ECT treatments in 12 patients as determined by three methods: 1) observed motor seizure in a cuffed extremity during the ECT treatment, 2) two blinded readings of MECTA SR1 EEG strips, and 3) two blinded measurements of quantitative EEG (qEEG) data from a Cerebro Trac 2500+ brain monitor, derived from spectral analysis and display of the EEG as a dot-density modulated spectral array with spectral edge frequency (SEF 90%).

We found the absolute differences between the MECTA readings to be 4.3 $\pm$ 1.1 (SEM) seconds and between the qEEG measurements to be 2.3 $\pm$ 0.6 seconds, indicating that the reliability is greater for the qEEG than the MECTA EEG. Using an experienced neuropsychologist's qEEG measurement as a "gold standard," the MECTA EEG reading appeared to be more valid than the observed motor seizure: the absolute difference between the qEEG measurement and the two MECTA readings were 8.4 $\pm$ 1.2 seconds and 7.1 $\pm$ 1.2 seconds, respectively, compared to 17.8 $\pm$ 1.7 seconds between the qEEG and the observed motor seizure. The clinical implications of these findings will be reviewed, and examples of cuff, MECTA EEG, and qEEG data will be presented.

NR105 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

BUSPIRONE: SEDATIVE OR STIMULANT EFFECT?

Rocco L. Manfredi, M.D., Psychiatry, Penn State University, 500 University Drive, Hershey, PA 17033; Edward O. Bixler, Ph.D., Charles M. Falcone, B.A., Melda A. Isaac, B.S., Roger J. Cadieux, M.D.

Summary:

A major advantage of buspirone is its reported lack of sedation. However, one side effect noted is insomnia. We evaluated buspirone in a 10 mg hs dose in the sleep lab in order to determine objectively its effects on sleep efficiency: sleep latency (SL), wake time after sleep onset (WTASO) and total wake time (TWT). Six insomniac subjects were assessed in a 16-night sleep laboratory protocol which included four placebo-baseline nights followed by seven nights of drug administration and five placebo-withdrawal nights. On the first three drug nights (nights 5-7), and final three drug nights (nights 9-11) SL changed minimally. However, WTASO increased by 95.2% ($P < 0.05$) on the first drug night (night 5). In addition, WTASO and TWT increased by 39.3% and 24.7% (NS) respectively, during the entire short-term drug condition, and by lesser degrees, 27.1% and 16.2% (NS), respectively, during continued drug administration (nights 9-11). These data confirm lack of sedative effect for buspirone but also suggest some initial sleep disruption produced by the drug. Following drug termination, there was some evidence of a delayed increase in sleep difficulty above baseline during the fourth and fifth withdrawal nights (nights 15 and 16). Regarding sleep stage variables, there was a significant decrease in REM sleep during the first third of the night both during initial (nights 5-7) and continued (nights 9-11) drug administration ($p < 0.05$ and 0.01, respectively). The percentage of REM sleep for the entire night did not change significantly, nor were there any significant changes or trends in other sleep stage variables. In summary, our data confirm the lack of sedative effects for buspirone. However, clinicians need to be aware that the drug can produce mild to moderate degrees of initial sleep difficulty and, following withdrawal, possible mild and delayed sleep disturbance.

NR106 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

TRANYLCYPROMINE WITHDRAWAL PHENOMENA

Mark T. Halle, M.D., Psychiatry, Penn State University, 500 University Drive, Hershey, PA 17033; Steven C. Dilsaver, M.D.

Summary:

The effect of withdrawing tranylcypromine was systematically studied in 18 adult patients who were being treated with 20 mg to 140 mg of this drug daily. The withdrawal of tranylcypromine produced anxious and depressed mood, agitation, fatigue, nausea, headaches, cognitive slowing, and impairment of concentration and memory. The rate of withdrawal appears to be a critical variable. The severe anxiety and agitation produced by the abrupt withdrawal of tranylcypromine responds to benzodiazepines. The literature documents three to five cases in which the withdrawal of tranylcypromine produced delirium and psychosis characterized by auditory and visual hallucinations and paranoid delusions. These effects were not observed in this study. Tranylcypromine withdrawal symptoms can nonetheless be incapacitating. Even the more severe withdrawal states, however, respond to treatment with a benzodiazepine. Our patients tolerated a reduction in the daily dose of tranylcypromine of 10 mg/week. However, most patients still reported an increase in their level of anxiety. Case vignettes of patients having severe withdrawal symptoms will be presented and management of these patients will be addressed.

NR107 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

MANAGEMENT OF MANIA WITH BENZODIAZEPINES, LITHIUM AND ANTICONVULSANTS

Mark T. Halle, M.D., Psychiatry, Penn State University, 500 University Drive, Hershey, PA 17033; Valerie J. Del Medico, M.D., Steven C. Dilsaver, M.D.

Summary:

The management of mania commonly involves high doses of antipsychotic agents (the "traditional treatment"). Many bipolar patients are treated with these agents for indefinite periods. An APA task force estimated that 26% of all patients chronically treated with antipsychotics develop tardive dyskinesia. Further, bipolar patients may be at an increased risk for the development of this disfiguring movement disorder. The avoidance of neuroleptic agents in the management of individuals with bipolar disorder is thus highly desirable. An "alternative" to the traditional treatment is described. Eight consecutive patients with dysphoric (n = 5) or mixed (n = 2) mania with psychosis and a rapid-cycling (n = 1) manic patient received the alternative regimen. Five of these patients bore the diagnosis of schizophrenia or schizophreniform psychosis and had been treated with high doses of neuroleptics (> 1000 chlorpromazine equivalents daily). The alternative treatment described here utilized a combination of clonazepam, carbamazepine or sodium valproate, and lithium. This treatment acted with 24 hours, and mania remitted within 24-48 hours in most cases. Clonazepam was discontinued prior to discharge in seven cases. Three patients relapsed when their serum level of anticonvulsant (n = 2) or lithium (n = 1) fell due to noncompliance or supervised dose reduction. All rapidly recovered when dosage was adjusted. Four patients stated that they preferred the alternative treatment, while none expressed preference for the traditional treatment.

NR108 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

SIMILARITIES BETWEEN THE DOPAMINE D2 RECEPTOR AND CALMODULIN

Patrick J. Rogue, M.D., Center of Neurochemistry, 5 Rue Blaise Pascal, Strasbourg 67084, France; Jean Zwiller, Ph.D., Anant N. Malviya, Ph.D., Guy Vincendon, M.D.

Summary:

The phenothiazine-type neuroleptics have calmodulin antagonist effects. The naphtalenesulfonamide derivatives are widely used calmodulin antagonists. We have investigated whether these and similar compounds could bind to striatal dopamine D2 receptors. The calmodulin antagonist W7 was the most potent D2 receptor antagonist. W7 displaced (3H) spiperone binding competitively with an IC50 close to the one for the inhibition of calmodulin-activated enzymatic activities. The chronic administration of this compound induced an up-regulation of striatal D2 receptors. The sequence of calmodulin and of the rat striatal dopamine D2 receptor was compared using the ANA computer program. This algorithm revealed a 28.6% sequence homology between a region of calmodulin located in the third calcium binding domain and part of the fifth transmembrane segment of the D2 receptor. The former contains the phenothiazine binding site, and the latter is part of the hydrophobic core which is supposed to constitute the ligand binding site of the receptor. The percent match rises to 57% when conservative substitutions are included. Thus W7 may act at a structurally similar site present both on calmodulin and on the dopamine D2 receptor.

NR109 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

CHARACTERIZATION OF ETHANOL-INDUCED CALCIUM RELEASE

Patrick J. Rogue, M.D., Center of Neurochemistry, 5 Rue Blaise Pascal, Strasbourg 67084, France; Anant N. Malviya, Ph.D., Guy Vincendon, M.D.

Summary:

There are at least two non-mitochondrial calcium pools, one that is not sensitive (IICP) to inositol, 1,4,5-triphosphate (IP3) and one that is (ISCP). The IP3 receptor is a 260kD protein that mediates calcium release through an ion channel of which it is probably a part. GTP can release calcium from both pools by means of a carrier-type mechanism. It has been suggested that GTP enlarges the ISCP at the expense of the IICP, a process that could be regulated by inositol 1,3,4,5-tetrakiphosphate.

Ethanol release calcium from intracellular stores. The ethanol-sensitive calcium pool (ESCP) is different from the ISCP. Ethanol-induced calcium release shows similarities, such as temperature sensitivity, with GTP-induced calcium release from the IICP. In the present study, the measure of calcium-45 uptake and release in microsomal preparations was used to further characterize the ESCP. The results will be discussed with respect to the relationship between ethanol-induced rise in intracellular calcium and the multiple cellular effects of ethanol abuse.

NR110 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

PERSONALITY ORGANIZATION IN ANALYTIC AND INPATIENTS

Norman R. Doidge, M.D., Psychiatry, Columbia University, Box 85 722 West 168th Street, New York, New York 10032; Andrew E. Skodol, M.D., John M. Oldham, M.D., H. David Kellman, M.D., Lyle Rosnick, M.D., Ron G. Goldman, M.D.

Summary:

Many clinicians who treat Axis II pathology use a diagnostic system that divides personality into neurotic, borderline and psychotic organizations on the basis of the presence of primitive defenses, identity diffusion, and reality-testing. Oldham et al. have developed a self-report questionnaire that measures personality organization according to these three factors. We have given the questionnaire, as well as SCID I and SCID II structured interviews to two demographically matched groups: 1) applicants for psychoanalysis at the Columbia Center (N=28) and 2) applicants to the Clinical Research Service at Psychiatric Institute, which specializes in the evaluation and treatment of patients with severe personality disorders (N=19). On the basis of their SCID diagnosis, patients were grouped into neurotic, borderline and psychotic categories. The questionnaire has shown good test-retest reliability (0.89). The mean profile score for psychotic patients was 424, borderline 336 and neurotic 276. A comparison of psychotic and neurotic group means was highly significant ($t=5.04$ $df=18$ $p.<0005$) as was the borderline and neurotic mean comparison ($t=3.33$ $df=38$, $p.<0005$). This study lends support for the validity of levels of personality organization as assessed by self-report in patients rigorously diagnosed by DSM-III-R criteria.

NR111 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

ECT THERAPY WITH BENZODIAZEPINES

Marc Auriacombe, Centre Carreire, 121 Rue De La Bechade, Bordeaux 33076, France; Denis Grabot, Pierre Marie Lincheneau, Jean Tignol, M.D.

Summary:

It is often asserted that patients receiving benzodiazepines (BZ) should not receive electroconvulsive therapy (ECT) because anti-convulsive properties of the drug could modify seizures and perhaps decrease the anti-depressive action of ECT. We have reviewed the international literature and could find no study which directly addressed this important issue. Two studies have reported that seizures induced by ECT in patients receiving BZ's are shorter of duration than when the drug is absent (STROMBREN et al., 1980 and STANDISH-BARRY et al., 1985). Recently another study found no effect of BZ's on seizure duration (OLESEN et al., 1989). In order to directly address this question, 15 patients were randomly assigned to either ECT with methohexatol (1 mg/kg) for anesthesia, or ECT with midazolam (0.1 mg/kg), a short-acting BZ used for anesthesia in cardiovascular surgery. All patients met *DSM-III-R* criteria for major depressive disorder and had agreed by an informed consent procedure to both ECT and random assignment to the two drug conditions. Both groups were similar for age (55.3 ± 14 vs 54.3 ± 17). Evaluation of seizure duration, depression (Montgomery Asberg Depression Rating Scale) and memory (combination of different tests for evaluation of digit span, anterograde and retrograde amnesia with verbal and non verbal material) were done on each patient prior to administering the ECT and without the tester knowing the group assignment of each patient. This testing was repeated after each odd numbered ECT. There were no differences in mean seizure duration between the two groups (36.2 ± 8.4 vs 36.4 ± 6.2 seconds, $p = 0.93$, NS) and in number of total ECT (6.8 ± 2 vs 6.2 ± 1.7, $p=0.56$, N.S.). Prior to beginning treatment the two groups were equivalent in depression ratings on the Montgomery-Asberg scale (MADRS) and there were no significant differences between the two groups 48 hours after termination of the last ECT (pre-treatment MADRS score 39.7 ± 6.7 vs 38.7 ± 7.2; post-treatment 9.7 ± 5.9 vs 6.2 ± 3.9, $p=0.26$, N.S.). Memory evaluation, likewise, showed no differences between the two groups. Our preliminary results, therefore, do not support the statement that BZ therapy diminishes the therapeutic efficacy of ECT.

NR112 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

PSYCHIATRIC MARKERS IN DIABETES CONTROL

Cynthia B. Stevens, M.D., 3 Washington Circle NW Ste 405, Washington, DC 20037; Abbey Wellman, M.D., David Reiss, M.D., Robert E. Ratner, M.D.

Summary:

To test the hypothesis that there are personality differences among poorly-controlled hypoglycemic, poorly-controlled hyperglycemic, and euglycemic Type I diabetics with equivalent levels of diabetes education, 53 subjects completed the Toronto Alexithymia, Hysteroid-Obsessoid, and CES-D Depression scales under blind conditions. Clinical assessment of the state of each subject's diabetes was recorded on the Health Provider Rating Scale designed by the researches. Each scale was scored by total and subscale scores. There were no statistically significant differences among the groups in total scores on all scales. The Alexithymia Feeling and Fantasy subscales did distinguish among the groups, however. In addition, CES-D values revealed a significant correlation with daily mean glucose values calculated for the two days preceding and the day the scales were completed. These results suggest that poorly-controlled diabetics are less able to monitor internal feeling and fantasy states than well-controlled diabetics and indicate the possible value of teaching patients to attend to mood and other inner feeling states in diabetes education programs or in targetted psychotherapy.

NR113 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

MEDICATION COVERAGE: PREVALENCE AND ATTITUDES

Richard Goldberg, M.D., Psychiatry, Univ of Connecticut, Health Center, Farmington, CT 06032; Michelle Riba, M.D., Allan Tasman, M.D.

Summary:

Although medication coverage—the provision of medications, by psychiatrists, to patients receiving psychotherapy from nonmedical professionals—is widely practiced, there is scant literature to guide the practitioner. As a step towards the establishment of guidelines, the authors surveyed a sample of Connecticut psychiatrists to determine the prevalence of medication coverage and the attitudes of those who practice it.

A randomly sampled group of 222 APA-member psychiatrists in Connecticut were sent a written survey instrument and were asked to mail it back in a prepaid envelope. Questions were asked concerning the numbers of patients seen for medication, the numbers of patients who have split therapy (medications dispensed by the psychiatrist and therapy given by a nonpsychiatrist), the ways the psychiatrists communicate with the nonpsychiatrist therapists, and the problems that arise or that may arise for the patient, the psychiatrist and the therapist. One hundred (45%) surveys were returned. Important findings were that while 66% of respondents were currently providing medical coverage, many had serious doubts about the ethics, obligations, and standardization of the practice. The authors then use the attitudes expressed to propose specific areas that need further study before professional guidelines can be considered.

NR114 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

CARDIOVASCULAR ACTIVITY AND RESPONSE IN SCHIZOPHRENIA

Dr. Hans-Peter Volz, Psychiatry, FU Berlin, Eschenallee 3, Berlin West 19 D 01000, Fed. Rep. Germany; Dr. Arthur Mackert, Albert Diefenbacher, M.D., Ingrid Keiler, Dr. Wolfgang Gaebel, Prof. Dr. Gunter Stock

Summary:

Studies of autonomic nervous system activity in schizophrenics by examining cardiovascular activity and other parameters are well-established tools in biological schizophrenia research. ZAHN (1975, 1988) reported high baseline levels of cardiovascular activity and electrodermal activity, slow rates of adaption, and attenuated reactivity. These patterns predicted a poor outcome on a 3-months follow-up. Based on these investigations, we examined base levels of 20 acutely ill, untreated schizophrenics (RDC), their reaction to a modified orthostatic challenge, and their reaction toward a test-dose of 150mg perazine (oral application). Cardiovascular active hormones (argine-vasopressine, angiotensine-2, aldosterone, renine) were also determined during the study.

The schizophrenic group showed in relation to 10 age-matched healthy volunteers a significantly elevated heart rate and elevated systolic and diastolic blood pressure. After the test-dose, the responders (BPRS-improvement after 4 weeks of neuroleptic treatment at least 33 percent) showed a significantly increased heart rate response in relation to nonresponders (32.4 vs. 31.4 beats/minute) during orthostatic challenge test. The examination of the cardiovascular active hormones could only partly explain these observations.

Results are discussed in relation to autonomic nervous system activity and to dopaminergic regulation of cardiovascular system.

NR115 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

VBR AND NEUROPSYCHOLOGICAL FINDINGS IN SCHIZOPHRENIA

John DeQuardo, Psychiatry, University of Michigan, 1500 E. Medical Center Drive, Ann Arbor, MI 48109; Rajiv Tandon, M.D., James H. Meador-Woodruff, M.D.

Summary:

Cerebral atrophy and ventricular enlargement (VBR) are reported to be associated with a variety of clinical and biological variables in schizophrenia. VBR has been found to correlate with cognitive impairment, lower I.Q., low educational achievement, and poor premorbid function; these associations have not been uniformly confirmed, however. In an effort to further evaluate this relationship, we studied 52 drug-free schizophrenic patients (*DSM-III-R* and RDC) admitted to the University of Michigan Schizophrenia Program. Computerized tomography of the brain was performed and VBR determined via computer-enhanced video digital planimetry. A neuropsychological assessment (including WAIS-R) was performed, total years of education were determined and premorbid function assessed by the Premorbid Adjustment Scale.

We found no inverse correlation between VBR and cognitive impairment, IQ, or low educational achievement. In fact, a trend ($p < 0.10$) toward direct correlation between VBR, IQ, and educational level was found. This finding suggests that at least two developmental processes operate in the genesis of schizophrenia:

(i) Adolescent onset of social dysfunction associated with increased VBR, fairly normal childhood function, higher academic achievement and IQ;

(ii) childhood onset of social dysfunction associated with low educational achievement and IQ, and variably with VBR.

NR116 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

ASSESSMENT OF DEPRESSION IN SCHIZOPHRENIA

Israel Liberzon, M.D., Psychiatry, University of Michigan, 1500 E. Medical Center Drive, Ann Arbor, MI 48109; Rob Goldman, Ph.D., Rajiv Tandon, M.D.

Summary:

Depressive symptomatology occurs commonly at various stages of schizophrenic illness and is most frequently assessed by the Hamilton rating scale for depression (Ham-D). A major unanswered question is whether the Ham-D is a valid measure of depressive symptomatology in schizophrenic patients, since the instrument was originally developed for use with a depressive population. Seventy-five schizophrenic (*DSM-III-R* and SADS/RDC) inpatients were administered the Ham-D, the 18-item BPRS, and the Scale for the Assessment of Negative Symptoms (SANS) at drug-free baseline and after four weeks of neuroleptic treatment. The same factor analytic procedure used in Hamilton's original validation studies was applied to this sample of schizophrenic patients.

We obtained a four factor solution, with the factors in order of decreasing variance as follows: somatic, agitation, negative symptoms, and a depression factor which accounted for only 6 percent of the total variance. The depression factor was comprised of depressed mood, guilt, and middle insomnia. This differed from the depression factor in Hamilton's studies which consisted of guilt, depressed mood, suicidality, retardation, and loss of insight. In our study with schizophrenic patients, retardation, loss of insight, along with anhedonia, comprised the second factor; this factor correlated highly with both the BPRS negative symptom factor ($r = 0.8$; $p < 0.001$) and the SANS total score ($r = 0.7$; $p < 0.001$). Therefore, we concluded that this second factor was indeed a negative symptom cluster, distinct from the depression factor. Findings did not differ after neuroleptic treatment.

Our findings call into question the use of the Ham-D as a measure of depressive symptomatology in schizophrenia. Furthermore, previous findings of correlations between depressive symptoms (measured by the Ham-D) and negative symptoms in schizophrenia are confounded by the fact that the Ham-D total score includes a significant contribution from negative symptoms.

NR117 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

EFFECTS OF BIPERIDEN ON SCHIZOPHRENIA SYMPTOMS

Jon K. Zubeita, M.D., Psychiatry, University of Michigan, 1500 E. Medical Center Drive, Ann Arbor, MI 48109; Rajiv Tandon, M.D., Nancy A. Mann, R.N., William E. Eisner, R.N.

Summary:

Anticholinergic drugs are commonly used in the treatment of extrapyramidal side effects, which accompany neuroleptic treatment in schizophrenia. While it is assumed that these drugs have no effect on schizophrenic symptomatology, studies indicate that anticholinergic agents may aggravate positive symptoms and antagonize therapeutic effects of neuroleptics. These adverse effects of anticholinergic drugs in schizophrenia appear to be confined to positive symptoms, however, and some investigators have observed that anticholinergic agents benefit negative symptoms. There are virtually no controlled studies on the effects of anticholinergics on symptoms in drug-free schizophrenic patients.

In this study, we examined the effects of biperiden, on positive and negative symptoms in 30 otherwise drug-free schizophrenic inpatients. After being medication free for at least two weeks, patients received 4 mg of biperiden orally twice a day for two days. Patients were independently rated on the BPRS by two nurse-clinician raters, blind to medication-status, at baseline and after two days-biperiden. Paired t-tests were performed to compare symptom ratings at baseline and after biperiden.

There was significant increase in positive symptom severity following biperiden ($t = 6.5$, $df = 29$, $p < 0.01$), and a trend toward a decrease in the severity of negative symptoms ($t = -2.03$, $df = 29$, $p < 0.05$). These findings suggest that anticholinergic agents, commonly employed in schizophrenia, significantly affect schizophrenic symptomatology and that this effect may be obscured by the neuroleptic agents with which they are employed. These findings also indicate the importance of cholinergic mechanisms in schizophrenic pathophysiology and support the recently proposed model of dopaminergic/cholinergic mechanisms in schizophrenia.[1]

NR118 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

SLEEP ONSET REM PERIODS IN SCHIZOPHRENIC PATIENTS

Stephan F. Taylor, M.D., Psychiatry, University of Michigan, 1500 E. Medical Center Drive, Ann Arbor, MI 48109; Rajiv Tandon, M.D., James E. Shipley, M.D., Alan S. Eiser, Ph.D., Joann Goodson, B.Sc.

Summary:

Sleep onset REM periods (SOREM), defined here as the onset of REM sleep within 10 minutes of sleep onset, have been found in depressed patients and are associated with greater illness severity, psychotic depression, older age, and dexamethasone nonsuppression. Because shortened REM latencies are also associated with schizophrenics, we undertook to explore the frequency and clinical correlates of this phenomenon in a group of 40 medication-free schizophrenic patients diagnosed by SADS/RDC and *DSM-III-R* criteria and studied by sleep EEG in their own hospital beds. After a first night as adaptation and to rule out primary sleep disorders, on the second night of recording, 7 of the 40 patients exhibited REM latency in less than 10 minutes. This SOREM group had greater global severity as measured by higher BPRS scores (53.7 ± 8.2 S.D. vs. 45 ± 7.5; $p < 0.05$) and higher ratings of negative symptoms as assessed by SANS (16 ± 1.8 vs 11.3 ± 4.1; $p < 0.01$) compared to the 33 patients without SOREM (mean REM latency $= 65 \pm 28.7$ min). Patients in the SOREM group had higher post-dexamethasone cortisol levels on the DST (11 ± 7.2 mcg/dl vs 4.38 ± 3.01 mcg/dl; $p < 0.01$) and were more likely to be non-suppressors (X^2 with continuity correction $= 3.91$; $p < 0.05$). The SOREM group did not differ from the non-SOREM group in age, sex, Hamilton rating scores for depression, ventricular brain ratios, positive symptom subscale ratings, time or percentage of delta slow-wave sleep, or REM density. After four weeks of neuroleptic treatment, clinical improvement was observed in both groups, although the SOREM group persisted with higher SANS scores (11.9 ± 3.7 vs. 7.6 ± 2.9; $p < 0.01$) and higher ratings of global severity by total BPRS scores (39 ± 5.2 vs. 33.4 ± 6.8; $p < 0.05$). These findings of an association between SOREM and DST non-suppression are similar to what we have reported with depressed patients, suggesting the need for further investigation of similarities and differences in the pathophysiology of sleep and HPA changes in depression and schizophrenia.

NR119 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

CLINICAL PREDICTORS OF OUTCOME IN SCHIZOPHRENIA

Saulo C.M. Rebeiro, M.D., Psychiatry, University of Michigan,, 1500 E. Medical Center Drive, Ann Arbor, MI 48109; Rajiv Tandon, M.D., Rebecca Ricoy, M.D.

Summary:

In view of the heterogeneity of outcome in schizophrenia, there is a clear need to identify reliable predictors of outcome. Clinical features that have been studied include premorbid function, sex, intelligence, age and type of onset, precipitating events, duration of symptoms, subtype of illness, and the presence and severity of positive, negative, and depressive symptoms. In an effort to evaluate the prognostic value of these clinical features we prospectively studied 60 schizophrenic patients (SADS/RDC and *DSM-III-R*) and assessed outcome after one year of standard neuroleptic treatment. Positive, negative, and depressive symptoms were assessed by the BPRS, SANS, and Hamilton Depression scales, respectively, at medication-free baseline and four weeks after treatment. Outcome was assessed by the Strauss-Carpenter Scale.

Post-treatment positive and negative symptom ratings and total BPRS scores were positively correlated ($p < 0.01$) with poor outcome, and post-treatment SANS strongly predicted ($p < 0.001$) poor outcome at one year. Baseline severity of various symptom measures (pre-treatment BPRS and SANS), and Hamilton scores at either point, were unrelated to outcome.

These findings suggest that persistent positive and negative symptoms after four weeks of treatment, but not at baseline, predict poor outcome at one year. Depressive symptoms seem to be unrelated to outcome and do not carry any prognostic value. The various clinical features accounted for 50 percent of the variance in outcome, suggesting that it is possible to make reasonable clinical predictions of one-year outcome in schizophrenia based on clinical parameters.

NR120 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

CLOZAPINE-INDUCED WEIGHT GAIN IN THE CHRONICALLY MENTALLY ILL

Robert A. Leadbetter, M.D., Western State Hospital, P.O. Box 2500, Staunton, VA 24401; Diane Pavalonis, M.S.N.

Summary:

Clozapine is an atypical antipsychotic with unique psychopharmacologic and endocrine effects for use in patients with treatment resistant psychosis. Standard antipsychotic drugs, particularly low potency neuroleptics, have been implicated in inducing weight gain. World-wide, weight gain has been reported to occur in less than one percent of patients treated with Clozapine. However, there is one report of a persistent increase in appetite and concomitant weight gain in 9 of 13 patients treated with this drug. We treated 15 patients who failed standard neuroleptics with Clozapine for 12 weeks. They were weighed weekly in a consistent manner while hospitalized on a research unit for the chronically mentally ill. Of these, 10 (67%) gained a statistically significant ($p < .001$) amount of weight. This weight gain was superimposed on that induced by standard neuroleptics. The gain in weight correlated with Clozapine dose ($p < .005$), younger age ($p < .025$), and improvement as reflected by total BPRS score ($p < .025$). Theories to explain this include histamine receptor blockade, a unique ration of D1 to D2 receptor blockade, changes in metabolism due to alterations in endocrine functioning and/or variables unique to patient population and setting.

NR121 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

IN VIVO ASSESSMENT OF PUTAMEN VOLUME IN DEPRESSION

Mustafa M. Husain, M.D., Psychiatry, Duke University, P.O. Box 3215, Durham, NC 27710; William M. McDonald, M.D., Murali Doraiswamy, M.D., Gary S. Figiel, M.D., Orest B. Boyko, M.D., Everett H. Ellinwood, Jr., M.D., Charles B. Nermeroff, M.D., K. Ranga R. Krishnan, M.D.

Summary:

The role of basal ganglia (BG) is increasingly being recognized in cognitive and behavioral functions. Patients with BG lesions have been shown to exhibit significant affective symptoms including apathy, depression, and psychosis. We therefore decided to assess the volumes of various prosencephalic ganglia in patients with major depression. In this report, we present the findings on the changes in the putamen nuclei in a group of 38 depressed (*DSM-III-R*) patients (mean age $\pm$ SD, 53.2 $\pm$ 18.6, 15 males) and 36 controls (52.9 $\pm$ 19.1, 14 males). Both groups were free of any major medical conditions and neurological deficits. Age was negatively correlated with putamen volume in both the depressed ($r = -0.55$, $p = 0.0003$) as well as in control groups ($r = 0.74$, $p = 0.0001$). There was a significant decrease in the putamen volume in depressed patients (7.82 $\pm$ 1.05) compared to controls (10.46 $\pm$ 2.41ml) ($t = 5.11$, $df = 72$, $p = 0.0001$, two tailed t-test). These findings further support the roles of BG structural changes in major depression.

NR122 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

NEUROLEPTIC RESPONSIVENESS AND EPS: IS LESS MORE?

Robert Perovich, M.D., Psychiatry, Hill Side Hosp LIJMC, P.O. Box 38, Glen Oaks, NY 11004; Celeste Johns, M.D., Peter J. Weiden, M.D., Jose Ma. Alvir, D.P.H., Kathleen Frechen, M.D., Gustav Degreef, M.D., John M. Kane, M.D.

Summary:

GOALS The relationship between neuroleptic drug response and extrapyramidal (EPS) side effects in the treatment of schizophrenia has been controversial. Determining whether EPS is a predictor of neuroleptic response is a clinically and theoretically important question.

METHODS The study design was as follows: 1) acutely-ill schizophrenic patients were given a fixed daily dose of 20 mg fluphenazine HCL and prophylactic benztropine at 6 mg for 4 weeks, 2) EPS was measured weekly with the Simpson-Angus EPS scale, 3) clinical response was measured with weekly BPRS and CGI ratings, 4) fluphenazine levels were determined at weeks 3 and 4, and, 5) at the end of the study, at week 4, the patient's overall response to treatment was rated and categorized as responder vs nonresponder. Nonresponders were defined by a priori criteria of remaining moderately ill (4 or greater) on any of the four psychotic items of the BPRS, and being rated as only minimally improved on the CGI.

RESULTS To date, 54 patients have completed the study. Nineteen (35 percent) were responders and 35 (65 percent) were nonresponders. As shown below for week 4, the neuroleptic responders had less EPS than the nonresponders.

	Akinesia mean(SD)	*Akathesia* mean(SD)	*Gait* mean(SD)	*Rigidity* mean(SD)	*Cogwheeling* mean(SD)
Responder (N = 19)	.16(.38)	.32(.75)	.26(.45)	.37(.60)	.37(.50)
Nonresponder (N = 35)	.68(.81)	.56(.75)	.44(.79)	.76(.90)	.82(.77)
Statistic (DF = 51)	t = 3.19 p. < 005	t = 1.14 NS	t = 1.05 NS	t = 1.87 p < .1	t = 2.54 p < .02

The results from weeks 1, 2, and 3 are similar to week 4, suggesting that this association begins early on. Our finding cannot be explained by differential metabolic or compliance effects because the fluphenazine blood levels did not differentiate these groups.

SIGNIFICANCE Neuroleptic nonresponsive patients seem to develop more EPS, which is not an artifact of clinical treatment decisions, compliance, or drug metabolism.

NR123 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

THE MCPP CHALLENGE TEST IN SCHIZOPHRENIA

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Summary:

Biological research in schizophrenia has focused on dopamine hypothesis (DA). Recently studies using medications with serotonin (5HT2) antagonistic properties such as clozapine, setoperone and risperidone have shown significant improvement in symptomatology, particularly negative symptoms. We studied 10 medication free patients with a diagnosis of schizophrenia in a double-blind method, utilizing a selective serotonin agonist, m-chlorophenylpiperazine (MCPP) challenge test. Behavioral assessments (positive and negative systems, mood, anxiety and affect) and hormones under serotonergic control (acth, cortisol and prolactin) were made. Each patient participated in two tests (active and placebo) one week apart. The test was from (9:00 A.M. - 1:30 P.M.) with hormonal assessments every 30 minutes and behavioral assessments every hour except for the last rating which was done at 30 minutes internal (1:30 P.M.). The dose of MCPP used was 0.25 mg/kg, given after one hour adaptation time at 10:00 A.M. Behavioral and hormonal data on schizophrenia patients will be compared with the same number (n = 10) of age- and sex-matched groups of normal controls and patients with a diagnosis of major depression and panic disorder. It is clear that other neurotransmitters besides dopamine need to be evaluated to understand the biological heterogeneity of schizophrenia.

NR124 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

EFFECTS OF SKF-38393 (D-1 AGONIST) ON SCHIZOPHRENIA

Nancy A. Breslin, M.D., CBDB, NIMH Neurosci Center, 2700 Martin L. King Jr. Ave SE, Washington, DC 20032; David G. Daniel, M.D., James M. Gold, Ph.D., Bhaskar S. Kolachana, Ph.D., Joel E. Kleinman, M.D., Daniel R. Weinberger, M.D.

Summary:

As dysfunction of the prefrontal cortex has been implicated as the source of some schizophrenic deficits, the "dopamine hypothesis" of schizophrenia has been extended by the notion that overactivity of the mesolimbic dopamine system may be a secondary manifestation of cortical dysfunction. This model suggests that activation of prefrontal cortex, with agents such as dopaminergic agonists, might ameliorate schizophrenic symptoms. We are currently studying the effects of chronic treatment with combined administration of SKF-39393 (a D1 agonist) and molindone (the most selectively D2 of marketed neuroleptics) designed to exploit the fact that most primate cortical dopamine receptors are of the D1 type. Preliminary analysis of the first five patients to complete this double-blind, crossover design study found the following: 1) patients showed no worsening of positive or negative symptoms while maintained on molindone and high doses of SKF-38393 (1200 mg/day); 2) the patients showed no change of choreoathetotic or extrapyramidal symptoms; 3) there was a trend toward an improvement in blood flow (Xe-133 SPECT) to the front cortex when patients on SKF-38393 were challenged with the Wisconsin Card Sort; 4) CSF from subjects contained above 2 ng/ml of SKF-38393. Expanded results, including the data from additional patients, will be presented.

NR125 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

NEUROLEPTIC DOSE VERSUS BLOOD LEVELS IN CHRONIC PATIENTS

Rimal B. Bera, M.D., Psychiatry, Univ of California Irvine, 3 Terraza, Irvine, CA 90274; Jerome F. Costa, M.D.

Summary:

There have been a number of studies performed that explore the relationship between neuroleptic dosage and neuroleptic blood level in non-chronic psychiatric patients. Based on these results, certain neuroleptics, like haloperidol, have been felt to have a blood level range where the therapeutic effect is seen. The purpose of this study was to determine if chronic psychiatric patients require higher doses of neuroleptics in order to achieve a therapeutic blood level, as compared to more acute psychiatric patients. The charts of 100 patients at Metropolitan State Hospital in Norwalk, California, were reviewed for diagnosis, neuroleptic dose and level, age, sex, weight, and duration of illness. Our hypothesis was that chronic psychiatric patients require higher doses of neuroleptics in order to achieve an appropriate blood level.

Preliminary results indicate that the above hypothesis is correct. We have found a general trend of higher neuroleptic doses required in the more chronic population in order to achieve similar blood levels as the acute population which are on a lower dose of neuroleptics.

These findings should lead to improved guidelines of neuroleptic administration in chronic psychiatric patients.

NR126 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

SPECT IN SCHIZOPHRENIA WITH STIMULANT ACTIVATION

David B. Bresnahan, M.D., Psychiatry, Medical College of Wisconsin, 8700 W. Wisconsin Avenue, Milwaukee WI 53226; Michael Goldstein, Ph.D., John M. Davis, M.D., Rajiv P. Sharma, M.D., Ronald Tikofksy, Ph.D., Robert S. Hellman, M.D.

Summary:

The authors report preliminary results in a study of rCBF patterns in schizophrenia vs. normals following intravenous methylphenidate challenge. Seven subjects (3 schizophrenic; 4 normal control) have been studied with iodoamphetamine SPECT following both placebo and methylphenidate infusion (0.5 mg/kg). The feasibility of this study approach has been assessed as well as examination of the effects of methylphenidate on rCBF patterns. Schizophrenic subjects following methylphenidate showed noticable behavioral activation, exhibiting a 10 to 20 point increase on the BPRS following methylphenidae. All SPECT images for this study (14 in all) were mixed with a larger group of 40 clinical SPECT studies and blindly rated by members of the nuclear medicine division. The SPECT studies were rated for overall image quality and presence or absence of movement artifact. There was no deterioration in SPECT image quality following methylphenidate infusion despite noticeable behavioral activation produced. We have calculated rations for regions of interest compared with average total cortical activity. Owing to small sample sizes, we have not detected statistically significant differences in patters of rCBF in schizophrenia following methylphenidate infusion. There appears to be a trend toward activation of the left prefrontal cortex in schizophrenia when compared with normal controls. Preliminarily, this appears to be feasible methodology and may hold promise for studying the pathophysiology for schizophrenia.

NR127 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

POSITIVE AND NEGATIVE SYMPTOMS: A ONE-YEAR FOLLOW-UP

John T. Moranville, M.D., Psychiatry, Univ of Calif San Diego, 3427 Fourth Avenue, San Diego, CA 92103; David L. Braff, M.D., Robert K. Heaton, Ph.D., Julia Kuck, M.A., John R. Montague, Ph.D., Ana Maria Andia, M.D., Sidney Zisook, M.D.

Summary:

The SANS and SAPS are widely used for the assessment of negative and positive symptoms, yet little information regarding stability of these symptoms over time exists. Theoretically negative symptoms remain stable over time, while positive symptoms fluctuate. To test the stability of both negative and positive symptoms, we compared baseline and one-year ratings from 25 chronic schizophrenic outpatients. SANS and SAPS totals were not significantly different between the two rating sessions. In a minority of patients, however, the individual global ratings did increase or decrease over time. In seven patients, the change in symptoms changed the Andreasen subtype. In these patients, positive and negative symptoms appeared to vary independently. These results suggest that despite marked stability of both positive and negative symptoms in the majority of clinically stable schizophrenic outpatients, a small minority of patients may experience fluctuations over time of either or both types of symptoms. State related issues such as medication changes and stage of illness will be reviewed. The implications for course of illness will also be discussed.

NR128 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

SUBSTANCE ABUSE AND PSYCHOSIS: PAST AND PRESENT

John T. Moranville, M.D., Psychiatry, Univ of Calif San Diego, 3427 Fourth Avenue, San Diego, CA 92103; John Tsuang, M.D., Sidney Zisook, M.D., Julia Kuck, M.A., David L. Braff, M.D., Robert K. Heaton, Ph.D.

Summary:

Schizophrenics often use psychoactive substances. Previous studies suggest exacerbation of psychotic symptoms from use of amphetamines, hallucinogens, and marijuana, but little evidence is available on the long-term association between use of these substances and symptom severity in schizophrenia. To assess the association between prior substance use and severity of psychotic symptoms in schizophrenic patients, we compared SANS, SAPS, and BPRS scores of 27 past abusers to 13 nonabusers. Past abusers had previously experimented with or abused one or more substances but denied current abuse. Nonabusers denied ever using any psychoactive substance. SANS, SAPS, and BPRS total scores were not significantly different, and the two groups did not differ in age at first psychiatric contact, neuroleptic dose, or paranoid/nonparanoid subtype. Males, however, were more likely to have a history of psychoactive substance use than females ($X^2 = 4.00$, $df = 1$, $p \leq 0.05$). Admittedly, the implications of a cross-sectional comparison are limited. However, these results suggest the need for longitudinal studies of the interaction between schizophrenic pathology and substance abuse.

NR129 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

EXPRESSED EMOTION AND POSITIVE/NEGATIVE SYMPTOMS IN SCHIZOPHRENIA

Ernesto Mujica, M.A., Psychiatry, Cornell Univ Med College, Payne Whitney Clin 525 E 68th, New York, NY 10021; Gretchen L. Haas, Ph.D., Denise Hien, M.S., Dodi Goldman, M.A., Steven Passik, M.S., Glynn Rudich, M.S.W.

Summary:

Background: "Expressed Emotion (EE) has been associated with increased likelihood of relapse in schizophrenia. A largely unstudied question concerns the association of EE with patient symptomatology during the acute phase of illness. The few investigations that have addressed this question have focussed almost exclusively on positive symptoms. This study investigates the association between EE and specific positive and negative symptom dimensions during the acute phase of schizophrenia. *Methods:* 41 consecutive admission inpatients (aged 18 to 45) with DSM-III-R schizophrenia were assessed at hospital admission with a broad battery of clinical measures (GAS, BPRS, SANS and SAPS). EE measures (critical comments, emotional overinvolvement and warmth) were generated from the Camberwell Family Interview (CFI) at admission with the key parent who had regular contact with the patient during the three months prior to admission and during hospitalization. *Results:* Parental criticism (CC) and overinvolvement (EOI) contributed significantly to variance in the global measure of anhedonia/asociality from the SANS ($p < .01$). Patients who showed severe levels of anhedonia/asociality tended to have parents with *high* levels of EOI and *low* levels of CC. CC was positively associated with severity of formal thought disorder, as measured on the BPRS ($p < .05$), and the SAPS ($p < .10$). Further analysis indicated that these results could not be accounted for by chronicity of illness or demographic variables. These findings support the notion that parental criticism and overinvolvement may be differentially associated with acute symptoms. Parental criticism may be most frequent in the presence of specific forms of symptomatology, namely thought disorder. In contrast, high parent emotional overinvolvement in the absence of criticism may be most strongly associated with patient deficits in social functioning.

NR130 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

BIZARRE DELUSIONS IN DSM-III-R SCHIZOPHRENIA

Denise Hien, M.S., Psychiatry, Cornell Univ Med College, Payne Whitney Clin 525 E 68th, New York, NY 10021; Dodi Goldman, M.A., Gretchen L. Haas, Ph.D., John A. Sweeney, Ph.D., Allen J. Frances, M.D.

Summary:

Goals: Despite a lack of empirical evidence to date, DSM-III-R assigns bizarre delusions substantial weight among criteria used to diagnose the group of schizophrenias. A total of 152 schizophrenic, schizophreniform and schizoaffective patients were assessed for the presence of bizarre delusions using DSM-III-R SCID-P criteria. Methods: Schizophrenic patients (n=119) were assessed at admission and discharge with a broad battery of clinical measures of premorbid adjustment (PAS), clinical symptomatology (SAPS, SANS, BPRS), intelligence (Ammon's IQ Test) and overall functioning (GAS). An equivalent high percentage of schizophrenic, schizophreniform and schizoaffective patients had bizarre delusions (X=78%). At admission the schizophrenics with bizarre delusions had more overall psychiatric symptoms as measured on the BPRS ($p<.02$), more severe positive symptoms on the SAPS ($p<.001$), but less severe negative symptoms on the SANS ($p<.04$) than patients without bizarre delusions. History of bizarre delusions was also associated with more severe positive symptoms at discharge ($p<.03$), although there were no differences on indices of treatment response, including length of stay, neuroleptic dosage at discharge, and change on symptom measures. No significant differences in premorbid adjustment were found across groups. Patients with bizarre delusions had significantly higher IQ ($p<.04$), higher level of education ($p<.05$), and a trend for later mean age of onset (24.0 vs. 21.0 years). Our results call into question the weight given to bizarre delusions in the current DSM-III-R criteria for schizophrenia. Presence of bizarre delusions did not distinguish a group of patients with poor treatment response in hospital.

NR131 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

NEUROCOGNITIVE DEFICITS AS DISCRIMINATORS IN SCHIZOPHRENIA

Richard S.E. Keefe, M.A., Psychiatry, Mount Sinai School of Med, One Gustave Levy Place, New York, NY 10029; Richard C. Mohs, Ph.D., Larry J. Siever, M.D., Philip D. Harvey, Ph.D., Harold A. Sackeim, Ph.D., Kenneth L. Davis, M.D.

Summary:

Schizophrenics perform worse than normal controls on eye tracking, continuous performance test (CPT), and backward masking tasks. The relative discriminating power of these deficits and their relation to one another in schizophrenia has been largely unaddressed. This study tested the optimal linear weighting of key eye tracking, CPT, and backward masking variables in a discriminant function analysis between 32 DSM-III-R chronic schizophrenics and 17 normal controls. Intelligence was assessed with WAIS-R vocabulary and block design subtests. Performance on all tasks contributed significantly ($p<.01$) to the discriminant function, and 82% of subjects were correctly classified. CPT response sensitivity (d') was the most powerful discriminating variable, yielding structure coefficients of .88 for nondegraded and .70 for degraded conditions. Structure coefficients were .47 and .43 for monitor and nonmonitor eye tracking qualitative ratings, and .51 and .42 for backward masking performance at 120 and 180 msec stimulus onset asynchronies. In multiple regression analyses, CPT d' accounted for 17.6% ($p<.0005$) of diagnostic variance above and beyond intelligence (27.7%, $p=.0001$). Variables from eye tracking and backward masking tests did not further contribute to the overall diagnostic variance. These data suggest that while all three of these tasks are powerful in discriminating schizophrenics and normals, the deficits measured by eye tracking and backward masking may not significantly contribute to an understanding of the neurocognition of schizophrenia beyond the attentional factors assessed by the CPT.

NR132 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

PRINCIPAL COMPONENTS OF NEGATIVE SYMPTOMS AND FORMAL THOUGH DISORDER IN SCHIZOPHRENIA

Richard S.E. Keefe, M.A., Psychiatry, Mount Sinai School of Med, One Gustave Levy Place, New York, NY 10029; Philip D. Harvey, Ph.D., Lindsey Bergman, B.A., Mark R. Serper, M.A., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

Summary:

Recent conceptualizations of negative symptoms and formal thought disorder in schizophrenia contend that each is comprised of several dimensions. Various methods have been developed to assess these components of schizophrenic symptomatology, but little is known about the interrelationships of symptoms within them. This study investigated the factor structure of negative symptoms based on data collected from the Scale for the Assessment of Negative Symptoms (SANS) and the factor structure of formal thought disorder from the Thought, Language and Communication Scale (TLC) on 130 hospitalized DSM-III-R chronic schizophrenics. A principal components factor analysis with varimax rotations was performed on both scales. The SANS yielded four factors. The largest factor, diminished expression, accounted for 35% of the total variance among SANS scores. Items related to social amotivation, impaired organization, and impaired concentration accounted for 11%, 9% and 6%, respectively, of the variance. The TLC yielded six factors, the largest of which are described as positive formal though disorder (29%), (e.g., incoherence, derailment), negative formal though disorder (9%), (e.g., poverty of speech, poverty of content of speech), and verbosity (9%), (e.g., circumstantiality and pressure of speech). These data provide empirical support for theoretical notions that negative symptoms are comprised primarily of two major factors, diminished expression and social amotivation, and that formal thought disorder is comprised of positive and negative components.

NR133 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

IMMUNOBLOTTING TO HSV IN SCHIZOPHRENIA

Anthony L. Pelonero, M.D., Psychiatry, Medical College of VA, Box 710 MCV Station, Richmond, VA 23298; Daniel H. Conrad, Ph.D., Anand K. Pandurangi, M.D.

Summary:

We previously reported a study of IgG antibodies to herpes group viruses in a sample of 38 patients with RDC schizophrenia and controls. A subgroup of 32% (12) of these patients had high titers to herpesvirus hominus by an indirect ELISA technique; 73% of this subgroup had mild cortical atrophy on Magnetic Resonance Imaging scans. To further investigate the immunology of this subgroup, immunoblotting was performed. We hypothesized that there is an immunologic variance or aberrancy in this subgroup, and that the IgG antibody would not recognize the same antigenic determinants (epitopes) in both groups. The sera of eight patients and eight controls known to have high antibody titers by ELISA to herpes simplex virus (HSV) was studied. A "Western" blotting technique was used. HSV antigens were solubilized in sodium dodecyl sulfate (SDS), run in a SDS-polyacrylamide gel immunoelectrophoresis, transferred to nitrocellulose paper, and then incubated with nonspecific protein to block empty sites. After reaction with subject serum and then a detection reagent, the strips were developed with I^{125} labeled antihuman IgG. The immunoblotting technique will be diagramed for presentation. Results of the study and a discussion will be presented.

NR134 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

MANAGEMENT OF RISK OF RELAPSE IN SCHIZOPHRENIA

William Wirshing, M.D., Psychiatry, UCLA Brentwood VA, Wilshire & Sawtelle Blvds, Los Angeles, CA 90073; Thad Eckman, Ph.D., Stephen R. Marder, M.D., Robert P. Liberman, M.D.

Summary:

The interim results of a controlled clinical trial of low-dose fluphenazine decanoate (5 mg every two weeks)) combined with skills training of medication and symptom self-management will be presented. Chronic schizophrenic outpatients are randomly assigned to two medication conditions that offer time-limited placebo or oral fluphenazine at times of prodromal signs of relapse, and also to two psychological condition—either skills training or supportive group therapy, both delivered in groups for four hours per week over a six-month period. Patients are evaluated blindly for symptoms (BPRS, GAS, SCL-90), social functioning (Social Adjustment Scale, Assessment of Interpersonal Problem Solving, Social Skills in Medication and Symptom Self-Management) for a two-year follow-through period. The skills training condition is delivered through structured and prescribed modules employing seven learning activities (video modeling, role play, problem solving exercises, in vivo exercises). Results with 20 subjects in each condition have revealed significant improvements in social skills in the skills training (but not supportive therapy) condition and an interactional effect in reducing relapse and exacerbations of psychosis in subjects given the supplementary fluphenazine and skills training.

NR135 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

ILLNESS DURATION EFFECTS IN FIRST EPISODE SCHIZOPHRENIA

Antony D. Loebel, M.D., Research, Hillside Hosp LIJMC, 266th St & 76th Ave Lowenstein, Glen Oaks, NY 11004; Jeffrey A. Lieberman, M.D., Darlene Jody, M.D., Sally Szymanski, M.D., Jose Ma. Alvir, D.P.H., Michael Borenstein, Ph.D.

Summary:

This study assessed the impact of illness duration prior to hospitalization on overall outcome in first episode schizophrenia. Previous outcome studies have suggested that extended duration of untreated illness may predict poor outcome.[1] It is not known whether this is related to delay in the institution of neuroleptic medication itself or other associated illness factors.

We examined data from ongoing prospective outcome study patients undergoing their first episode of schizophrenia. None of these patients had prior treatment exposure. All patients received a structured diagnostic interview; potential biological and clinical markers of illness course and outcome were obtained. Treatment was provided according to a standardized protocol. Patients were rigorously evaluated in a structured manner throughout their course.

We will describe results from the first 57 patients in this study. The relative contribution of illness duration prior to index hospitalization on subsequent treatment course and outcome will be presented. In addition, the role of other potentially important variables in the prediction of outcome including age of onset, mode of onset and premorbid adjustment, will also be discussed.

NR136 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

A TRIAL OF L-DOPA AND MOLINDONE IN SCHIZOPHRENIA

David G. Daniel, M.D., NRH, NIMH, 2700 Martin L. King Ave SE, Washington, DC 20032; Nancy A. Breslin, M.D., James Clardy, M.D., James M. Gold, Ph.D., Joel E. Kleinman, M.D., Daniel R. Weinberger, M.D.

Summary:

Recent evidence from animal and human studies suggests that selective augmentation of cortical dopamine subtype I receptors may enhance cortical function in schizophrenia. To explore this possibility clinically, we administered L-dopa in combination with the relatively selective dopamine subtype II receptor antagonist, molindone, to schizophrenic patients in a double-blind, placebo-controlled, randomized, crossover design (eight weeks active, eight weeks placebo). Statistical analyses were carried out with a paired t-test using each patient as his or her own control. In the first seven patients to complete the study, physician and nursing ratings showed a nonsignificant trend toward improvement in negative symptoms. Results of regional cerebral blood flow measurement (Xe-133 Dynamic SPECT) and cognitive testing revealed no significant effect of L-dopa. The results of additional subjects, as well as the implications of the findings on the hypothesis that relatively selective augmentation of cortical dopamine activity might enhance cortical function in schizophrenia will be discussed.

NR137 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

NATURAL KILLER CELL ACTIVITY IN SCHIZOPHRENIA AND SCHIZOAFFECTIVE DISORDER

John S. McDaniel, M.D., Psychiatry, Emory University, P.O. Box AF, Atlanta, GA 30322; Samuel C. Risch, M.D., Rita D. Jewart, Ph.D., Mary B. Eccard, M.S.N, William E. Pollard, Ph.D., Jane Caudle, M.S., Mark Stipetic, B.S., Emile D. Risby, M.D., Richard Lewine, Ph.D.

Summary:

Impairment in natural killer cell activity (NKA) has been widely reported in depressed and bereaved individuals (1). Few studies have determined NKA in nonmedicated schizophrenic patients, and to our knowledge there have been no reports of NKA in patients with schizoaffective disorder (2). We have prospectively studied NKA in 13 medication-free schizophrenic patients and seven medication-free patients with schizoaffective disorder, depressed type, as compared with age- and sex-matched normal controls. To date, NKA in schizophrenic patients does not differ significantly from that in controls (35.0 $\pm$ 49.0 schizophrenia vs. 23.9 $\pm$ 23.4 normals, $t = 1.29$, $df = 12$, $p < .221$ [2-tailed probability]), nor does NKA in schizoaffective patients significantly differ from that in controls(33.5 $\pm$ 20.5 schizoaffective vs. 19.3 $\pm$ 18.0 normals, $t = 1.20$, $df = 6$, $p < .276$ [2-tailed probability]). In neither group were there statistically significant correlations among age, Brief Psychiatric Rating Score, Hamilton Depression Rating Scale score, and NKA. The 95% confidence interval for the difference between the means of the schizophrenic patients and controls ranged from -7.64 to 29.81, and for the schizoaffective patients the 95% confidence interval ranged from -14.74 to 43.03. These findings may indicate that the alterations in NKA may be nosologically more specific to depressed and bereaved states.

NR138 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

CAVUM SEPTUM PELLUCIDUM IN PSYCHOSIS

George J. Jurjus, M.D., Psychiatry, Ohio State University, 473 West 12th Avenue, Columbus, OH 43210; Stephen C. Olson, M.D., Jeffrey A. Coffman, M.D., Steven b. Schwarzkopf, M.D., Henry A. Nasrallah, M.D.

Summary:

Since 1851, congenital neural abnormalities including CSP have been associated with schizophrenia. We conducted a magnetic resonance imaging (MRI) study to compare rates of CSP in schizophrenia (n=67) with those in psychiatric controls (bipolar and schizoaffective, n=60) and normal controls (n=37). Exclusion criteria included significant medical or neurologic illness and severe substance dependence. T_1 weighted 5 mm coronal images were visually rated for presence and size of a CSP by a researcher blind to diagnosis.

We found that 18.9% of controls and 18.1% of all psychotic subjects had a CSP of any size, and that there was no difference in the incidence of large cavae (moderate-severe) between controls, schizophrenics and psychiatric controls. Males had higher rates of CSP (25% vs. 9.7%; p=0.01) in all groups, and schizophrenics had higher rates than psychiatric controls (25% vs. 10%; p=0.02). When males and females were analyzed separately, no significant differences emerged, reflecting an excess of males in the schizophrenic group. Our results indicate that MRI detects more CSP than CT and that males are more frequently affected. We found no association between CSP and psychosis in general. Subjects with and without CSP will be compared on clinical variables to identify implications of this development variant for the pathogenesis of schizophrenia.

NR139 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

OBSESSIVE COMPULSIVE SYMPTOMS IN SCHIZOPHRENIA

Ileana Zaharovits, M.D., Psychiatry, Maimonides Hospital, 950 49 Street #10G, Brooklyn, NY 11219

Summary:

There is a controversy over the role of obsessive compulsive symptoms in schizophrenia. Some authors have said that obsessive-compulsive symptoms prevent personality disintegration in schizophrenics. A more recent study, however, showed that obsessions and compulsions in schizophrenic patients represent a poorer prognosis. The present study was initiated in order to observe the functioning level of obsessive schizophrenics compared with nonobsessive schizophrenics currently in treatment in our clinic. One hundred twenty patients who met the DSM-III-R criteria for schizophrenia were examined by chart review and therapist interviewing. The investigator developed a structured questionnaire designed to assess the subjects' symptomatology and their level of functioning. The preliminary results showed that the prevalence of obsessive-compulsive symptoms in schizophrenia is much higher than in the general population; approximately 15% of the examined schizophrenics were diagnosed with severe obsessions or compulsions. The obsessive schizophrenics presented a poorer prognosis, confirming the findings published by Fenton and McGlashan in 1986. The study showed that there is a direct correlation between the hospitalization days and the degree of severity of obsessive-compulsive symptoms. Also the obsessive schizophrenics presented a lower level of functioning with poorer employment history, more social isolation, poorer financial management and less independent life.

NR140 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

STRIATAL D1, D2 RECEPTORS UNCHANGED BY CORTEX LESIONS

Zafa A. Sharif, M.D., Psychiatry, NY State Psych. Inst., 722 West 168th Street, New York, NY 10032; Sage Przedborski, M.D., Jean L. Cadet, M.D.

Summary:

Schizophrenia is a chronic neuropsychiatric illness characterized by positive symptoms which suggest increased mesolimbic (ML) dopamine (DA) activity, and negative symptoms that might be secondary to decreased mesocortical (MC) DA activity. To reconcile this apparent paradox, Weinberger has postulated that prefrontal cortical neurones my exert feedback control over ML DA activity with dysfunction of MC DA transmission resulting in increased transmission in the ML system. A replicated postmortem finding in schizophrenia is an increase in the numbers of striatal D2 receptors. If it could be demonstrated that an increase in subcortical D2 receptors occurs secondary to a selective prefrontal cortical lesion in rats, the implications for the pathophysiology of schizophrenia are apparent. We made selective unilateral orbitofrontal cortical lesions in rats using ibotenic acid which destroys neuronal cell bodies. Sham lesions with saline were made in controls. After three weeks, animals were sacrificed; D1 and D2 receptors densities were measured using quantitative receptor autoradiography. Experimental animals showed no difference in striatal D1 or D2 receptor densities compared with controls. There were also no differences between lesioned and unlesioned sides of experimental animals. Our results failed to document subcortical receptor changes secondary to orbitofrontal cortical lesions in rats.

NR141 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

SEXUAL INTEREST AND MENSTRUAL CYCLE PHASE IN LATE LUTEAL PHASE DYSPHORIC DISORDER

Tung-Ping Su, M.D., BPB, NIMH Bldg 10 Room 3N238, 9000 Rockville Pike, Bethesda, MD 20892; Kari L. Muller, B.A., David R. Rubinow, M.D.

Summary:

We investigated the effect of menstrual cycle (MC) phase on self ratings of enhanced and diminished sexual interest in 21 patients with LLPDD and in 19 controls. After prospective diagnostic confirmation, subjects completed daily ratings of sexual interest and affective symptoms over two menstrual cycles with 6-point intensity scales. ANOVA-R revealed significant phase by diagnosis effects for both increased and decreased sexual interest. Sexual interest was significantly decreased during the premenstrual phase and increased during the postmenstrual phase in patients compared with controls ($p < .005$ and $p < .05$, respectively). Stepwise regression analysis revealed that irritability accounted overwhelmingly for the variance (27% to 58%) of the less sexual interest (LSI) measure in patients irrespective of MC phase, while mood seemed unrelated to the more sexual interest (MSI) measure. Further, in the controls, appetite overwhelmingly accounted for the variance (19% to 34%) in both LSI and MSI measures. These data suggest the following: sexual interest does not vary with MC phase in controls, ratings of LSI increase (more severe) during the premenstrual phase and are correlated with irritability in patients with LLPDD; ratings of MSI increase in the postmenstrual phase in LLPDD patients compared with controls. These findings support the concept of MC phase-related state change in LLPDD patients and the distinctiveness of the postmenstrual "euphoria."

NR142 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

ULTRASHORT TRANSITION FROM METHADONE TO NALTREXONE

Norbert Loimer, M.D., Psychiatry, University of Vienna, Waehringer Gurtel 18-20, Vienna 01090, Austria; Kurt Lenz, M.D., Otto Presslich, M.D., R. Schmid, Ph.D.

Summary:

In an open clinical trial, methadone detoxification was carried out in seven opiate addicted subjects by intravenous administration of naloxone. The acute onset of withdrawal distress was suppressed by means of a short-term benzodiazepine sedation started before naloxone administration. Afterwards, the benzodiazepine sedation was antagonized by means of repeated doses of flumazenil.

To protect the patients from a late onset of withdrawal distress, after the pharmacological action of naloxone had worn off, the patients received naltrexone p.o. (50 mg/24h) until no more opiates were detectable in their urine specimens.

This safe and rapid technique allows an easy and safe transition from methadone to naltrexone. Naltrexone medication can be stopped without causing any withdrawal distress when the patient is completly opiate free or might be continued as maintenance therapy.

This withdrawal therapy means an alternative to standard opioid detoxification procedures by means of steadily decreasing doses of oral methadone in respect to its speed, effectiveness, and safety.

NR143 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

COGNITION AND DEPRESSION IN SUBSTANCE ABUSERS

Mary H. Closser, D.O., Department of Psychiatry, Yale School of Medicine, The APT Foundation, 914½ Howard Ave., New Haven, CT 06519; Kirk J. Brower, M.D., Frederic C. Blow, Ph.D., Rosalind Fantone, R.N., Thomas P. Beresford, M.D.

Summary:

Depressive symptoms and subtle cognitive deficits in substance abusers may adversely affect clinical decision making and outcome since traditional rehabilitation programming relies on psychotherapy and education. Depression is readily diagnosed by clinical interview and symptoms quantitated by interview or self-rating. Screening neuropsychological batteries, however, are impractical in earliest assessment. We administered the Modified Mini-Mental State (3MS) Examination, a bedside cognitive screen, and the Structured Interview Guide for the Hamilton Depression Rating Scale to 142 consecutive admissions to an inpatient rehabilitation program. Seventy-five percent (107) were alcohol-, 44 percent (63) cocaine- and 21 percent (30) cannabis-dependent. While 2.5 (3) percent showed significant cognitive impairment (3MS < 80) versus 2.5 percent (3) by clinical diagnosis, at least 14 percent (20) had significant difficulty with program learning tasks because of apparent deficits. Although 25% (28) had significant depressive symptoms on admission (SIGH-D > 18) only 2 percent (4) had mood disorder diagnoses made post-detoxification. Depressive symptoms did not appear to affect program task performance. As the low variability and sensitivity of the 3MS became apparent, we added the Symbol-Digit Modalities Test (SDMT); early results indicate that similar instruments may be more useful in rapidly screening for clinically significant deficits in substance abusing populations.

NR144 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

A SUBSTANCE USE CONSULTATION/LIAISON SERVICE: CHARACTERISTICS OF PATIENTS AND PEDAGOGICAL POTENTIAL

Frances Rudnick-Levin, M.D., Univ of MD/NIDA ARC, Box 5180, Baltimore, MD 21224; William W. Weddington, M.D., Charles A. Haertzen, Ph.D., Arthur Cohen, M.A., D.A. McDuff, M.D.

Summary:

Substance use disorders occur commonly among persons who use medical, surgical, or psychiatric clinical services. In spite of high prevalence rates, physicians often fail to detect substance abuse disorders, particularly alcoholism. A method to teach medical students or residents as well as to offer intervention services to substance abusing patients in a teaching hospital is to offer a substance abuse consultation service (SACS). To learn if a SACS had clinical or teaching potential, we conducted this pilot study to determine characteristics of patients referred to a SACS in a 700-bed university hospital. Two hundred eighty-nine inpatients were referred over a three-month study period. A majority of patients were on the medical service, although one-third were psychiatric inpatients. Excluding nicotine dependence, polysubstance abuse was frequent; over 60% of patients reported ever abusing two or more substances concurrently. Alcohol was the most frequently abused substance (68% of patients), followed by cocaine (53%), opiates (46%), and marijuana (22%). The SACS provided patients from a variety of services to trainees for interviewing, diagnosing, demonstrating confrontational techniques appropriate to addicts who denied their condition, offering recommendations regarding pharmacological and behavioral managements, and referring to community treatment or self-help programs.

NR145 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

TAKEN AS NEEDED MEDICATION USE AS A PREDICTOR OF ALCOHOLIC RECIDIVISM

Nathaniel Marvel, Jr., M.D., Psychiatry, Cincinnati VAMC, 3200 Vine Street, Cincinnati, OH 45220; Thor Tangvald IV, M.D., Van Silka, M.D.

Summary:

The charts of 35 consecutively admitted alcohol dependent veterans were reviewed two years after their admission to a VA medical center inpatient detoxification unit. The average number of doses per day was calculated for both PRN and scheduled detox meds as well as for other PRN medications. Of the 35 patients, nine (25%) returned to this detox unit within two years (recidivists). They took 0.7 doses/day of PRN detoxification medications while the non-recidivists took only 0.3 doses/day ($p < .005$). Other PRN medications were also consumed by the recidivists (0.8 doses/day) at twice the rate of the non-recidivists (0.4 doses/day) ($p < .005$). The average length of stay of the recidivists was five days, compared to the non-recidivists average of 6.9 days ($P < .05$). During this time, the recidivists received less scheduled detoxification medication than the group of non-recidivists (NS). We found it interesting that the group of recidivists received less scheduled detoxification medication and had a shorter average length of stay, yet they requested more PRN medication than the non-recidivists. We feel that this is useful from both a treatment point of view as well as having value as a prognostic indicator.

References:
(1) Rounsaville B, et al: Psychopathology as a predictor of treatment outcome in alcoholics. Arch Gen Pscyhiatry 44:505, 1987.
(2) McLellann, et. al: Predicting response to alcohol and drug abuse treatment: role of psychiatric severity. Arch Gen Psychiatry 40:620, 1983.

NR146 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

QUANTITATIVE EEG CORRELATES OF DSM-III-R CRACK COCAINE DEPENDENCE

Kenneth R. Alper, M.D., Psychiatry, NY Univ Med Ctr, 550 First Avenue, New York, NY 10016; Robert J. Chabot, Ph.D., Anthony Kim, M.D., Leslie S. Prichep, Ph.D., E. Roy John, Ph.D.

Summary:

Evidence for a distinctive withdrawal state associated with cocaine dependence has accumulated from behavioral, neurophysiologic, and preclinical and clinical pharmacologic studies. We report here on the results of a preliminary investigation of the quantitative EEG (QEEG) correlates of severe chronic DSM-III-R crack cocaine dependence in seven patients abstinent from crack for two to 63 days. Increased alpha relative and absolute power were noted at all leads. Increased alpha has also been noted in multiple studies of patients with unipolar major depression (Alper and Cancro, 1990). This series of patients showed significant depressive morbidity, with four patients having attempted suicide subsequent to their beginning crack use, and the group mean Beck depression scale score was 18.8. These results compliment other phenomenologic and preclinical and clinical studies indicating disturbance of neurotransmitter systems subserving reward-mediated behavior in cocaine withdrawal and depression. QEEG may contribute to an understanding of the neurophysiologic basis of cocaine dependence, and prospective studies correlating QEEG measures with subsequent response to pharmacologic intervention should be considered.

NR147 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

ALPRAZOLAM ATTENUATES EFFECTS OF MCPP IN NORMALS

Avi Molcho, M.D., Psychiatry, Albert Einstein, 1300 Morris Park Avenue, Bronx, NY 10461; Serge Sevy, M.D., Serena-Lynn Brown, M.D., Moshe Kotler, M.D., Robert Plutchik, Ph.D., Herman M. van Praag, M.D.

Summary:

The effects of alprazolam, an anxiolytic triazolobenzodiazepine, on physiological and behavioral responses induced by m-chlorophenylpiperazine (MCPP), a serotonin (5-hydroxytryptamine or 5HT) receptor agonist, were investigated in 10 healthy male subjects. Alprazolam (0.5 mg) or placebo was given one hour prior to MCPP (0.5 mg/kg) or placebo. Four tests were conducted in each subject over a 210-minute period: (1) alprazolam + MCPP, (2) alprazolam + placebo, (3) placebo + MCPP, and (4) placebo + placebo. Physiologically, MCPP increased cortisol, prolactin, and growth hormone release, as well as heart rate and body temperature. Alprazolam decreased cortisol plasma level and body temperature. Alprazolam also caused a decrease in MCPP-induced cortisol, heart rate, and body temperature responses, but not in MCPP-induced prolactin and GH release. Behaviorally, MCPP was found to increase anxiety level. Moreover, in three subjects, MCPP induced physical symptoms suggestive of a panic attack. Alprazolam was found to inhibit these MCPP-induced behavioral effects. These results are discussed in light of their important implications for the serotonin hypothesis of anxiety, suggesting that the anxiolytic action of alprazolam may be related to an inhibition of 5HT activity.

NR148 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

NEGATIVE AND DEPRESSIVE SYMPTOMS IN SUICIDAL SCHIZOPHRENICS

Sidney J. Jones, M.D., Neurochemistry, NYS Psychiatric Inst., 722 West 168th Street, New York, NY 10032; Barbara Stanley, Ph.D., Jeannine Guiido, M.A., Ronald M. Winchel, M.D., Michael Stanley, Ph.D.

Summary:

This study examines the importance of depressive and negative symptoms as well as the value of the dexamethasone suppression test (DST) in differentiating schizophrenics with and without a history of suicide attempts.

We evaluated 59 schizophrenic patients, 25 of whom had a history of at least one suicide attempt. The Hamilton Depression Scale (HAM-D) was used to assess depression. The severity of negative symptoms was evaluated by summing Brief Psychiatric Rating Scale (BPRS) items emotional withdrawal, motor retardation, and blunted affect. Dexamethasone (1 mg) was given at the end of a two-week neuroleptic free evaluation period at 11 p.m. Serum cortisol levels were drawn at 9. a.m. and 4 p.m. the following day.

Total HAM-D scores differentiated schizophrenic attempters versus nonattempters, with attempters displaying more depressive symptoms than nonattempters ($t=3.4$, $df=56$, p.002). BPRS negative symptom scores did not distinguish between the groups. Both a.m. and p.m. cortisol levels correlated with the total HAM-D score ($r=.62$, $n=20$, p.01; $r=.66$, $n=22$, $p<.01$; respectively), while they did not correlate with the BPRS negative symptom scores. These findings reinforce that depressive and negative symptoms are separate constructs.

NR149 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

FAMILY HISTORY AND ADOLESCENT SUICIDALITY

James K. Zimmerman, Ph.D., Psychiatry, Montefiore Med Center, 111 E. 210th Street, Bronx, NY 10467; Gregory M. Asnis, M.D., Herman M. van Pragg, M.D., Laura C. Lemle, Ph.D.

Summary:

Past research has examined the influences of family history on adolescent suicidality. A recent study using a random sample of inner city high school students found that 9% reported having made suicide attempts; among attempters, there was a family history of suicide attempts in 33% of the cases (Harkavy Friedman, Asnis, et al, 1987). This poster will report findings using an extensive self-report measure of suicidality (Harkavy Friedman and Asnis, 1989). Data were collected on adolescents referred to a suicide prevention program and on their parents or custodial family members. Preliminary data on 40 cases include 29 attempters, and show a rate of 28% suicide attempts in the nuclear family of adolescents who had attempted suicide, confirming previous findings. Twenty-one percent of adolescent attempters had mothers who were attempters, while only 9% of mothers of nonattempters were attempters themselves; this difference is not statistically significant. However, in 59% of adolescent attempter cases, there were attempts in the extended family, while a family history of attempts was found in only 9% of nonattempters ($X^2=6.03$, $p<.02$). The implications of these findings regarding psychosocial, environmental, and genetic factors in adolescent suicide will be discussed.

NR150 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

PINEAL CALCIFICATION: MARKER OF TARDIVE DYSKINESIA

Reuven Sandyk, M.D., Psychiatry, Albert Ein Coll of Med, 1500 Waters Pl. Research Unit, Bronx, NY 10461; Gavin I. Awerbuch, M.D., Stanley R. Kay, Ph.D., J. Daniel Kanofsky, M.D.

Summary:

We reported recently increased spontaneous abnormal perioral movements in haloperidol-treated pinealectromized rats, which may implicate decreased melatonin secretion in the pathophysiology of tardive dyskinesia (TD). Since both preclinical and clinical studies suggest that the process of pineal calcification (PC) is accelerated by diminished melatonin secretion, we examined CT scans for prevalence of PC and other indicators of cerebral atrophy in 171 neuroleptic-treated chronic psychiatric inpatients (mean age 44.3, SD 10.9). Patients were rated for TD on two occasions, six months apart, using the AIMS. PC was rated independently by one of the investigators who was blind to the study hypothesis. Interrater and test-retest reliabilities for TD were high, and data from the second assessment were analyzed. The overall prevalence of persistent TD was 52.1 percent. Multiple stepwise regression analysis revealed that age, sex, current neuroleptic and anticholinergic dose, and EEG abnormalities, were not significant predictors of TD. The prevalence of PC in the TD group was 88.8 percent as compaired to 25.6 percent in the non-TD group ($p<0.001$) and 4.1 percent in the general population. Prevalence of PC was the only nueroradiological abnormality related to TD, suggesting that diminished melatonin secretion may be implicated in its pathophysiology. Our finding suggest that PC may serve as a neuroradiological marker of vulnerability to develop persistent TD.

NR151 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

LOW DOSE BROMOCRIPTINE IN THE TREATMENT OF TARDIVE DYSKINESIA

Lauren B. Marangell, M.D., Albert Ein Col of Med, Bronx Psych Ctr 1500 Waters Pl, Bronx, NY 10461; Stanley R. Kay, Ph.D., Jean-Pierre Lindenmayer, M.D.

Summary:

Dopamine (DA) agonists can be used in low doses to preferentially stimulate presynaptic autoreceptors, thereby decreasing DA synthesis and release. Clinical application of this principle to treat conditions such as tardive dyskinesia and psychosis, where DA hyperactivity or supersensitivity is central to the pathophysiology, has been hindered by uncertainty as to which doses in humans will lead to attenuation of DA activity, as opposed to the classical postsynaptic agonist effect.

We conducted a six-week, single-blind randomized study of adjuvent bromocriptine, 2.5 mg/day, in seven neuroleptic-treated chronic schizophrenic patients with tardive dyskinesia. Improvement in tardive dyskinesia, measured by the Abnormal Involuntary Movement Scale, was significantly greater under bromocriptine as compared to the control conditions (paired $t = 3.15$, $p<.02$). Psychopathology, measured by the Positive and Negative Syndrome Scale, showed trends toward improvement, particularly in thought disorder and activation. The data suggest that bromocriptine in doses of 2.5 mg/day ameliorates tardive dyskinesia and possibly psychopathology, theroretically due to preferential stimulation of presynaptic autoreceptors.

NR152 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

TESTING THE GABA HYPOTHESIS OF TARDIVE DYSKINESIA

Shawn L. Cassady, M.D., Research Center, Maryland Psychiatric, P.O. Box 21247, Baltimore, MD 21228; Adrian Birt, M.D., Richard Ellsberry, B.A., Gunvant K. Thaker, M.D., Carol A. Tamminga, M.D.

Summary:

A leading theory on the mechanism of tardive dyskinesia (TD) asserts decreased GABAergic efferent activity from the substantia nigra reticulata (SNR). We found that GABA agonists reduce dyskinetic symptoms, and that there is decreased CSF GABA in TD. In monkey, disruption of SNR GABA efferents produces inappropriate eye saccades. We evaluated saccadic control in 35 schizophrenic patients with TD, 25 without TD and 14 normals. Results suggest a twofold increase in saccadic distractibility (SCD) in TD compared to non-TD and normal controls ($p > .0001$). We hypothesize that GABAergic augmentation will decrease SCD and TD score in these patients, supporting the GABA hypothesis of TD. In a double-blind, placebo-controlled study, we administered clonazepam in doses up to 1.25 mg, and muscimol, a GABA agonist, in doses up to 5 mg. Volitional saccade latency (VSL) was recorded as a measure of sedation, a potential confound of these pharmacologic probes. Our preliminary results show that clonazepam increased VSL approximately 23% per mg, and SCD increased approximately 18% per mg. The large and increasing sedative effect renders clonazepam useless in testing our hypothesis. Results of muscimol trials will also be reported. We expect a larger effect size with less confounding sedation.

NR153 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

DIAGNOSIS OF POST TRAUMATIC DISORDER

Eitan D. Schwarz, M.D. Psychiatry, Evanston Hospital, 2650 Ridge Avenue Room 5321, Evanston, IL 60201; Janice M. Kowalski, Ph.D.

Summary:

This report examines the diagnosis of Post-traumatic Stress Disorder (PTSD) according to *DSM-III*, *DSM-III-R*, and proposed *DSM-IV* criteria sets in a cohort of 62 children and 48 adults 6 to 14 months after exposure to a single man-made disaster. Local school professionals interviewed the children and enabled access to a traumatized population. Subjects demonstrated a continuum of severity of PTSD. Difference among symptom thresholds had a more robust effect on diagnosis and incidence than difference among criteria sets. *DSM-III-R* was most restrictive, and there is considerable exclusion among the criteria sets.

NR154 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

SEROTONIN AND VICTIMS OF CHILDHOOD SEXUAL ABUSE

Mark H. Corrigan, M.D., CRU, Dorothea Dix Hospital, South Boylan Avenue, Raleigh, NC 27611; James C. Garbutt, M.D., Gregory M. Gillette, M.D., George Mason, Ph.D., Stanley Carson, Pharm. D, Robert N. Golden, M.D.

Summary:

Serotonergic dysregulation has been implicated in a number of psychiatric conditions. We investigated central serotonergic function, as measured by the neuroendocrine response to acute intravenous clomipramine (CMI) challenge, in 10 female adult psychiatric inpatients with histories of sexual abuse prior to age 14. We compared them to age- and sex-matched healthy volunteers and found that the sexual abuse victims had significantly blunted prolactin ($p = .05$) and cortisol ($p < .02$) responses, indicating reduced central serotonergic function. Since one-half of the patients carried a diagnosis of depression, we questioned whether the finding was due to affective illness. However, the prolactin and cortisol responses were not significantly different between sexual abuse victims with depression and those without. Furthermore, there was no correlation between the severity of depressive symptoms and the degree of blunting in the neuroendocrine responses to CMI. These data support the hypothesis that sexual abuse during a developmentally vulnerable period can lead to perturbations in central neurobiologic systems that persist into adulthood.

NR155 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

SENSORY MODALITIES OF FLASHBACKS: POST-TRAUMA

Heidi S. Resnick, Ph.D., Psychiatry, MUSC, 171 Ashley Avenue, Charleston, SC 29425; Dean G. Kilpatrick, Ph.D., Julie A. Lipovsky, Ph.D., Angelyne Amick, Ph.D., Connie L. Best, Ph.D., Benjamin E. Saunders, Ph.D., Ellie Sturgis, Ph.D.

Summary:

Little is known about the symptom of flashbacks related to traumatic events, which is included in DSM-III-R criteria for post-traumatic stress disorder (PTSD). Based on the prominence of sleep disturbances and abnormal REM patterns observed in this disorder, it has been suggested that this symptom may relate to the process of REM phenomena occurring during waking (1). Others have suggested similarities between this symptom and the phenomenon of panic attacks (2). This is a report of descriptive data on the frequency of flashbacks across sensory modalities within a general population sample of 1,414 women included in a National Institute on Drug Abuse funded study of potential mental health consequences, associated with trauma exposure and family history of substance abuse. Subjects were located and interviewed, following a structured interview schedule that included DSM-III-R criteria for PTSD, by female interviewers from a national survey research firm. Thirteen percent of the women with positive histories of traumatic events including criminal victimization, reported that they had had a flashback following an event experienced, that had persisted for at least one month. Of this group, 57% reported visual flashbacks, 31% reported auditory flashbacks, 29% reported tactile flashbacks, and 10% reported olfactory flashbacks. Clinical and research implications will be discussed.

NR156 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

THE ACUTE EFFECTS OF AEROBIC EXERCISE ON MOOD IN NORMAL MEN

Joshua Simon, Ed.D., Psychiatry, Michigan St. Univ, 6132 Coach House Drive, East Lansing, MI 48823; Dale A. D'Mello, M.D., Peter C. Douris, Ed.D.

Summary:

The acute effects of a single bout of aerobic exercise on mood are not well documented. To investigate these effects, 30 men (mean age = 45.4 yrs) from a corporate fitness center with no prior history of mental illness cycled on an ergometer and ran on a treadmill for 15 or 30 min on two separate days (counterbalanced to reduce order effects) at 70-85 percent of maximal heart rate. The Profile of Mood States questionnaire was filled out 5 minutes before exercising and just after the exercise to answer the question, "How do you feel right now at this moment?" Total mood scores were more positive ($p<.05$) prior to beginning 15 min of exercise compared to 30 min of exercise. Total mood scores changed positively, i.e., improved, ($p<.02$) following either 15 or 30 min of exercise. These positive changes were not significantly different from each other. These results suggest the following: (1) aerobic exercise has a positive acute effect on mood; (2) 15 min of exercise is as effective as 30 min in improving mood; and (3) anticipation of 30 min of exercise, compared to 15 min, has an acute negative effect on mood.

NR157 **Monday, May 14, 3:00 p.m. - 5:00 p.m.**

PREMENSTRUAL SYNDROME IN A PSYCHIATRIC SETTING

Catherine Hair, M.D., Psychiatry, Univ of Conn. Hlth Ctr., 263 Farmington Avenue, Farmington, CT 06032; Richard Schramm, M.D., Susan Caruso, Ph.D., Mahlon S. Hale, M.D.

Summary:

In the DSM-III-R, premenstrual syndrome (PMS) was proposed as a psychiatric disorder as Late Luteal Phase Dysphoric Disorder (LLPDD). As part of a consultation-liaison activity for psychiatric residents, an outpatient evaluation service for PMS was established in 1988, at the University of Connecticut Health Center. Goals have been to study the diagnosis of LLPDD and to determine whether it occurs independent of other psychiatric diagnoses.

We have evaluated 33 women for the presence of LLPDD and other psychiatric disorders. The protocol incudes: psychiatric, gynecologic and medical histories, the Premenstrual Assessment Form (Halbreich, et al.), the Daily Rating Form (Endicott, et al.), the LLPDD Form (DSM-III-R), and the SCL-90-R (DeRogatis).

Demographic findings of the study population are presented along with results from the protocol. Our findings indicate that PMS rarely occurs independent of other psychiatric disorders. Women referred with the complaint of LLPDD or PMS have primarily exacerbation of underlying clinical or subclinical psychiatric disorder during the late luteal phase, or carry a dual diagnosis of a psychiatric disorder with subclinical LLPDD.

These findings question the validity of LLPDD as an independent disorder. Implications for assessment and treatment of LLPDD are presented.

NR158 **Tuesday, May 15, 9:00 a.m. - 10:30 a.m.**

BRAIN MORPHOLOGY AT THE ONSET OF SCHIZOPHRENIA

Lynn E. DeLisi, M.D., Psychiatry, Suny, Stony Brook, HSC, T-101, Stony Brook, NY 11794; Anne L. Hoff, Ph.D., Joseph Schwartz, Ph.D., Gail Shields, M.D., Shree Halthore, M.D., Azad Anand, M.D.

Educational Objectives:

The objectives are to examine the questions of whether brain abnormalities are present at the onset of psychosis and are they progressive? Evidence for and against these issues from previous publications and new data will be presented and discussed.

Summary:

Structural brain changes are known to be present in patients with chronic schizophrenia; however, little is known about the timing of these findings. Only a small number of studies are reported of differences between first episode patients and controls, and these only examined ventricular size. We have recently begun a prospective longitudinal study of first episode cases in order to examine multiple brain regions (by MRI) at the onset of illness and to determine whether there is progressive structural change with time. Data will be reported on 30 first episode cases, 15 chronic schizophrenics, and 20 controls.

Statistical analyses of computerized measurements from initial scans (using a MANCOVA controlling for total brain volume) showed significantly increased lateral ventricular size ($p = .02$; left > right) in both patients groups compared with controls and reduced left temporal lobe size in the chronic patients only (p. = 05). Left lateral ventricular size was inversely correlated with age of onset of behavioral change ($r = -.38; p = .02$), so that the earlier the change, the larger the ventricles, while reduced temporal lobe size was uncorrelated with age of onset, but was correlated with time since onset (right: $r = -.43, p = .004$; left: $r = -.40, p = .008$). These findings suggest that some morphological change may already be present at the clinical onset of psychosis, particularly in patients with an early onset, while other structural change may progress with the duration of illness.

References:

1) Weinberger DR, DeLisi LE, Perman GP et al: Computed tomography in schizophreniform disorder and other psychiatric disorders. *Arch. Gen. Psych.* 39: 778-783, 1982.

2) DeLisi LE, Dauphinais ID, Gershon ES: (1988) Reduced size of brain limbic structures, *Schiz. Bull.* 14:185-191.

NR159 **Tuesday, May 15, 9:00 a.m. - 10:30 a.m.**

AUDITORY HALLUCINATIONS AND LANGUAGE AREAS OF THE BRAIN IN NEUROLEPTIC-FREE SCHIZOPHRENICS

John M. Cleghorn, M.D, Psychiatry, McMaster University, 1200 Main Street West, Hamilton Ontario, Canada L8N 3Z5; E. Steven Garnett, M.B., Claude Nahmias, Ph.D., Sheryl Franco, R.N., Barbara Szechtman, M.A., Ronald D. Kaplan, Ph.D., Henry Szechtman, Ph.D., Gregory M. Brown, M.D.

Educational Objectives:

To examine the evidence that auditory hallucinations are mediated by brain mechanisms mediating the production of language.

Summary:

We predicted that language regions of the brain would be metabolically activated while schizophrenic patients experienced auditory hallucinations and that the level of metabolism would be correlated with hallucination scores. Twenty-one *DSM-III* schizophrenics (16 drug naive first episode), 5 long free of neuroleptics) were examined by positron emission tomography (PET) with [^{18}F] fluorodeoxyglucose ([^{18}F] FDG). Auditory hallucinations (H) were scored after the uptake of [^{18}F] FDG using the hallucination scale of the SAPS. Eleven patients hallucinated during this period and 10 did not. These two groups did not differ in respect to age, sex, prior neuroleptic medication, age of onset, and prior substance abuse.

Results: Relative metabolism in Broca's region was significantly greater in the H group than in the nonH patients ($t = 2.06$, $p = .05$) and significantly less in right auditory cortex ($t = 2.26$, $p = .03$). Left supramarginal cortex metabolism was significantly lower in the H than nonH group. The left striatum was more active metabolically in the H than nonH patients ($t = 2.51$, $p = .02$).

Hallucination scores correlated significantly with metabolism in the striatum ($r = +.83$, $p < .001$) and anterior cingulate ($r = +.68$, $p = .02$).

Superior temporal and cingulate regions were also implicated in our study of neuroleptic treated chronically hallucinating patients (Cleghorn et al, *British Journal of Psychiatry*, in press).

References:

1) Bick, P.A. and Kinsbourne, M. Auditory hallucinogens and subvocal speech in schizophrenic patients. *American Journal of Psychiatry*, 144:222-225, 1987.

2) Cleghorn, J.M., Garnett E.S., Nahmias, C., Brown, G.M., Kaplan, R.D., Szechtman, H., Szechtman, B., Dermer, S.W., Cook, P. Regional brain metabolism during auditory hallucinations in chronic schizophrenics. *Br. J. Psychiatry* (in press).

NR160 **Tuesday, May 15, 9:00 a.m. - 10:30 a.m.**

QUANTITATIVE DATA AND THE GENETICS OF SCHIZOPHRENIA

Steven O. Moldin, Ph.D, Psychiatry, Washington University, 216 South Kingshighway Blvd, St. Louis, MO 63110

Educational Objectives:

To show that adjunct consideration of both qualitative (affection status) and quantitative (correlated liability indicator) data can: (1) lead to more valid phenotypes that would be useful in linkage and other genetic analyses of schizophrenia, and (2) increase the power of segregation analysis for investigating schizophrenia's mode of inheritance and estimating morbid risk.

Summary:

Increased understanding of the genetics of schizophrenia depends on valid determinations of the disease and "spectrum" conditions. A quantitative co-segregating correlate of liability can be used conjointly with diagnostic criteria for ascertaining probands, clarifying etiologic heterogeneity, resolving the mode(s) of inheritance, and identifying unexpressed genotypes. As an illustration, I discuss the utility of a cost-effective quantitative index from the Minnesota Multiphasic Personality Inventory. Results are presented from investigations of 179 parents and 171 offspring in the New York High-Risk Project, as well as a sample of 83 state hospital inpatients: (1) logistic regression analysis demonstrates that the index has moderate-high sensitivity, specificity, and predictive power (.64-.92) on cross-replication for discriminating schizophrenia from affective illness; (2) admixture analysis identifies a latent class of offspring at greatest risk; (3) segregation analysis of 65 normal control families shows that the index is highly familial; and (4) bivariate segregation analysis of 52 families with a schizophrenic parent demonstrates a moderate (.4) correlation between the index and liability, with psychometric data making a significant contribution to risk prediction. General implications of using quantitative indicators with diagnostic criteria to obtain more valid phenotypes for linkage analysis of psychiatric illnesses are discussed.

References:

Transmission of a psychometric indicator for liability to schizophrenia in normal families. S.O. Moldin, J.P. Rice, I.I. Gottesman, & L. Erlenmeyer-Kimling, *General Epidemiology*, in press; J.M. Lalouel, L. Mignon, M. Simon, R. Fauchet, D.C. Rao, & N.E. Morton, Genetic analysis of idiopathic hemochromatosis using both qualitative (disease status) and quantitative (serum iron) information, *American Journal of Human Genetics*, 37:275-286, 1985.

NR161 **Tuesday, May 15, 9:00 a.m. - 10:30 a.m.**

SCHIZOTYPY AND SUSTAINED ATTENTION

Mark F. Lenzenweger, Ph.D., HDFS, Cornell University, G-65 Van Rensselaer Hall, Ithaca, NY 14853; Barbara Cornblatt, Ph.D.

Educational Objectives:

At the end of the paper presentation, the learner should be able to appreciate/understand the psychometric high-risk strategy, basic signal detection theory indexes and computerized assessment of attentional functioning. The learner will also gain an appreciation for the relevance of attentional dysfunction in clinical schizotypes.

Summary:

The present study examined global sustained attentional functioning in 32 hypothetically psychosis prone (schizotype) and 43 normal control subjects drawn from a large randomly ascertained nonclinical university population (N = 726). Hypothetical psychosis proneness (or schizotypy status) was determined using a psychometric high-risk selection strategy which employed the Perceptual Aberration Scale, a prominent psychometric index of schizotypy. Sustained attention was measured objectively using a computerized high-processing load continuous performance test, i.e., the Continuous Performance Test-Identical Pairs Version (CPT-IP). Schizotypal subjects displayed significantly power global sustained attentional performance relative to control subjects as measured by the signal detection theory index d' and overall hit rate, a pattern of results often found among actual schizophrenic patients. Although schizotypic subjects evidenced greater levels of anxiety and depression during laboratory testing, sustained attention performance was not significantly associated with these mental factors. Our results support the trait-like liability indicator status of a relative sustained attention deficit among schizotypes and are interpreted in light of previous attention research conducted with actual schizophrenic patients as well as children at risk for schizophrenia. We also discuss the research utility of the psychometric high-risk strategy in schizophrenia-related investigations executed using nonclinical populations.

References:

Lenzenweger, M.F., & Loranger, A.W. (1989), Detection of familial schizophrenia using a psychometric index of schizotypy. Archives of General Psychiatry, 46, 902-907; Cornblatt, B.A., Lenzenweger, M.F., & Erlenmeyer-Kimling, L. (1989). The Continuous Performance Test, Identical Pairs Version. Psychiatric Research, 29, 65-85.

NR162 **Tuesday, May 15, 9:00 a.m. - 10:30 a.m.**

MCPP EFFECTS IN SCHIZOPHRENIC PATIENTS

John H. Krystal, M.D., Psychiatry, Yale Univ Sch of Medicine, West Haven VA Medical Center, West Haven, CT 06156; John P. Seibyl, M.D., Lawrence P. Price, M.D., Scott W. Woods, M.D., George R. Heninger, M.D., Dennis S. Charney, M.D.

Educational Objectives:

1) To describe a role for serotonin systems in the symptoms of schizophrenia; 2) highlight serotonin systems as a focus of novel treatment strategies for refractory patients.

Summary:

Serotonergic (5-HT) contributions to the pathophysiology of schizophrenia have come under intense scrutiny since the recent finding that high potency at 5-HT receptors may contribute to the enhanced efficacy of atypical neuroleptics, such as clozapine. 5-HT contributions to the symptoms of schizophrenia were studied using the 5-HT agonist, m-chlorophenylpiperazine (MCPP) in schizophrenic patients off neuroleptics and after treatment with typical neuroleptic medications. *Methods:* In an ongoing study, schizophrenic patients off neuroleptics for at least two weeks (N = 12) participated in two test days in a randomized order during which they received MCPP (0.1 mg/kg, i.v. over 20 minutes) or placebo. MCPP and placebo tests were also performed on a comparable healthy subject group (N = 12). Behavioral and neuroendocrine measures were obtained. Repeat MCPP and placebo test days were conducted in a subset (N = 5) of these patients who received four weeks of neuroleptic treatment. *Results:* 10/12 schizophrenics and 0/12 healthy subjects experienced significant MCPP-induced increases in the Brief Psychiatric Rating Scale (BPRS) psychotic symptoms, including visual and auditory hallucinations, conceptual disorganization, and suspiciousness. Anxiety responses to MCPP in patients were comparable to healthy controls and showed a different time course than psychotic worsening. Neuroleptic-free patients did not differ from healthy subjects in their growth hormone, cortisol, or prolactin responses to MCPP. Preliminary analyses suggest that typical neuroleptic treatment for four weeks reduced, but did not block, MCPP responses. *Implications:* MCPP appears to exacerbate psychosis in a high percentage of schizophrenic patients, suggesting that 5-HT systems play an important role in the pathophysiology of schizophrenia. The high affinity of MCPP for the 5-HT_2, 5-HT_{1C}, and 5-HT_3 receptors supports the impression that drugs that block these receptors may be useful in treatment of schizophrenia. In addition, the failure of neuroleptics to block the exacerbation caused by MCPP suggests that MCPP effects are specific to 5-HT systems and are unlikely to be due to a non-specific exacerbation of psychosis.

References:

Kane J, Honigfeld, G, Singer J, Meltzer H, and the Clozaril Collaborative Study Group: Clozapine for the Treatment-resistant schizophrenic: A double-blind comparison with Chlorpromazine. *Arch. Gen Psychiatry*, 45:789-796, 1988.

Hoyer D: Functional Correlates of serotonin 5-HT_1 recognition sites. *J. Rec Res* 8(1-4), 59-81, 1988.

NR163 **Tuesday, May 15, 9:00 a.m. - 10:30 a.m.**

IS SIX-MONTHS CRITERION NEEDED FOR DSM-IV SCHIZOPHRENIA?

Ming T. Tsuang, M.D, Psychiatry, Harvard Medical School, Brockton VAMC-116A 940 Belmont, Brockton, MA 02401

Educational Objectives:

At the end of this program one should recognize that six months duration of symptoms for diagnosing schizophrenia may not be necessary, and that a shorter duration should be considered for *DSM-IV* Schizophrenia.

Summary:

With *ICD-10* and *DSM-IV* in preparation, it is an excellent time to reassess the "duration of symptoms" criterion in schizophrenia. Although *DSM-III-R* uses "six months," there is no clear theoretical or empirical justification for this cut-off point. To examine this question empirically, we analyzed a group of 510 consecutively admitted and clinically diagnosed schizophrenics in terms of the relationship between duration of symptoms at diagnosis and long-term outcome. Of that group, complete information about duration and 30-40 year outcome data were available for 465 patients. Duration categories were defined in terms of one-month increments with the last category being "greater than six months." Long-term outcome was assessed according to occupational and psychiatric status at follow-up. Our results indicate that the proportion of "good" occupational outcome (employed) and good psychiatric outcome (no symptoms) sharply declines for those patients with a three-month or more duration of symptoms at index admission. At follow-up, 30-40 years later, of the patients who had less than three months duration of symptoms at admission, 56 percent were rated as employed, retired, or working at home and 41 percent were rated as having no psychiatric symptoms. When the duration of symptoms was greater than three months, the comparable percentage of good ratings decreased significantly to 37 percent for occupational status and 26 percent for psychiatric status. Our analyses suggest that based on long-term outcome, three months rather than six months should be considered for the "duration of symptoms" criteria for *DSM-IV* schizophrenia. Implications of these results will be discussed.

References:

Coryell W and Tsuang MT: *DSM-III* schizophreniform disorder: Comparisons with schizophrenia and affective disorder. *Arch Gen Psychiatry*, 39:66-69, 1982.

Coryell W and Tsuang MT: Outcome after 40 years in *DSM-III* schizophreniform disorder. *Arch Gen Psychiatry*, 43:324-328, 1986.

NR164 **Tuesday, May 15, 9:00 a.m. - 10:30 a.m.**

PRE-VIETNAM SERVICE MEDICAL RECORDS OF PTSD VETERANS

Roger K. Pitman, M.D., VA Research Service, 228 Maple Street, Manchester, NH 03103; Scott P. Orr, Ph.D., Michael Macklin, B.A., Bruce Altman, Psy. D.

Educational Objectives:

At the end of the program, the learner should be able to understand the role of pre-combat military records in elucidating the contribution of pre-stressor factors to the development of post-traumatic stress disorder.

Summary:

Pre-Vietnam military medical and personnel records were compared in previously defined (Pitman et al, 1989) cohorts of 47 PTSD and 83 non-PTSD, wounded Vietnam veterans. The two groups were comparable across the great majority of variables studied. These included: personal and family health statements, number of historical medical symptoms, historical psychiatric symptoms (including insomnia, nightmares, sleepwalking, depression, amnesia, bed wetting, nervousness, drug and alcohol use, and suicide attempts), and historical legal problems, as reported at the time of military induction; blood pressure and number of abnormal physical findings at the induction examination; Armed Forces Qualifying Test scores; number of military sick call visits prior to transfer to Vietnam; and pre-Vietnam military conduct ratings. Opposite to our prediction, there was a trend for military induction examination pulse rates to be (5 BPM) lower in the PTSD group. There were also trends for more PTSD veterans to have reported pre-military school difficulties and to have a pre-Vietnam military efficiency rating below excellent, but for fewer PTSD veterans to have had pre-Vietnam military AWOLs and non-judicial punishments.

Taken as a whole, the results support the absence of significant premorbid medical, psychiatric, or behavioral abnormalities in post-traumatic stress disorder in Vietnam veterans. Additional analyses are in progress and will be reported at the time of the presentation.

References:

1. Pitman RK, Altman B, Macklin ML. Prevalence of post-traumatic stress disorder in wounded Vietnam veterans. *American Journal of Psychiatry*, 146:667-669, 1989.

2. Foy DW, Rueger DB, Sipprelle RC, Carroll EM: Etiology of posttraumatic stress disorder in Vietnam veterans: analysis of premilitary, military, and combat exposure influence. *Journal of Consulting and Clinical Psychology*, 52:79-87, 1984.

NR165 **Tuesday, May 15, 9:00 a.m. - 10:30 a.m.**

SLEEP IN SURVIVORS OF THE NAZI HOLOCAUST

Jules Rosen, M.D., Univ of Pitts. Sch of Med, 3811 O'Hara Street, Pittsburgh, PA 15213; Charles F. Reynolds, M.D., Patricia R. Houk, M.S.W., Amy L. Yeager, B.A., Linda F. Hurwitz, M.A.

Educational Objectives:

To understand the nature of sleep in a community based population of people exposed to extraordinary emotional trauma 45 years ago.

Summary:

Sleep disturbances are commonly reported by victims of extraordinary stress and have been known to persist for decades. Using the Pittsburgh Sleep Quality Inventory (PSQI), this study compares the sleep of community-based survivors of the Nazi Holocaust (N = 42) to elderly depressed patients (N = 37) and controls (N = 54) in their home environments during the preceding one month period. Approximately 2/3 of the survivor group had total PSQI scores in the impaired range. The survivors had significantly more sleep problems than controls, but fewer than depressives ($F = 61.69$, $p < .0001$). Survivors reported awakenings due to bad dreams significantly more often than the other two groups with 35 percent experiencing nightmares at least once per week. The survivor group had significantly less daytime dysfunction due to loss of enthusiasm than the depressed group ($X^2 = 7.73$, $p < .005$), suggesting that sleep and mood disturbances are not necessarily linked among survivors. Sleep disturbance and frequency of nightmares correlated positively with the duration of internment in concentration camps ($r = .39$, $p < .01$). These findings suggest that for some Holocaust survivors, impaired sleep and frequent nightmares are significant problems 45 years after liberation.

References:

1. Buysse DJ, Reynolds CF III, Monk TH, et al: The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatric Res* 28:193-213, 1989.

2. Kaminer H, Lavie P: Dreaming and the long-term adjustment to severe trauma. *Sleep Res* 18:146, 1989.

NR166 **Tuesday, May 15, 9:00 a.m. - 10:30 a.m.**

COMORBIDITY OF PANIC DISORDER SEIZURES: AFFINITY OR ARTIFACT?

Richard Neugenbauer, Ph.D., Sergievsky Ct., Columbia University, 630 West 168th Street, New York, NY 10032; Robert Ouellette, M.P.H., Myrna M. Weissman, Ph.D., Jeffrey Markowitz, Ph.D.

Educational Objectives:

To examine epidemiologic, data analytic, and clinical issues that arise when assessing whether the co-occurrence of two disorders in the same individual represents diagnostic error, chance association of entirely separate disease entities or a causal link.

Summary:

Occurrence in the same individual of panic disorder and seizures, especially partial complex seizures, has prompted speculation of an affinity between these two conditions. The Epidemiologic Catchment area (ECA) study, an epidemiologic survey of psychiatric disorder in probability samples drawn from five U.S. communities (N = 18,000), affords the first opportunity to investigate this question of comorbidity in a sample free of selection bias. At each site lifetime prevalence of psychiatric disorder was based on subjects' responses to the Diagnostic Interview Schedule (DIS) converted to *DSM-III* diagnoses using computer algorithm. At one site, New Haven, lifetime prevalence of seizures was assessed in a separate medical questionnaire administered prior to the DIS. At the other sites, seizure history was assessed in the DIS section on somatization disorder. At New Haven (N = 4882), the odds of a person with a history of panic disorder (N = 60) also reporting a history of seizures was 6.6 fold the odds of a person with no lifetime history of psychiatric disorder (N = 3628) reporting a seizure history (95 percent confidence interval[CI] 2.4-18.2). The corresponding odds ratio for persons with panic disorder reporting a seizure history compared to persons with other psychiatric disorders (N = 788) reporting such a history is 5.4 (95 percent) CI 2.0-14.8). In the other four ECA sites combined, these odds ratios were 3.4 (95 percent CI 1.8-6.2) and 2.0 (95 percent CI 1.1-3.5), respectively. All analyses were adjusted for sociodemographic and a wide range of other potentially confounding variables (e.g., alcohol abuse, head injury). Given the similarity of panic disorder symptoms and partial complex seizures, this association may reflect merely "diagnostic" error in the present study as well as in either, clinical investigations. However, the strength and specificity of the association in these controlled analyses, the independent replication of the finding in the other ECA sites (both separately and combined), and the biological plausibility of the link, suggest strongly that the two disorders are casually, not artifactually, linked.

References:

Harper, M and Roth, M. Temporal lobe epilepsy and the phobic anxiety-depersonalization syndrome. Part I: A comparative study. *Compr Psychiatry* 3:3:129-151, 1962.

Signer, S.F. Seizure disorder or panic disorder? *Am J Psychiatry* 145:2:275-276, 1988.

NR167 **Tuesday, May 15, 9:00 a.m. - 10:30 a.m.**

ACTH RESPONSE TO PENTAGASTRIN IN PATIENTS WITH PANIC DISORDER AND HEALTHY CONTROL SUBJECTS

James L. Abelson, M.D., Psychiatry, Univ of Michigan, 1500 Medical Center Drive, Ann Arbor, MI 48109; Randolph M. Neese, M.D., Aaron Vinik, M.D.

Educational Objectives:

(1) Increase understanding of hypothalamic-pituitary-adrenal axis function in panic disorder, specifically contrasting ACTH responses to CRH and pentagastrin. (2) Illustrate how clinical observations and research can interact with basic science to generate new ideas about pathophysiology and treatment.

Summary:

Patients with panic disorder have blunted corticotropin (ACTH) responses to corticotropin-releasing hormone (CRH). This abnormality suggests that CRH may play a role in the pathophysiology of panic disorder. However, ACTH is under multihormonal control and its co-modularity neuropeptides have received little attention. Pentagastrin is a pentapeptide that has an active-site structure identical to the terminal amino acid sequences of gastrin and cholecytokinin (CCK). Both of these peptides are found in the pituitary co-localized with ACTH. CCK is a known modulator of hypothalamic-pituitary-adrenal (HPA) axis activity and an ACTH secretagogue. Intravenous pentagastrin, which is used as a provocative test for endocrine tumors, can produce symptoms identical to those of a panic attack. These observations led us to infuse pentagastrin into five patients with panic disorder and five healthy control subjects. All subjects received 0.6 microgram/kg of pentagastrin intravenously at 9:00 a.m. after an overnight stay in a clinical research center. Pentagastrin produced a significant increase in ACTH levels. In contrast to their response to CRH, patients with panic disorder did not have blunted ACTH responses to pentagastrin. There were significant differences between patients and controls in their cardiovascular response to the infusion. Our data support the hypothesis that the origin of HPA axis dysfunction in panic disorder is at or above the level of the hypothalamus. This first demonstration of an ACTH response to pentagastrin in patients may provide us with a new tool for dissection of HPA axis dysfunction. It also suggests new directions for speculative thinking about the biological treatment of panic disorder.

References:

Reisine TD, Alexrod J: Regulation of ACTH secretion and synthesis. In Hormonal Proteins and Peptides, Vol. 13, Corticotropin. Edited by Li CH, Orlando, Academic, 1987, pp. 173-96. Abelson JL, Neese RM, Vinik A: Treatment of panic-like attacks with a long-acting analogue of somatostatin. *J Clin Psychopharmacol.*, in press.

NR168 **Tuesday, May 15, 9:00 a.m. - 10:30 a.m.**

COGNITIVE THEORY FOR PANIC: COMPARATIVE EFFICACY

David M. Clark, D.Phil., Psychiatry, University of Oxford, Warneford Hospital, Oxford OX3 7JX, England; Michael Gelder, D.M., Paul Salkovskis, M. Phil., Ann Hackmann, M.Sc., Hugh Middleton, M.D., Pavlos Anastasiades, B.Sc.

Educational Objectives:

To provide a comparative evaluation of leading psychological and pharmacological treatments for panic disorder.

Summary:

Several studies have found that cognitive therapy is an effective treatment for panic. However, it is not known how cognitive therapy compares with other empirically validated treatments for panic. In order to investigate this question, 64 patients meeting *DSM-III-R* criteria for panic disorder without severe avoidance were randomly allocated to either cognitive therapy, applied relaxation, imipramine (up to 325 mg/day, mean 233 mg/day), or wait-list. All three treatments were given in conjunction with self-exposure instructions. Patients receiving cognitive therapy or applied relaxation had 12 sessions of treatment over a period of three months. Patients receiving imipramine were given a similar number of sessions and then maintained on the drug for a further three months before being withdrawn. Outcome measures included patient and blind assessor ratings of panic frequency and severity, panic diaries, Beck Anxiety Inventory, Beck Depression Inventory, laboratory psychophysiological assessment, and measures of catastrophic misinterpretations of bodily sensations. Immediate post-treatment (3 mths and 6 mths) results are presented. Comparisons between treatment groups and wait-list indicated that all three treatments were effective. There were no significant differences between applied relaxation and imipramine. On several measures cognitive therapy was significantly more effective than either applied relaxation or imipramine.

References:

Clark, D.M., A cognitive approach to panic *Behaviour Research Therapy*, *24* 461-470, 1988

Clark, D.M., Salkovskis, P.M., Gelder, M.G. *et al*: Tests of a cognitive theory of panic. In Hand and Wittchen (ed) *Panic and Phobias 2*, Springer-Verlag, 1988

NR169 **Tuesday, May 15, 9:00 a.m. - 10:30 a.m.**

TYPES OF SYMPTOMS AND RESPONSE TO CLOMIPRAMINE IN OBSESSIVE COMPULSIVE DISORDER

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Educational Objectives:

To present data on the types of OC symptoms found in a very large cohort OCD patients. Also, to examine the relationship between drug response and symptom content.

Summary:

There has been considerable interest in identifying meaningful subtypes of obsessive-compulsive disorder (OCD) based on the types of obsessive (O's) and/or compulsions (C's) present. We examined the types of obsessive-compulsive (OC) symptoms (sxs) in a very large (N = 544) cohort of nondepressed OCD outpatients who participated in a multicenter trial of clomipramine (CMI) vs. placebo. In this study, CMI was shown to be significantly better than placebo. *Methods:* The types of OC sxs were determined from pretreatment endorsements of the Y-BOCS Symptom Check List (Y-BOCS-SCL), a clinician-rated inventory of 54 types of O's and compulsions divided into 15 larger categories according to thematic content (e.g., aggression or contamination) or behavioral expression (e.g., washing or checking) of the sxs. *Results:* The majority of items were frequently endorsed and the majority of patients endorsed multiple items (mean # different items endorsed = 13.8 ± 11.3). Based on the 15 larger SCL categories, 84 percent had $1 >$ type of obsession (eg, 34 percent had $4 \geq$ types) and 87 percent had > 1 type of compulsion (eg, 48 percent had ≥ 4 types). The most frequently endorsed of the 15 symptom categories were "aggressive" (69 percent) and "contamination" (69 percent) O's and "cleaning/washing" (71 percent) and "checking" (73 percent) C's. The baseline severity of OCD was independent of the number of items endorsed on the SCL. Further analysis of the SCL and correlations of symptom categories with treatment response will be presented. *Conclusions:* These data suggest that it may be difficult to resolve OCD into discrete subtypes based solely on the content of OC sxs. There was extensive overlap between OC sxs viewed traditionally as distinct subgroups of OCD (eg, "checkers" vs. "washers"). A preliminary analysis of the data also suggests that content may not be very helpful in predicting response to drug therapy. Biological heterogeneity in OCD may not be expressed as differences in the content of OC sxs.

References:

1. Goodman WK, Price LH, Rasmussen SA et al. The Yale-Brown Obsessive Compulsive Scale I. Development, Use, and Reliability, *Arch Gen Psychiatry* 46:1006-1011, 1989.

2. DeVeaugh-Geiss J. Landau P, Katz R; Treatment of obsessive compulsive disorder with clomipramine, *Psychiatric Annals*, 19:97-101, 1989.

NR170 **Tuesday May 15, 12 noon - 2:00 p.m.**

TRIUNE BRAIN: CLINICAL APPLICATIONS FOR PSYCHIATRY

Elliot S. Cohen, M.D., Pain Management Centre, 2850 Serendipity Circle West, Colorado Springs, CO 80917; Arun V. Hejmadi, Ph.D., Patricia J. Lyall, B.S.

Summary:

Recent advances in psychophysiology and psychoimmunology have rekindled interest in relationships between emotion, thought, behavior, and physiology. The authors will present Subcortical Learning and Integration Construct (SLIC), and a viable model for understanding and impacting these relationships and will describe and demonstrate its clinical applications. SLIC begins with the triune brain concept (MacLean), which integrates structure (cortex/subcortex) with function and behavior. Brown's theory clarifies cortical and subcortical cognition: Cortical levels are mostly logical, rational, and capable of language; subcortical cognition is non-rational, non-logical, incapable of expressive verbal language, and similar in quality to early ontogenic stages of cognitive development. These latter processes have also been called "magical thinking." Often, the disjunction between logical and magical thinking processes in patients can impede therapeutic progress. SLIC provides a framework within which it is possible to understand, utilize, and integrate these different, and often conflicting levels of cognition to therapeutic advantage. SLIC has been used with success with anxiety disorders (DSM-III-R), depression, and functional illnesses. Clinical application will be illustrated with case discussions, audio tapes, and videotapes. Papers on this approach will be available.

NR171 **Tuesday May 15, 12 noon - 2:00 p.m.**

ETOMIDATE ANESTHESIA IN ECT

Paula T. Trzepacz, M.D., Psychiatry, Western Psychiatric Inst. and Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213; Fred C. Weniger, Jr., M.D., Joel Greenhouse, Ph.D.

Summary:

We reviewed charts of 47 consecutive depressed inpatients who received ECT to compare the effects of thiopental and etomidate anesthesia on seizure duration. All had diagnoses of major depression with or without delusions, bipolar depression, or major depression with primary degenerative dementia (DSM-III). Their ages ranged from 19-85 years. and 34 were geriatric ($\geq$ 62 yrs). A subgroup of 28 patients, whose mean age was 64 years, received both etomidate and thiopental during their course of ECT, sometimes in alternating fashion. In this subgroup, seizure durations were significantly longer ($p < .001$) for the etomidate treatments ($n = 110$) vs. the thiopental treatments ($n = 91$). Their mean seizure duration was 42.5 ± 15.4 sec. for etomidate and 30.6 ± 10.5 sec. for thiopental. In addition, 12 other patients (mean age = 57 years) received exclusively thiopental anesthesia and 6 patients (mean age 69 years) received only etomidate throughout their courses of ECT. No differences in seizure duration were found between these unmatched subgroups who were homogeneously treated with either agent. The etomidate-only subgroup may have had a higher seizure threshold and/or shorter seizures due to older age than the thiopental-only subgroup. Interestingly, etomidate produced seizure durations over 100 seconds on several occasions. We feel that etomidate, when compared intra-patient to thiopental, allows for longer seizure durations during ECT. While we did not measure improvement, 41 of 46 cases responded to the ECT course; 1 had more dementia than depression, and 4 were transferred to a medical service for unrelated medical problems before ECT was completed.

NR172 **Tuesday May 15, 12 noon - 2:00 p.m.**

THREE YEAR COMMUNITY FOLLOW-UP ON CONNECTICUT'S NOT GUILTY BY REASON OF INSANITY

Robert T. M. Phillips, M.D., Whiting Forensic Inst., O'Brien Drive, Middletown, CT 06457; Deborah Scott, M.S.W., Martha Lewis, M.S.W.

Summary:

An analysis of the insanity acquittees conditionally released and followed for a three year period by the Psychiatric Security Review Board of Connecticut will be presented. The data presented will show a comparison of the group that have been successful, i.e. the Psychiatric Security Review Board has revoked the conditional release, with those who were not revoked. Factors compared are demographic information, crime, diagnosis, type of community psychiatric treatment, type of supervision, type of residence, family support, type of medication orders. The analysis shows significant trends in which variables such as family support, substance abuse history and Axis II diagnosis increase risk of failure in the community. The major reason for a revocation of condition release is drug abuse. Connecticut acquittees have experienced a low rearrest rate, less than 15%, but the rate of rehospitalization is approximately 33%.

The Connecticut data are compared to the data from Oregon, which also uses the Psychiatric Security Review Board model. Data from other jurisdictions, California, New York and Maryland will also be presented.

NR173 **Tuesday May 15, 12 noon - 2:00 p.m.**

BETA-1 RECEPTOR RESPONSE IN NORMALS ON DESIPRAMINE

Robert B. Pohl, M.D., Psychiatry, Wayne State University, 951 Lafayette, Detroit, MI 48207; Vikram K. Yeragani, M.D., Richard Balon, M.D., Debra A. Glitz, M.D., Richard Berchou, D. Pharm., C. Ramesh, M.D.

Summary:

Tricyclic antidepressant (TCA) induced down-regulation of beta-receptors in animals appears to be selective for beta-1 adrenoceptors, while beta-2 receptors are unaffected. This phenomenon is of interest because the time course of down-regulation matches the delayed therapeutic response to TCAs. However blood element beta-receptors are of the beta-2 type. To test whether there is a TCA-induced decrease in the beta-1 receptor responsiveness in man, we measured the heart rate response to logarithmically increasing doses of isoproterenol before, during, and after three to four weeks of 75 mg of desipramine daily in normal controls. Regression lines are calculated for postinjection heart rate increases as a function of isoproterenol dose. The chronotropic dose 25 (CD25), the dose of isoproterenol that raises heart rate by 25 beats per minute, was calculated from each subject's regression equation. In the first seven subjects, there was a significant difference between the pretreatment (1.66 ± 1.23 ug) and posttreatment CD25 (5.2 ± 4.6 ug) ($t = 2.2$, df;6, $p < 0.05$), one tailed). There was a smaller increase in CD25 at 4-5 days of treatment (3.3 ± 2.9 ug). These data support the hypothesis that TCAs taken chronically result in a decreased response to beta-1 receptor stimulation.

NR174 **Tuesday May 15, 12 noon - 2:00 p.m.**

DEPRESSION, BLPH.BE AND ACTH IN CUSHING'S DISEASE

Monica N. Starkman, M.D., Psychiatry, Univ of Michigan, 1500 E. Medical Center Drive, Ann Arbor, MI 48109; David E. Schteingart, M.D.

Summary:

Cushing's Disease (CD) is associated with a depressive syndrome. In 11 patients, we studied profiles of ACTH and BLPH.BE cosecretion on the basal day (B) and with metyrapone (Met) stimulation and 2 and 8 mgm/day dexamethasone (DX) suppression. Depressed mood scores and modified 17-item Hamilton Depression Scales were obtained at B. Six were categorized as mildly depressed, 5 as more severely depressed. ACTH and BLPH.BE were measured by RIA. Patterns of cosecretion were categorized as parallel (P) if synchronized at most points, or nonparallel (NP) if major dissociation occurred. Cosecretion in patients with more severe depression was NP in 15 and P in 8 testing conditions; in mild depression, cosecretion was NP in 3 and P in 23 testing conditions ($p < .001$). With metyrapone stimulation, there were trends for smaller peptide peak response to occur in the severely depressed: ΔBLPH.BE (peak-baseline) was 14 ± 25 fm/ml versus 85 ± 75 in the mildly depressed ($p = .07$). Peaks in the severely depressed were also less synchronous: at the ACTH peak, ΔBLPH.BE (peak-baseline) was 20 ± 34 versus 77 ± 80 fm/ml in the mildly depressed ($p < .04$).

These results suggest that severity of depression in CD may be associated with greater dysregulation of cosecretion of POMC-derived peptides.

NR175 **Tuesday May 15, 12 noon - 2:00 p.m.**

PLASMATIC NEUROTENSIN AND VIP MODIFICATIONS IN MOOD AND ANXIETY DISORDERS

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Summary:

Neurotensin and VIP have been proposed to be involved in stress responsiveness and locomotor activity and might have a role in some neuropsychiatric disorders.

We have studied 18 patients diagnosed of Major Depression and 22 patients diagnosed of Agoraphobia with or without panic attacks following DSM III-R criteria. A control group of 20 healthy people was used. All the groups were matched in age and sex.

Morning blood samples were taken in fasting conditions and stored with calcium EDTA and Traxylol. Quantification of Neurotensin and VIP was performed by RIA commercial methods.

Determinations were made when untreated and after a twelve week randomized treatment with either Imipramin (2 mg/kg body weight) or Phenelzine(1 mg/kg).

Results show a significant decrease of both neuropeptides levels in the patient group as a whole ($p < 0.01$). Levels normalized after recovering with Imipramin or Phenelzine treatment.

Moreover, Neurotensin decrease positively correlated with depression rating scores (MADRS).

Results are discussed taking into account central neurochemical aspects and considerations about peripheric factors.

NR176 **Tuesday May 15, 12 noon - 2:00 p.m.**

ENHANCED ALPHA EEG WITH CLOZAPINE RESPONSE

Steven G. Potkin, M.D., Psychiatry, UC Irvine Medical Center, 101 City Drive Rt. 88, Orange, CA 92668; Yi Jin, M.D., C.W. Chris Heh M.D., Bob Isenhart, Curt Sandman, Ph.D.

Summary:

Clozapine is a novel neuroleptic drug which is effective in one third of treatment-resistant schizophrenic patients. Eight DSM-III-R diagnosed schizophrenic patients were included in this photic-driving spectral EEG study. EEG's and clinical evaluations (BPRS) were performed for each patient at the end of the 3-week, drug-free period and at the end of the 5-week clozapine treatment. Four of the eight patients demonstrated clinical improvement (more than 35% improvement in BPRS). Four experimental conditions, i.e., one resting and three photic stimuli (2.4 Hz, 4.5 Hz, and 8.3 Hz), were randomly provided during the EEG test. Eight 10-second EEG sweeps for each condition were recorded at 100 Hz digitizing rate from both Fz and Pz and referred to the linked mostoids. A FFT was performed, and the data were normalized by dividing absolute value by the total power across the entire spectrum for each condition. Responders showed a greater increase in alpha power than nonresponders after treatment (ANOVA $F(1,6) = 50.58$, $p = 0.0004$). A positive correlation between the change in BPRS score and the change in alpha EEG power under the driving condition was found following treatment ($r = 0.77$, $p < 0.03$). A nonsignificant correlation was found between plasma clozapine and change in BPRS or change in alpha. These results suggest that a positive clinical response to clozapine is associated with improved cortical alpha spectral EEG power.

NR177 **Tuesday May 15, 12 noon - 2:00 p.m.**

HEART RATE VARIABILITY IN MAJOR DEPRESSION

Gregory W. Dalack, M.D., Clinical Psychiatry, NYS Psychiatric Inst., 722 West 168th Street, New York, NY 10032; Steven P. Roose, M.D., Alexander H. Glassman, M.D., Sally Woodring, R.N., J. Thomas Bigger, M.D.

Summary:

It has long been recognized that autonomic nervous system function is disrupted in individuals with affective disorder. Heart rate variability is a reflection of the interplay and balance between sympathetic and parasympathetic input on the cardiac pacemaker. Since peripheral autonomic tone reflects input from central autonomic centers, we hypothesized that the disruption of autonomic nervous system function in depressed patients would be manifested by abnormalities in heart rate variability.

We measured heart rate variability in 12 drug-free, otherwise healthy patients, aged 31-79 years, who had DSM-IIIR major depression, and 33 normal controls, aged 39-85. We further calculated the proportion of absolute differences between R to R intervals >50msec (pNN50), an index that measures high frequency variability and is a quantitative reflection of vagally driven respiratory sinus arrhythmia, i.e. parasympathetic activity. Though overall heart rate variability did not appear to be significantly altered in depressed patients, the high frequency component was markedly diminished compared to controls: 67% of the patients had pNN50 ≤ 2.5, compared to 27% of controls (Chi-square $= 4.25$, df $= 1$, $p < 0.05$).

These data would appear to indicate that patients with major depression have decreased parasympathetic activity as reflected by diminished high frequency variability. Since decreased parasympathetic tone lowers the threshold for ventricular fibrillation, it is intriguing to speculate whether the observation reported here may relate to the mechanism underlying the long observed phenomenon that depressed patients have a higher than expected mortality from sudden cardiovascular events, namely that depressed patients are vulnerable to fatal ventricular arrhythmias.

NR178 **Tuesday May 15, 12 noon - 2:00 p.m.**

IMIPRAMINE AND PAROXETINE BINDING WITH ZACOPRIDE

John C. Pecknold, M.D., Research, Douglas Hospital, 323A Grosvenor, Westmount PQ, Canada H3Z 2M3; Lorenz Luthe, M.Sc., Linda J. Iny, M.A., Michael J. Meaney, Ph.D.

Summary:

Evidence for serotonergic abnormality has been accumulating from basic sciences as well as from human pharmacological data. [3H] imipramine binding sites are associated with the serotonin transport complex in brain and platelets and [3H] paroxetine has been suggested as a more specific marker. Preliminary results from our center indicate that the BMax of [3H] imipramine and [3H] paroxetine are significantly lower in the blood platelets in the patients suffering from DSM III-R diagnoses of major depression, dysthymia and especially generalized anxiety and panic disorder in comparison with normal controls.

Zacopride is a 5HT3 receptor antagonist with preliminary evidence of anxiolytic efficacy. In this 4-week multi-center, double blind, dose response study of Zacopride and placebo in patients with DSM III-R generalized anxiety disorder, 18 patients participated. All 18 patients had platelet paroxetine binding at baseline, but only 13 patients had this binding at the end of the study. Dose ranges were from 0.1 mg to 100 mg of Zacopride or placebo QID. All on the higher dosage improved on the HAM-A, whereas only 36 of those on placebo or low dose improved ($X^2 = 6.5$ $p < .03$). Those patients with a higher initial HAM-A score tended to have a greater increase on the final BMax of the imipramine binding ($r = -.74$ $p < .1$). Patients with a higher initial HAM-A score had an increased BMax of the paroxetine binding at the end of the study ($r = 0.56$ $p < .05$). We were unable to find significant results for a Zacopride dose curve on either the imipramine nor the paroxetine bindings. This may be due to the small numbers and dose range. A further study using higher doses of Zacopride is currently under way.

NR179 **Tuesday May 15, 12 noon - 2:00 p.m.**

EFFECT OF SLEEP DEPRIVATION ON MOOD AND ARDEN RATIOS

Christopher Reist, M.D., Psychiatry, Long Beach VAMC, 5901 East Seventh Street, Long Beach, CA 90822; Kenneth N. Sokolski, M.D., Edward M. Demet, Ph.D.

Summary:

One night of sleep deprivation produces significant, but temporary, mood improvements in about two out of three depressed patients. While the mechanism of this improvement is unknown, some evidence suggests a dopaminergic role in the action. The Arden ratio (eye potential in bright light divided by eye potential with dark adaptation) is a putative non-invasive measure which may reflect dopaminergic sensitivity. A previous study has shown decreased Arden ratios in depressed patients. The present study examined Arden ratios of depressed patients prior to and following a night of sleep deprivation. Patients were divided into two groups on the basis of symptom severity. A high group had Hamilton depression scores of ≥ 25; and a low group had scores of ≤ 10. Baseline Arden ratios of the high group were significantly lower than either the low group or normal controls. Sleep deprivation significantly improved depressive symptoms and increased Arden ratios of the high group. An inverse relation between clinical response and Arden ratios was found in non-responders. The results support a possible dopaminergic role in the mechanism of sleep deprivation and underscore the possible usefulness of Arden ratios as a diagnostic marker of depressive illness.

NR180 **Tuesday May 15, 12 noon - 2:00 p.m.**

CORRELATES OF PLASMA DEXAMETHASONE LEVELS IN DEPRESSION

Jacqueline A. Samson, Ph.D., Research Facility, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Anthony J. Rothschild, M.D., Joseph J. Schildkraut, M.D., Monica Luciana, B.S., Herbert Y. Meltzer, M.D., Alan F. Schatzberg, M.D.

Summary:

A number of investigators now report that plasma dexamethasone (DEX) levels are lower in depressed patients who show nonsuppression on the Dexamethasone Suppression Test (DST), and that DEX levels correlate inversely with plasma cortisol (COR) levels (1). Although it is known that depressed patients are heterogeneous with respect to rates of DEX metabolism, the mechanisms governing DEX metabolism are not fully understood (2). In a sample of 23 *DSM-III-R* drug-free unipolar nonpsychotic depressed patients (6 males, 17 females, mean $\pm$ SD age = 34 ± 9 years) we examined plasma catecholamines (NE, E, DA) and related measures (HVA, DBH) as well as plasma COR at 8am and 4pm before and after ingestion of 1mg DEX at 11pm. DEX levels were assessed at 4pm after DEX ingestion. A significant correlation was found between DEX level and age ($r = .45$, $p = .03$), but not sex ($r = .05$, NS). After statistically controlling for the effects of age, DEX levels correlated inversely with both 8am and 4pm post-DEX COR (8am $r = -.44$, $p < .05$; 4pm $r = -.45$, $p < .05$). Moreover, after controlling for age, sizeable positive partial correlations were found between DEX levels and 8am and 4pm post-DEX NE (8am $r = .35$, $p = .10$; 4pm $r = .48$, $p = .03$). Surprisingly, positive partial correlations were also found between DEX levels and 8am and 4pm pre-DEX NE (8am $r = .46$, $p = .03$; 4pm $r = .34$, $p = .12$). Lastly, a multiple regression analysis performed using pre-DEX measures and age as predictors of DEX levels, showed that age and 8am pre-DEX NE accounted for 37 percent of the variance in DEX levels (Multiple $R = .61$, $F = 5.28$, $p = .02$). Findings will be discussed in relation to interpretation of the DST, the pathophysiology of depressive disorders, as well as the implications for understanding interactions between catecholamines and HPA activity.

NR181 **Tuesday May 15, 12 noon - 2:00 p.m.**

CATECHOLAMINE OUTPUT VERSUS RECEPTOR FUNCTION

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Summary:

Could abnormalities of adrenergic receptor function in psychiatric illness simply reflect altered catecholamine output? To test this, we chose adenylate cyclase (AC) activity to measure receptor function and an integrated measure of extraneuronal norepinephrine (NE) to measure catecholamine release. The relationship of NE to AC activity has not been reported, although it has been suggested that circulating levels of NE influence the regulation of adrenergic receptors, AC activity and ultimately cell activity. We measured free plasma NE, free and conjugated urinary NE, normetanephrine, MHPG, VMA, and AC activity in platelets (PLT) and lymphocytes (LMP) (basal and following stimulation with GPP(NH)P and CsF) in 10 healthy volunteers. Free plasma and urinary NE did not correlate with AC activity. However, "NE release" (NE+NM/NE+NM+MHPG+VMA) significantly correlated positively with PLT basal AC activity (R=0.76, P=0.01) and negatively with LMP basal activity (R=-.70; P=0.02). "NE release" significantly correlated positively with GPP(NH)P and CsF stimulated AC activity in PLT and negatively with GPP(NH)P and CsF stimulated AC activity in LMP. This provides the first demonstration in humans that both basal and stimulated AC activity may be a function of the average extraneuronal NE output in the absence of pharmacologic stimulation.

NR182 **Tuesday May 15, 12 noon - 2:00 p.m.**

SENSITIVITY OF TRH TEST VERSUS TSH IN HYPOTHYROIDISM

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Summary:

The early stages of hypothyroidism can be identified by increased TSH response to TRH stimulation or elevated baseline TSH, prior to the development of low T4 or classic signs and symptoms. Such subclinical hypothyroidism has been reported in up to 10-15 percent of psychiatric patients, and has been associated with a positive response to thyroid hormone potentiation of antidepressants and a tendency in bipolar patients to rapid mood cycles. Autoimmune thyroiditis is the most common etiology. In order to determine if baseline TSH measurement obviates the need for the TRH test in identifying subclinical hypothyroidism, we reviewed 20 consecutive psychiatric inpatients who had a TRH test and either elevated baseline TSH (>4.0 uIU/ml by RIA) or increased TSH response to TRH (delta TSH >25.0 uIU/ml). Of 18 patients with delta TSH >25.0, only eight had baseline TSH >4.0. However, of 10 patients with baseline TSH >4.0, eight had delta TSH >25.0 and two had delta TSH >20.0. Of the 10 patients with positive antithyroid antibody titers, four could be identified by elevated baseline TSH, whereas eight could be identified by increased TSH response to TRH. These data suggest that TRH testing doubles the sensitivity of baseline TSH levels alone in identifying subclinical hypothyroidism in psychiatric patients.

NR183 **Tuesday May 15, 12 noon - 2:00 p.m.**

A PRIMATE MODEL FOR EVALUATING NOVEL ANTIPSYCHOTICS

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Summary:

An animal model has been developed using primate social colony paradigm to conduct an initial evaluation of new compounds for potential antipsychotic activity and motor side effects. This model is based on model psychosis with has been used to induce behavioral changes which resemble positive and negative symptoms of psychosis. Two one hour behavioral observation sessions are conducted each day. Following documentation of normal colony behavior and apomorphine (1 mg/kg, i.m.) induced behavior, at least four doses of the test antipsychotic compound is administered to selected members of the adult Stumptail macaque social colonies twice daily for 2-3 days in escalating doses with only one dose given per week. During the initial observation each day, the behavioral effects of the antipsychotic candidate alone is recorded. Apomorphine is then administered 15 min. before the second observation to examine the effect of the drug on the model psychosis. Standard antipsychotics such as trifluoperazine and haloperidol produced a dose dependent reversal of the model psychosis and an increase in Parkinson-like movement abnormalities and sedation. Two novel antipsychotic candidates gevotroline and BMY14802 produced a reversal of the model psychosis with reduced or no movement abnormalities.

N4184 **Tuesday May 15, 12 noon - 2:00 p.m.**

NEUROENDOCRINE EFFECTS OF SM3997

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Summary:

A new class of non-benzodiazepine anxiolytics have recently been introduced which are selective serotonin $(5HT)_{1A}$ partial agonists. These drugs are rapidly metabolized and one common metabolite is 1-phenyl piperazine (1-PP). Tandospirone (SM-3997), a member of this class, is one such compound currently in phase II clinical trials designed to assess both anxiolytic and antidepressant activity. This study investigates the pharmacokinetic and neuroendocrine profile of SM-3997 in healthy human males. *Method:* Seven healthy male subjects (Mean ± SD age; 26.3 ± 3.1) were tested in a double-blind protocol involving balanced, random assignment to 30 mg oral SM-3997 or placebo. Six subjects received two further tests in a single-blind fashion involving 40 mg and 50 mg oral SM-3997. Tests started at 8 am and were one week apart. Plasma for hormones and levels of SM-3997 and 1-PP were collected at 20 and 5 minutes before and 30, 90, 120, 150, 210, and 240 minutes after administration of drug of placebo. *Results:* Plasma Sm-3997 peaked within 30 minutes and 1-PP reached levels 5 to 20 times that of SM-3997 1 to 2 hours after oral administration. There was no significant placebo-drug difference in peak minus base plasma prolactin or cortisol. Peak minus base growth hormone values (mean ± SD) were 0.1 ± 1.2 ng/ml after placebo, and 7.3 ± 7.1 ng/ml ($p<.05$), 9.2 ± 7.6 ng/ml ($p<.05$),and 7.7 ± 8.4 ng/ml ($p<.09$) after 30 mg, 40 mg, and 50 mg SM 3997, respectively. *Implications:* Metabolism of SM-3997 into 1-PP and other metabolites is rapid after oral administration. The relatively high plasma levels of 1-PP raise questions about the role of 1-PP in the anxiolytic and antidepressant activity associated with $5HT_{1A}$ partial agonists. Increases in growth hormone but no change in prolactin or cortisol at these doses was surprising and suggest differential regulation of these hormones by serotonin receptor subtypes and/or that 1-PP may have actions at other neurotransmitter systems such as the adrenergic system which confound interpretation of neuroendocrine measures.

NR185 **Tuesday May 15, 12 noon - 2:00 p.m.**

PHOTOAFFINITY LABELING OF THE GBR BINDING SITE

S. Paul Berger, M.D., NIMH, Bldg 10 RM 4N214, 9000 Rockville Pike, Bethesda, MD 20982; Russel Martensen, Ph.D., Peter Laing, Ph.D., Steven M. Paul, M.D.

Summary:

In order to develop a photoaffinity probe for the dopamine reuptake carrier probe, a tritiated azido derivative of the dopamine reuptake inhibitor, GBR-12935 has been synthesized. The reversible binding of the azido GBR-12935 derivative in the dark to striatal membranes was characterized. Like [3H] GBR-12935 binding complete sodium dependence was observed and there was a strong correlation between a series of drugs ability to inhibit binding and dopamine reuptake. Stereospecificity was observed between the plus and minus enantiometers of cocaine. GBR 12935 inhibited binding with a hill coefficient close to one whereas cis-flupenthixol an inhibitor of the binding of GBR compounds to a piperazine site, did not significantly inhibit binding. Incubation of membranes with the tritiated azido GBR-12935 derivative, followed by ultraviolet irradiation leads to the covalent incorporation of the probe into a peptide of Mr = 80,000 as assessed by autoradiography of gels after sodium dodecyl sulfate- polyacrylamide gel electrophoresis. Labeling of this Mr = 80,000 peptide is sodium dependent and can be blocked stereospecifically by (–) but not (+) cocaine. Dopamine reuptake inhibitors likewise blocked incorporation into the Mr= 80,000 peptide was not present in the cerebelum an area of sparse dopaminergic terminals. Following WGA lectin chromatography the Mr = 80,000 peptide was detected exclusively in the NAG eluent.

NR186 **Tuesday May 15, 12 noon - 2:00 p.m.**

MEMBRANE PHOSPHOLIPID CONTENT IN BIPOLAR DISORDER

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Summary:

Phospholipids (PLs) are major structural components of the cell membrane, that interact with membrane enzymes and transport molecules. To assess the hypothesis that altered membrane PL composition occurs in bipolar affective disorder, we performed a preliminary analysis of data from an ongoing investigation. PL composition of erythrocyte (RBC) membranes was determined with a novel method based on two-dimensional high performance thin layer chromatography and scanning laser densitometry. The method separates nine classes of amino-, choline-, and inositol-PLs or lysoPLs, and can quantitate amounts of PL corresponding to <15 ng of lipid phosphorous. Data are currently available from 12 patients with bipolar disorder and 11 normal control subjects. All subjects were drug-free and physically healthy. Patients did not differ significantly from controls in the proportion of males/females (4/8 vs. 4/7), mean age (33.9 vs. 39.1 yrs), or mean body mass index (BMI, 27.3 vs. 25.4 kg/m^2). Choline- and inositol-PLs did not differ between patients and controls. For the amino-PLs [phosphatidylethanolamine (PE) and phosphatidylserine (PS)], the ratio of PE/PS was significantly lower in bipolar patients than in controls (Mann-Whitney test, $p<0.01$). In the bipolar group, but not in the control group, PS was inversely correlated with both NA^+–Li^+ countertransport activity ($p<0.03$) and BMI ($p<0.02$). These findings suggest possible membrane PL alterations in bipolar disorder, as well as a potential interaction between ion transport processes and the PL matrix. Although not necessarily of importance to the RBC, these PL alterations could reflect an underlying physiological defect in bipolar disorder that affects cells in the CNS, and that could have a role in the pathogenesis of depressive or manic episodes.

NR187 **Tuesday May 15, 12 noon - 2:00 p.m.**

HIPPOCAMPAL LESIONS AND BRAIN DOPAMINE SYSTEMS

Barbara K. Lipska, Ph.D, CBDB, NIMH, 2700 Martin L. King Jr Ave SE, Washington, DC 20032; George E. Jaskiw, M.D., Farouk Karoum, Ph.D., Joel E. Kleiman, M.D., Daniel R. Weinberger, M.D.

Summary:

The purpose of this study was to determine the influence of intrinsic hippocamal neurons on regional brain catecholamine turnover and locomotion in the rat. Rats were lesioned bilaterally (coordinates from bregma AP –3.0 mm, ML + 2.2 mm, VD -3.9 mm) with ibotenic acid (IA) (ug in 0.5 ul) or vehicle (buffered saline). Locomotion was assessed on the 14th and 28th days postoperatively. In IA lesioned rats spontaneous but not d-amphetamine (1.5mg/kg) induced locomotion was increased on the 14th but not 28th day after lesion. The levels of DA, DOPAC, HVA were assayed by HPLC in medical prefrontal cortex, nucleus accumbens, hippocampus, olfactory tubercle and anteromedial caudate and will be discussed in light of the behavioral results.

NR188 **Tuesday May 15, 12 noon - 2:00 p.m.**

HEAT LOADING IN HALOPERIDOL-TREATED SCHIZOPHRENICS

Haggai Hermesh, M.D., Geha Psych Hospital A., P.O. Box 72, Petah Tiqva 49100, Israel; Moshe Birger, M.D., Arik Shalev, M.D., Yoram Epstein, Ph.D., Hanan Munitz, M.B., Suzy Floru, M.D.

Summary:

We attempted to clarify some of the ongoing pathophysiological disturbances that underlie 3 serious hyperthermic syndromes related to schizophrenia and neuroleptic treatment; heat stroke, febrile catatonia and neuroleptic malignant syndrome. Eight male schizophrenic outpatients, stabilized with haloperidol (HPL) depo 100-150 mg/month underwent a standard heat loading procedure in a climatic chamber. Participants paced on a treadmill for 50 min. x 2 and were exposed to an ambient temperature of 36°C and a relative humidity of 60%. Skin, body, and rectal temperature, sweat rate, serum creatinine phosphokinase and prolactin were measured before, during and after exposure. When compared to normal age-matched male controls, patients had a higher dropout rate (5/8 vs 0/8, Fisher's exact test, $p=.012$) attributed either to exhaustion or the reaching of upper safety limit temperature (39°C). The patients' sweat rate (432 ± 216 vs 904 ± 246 gr/h, $p<.002$) as well as their heat conductance from body core to the periphery (219 ± 22 vs 240 ± 13, $p<.05$) were significantly lower. These findings indicate the presence of a persistent thermoregulatory disturbance in schizophrenic patients treated with HPL.

NR189 **Tuesday May 15, 12 noon - 2:00 p.m.**

LOW-DOSE CLOMIPRAMINE FOR REFRACTORY AKATHISIA

Haggai Hermesh, M.D., Geha Psych Hospital A., P.O. Box 72, Petah Tiqva 49100, Israel; Dov Aizenberg, M.D., Galia Friedberg, M.D., Zvi Zemishlani, M.D., Hanan Munitz, M.B.

Summary:

Four patients, with acute neuroleptic induced akathisia (NIA) responded favorably to the serotonergic tricyclic clomipramine (CMI) 20-50 mg/d. The patients' NIA had previously failed to respond to adequate doses of either anticholinergics, propranolol or clonidine. In a second prospective open study examining CMI efficacy for NIA, that were resistant to trihexyphenidyl 10mg/d and propranolol 120-160 mg/d results seem confirmatory. Eight patients out of 10 demonstrated an improvement greater than 65 percent. In the entire CMI-treated group, NIA scores were abated significantly, ($P_s < 0.05$, all paired, post-hoc, Student's t tests, following significant one way ANOVA). Our conclusion from the above 2 observations is that CMI has an anti-NIA potential and probably offers a novel addition to the anti-NIA arsenal. The relatively low doses of CMI used against NIA as well as the immediate improvement (i.e. within 1-3 days) imply that the anti-NIA influence of CMI is mediated through a mechanism not identical to the antidepressant one. The failures of anticholinergics and 2 adrenergic agents to remedy NIA, together with the efficacy of a mainly serotonergic drug suggests involvement of 5-HT in the pathophysiology of NIA. Other indirect psychopharmacological evidence that support this intriguing hypothesis will be discussed, as well as the speculation that modulation of the neuroleptic-blocked DA mesocortical tract by 5-HT, is the mechanism by which CMI reduces NIA.

NR190 **Tuesday May 15, 12 noon - 2:00 p.m.**

INTERGENERATIONAL EFFECTS OF POSTPARTUM PSYCHOSIS

John J. Sigal, Ph.D., Psychiatry, Jewish General Hospital, 4333 Cote Ste Catherine Road, Montreal Quebec, Canada H3T 1E4; Jacqueline Royer, M.D.

Summary:

We predicted that ongoing concern on the part of parents and alternate caretakers that a mother, once she had had a postpartum psychosis, might fall ill again, would result in the offspring born at the time or after the psychosis being more psychologically vulnerable than those born before. Thuwe provided us with follow-up data over 45 or more years on the psychiatric contacts of 67 late-adolescent and adult children of 13 mothers who had postpartum illnesses around the turn of the century. We used two methods of data analysis that took family size into account. In the first, we used the paired comparison test to compare the *proportion of probands within each family* who were born before the mother's illness to those born at the time or after it. In the second, we determined the *number of families* in which the proportion of probands who later required psychiatric care that were born at the time of or after the mother's illness was greater than the proportion born before, and the number in which the reverse was true. The numbers were compared to what might be expected by chance alone. The prediction was confirmed in both tests ($p < .05$, and $p > .01$, respectively); probands born before the mother's first postpartum psychosis had fewer psychiatric contacts than those born at the time of or after it. Replication with larger samples is required.

NR191 **Tuesday May 15, 12 noon - 2:00 p.m.**

WITHDRAWN

NR192 **Tuesday May 15, 12 noon - 2:00 p.m.**

A PROSPECTIVE STUDY OF DEPRESSION IN NURSING HOMES

Barry W. Rovner, M.D., Psychiatry, Johns Hopkins University, J.H. Hosler 320 600 N Wolf St, Baltimore, MD 21205; Pearl German, Sc.D., Larry Brant, Ph.D.

Summary:

We determined the prevalence and incidence of depression in a prospective study of new admissions (N = 455) to nursing homes. Psychiatrists examined each case using the Modified Present State Exam, the Hamilton Depression Scale, and the Mini-Mental Exam, and made diagnoses according to *DSM-III-R* criteria. On admission, 57 patients (prevalence rate = 12.5 percent) had major depression and the majority (80 percent) were untreated.

Two months later, 36 new cases of depression developed (incidence rate = 11.5 percent). Incident depressed cases more likely had past psychiatric treatment and were younger than nondepressed cases (24.0 percent vs. 8.3 percent, X2 = 11.6, p less than .001) and (78.2 yrs vs. 81.3 yrs, t = -2.02, p less than .05), respectively. The onset of depression was associated with changes in cognition, behavior, and functional capacity.

We conclude that major depression is a prevalent condition in nursing homes, is frequently untreated, and is associated with functional decline. Past psychiatric treatment and younger age are risk factors which predict the onset of depression. These characteristics can be used to target patients for appropriate preventative interventions.

NR193 **Tuesday May 15, 12 noon - 2:00 p.m.**

CRITERION PREVALENCE OF ADHD IN A SUBURBAN TOWN

Kerim Munir, M.D., Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139; David Boulifard, B.A., Eva Deykin, D.P.H.

Summary:

Attention Deficit Hyperactivity Disorder (ADHD) represents one of the most common and serious neurobehavior disorders of childhood, affecting children from early childhood to adult life. The entity we today label ADHD has undergone multiple transformations. We are conducting an epidemiological study to determine the prevalence and risk factors for ADHD in an enumerated suburban Massachusetts town. The first stage of this population-based study consists of independent surveys of parents and teachers by means of a questionnaire designed to screen 5- to 15-year-olds for this disorder by the DSM-III and DSM-III-R versions. Our findings to date on those individuals screened by both parents and teachers suggest that the criterion prevalence is higher for the DSM-III-R ADHD than the DSM-III ADHD, and that teachers are more likely than parents to screen children positively (ADHD: Parent 3.1%, Teacher 5.5%; ADDH: Parent 2.8%, Teacher 3.9%; N = 688). Sample stratification by sex suggests that females account relatively more than males for the higher DSM-III-R criterion prevalences (Females: ADHD-parent 0.6% vs. ADDH-parent 0.3%, ADHD-teacher 1.3% vs. ADDH-teacher 0.7%; Males: ADHD-parent 2.5% vs. ADDH-parent 2.5%, ADHD-teacher 4.3% vs. ADDH-teacher 3.2%).

NR194 **Tuesday May 15, 12 noon - 2:00 p.m.**

CORRELATES OF CLINICALLY DIAGNOSES DEMENTIA

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Summary:

Paquid is an epidemiological study designed to gather and follow-up a cohort of 4,000 elder subjects (65 years and older) living at home. These subjects were randomly chosen in the general population of 75 communities of South-Western France. The major goal of Paquid is to study normal and pathological brain aging. We present the results of the data collected from 2792 subjects on the prevalence and the correlates of clinically diagnosed dementia. The DSM III criteria for dementia were met by 101 subjects (3.62%). These cases were reviewed by a neurologist to confirm the diagnosis and to determine the etiology of dementia using NINCDS-ADRDA criteria. 43 subjects were classified as probable Alzheimer's disease; 8 as possible Alzheimer's disease; 5 as vascular dementia; 5 as Parkinson's disease with dementia; 2 as alcoholic dementia; 2 as dementified psychosis; and 1 unclassified. Fifteen patients refused to see the neurologist, 18 were false positives, and 2 died before the visit of the neurologist. Using the NINCDS-ADRDA criteria, the prevalence of dementia decreased to 1.6%. The prevalence of dementia increased with age, but more interestingly, it decreased dramatically as educational level increased. For the verified cases, the prevalence is 5.4% for subjects with no education, 1.8% for subjects with grade school level, 0.6% for subjects with high school level and 0% for subjects with university degrees. The relationship between dementia and educational level is still controversial in the literature. However, the fact that our study was based on a large and randomly selected sample, and that all the demented cases were verified by a neurologist using NINCDS-ADRDA criteria, suggests that educational level is an important correlate of dementia for French elderly community residents.

NR195 **Tuesday May 15, 12 noon - 2:00 p.m.**

RATES OF PSYCHIATRIC DISORDERS IN THE MEDICALLY ILL

George Fulop, M.D., Psychiatry, Mount Sinai Hospital, 1 Gustave Levy Place Box 1228, New York, NY 10029; James J. Strain, M.D.

Summary:

Elderly medical inpatients have been shown to have increased rates of concurrent psychiatric disorders. The nature and prevalence of specific psychiatric disorders and medical surgical conditions need to identified in order to study potential mechanisms of interaction and to focus psychosocial interventions on those patients at risk for a psychiatric comorbidity (PC).

METHOD: The computerized medical abstracts of 27,213 geriatric (age>65) admissions to the medical/surgical wards of the Mount Sinai Hospital in NYC from 1985 through 1987 were reviewed for the prevalence rates of DSM-III psychiatric disorders in the top 25 Diagnosis-Related Groups using the Utilization Information System database.

RESULTS: The prevalence of psychiatric comorbidity ranged from a low of 2.8% (Lens Procedure) to a high of 28.5% (Respiratory Infections). Specific DSM-III categories and the associated medical conditions follow:

DSM-III Disorder	Prevalence of Disorder	Medical/Surgical Disorders
Adjustment	2.7%	Amputation, Renal Infection, Metabolic, Congestive Heart Failure
Affective	6.6%	Nerve Diseases, Back Problems, Hip Fractures, Joint Procedures
Anxiety	2.0%	Nerve Diseases, Chronic Lung, Arrythmia, Myocardial Infarct
Delirium	19.6%	Respiratory Infections, Metabolic, Amputation, Urinary Tract Infection
Dementia	3.8%	Nerve Diseases, Respiratory Infections, Septicemia, Metabolic
Psychotic	5.5%	Nerve Diseases, Cerebrovascular Accidents, Chronic Lung, Operative Procedures
Substance	2.5%	Congestive Heart Failure, Respiratory Infections, Arrhythmia, Myocardial Infarct

The varying rates of psychiatric disorders associated with medical conditions suggest different mechanisms of interaction. These targeted medical conditions with high comorbidity rates may be the focus of the psychosocial interventions aimed at improving health and potentially reducing hospital costs and stay.

NR196 **Tuesday May 15, 12 noon - 2:00 p.m.**

RISK FACTORS FOR THE SCHIZOPHRENIA SYNDROME

Allen Y. Tien, M.D., Mental Hygiene, Johns Hopkins, 624 N. Broadway, Baltimore, MD 21205; William W. Eaton, Ph.D.

Summary:

Clinicians have observed that schizophrenics often manifest a range of non-psychotic psychopathology before the first episode of schizophrenia. Schizophrenics in remission also experience non-psychotic symptomalogy before the beginning of a new episode. This paper presents the first prospective analysis of antecedent psychopathology in schizophrenia with data from a community sample - the NIMH Epidemiologic Catchment Area Program. Three non-overlapping conditions were defined using DSM-III definitions as implemented by the Diagnostic Interview Schedule (DIS): (1) DSM-III Schizophrenia Criterion A; (2) Criterion A and Affective Episode; and (3) full Schizophrenia. In the one year followup period, the cumulative incidence rate of Criterion A was 0.79 per 100, for Criterion A with Affective Episode it was 0.17 per 100, and for Schizophrenia the rate was 0.20 per 100. In multivariable logistic models, the patterns of risk relationships between sociodemographic factors and Schizophrenia resembled patterns in clinically based and registry based literature. Males had an earlier peak onset than females and marital status and employment were strongly related to risk for Schizophrenia. An interaction between gender and never marrying was observed, indicating that never married males were about 50 times increased risk for Schizophrenia, never married females were at about 14 times increased risk, and married females were at about 2.5 times increased risk, relative to married males. After adjustment for sociodemographic factors, DIS/DSM-III Obsessive Compulsive Disorder and Social Phobia were both associated with over 3.5 times increased risk for Schizophrenia. Several other specific psychopathology items, including panic attacks, were found to be associated with increased risk for Schizophrenia. There were both similarities and differences in risk factor structure between Schizophrenia and the other two identified categories of case.

NR197 **Tuesday May 15, 12 noon - 2:00 p.m.**

SCHIZOPHRENIA SPECTRUM: PERSONALITY AND COGNITION

Allen Y. Tien, M.D., Mental Hygiene, Johns Hopkins, 624 N. Broadway, Baltimore, MD 21205; Gunvant K. Thakar, M.D., Paul T. Costa, Jr, Ph.D., William W. Eaton, Ph.D.

Summary:

Many studies support relationships between schizophrenia and "spectrum" abnormalities. Study of schizophrenia spectrum may help define the processes leading to schizophrenia. In this pilot study, subjects expected to have a high probability of spectrum characteristics were identified from the Baltimore Epidemiologic Catchment Area Survey sample. Thirty eight were recruited and examined by clinicians to assess DSM-III-R Axis II Traits and Disorders. To assess personality quantitatively, we used the NEO-PI, which scores the domains of Neuroticism, Extroversion, Openness to Experience, Conscientiousness, and Agreeableness. The Wisconsin Card Sorting Test (WCST), Continuous Performance Test (CPT), and smooth pursuit eye movements were assessed. About 40% were found to have spectrum features. Perseverative Errors (PE) on the WCST had correlations of -0.40 and -0.45 with the Openness and Conscientiousness scales on the NEO-PI. The Conscientiousness scale had a -0.41 correlation with Errors of Omission (EO) on the CPT. There were correlations of 0.58 and 0.52 between PE and EO with poor smooth pursuit. Intriguing differences between Schizotypal and Schizoid subjects in terms of the NEO-PI scores were observed with logistic regression models. Whereas the Schizotypal subjects were low on the Fantasy facet of the Openness domain, the Schizoid subjects combined high scores on Ideas (Openness facet) with low scores in Actions (Openness facet) and Assertiveness (from the Extroversion domain). One implication of these results is that cognitive and perhaps neurophysiologic abilities may underlie personality characteristics.

NR198 **Tuesday May 15, 12 noon - 2:00 p.m.**

TARDIVE DYSKINESIA IN ASIANS: MULTINATIONAL STUDY

Edmond H. Pi, M.D., Psychiatry, Univ of South California, 1934 Hospital Place, Los Angeles,CA 90033; Gregory E. Gray, M.D., Dong G. Lee, M.D., Zhongfu Ji., M.D., Yongzhen Weng, M.D., Chang K. Kim, M.D., Yong S. Kim, M.D., Tie M. Leung, M.D., Akira Kishimoto, M.D., Chen-I Wu, M.D.

Summary:

Although ethnic differences in drug response and side effects are frequently claimed, there have been few epidemiological studies of the prevalence of tardive dyskinesia (TD) among different ethnic groups. In the present study, 982 hospitalized psychiatric inpatients from Beijing (N-232) and Yanji (N=291) China; Hong Kong (N=155); Seoul, Korea (N=165); and Tottori, Japan (N=139) were examined for abnormal movements using the Abnormal Involuntary Movement Scale. Each patient was evaluated by the senior investigator (EHP) plus psychiatrists at each hospital. Schooler and Kane's RDC for TD were used to establish the diagnosis. Other demographic and clinical data were obtained from the patients' charts. The overall prevalence of TD was 17.0% (11.2% mild, 4.8% moderate, and 1.0% severe). Because of significant confounding of effects, multiple logistic regression analysis was used to estimate the effects of a given risk factor while controlling for all other risk factors. Using this approach, the significant risk factors identified were age 50+ years (odds ration [OR]=2.8), current neuroleptic dose < 200 mg CPZ equivalent (OR=1.9), and site, with patients outside Beijing having a 1.9-2.9 x greater risk than those in Beijing. Explanations for, and clinical implications of, the inter-site differences and the inverse relationship with current dosage will be discussed.

NR199 **Tuesday May 15, 12 noon - 2:00 p.m.**

DOES ECT CHANGE SEROTONERGIC FUNCTION?

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Summary:

Electroconvulsive therapy (ECT) remains one of the most effective treatments for severe depression, despite continued uncertainty about its mechanism(s) of action. In addition to multiple effects on dopamine systems, preclinical studies of electroconvulsive shock have shown increases in serotonergic receptor ($5\text{-}HT_2$) number and responsivity. To test serotonergic responsiveness in humans undergoing ECT, intravenous clomipramine (CMI), a tricyclic antidepressant relatively selective for 5-HT reuptake inhibition, was used as a pharmacologic probe. Five inpatients with major depression underwent infusion of CMI 12.5 mg IV after a 4-wk medication washout and again at least 5 days following completion of a course of ECT. Neuroendocrine and cardiovascular measures and subjective ratings were assessed prior to, and for 4 hr after the CMI infusion. All patients responded clinically to ECT. However, the prolactin response to IV CMI, which was blunted in the patients at baseline, did not normalize following treatment. There was no change in the plasma cortisol, ACTH, growth hormone, and vasopressin responses to CMI after ECT. In contrast, CSF concentrations of the major 5-HT metabolite, 5-HIAA, were increased by 16% to 185% in 4 of these patients. Thus, if ECT is altering components of the 5-HT system in the CNS, this effect is not manifested by changed responses to the more "physiologic" IV CMI probe.

NR200 **Tuesday May 15, 12 noon - 2:00 p.m.**

AXIS II PERSONALITY FEATURES IN THE FIRST DEGREE RELATIVE OF PROBANDS WITH SCHIZOPHRENIC DISORDER, AFFECTIVE DISORDER AND NO DISORDER (NORMAL CONTROLS)

Elizabeth Squires-Wheeler, Ph.D., Medical Genetics, NYS Psych. Inst., 722 West 168th Street, New York, NY 10032; L. Erlenmeyer-Kimling, Ph.D.

Summary:

Schizophrenic spectrum disorder has been defined historically as 1) any psychiatric disorder appearing in the biological relatives of schizophrenic probands at rates exceeding population base rates, 2) attenuated, schizophrenic-like signs and symptoms, and 3) the joint occurrence of 1 and 2 above. Investigators (Gottesman, 1975; Kendler, 1985) have advanced validity criteria for schizophrenic spectrum candidates identified by means of familial aggregation: proposed candidates should exhibit "maximal sensitivity and specificity in identifying relatives of schizophrenic patients."

In recently presented reports features and disorder from the DSM-III-R, Axis II, odd eccentric cluster (schizotypal, schizoid and paranoid disorder) have been examined using the validity criteria and have received inconsistent support. Other Axis II features and disorder (e.g., obsessive-compulsive disorder) have recently been proposed (Lewis et al., 1989).

To apply the validity criteria systematically to the range of spectrum candidates suggested to date, while imposing significance levels appropriate for the number of contrasts examined, we have taken the following approach. The rates of DSM-III-R, Axis II features and disorders were assessed in three offspring groups (ages 18 to 29) defined by parental diagnoses, including schizophrenic disorder (n = 90), affective disorder (n = 70), and no parental disorder (n = 161). The assessment was conducted by trained social workers and psychologists by means of a direct interview (Personality Disorder Examination). The interviewers were blind to the parental psychiatric status and to previous psychiatric assessments in the offspring.

The rates of Axis II Disorder (using DSM-III-R thresholds) are low across all groups. The mean raw dimensional scores for each Axis II Disorder and the associated correlation matrices are presented by group. A clinical profile encompassing comorbidity patterns provides a preliminary approach for achieving desired specificity.

NR201 **Tuesday May 15, 12 noon - 2:00 p.m.**

SIXTY PERCENT CONCORDANCE FOR ALZHEIMER'S DISEASE IN MONOZYGOTIC TWIN PAIRS

Kathleen Welsch, Ph.D., Psychiatry, Duke University, Box 3925 DUMC, Durham, NC 27710; John C.S. Breitner, M.D., Kathryn M. Magruder-Habib, Ph.D., Cynthia M. Churchill, M.D., C. Dennis Robinette, Ph.D., Marhsal F. Folstein, M.D.

Summary:

The N.A.S. registry of aging twin veterans contains 10,000 pairs born in 1917-1927. The 442 pairs (884 subjects) residing in the Carolinas, Virginia, DC or Maryland were studied for Alzheimer's disease (AD) using a brief telephone interview for cognitive symptoms, telephone history interviews with spouses or other informants, and in-person examination of screen-positive subjects. One of 10 screen-positive probands had cerebrovascular disease with depression. One monozygotic (MZ) pair of screen-positive subjects was concordant for Probable AD (NINCDS criteria). Remaining probands had Possible AD or "mild/ambiguous" cognitive disorder suggesting early AD. Their screen-negative co-twins were examined in person: 2 of 4 MZ co-twins showed symptoms suggesting early AD, but none of 3 DZ co-twins showed any abnormality. The results of this work suggest: 1) that systematic ascertainment of AD in the N.A.S. registry by the above methods is feasible; 2) that the prevalence of progressive cognitive disorder in the registry is about 2%; 3) that concordance for presumptive AD in MZ pairs (60% now, possibly more if other co-twins have later onsets) exceeds prior estimates; but 4) that such rates of concordance may become apparent only upon detailed evaluation of apparently normal co-twins as well as their impaired brothers.

NR202 **Tuesday May 15, 12 noon - 2:00 p.m.**

TIMING PRENATAL INSULT IN SCHIZOPHRENIA: TWIN STUDY

H. Stefan Bracha, M.D., Neuropsychiatry, Associate Professor, VAMC 116A1/NLR Psych Service, North Little Rock, AR 72114; Stephen R. Paige, Ph.D., E. Fuller Torrey, M.D.

Summary:

Fingertip ectodermal ridges are formed during the first half of the second prenatal trimester and are sensitive markers of an insult during that period. Prenatal rubella and CMV infections are well known examples; cleft palate and some cases of mental retardation are conditions with ridge count abnormalities in which early second trimester insult probably increases the penetrance of polygenic vulnerability. Studies suggest that in an adult low ridge count may indicate that the subject had been small for gestational age during the first half of the second trimester. A very high adult ridge count may indicate that the subject had been edematous during that prenatal period (implying infection.) We have examined ridge counts (using Slater's method) in 21 MZ twins, one of whom had schizophrenia adult onset (DSM III-R per SCID I and II). Minimum discordance was four years. Zygosity was determined by blood and HLA typing. *Results:* No significant differences were found: mean absolute finger ridge count was 168 $\pm$ 80 for the 21 unaffected co-twins and 173 $\pm$ 89 for their 21 monozygotic twins with schizophrenia; also, no difference or ridge asymmetries were found compared to control twin pairs. *Discussion:* Previous studies reported both increased and decreased ridge count in schizophrenia. Most of those studies, however, have methodological problems. Recent carefully conducted epidemiological studies strongly suggest that some patients with schizophrenia have been exposed to a second trimester insult. Earlier and later developmental markers are being studied in our laboratory in an attempt to continue "walking along" the prenatal period. The present negative study however, if further supported, may be the first indication that, unlike mental retardation, second trimester prenatal insults in adult onset schizophrenia are localized to not earlier than the *second half of the second trimester.* Supp. by MH43537, MH41176, and VA Merit Rev.

NR203 **Tuesday May 15, 12 noon - 2:00 p.m.**

PLATELET 5HT UPTAKE IN SONS OF ALCOHOLIC FATHERS

Jeffrey L. Rausch, M.D., Psychiatry, Univ of California, M-003, La Jolla, CA 92093; Maristela Monteiro, M.D., Marc A. Schuckit, M.D.

Summary:

Platelet serotonin uptake kinetics were examined in a carefully screened group of 28 male subjects, half of whom had an alcoholic father. Paired subjects were matched for a variety of characteristics including age, race, sex, substance use history, height/weight ratio, season, and time of day for platelet serotonin uptake. The family history positive group had a significantly ($p < 0.02$) higher mean Vmax for platelet serotonin uptake (64.1 $\pm$ 19. s.d.) compared to the control group without family histories of first degree relatives with alcoholism (53.8 $\pm$ 19). No significant differences in the affinity constant (Km) or in the Hill constant were found between groups. The results are consistent with the possibility that a higher Vmax of platelet serotonin uptake indicates a biological factor associated with alcoholism risk.

NR204 **Tuesday May 15, 12 noon - 2:00 p.m.**

GENETICS OF PSYCHOSES IN LARGE PEDIGREES OF QUEBEC

Michel Maziade, M.D., Univ Laval Robert-Giffard, Centre De Recherche, 2601 de la Canardiere, Beauport, Quebec, Canada G1J 2G3; Vincent Raymond, M.D., Marc De Braekeleer, M.D., Maria Martinez, Ph.D., Chantal Caron, M.D., Chantal Merette, Ph.D.

Summary:

Family, twin, and adoption studies indicate that the etiology of schizophrenia and bipolar disorders probably results from the interaction between environmental and genetic factors. Our group has undertaken a program to recruit large multi-generation and mid-size families densely affected by schizophrenia *or* bipolar affective disorders (BPAD). Eastern Quebec is exceptionally well suited for genetic studies: 1) large sibships (prevalent in older living generations), 2) genetic homogeneity, 3) demographic stability mainly due to language barrier, 4) tracking down progenitors through easy access to intact church baptism and marriage registers going back to the 17th century, 5) universal care system. With the collaboration of the psychiatrists of all 12 regional hospitals, after only eight months of screening, we have identified five large extended pedigrees (two of schizophrenia), each consisting of at least 350 living persons over three generations with at least 12-15 percent definitely affected members. Furthermore, 30 multiplex families ((BPAD or schizophrenia) with sibship sizes 7 to 16, (with two to five definitely affected sibs), have also been identified and not yet extended. These figures exceed those from similar screenings done in the U.S. (Pulver et al, 1989). Standardized clinical assessments, banking of cell lines, and genotype mapping are underway in the most informative branches and families.

NR205 **Tuesday May 15, 12 noon - 2:00 p.m.**

USE OF (AC)N REPEAT POLYMORPHISMS IN SCHIZOPHRENIA

Michael H. Polymeropoulos, M.D., LBG, NIMH, 2700 Martin L. King Ave SE, Washington, DC 20032; Hong Xiao, M.D., Lynn Delisi, M.D., L. James Weber, Ph.D., R. Carl Merril, M.D.

Summary:

The search for a genetic factor in schizophrenia has been hampered by the absence of any specific biological markers. Genetic linkage studies so far, have been limited to the study of candidate genes or candidate chromosomal loci, mainly because of the inability to screen the whole genome in a cost effective manner. A recently discovered class of DNA polymorphisms offers the potential for whole genome screening. These polymorphisms are based on tandem dinucleotide repeats of the (dCA)n.(dGT) type. Such polymorphisms may be studied using the Polymerase chain reaction to amplify short 100-200 b.p. DNA fragments containing the repeated sequences, followed by analysis of 6 percent PAGE sequencing gels. Alleles generally differ in size in multiples of two bases. These (CA)n repeat polymorphisms are highly informative with average PIC values of 0.60. It is estimated that between 7,000 to 12,000 informative markers of this type may be available. They appear to be distributed throughout the genome. Our study of a small three generation family with schizophrenia with 30 such markers has confirmed the efficiency of this approach and the high degree of informativeness of these markers.

NR206 **Tuesday May 15, 12 noon - 2:00 p.m.**

MAPPING GENES FOR MANIC DEPRESSION AND SCHIZOPHRENIA

William F. Byerley, MD., Psychiatry, Univ of School of Med., 50 North Medical Dr. RM 5R278, Salt Lake City, UT 84132; Mark Leppert, Ph.D., John Holik, B.A., Angela M. Lubbers, B.A., Steve Jensen, B.A., Ray White, Ph.D.

Summary:

There are data suggesting that a mutant gene localized to the Xq28 genomic area confers susceptibility to manic-depression in some families and that a gene predisposing to schizophrenia maps to 5q11-13. It is clear, however, that these putative genes are not etiologically involved in the pathogenesis of manic-depression and schizophrenia in other families. In order to map additional genes that cause these illnesses, we have initiated a systematic genomic mapping study using over 250 DNA markers. Seven multigenerational manic-depressive kindreds as well as eight schizophrenic families are being investigated. We will report our latest linkage data.

NR207 **Tuesday May 15, 12 noon - 2:00 p.m.**

FAMILIAL PEDIGREES OF PARAPHILIA

Alain Labelle, M.D., Psychiatry, Royal Ottawa Hospital, 1145 Carling Avenue, Ottawa Ontario, Canada, K1Z-7K4; Dominique Bourget, M.D., Pierre Tessier, M.D., Martin Alda, M.D., J.M.W. Bradford, M.B.

Summary:

Paraphilia or sexual deviation never established itself as a classical major mental illness such as schizophrenia or affective disorder and has often been considered to be an antisocial behaviour. Environmental influences have long been recognized. It was speculated that sexual behaviour in man was modulated by a learning and modelling process resulting from social and familial influences. However recent studies with sophisticated assessment techniques also tend to support the presence of biological factors underlying the development of paraphilia. Biological correlates such as testosterone levels definitely play a role in the production of aberrant sexual behaviour. The observation that paraphiliac behaviour seem to run over a number of generations in certain families has led us to question a genetic model of transmission. In order to study this hypothesis, it was first necessary to objectively establish the presence of a familial paraphiliac pattern. We have identified and studied a number of families with a high incidence of paraphilia among the members and proceeded to the construction of genograms on the basis of a standardized family history. Preliminary results indicate the heterogeneity of sexual deviation and further suggest that certain sexual behaviours may be genetically linked.

NR208 **Tuesday May 15, 12 noon - 2:00 p.m.**

PRELIMINARY ANALYSIS OF A LARGE STUTTERING PEDIGREE

Charles D. Mellon, M.D., Howard Hughes Med. Inst., 603 Wintrobe Building, Salt Lake City, UT 84132; Sandra Hasstedt, Ph.D., Marvin Hanson, Ph.D., Wendal Walton, Ph.D., Mark Leppert, Ph.D., Ray White, Ph.D.

Summary:

Segregation analysis and twin studies indicate a strong genetic basis for the phenotype of stuttering (Cox, 1988). We have located, in Utah, a six-generation pedigree with approximately 1,000 individuals all descended from a single male progenitor who was a stutterer. Preliminary analysis of the pedigree reveals that the second generation is composed of eight branches. Two of these branches, containing approximately 400 individuals, exhibit no stuttering, four branches exhibit low frequency stuttering, and one branch exhibits a high density of stuttering (a greater than 20-fold risk for stuttering over the general population). Likelihood analysis (Elston and Stewart, 1971) on this high density branch using prevalence rates of 1.5 percent for males and .5 for females favors a major locus model over a polygenic model.

Major Locus	$X^2=26.67$	$p<0.005$
Polygenic	$X^2=6.98$	$p<0.01$

We believe that this pedigree provides a unique resource to study the genetics of stuttering by use of the linkage paradigm. Stuttering may be an ideal phenotype for linkage studies in psychiatric disorders because of: (1) early age of onset, (2) uncomplicated phenotype, (3) little evidence for assortive mating, (4) better family cooperation with research, and (5) no medication effects.

NR209 **Tuesday May 15, 12 noon - 2:00 p.m.**

ALZHEIMER'S IN HISPANICS AND THEIR FAMILIES

Jacobo Mintzer, M.D., Psychiatry, University of Miami, 1611 NW 12th Avenue D-29, Miami, FL 33136; Margarita Lermo, M.D.

Summary:

Few cultural data are available on family caregiving for older relatives with or without dementia.

This report presents data collected by the Alzheimer's Disease Project Registry on 78 White Hispanic American (HA) and 257 White Non Hispanic (WNH) caregivers of demented patients of similar socioeconomic characteristics living in the Miami area.

Preliminary analysis of the data suggest that HA caregivers appear to be at higher risk for mental health problems, that family members wait longer to bring relatives for diagnostic workups, that family members know little about and use services less frequently than WNH and that caregiving responsibilities tend to be shared to a greater extent by family members other than the spouse in the HA families. It is likely that multiple cultural factors specific to the Hispanic American culture play an important role in the way dementia affects the behavior and mental health of family members.

The presentation will include a discussion on the clinical implications of these findings in the care of American Hispanic demented patients and their families.

NR210 **Tuesday May 15, 12 noon - 2:00 p.m.**

LITHIUM INDUCED POLYURIA AMELIORATED BY POTASSIUM

Mahmoud N. Musa, M.D., Psychiatry, Chicago Medical School, 3333 Green Bay Road, North Chicago, IL 60064; Bhaskara Tripuraneni, M.D., Hal Skopicki, Ph.D., Demitrios Zikos, M.D., Ramaswamy Lakshaman, M.D., John Caliendo, M.D.

Summary

Polyuria is a common side effect of lithium. Experiments with rats show that potassium supplementation ameliorates lithium induced polyuria without any effect on lithium levels or extracellular volume. However, no studies in humans have been reported. In this pilot study, we report the results of potassium supplementation on the first four patients with significant lithium induced polyuria. The patients received 20 milliequivalents of potassium per day for seven days. The mean (S.D.) of their 24 hour urine volume decreased from 3856 (926) ml to 2618 (994) ml, ($p=0.0064$). Their urine osmolality increased from 239 (89) to 361 (127), ($P=0.0368$). Discontinuation of potassium resulted in recurrence of polyuria. Potassium may be a safer and more easily available treatment of lithium induced polyuria than currently utilized diuretics such as the thiazides and amiloride.

NR211 **Tuesday May 15, 12 noon - 2:00 p.m.**

UTAH TOURETTE FAMILY STUDY

William M. McMahon, M.D., Medical Dept., Univ of Utah, 50 North Medical Drive, Salt Lake City, UT 84132; Mark Leppert, Ph.D., Francis Filloux, M.D., Ben J.M. Van De Wetering, M.D.

Summary:

This report presents the most recent results in the Utah Tourette's Syndrome family study. We detailed one very large kindred spanning four generations affected with Tourette's Syndrome. This pedigree offers a unique opportunity for study of the phenotypic spectrum of this protean condition, as well as for linkage analysis. We have identified 31 members with full Tourette Syndrome (category A-1 according to the Tourette unified rating system). This represents 23 percent of the 130 subjects interviewed undergoing structured interview to this time. In addition, chronic multiple tic disorder, obsessive compulsive disorder and attention deficit disorder are manifest in this kindred. These may represent varying phenotypic expressions of the putative Tourette gene in this family. Issues raised by this unique kindred relative to linkage will be discussed.

NR212 **Tuesday May 15, 12 noon - 2:00 p.m.**

VENTRICULOMEGALY IN SPORADIC SCHIZOPHRENIA

Steven B. Schwarzkopf, M.D., Department of Psychiatry, Ohio State University, 473 W. 12th Ave. 071 Upham Hal, Columbus, OH 43201; Bernhard Bogerts, M.D., Stephen C. Olson, M.D., Jeffrey A. Coffman, M.D., Henry A. Nasrallah, M.D.

Summary:

Intro: Cerebral abnormalities including ventricular enlargement and cortical atrophy have been identified in some schizophrenic patients. Some studies have suggested a positive relationship between cortical atrophy and genetic loading. Others suggest that ventricular enlargement is associated with perinatal complication or a lack of family history of psychosis. In this study, we evaluated cerebral abnormalities in patients with vs without a family history of psychosis.

Methods: 72 schizophrenic and schizoaffective patients were tested (DSM III-R), 53 schizophrenic, 19 schizoaffective). Family history was obtained by parental interview (FH RDC) and patients classified as FH positive (1st or 2nd degree relative with psychosis) or FH negative. T1 weighted MRI scans were obtained and rated for cortical atrophy, lateral ventricular enlargement, 3rd ventricular enlargement, and temporal lobe dysplasia (3 point scale).

Findings: No differences were found between the groups (family history positive/negative) on cortical atrophy 3rd ventricle enlargement, or temporal lobe abnormality. The family history negative group had a greater proportion with lateral ventricular enlargement than the family history positive group (47% vs 13%; P .006 chi square). Findings were significant in both the entire group and the schizophrenics analyzed alone. Family history negative patients were not older or more chronic than family history positive patients. These results support previous reports of ventricular enlargement predominantly in family history negative patients but fails to show increased cortical atrophy in family history positive patients.

NR213 **Tuesday May 15, 12 noon - 2:00 p.m.**

LOW FAMILY HISTORY IN SCHIZOPHRENIA WINTER BIRTHS

Steven B. Schwarzkopf, M.D., Psychiatry, Ohio State University, 473 West 12th Avenue, Columbus, OH 43210; Henry A. Nasrallah, M.D., Stephen C. Olson, M.D., Jeffrey A. Coffman, M.D.

Summary:

Several studies have shown excess "winter births" in schizophrenic patients. We report here an inverse relationship between family history of major psychiatric disorder and winter birth.

55 subjects with schizophrenia (SCID-R interview, 41 males, 14 females) were classified as familial (PH POS) or sporadic (FH NEG) using the criterion of criteria 1st degree relative with psychosis (FH RDC). Season of birth was designed as WINTER (Jan-Mar), SUMMER (Aug-Oct), or OTHER (other months), as per earlier studies Fisher's Exact and Chi Square tests were used to assess the relationship between winter birth and family history.

Using WINTER and SUMMER born subjects and the FH criteria, the number of FH NEG patients born in winter was 50% (9 of 18). Significantly fewer familial patients (1 of 12, 8.3%) were born in winter (P=.011), Fisher's Test, one tail). Chi Square analysis including the OTHER months patients showed the FH NEG group distributed as predicted by chance, whereas FH POS patients showed increasing frequency from winter to summer (P=.021, Chi Square).

The results are consistent with an inverse relationship between genetic loading and winter birth in schizophrenia. These findings suggest, as other authors have speculated, that in samples of schizophrenic patients not selected for high genetic risk, an inverse relationship between environmental insults and genetic predisposition exists. Family history, season of birth, and cerebral insult data may help define more homogenous subgroups in schizophrenia research.

NR214 **Tuesday May 15, 12 noon - 2:00 p.m.**

METHODOLOGICAL BIAS IN THE ASSESSMENT OF NEGATIVE SYMPTOMS OF SCHIZOPHRENIA

David H. Strauss, M.D., New York State Psychiatric, 722 W. 168th St., New York, NY 10032; Xavier F. Amador, Ph.D.

Summary:

In a pilot project aimed at the identification of valid clinical indicators of core "deficit" symptomatology in schizophrenia, the authors identified several biases inherent in widely used standard negative symptom rating scales which artificially inflated negative symptom scores. The tendency to over-rate stemmed in part from the "observation-only" or "behavioral" orientation of these scales. A second group of biases derived from clinical issues in schizophrenia: the relative difficulty in eliciting certain positive symptoms and the psychological preference of patients to reveal negative symptoms rather than the more stigmatizing positive symptoms of psychosis. The authors present case studies and data illustrating these biases in SANS and PANSS data and suggest methods for more accurate assessment of deficit symptomatology in schizophrenia.

NR215 **Tuesday May 15, 12 noon - 2:00 p.m.**

THE LONGITUDINAL COURSE OF SCHIZOPHRENIC SYMPTOMS

Jean M. Addington, Ph.D., Psychiatry, Univ of Calgary, Holy Cross 2210 2nd St. S.W., Calgary Alta, Canada, T2S 1S6; Donald E. Addington, M.D.

Summary:

Recent approaches to subtyping schizophrenia have made use of the concepts of positive and negative symptoms. It is sometimes assumed that positive and negative symptoms are distributed discontinuously or inversely. Many of the studies that have examined this concept are cross-sectional. This research examines the relationships among positive and negative symptoms in a sample of 50 DSM III diagnosed schizophrenics. Using the SANS and the SAPS, symptoms are assessed, first, in the acute phase of the illness and then 6 months later in a period of relative remission. Results showed that positive and negative symptoms were neither distributed discontinuously nor inversely at both phases of the illness. Secondly, in comparison to positive symptoms, negative symptoms were highly intercorrelated at both times. Thirdly, the presence of negative symptoms in the acute phase was highly predictive of the presence of negative symptoms at follow-up. Implications for the longitudinal course of symptoms in schizophrenia are discussed.

NR216 **Tuesday May 15, 12 noon - 2:00 p.m.**

COGNITIVE FUNCTIONING AND SCHIZOPHRENIC SYMPTOMS

Jean M. Addington, Ph.D., Psychiatry, Univ of Calgary, Holy Cross 2210 2nd St. S.W., Calgary Alta, Canada, T2S 1S6; Donald E. Addington, M.D.

Summary:

The present study examined a variety of cognitive functions in schizophrenics in order to explore the relationship between symptoms and cognitive performance. The Wechsler Adult Intelligence Scale and a battery of neuropsychological tests, developed at the Montreal Neurological Institute, were administered to fifty acutely ill, hospitalized schizophrenics. Patients were diagnosed using DSM III criteria for schizophrenia. Negative symptoms were assessed with the SANS and positive symptoms with the SAPS. Both the cognitive tests and the symptom rating scales were administered to this sample(n=39) at a six month follow-up period. Multiple regression analyses revealed that, at hospitalization, high negative symptom ratings but not positive symptoms were significantly associated with impaired intellectual functioning. Performance on the neuropsychological tests was deficient but was unrelated to either positive or negative symptoms.

At the 6 month follow-up, all symptoms had significantly improved. Intellectual functioning as measured by the WAIS had significantly improved but performance on the neuropsychological tests, particularly those which measure frontal lobe functioning did not significantly improve. Multiple regression analyses showed a significant association between poor intellectual functioning and the presence of a combination of positive and negative symptoms. An examination of the change in symptoms relative to the change in cognitive functioning revealed that improved cognitive functioning was related to an improvement in positive but not negative symptoms.

NR217 **Tuesday May 15, 12 noon - 2:00 p.m.**

LENGTH OF STAY AND RECIDIVISM IN SCHIZOPHRENIA

Lawrence Appleby, Ph.D., Mental Health, IL. State Psych, Inst., 1601 West Taylor, Chicago, IL 60612; Desai N. Prakash, M.D., Daniel J. Luchins, M.D., Robert D. Gibbions, Ph.D., Donald K. Hedeker, Ph.D., Russel A. Puetz, M.A.

Summary:

We undertook a retrospective study to determine whether length of hospital stay (LOS) effects the rate and rapidity of relapse in schizophrenic patients. Fifteen hundred cases were randomly selected from 10 state hospitals in Illinois and followed for 18 months after initial discharge in FY'85. Length of stay significantly influenced time to relapse after partialling out the effects of number of prior admissions and age ($p < .01$ at 30 days and $p < .03$ at 18 months). Facility location was not predictive but comparisons revealed that at urban hospitals patients were predominantly nonwhite, had shorter median stays, and yielded more total relapses; they also had more prior admission. Intrahospital effects were tested by examining the largest urban facility. After controlling for prior admission and age, LOS significantly predicted relapse again at 30 days ($p < .03$) and 18 months ($p < .05$). These results indicate that length of hospital stay is directly related to time-in-community before relapse: most critically, schizophrenic patients hospitalized for short stays are more likely to relapse within 30 days after discharge. Our findings challenge the present policy of short-term hospitalization, which may be appropriate for selected psychiatric populations but not for many seriously mentally ill individuals.

NR218 **Tuesday May 15, 12 noon - 2:00 p.m.**

NEGATIVE SCHIZOPHRENIC SYMPTOMS AND EEG ALPHA

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

Summary:

Although the literature is rich in descriptions of EEG findings in schizophrenia patients, there is less consistency than is generally acknowledged. In particular, both increased and decreased quantities and/or reactivity of alpha band activity have been reported. There is reason to suspect that such variables as recording conditions, chronicity, and treatment responsiveness may affect levels of alpha activity in schizophrenics. In addition, some authors have described a relationship between clinical ratings and alpha lateralization. We explored the relationship between clinical ratings performed at the time of EEG recording to alpha power and coherence in 14 medication free DSM-III schizophrenic inpatients.

Nine channels of unipolar EEG with eye movements monitored by EOG had been recorded during a resting with eyes open condition. The data were filtered at .5 and 35 Hz, digitized at 64 Hz, and edited off-line for artifact. FFT was performed on average reference and source derivation transformations of the remaining EEG in order to obtain spectral power and coherence, respectively. Patients were rated with the Brief Psychiatric Rating Scale (BPRS), from which subscales corresponding to negative symptoms, positive symptoms, paranoia, and anxiety/depression were derived. The subscales were entered into multiple regressions with repeated measures for (1) log alpha power in four bilateral leadpairs, and (2) alpha coherence between 12 within- and 16 between-hemisphere electrode pairs.

Negative symptoms varied inversely with alpha power ($p < .02$) and both within- ($p < .03$) and between-hemisphere coherence ($p < .05$). The possible implications of reduced alpha activity associated with negative symptoms are discussed.

NR219 **Tuesday May 15, 12 noon - 2:00 p.m.**

SOURCE DEVIATION EEG COHERENCE AND SCHIZOPHRENIA

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

Summary:

EEG coherence, the covariation by frequency between two recording channels, may reflect underlying patterns of brain activity. Using arrays of bipolar electrodes, we recently reported increased within-hemisphere theta coherence in medication-free schizophrenics. However, interpretation of bipolar coherences is not straightforward. We computed source derivation values from previously recorded EEG in order to obtain coherences between discrete electrode sites without the confounding influence of the common reference electrode.

14 medication-free schizophrenics, 9 affective controls, and 13 normal volunteers were studied during resting and task conditions. Eleven schizophrenics were restudied after neuroleptic treatment. Unipolar EEG was recorded from 9 electrodes with eye movements monitored by EOG. Signals were filtered at .5 and 35 Hz., digitized at 64 Hz., and stored on disk. Artifact-edited EEG was transformed to source derivation and analyzed by FFT. Group and medication effects on coherence between 12 within- and 16-between hemisphere electrode pairs in five standard frequency bands were tested with repeated measures ANOVAs.

Results differed considerably from those obtained previously. Within-hemisphere delta coherence was higher in affective patients ($p = .044$) as were specific within-hemisphere alpha coherences ($p = .037$). Both patient groups were higher than normals in specific between-hemisphere beta2 values ($p = .02$). Neuroleptic treatment increased overall between hemisphere theta ($p = .004$), alpha ($p = .016$), and beta1 ($p = .029$) coherence, and was associated with localized increases in within-hemisphere theta coherence ($p = .048$).

These findings suggest that the methodology used to measure coherence can drastically affect the conclusions reached about brain activity in psychiatric disorders.

NR220 **Tuesday May 15, 12 noon - 2:00 p.m.**

SACCADES IN SCHIZOPHRENIA: MORE THAN A MARKER

Frederic Flach, M.D., Psychiatry, NY Medical College, 420 E. 51st Street, New York 10022; Melvin Kaplan, O.D., Herbert Benglesdorf, M.D., Barbara Orlowski, Ph.D, Dennis Carmody, Ph.D.

Summary:

In a controlled study carried out on the inpatient service of the Psychiatric Institute, New York Medical College, Valhalla, NY, 57 inpatients with schizophrenia and affective disorders were compared with 60 control subjects, using various assessments of visuo-spatial management. A highly significant, profound dysfunction in visuo-spatial management was demonstrated in the patient group. Marked compression of perceived space, a serious reduction in focal-ambient accommodative function, and extensive loss of depth perception, binocularity, and the ability to fuse in response to motion were noted. Moreover, visuo-spatial dysfunction in schizophrenics could be differentiated from that in affective disorders. Analysis of variance significance: $p < .05 - < .001$.

These findings have theoretical and clinical importance. They position the established observations of abnormal saccades in such patients within the framework of an overall disturbance in mechanisms involved in spatial management. Whether the visuo-spatial management disturbance that has been identified is etiologic or results from the psychiatric disorder remains to be determined, but there is little question that it contributes importantly to functional, occupational, and social impairment. This study has implications for early diagnosis of schizophrenic and affective disorders. Moreover, since visuo-spatial performance can be improved with specialized treatment, there are important implications for prevention and rehabilitation.

NR221 **Tuesday May 15, 12 noon - 2:00 p.m.**

NOVEL QUANTITATIVE PSYCHOTHERAPY OUTCOME MEASURES

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Summary:

In the course of demonstrating a relationship between the helpfulness of therapist interventions in addressing the core theme" (HTI), and patient's insight, the author has come upon a novel type of process-derived psychotherapy outcome measures. As a final step in the study of a newly developed process measure, CCRT-W ("Work on CCRT," based on Luborksy's Core Conflictual Relationship Theme,) two independent judges rated HTI for each of 14 sessions of a time-limited psychodynamic therapy. HTI was highly reliably ratable (coef.alpha=.88) and was found to oscillate as widely as the patient's variables (e.g., Insight). The hypothesis that HTI would covary with the patient's variables (which were determined in the earlier research phase) for the entire therapy was disproved. However, when therapy was divided into the part before transference dominated) and the part after transference interpretations were elicited by the patient's negative reaction to the termination in sessions 8-9, there appeared significantly positive correlations between the HTI and Insight and Understanding (.78* and .77*, $p<.05$) for sessions 1-7. Although there were no significant correlations for sessions 8-14, this lack of covariance was found to be caused by two systematic "deviations" of the actual values of the patient's Insight in sessions 8-14 from the values predicted for it from HTI in sessions 8-14, according to the linear relationship between Insight and HTI in the sessions 1-7. The amount and duration of these deviations could be specifically determined, and they are individualized and quantitative outcome measures for this treatment. Generally, whenever there is a significant relationship between therapist and patient variables for a part of therapy, systematic deviations from that relationship and patient variables for a part of therapy, systematic deviations from that relationship in later phases can be used as outcome measures.

NR222 **Tuesday May 15, 12 noon - 2:00 p.m.**

CHOLECYSTOKININ, DOPAMINE AND SCHIZOPHRENIA

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Summary:

Hokfelt first described the neuropeptide cholecystokinin (CCK) as co-localizing with dopamine (DA) within some mesolimbic dopamine cells. Subsequent investigations have shown that CCK appears to have effects on both presynaptic mesolimbic cell activity and upon postsynaptic responses to its co-transmitter, DA.

We report CSF levels of immunoreactive CCK and of the dopamine metabolite homovanillic acid (HVA) in 11 drug-free *DSM-III* schizophrenics, age 27.2 + 8.3(SD) years, whose first episode of psychosis had occurred 5.2 + 3.4 years previously. Such CCK and HVA levels were compared with those of controls, age 27.7 + 10.0 years, studied under virtually identical conditions. Both groups were hospitalized, and had been drug free for at least 12 days prior to collection of an 8:00 a.m. blood sample for plasma HVA and a lumbar tap (following 10 hours NPO). CSF was placed into an ethanol-dry ice bath at bedside, and stored at or below-70°C until assayed. CCK was assayed by the double antibody method of Beinfeld; HVA in plasma and CSF was assayed by the HPLC method of Yao.

Mean drug-free CSF CCK was 15.5 + 4.5 pmol/ml (range 6.9-23.4) in the schizophrenics and 27.4 + 5.1 pmol/ml (range 19.8-33.0) in controls (Mann-Whitney, $z = 3.02$; $p<0.002$). Though there was no difference in CSF CCK in male and female controls (29.4 vs 27.0 p mol/ml, respectively), schizophrenic males had lower CSF CCK than schizophrenic females (12.7 + 3.4 vs 18.9 + 3.1, respectively) (Mann-Whitney, $Z = 2.37$; p0.01). Age and duration of illness were both poorly correlated with CSF CCK levels ($r_s=0.02$ and $r_s=0.35$). Drug-free CSF CCK correlated poorly with CSF HVA in both controls and in schizophrenics ($r_s=0.37$ and $r_s=-0.03$, respectively), and poorly with plasma HVA in controls ($r_s=-0.40$) and in schizophrenics ($r_s=-.011$). Using the SADS Summary Scores for the week prior to lumbar tap, schizophrenics with lower CSF CCK values (>2.2SD below the mean of controls) evidenced poorer social functioning ($p<0.04$), higher evidence of suicidal behavior ($p<0.001$) and less manic syndrome than schizophrenics with higher CSF CCK ($p<0.04$).

The rapidity of antipsychotic response to drug appeared to be ***inversely*** related to drug-free baseline CSF CCK levels. As contrasted to control CSF CCK values, schizophrenic patient groups with lower CSF CCK respond progressively ***less*** readily to drug ($r_s=-0.85$; $p<0.001$).

NR223 **Tuesday May 15, 12 noon - 2:00 p.m.**

MRI CORRELATES OF NEGATIVE SYMPTOMS IN SCHIZOPHRENIA

Peter C. Williamson, M.D., London Psych Hospital, 850 Highbury Avenue, London Ontario, Canada N6A 4H1; David Pelz, M.D., Harold Merskey, D.M., Sandra L. Morrison, M.A., Patrick Conlon, M.D.

Summary:

A number of authors have suggested that negative symptoms in schizophrenia might be related to frontal lobe pathology or dysfunction. The present study examined nuclear magnetic resonance imaging (MRI) correlates of negative symptoms, positive symptoms, and tardive dyskinesia in 24 schizophrenic patients meeting *DSM-III-R* criteria. Negative and positive symptoms were assessed with the Scale for the Assessment of Negative Symptoms (SANS) and the Scale for the Assessment of Positive Symptoms (SAPS) respectively. Tardive dyskinesia was assessed with the Extrapyramidal Symptoms Rating Scale (ESRS). MRI scans were done on a 1.5 tesla unit using standardized pulse sequences. T1 (span-lattice relaxation) and T2 (spin-spin relaxation) values were obtained for regions of interest (ROI) in frontal and temporal white matter and cortex, and the basal ganglia. Partial volume effects were controlled by a small ROI and careful localization. Field non-homogeneity was controlled by calibration with a phantom and the use of ratio values. T2 values were similar for comparable regions of the brain and standard deviations were very low using this procedure. Patients with high ratings of negative symptoms had significantly higher T2 values in the dorsolateral prefrontal cortex than those patients with low ratings of negative symptoms (up to $p < .002$ on ratio values). This finding was unrelated to age, dose of medication, length of illness, or handedness. No T1 or T2 changes were found to be associated with positive symptoms or tardive dyskinesia in the regions examined. The findings suggested that frontal lobe tissue changes, reflected by increased T2 values, may be associated with negative symptoms in schizophrenia.

NR224 **Tuesday May 15, 12 noon - 2:00 p.m.**

NEUROLOGICAL SIGNS, VBR AND NEUROLEPTIC RESPONSE IN SCHIZOPHRENIA

Gyorgy Bartko, M.D., Natl. Inst. Nerv Ment Dis, Budapest PF.1 01281, Hungary; Gyorgy Zador, M.D., Arpad Kulin, M.D., Gaspar Biro, M.D.

Summary:

The relationship between neurological signs, cerebral ventricular size and the outcome of a 28-day haloperidol treatment were studied in 24 chronic schizophrenic (DSM-III-R) patients admitted for relapse. Handedness, neurological "soft" signs, abnormal voluntary movements were rated and spontaneous blinks were counted before treatment. Blink rate response to a test dose of haloperidol was evaluated 4hrs later and was followed by fixed dose treatment with haloperidol. BPRS was used to rate psychopathological symptoms before treatment and on day 28. CT scans of the brain were obtained and VBR were measured. Neither neurological signs assessed before treatment nor VBR were related to the outcome of neuroleptic treatment. However, blink rate response to haloperidol correlated significantly ($p < 0.01$) with the neuroleptic response. There was a significant negative ($p < -0.05$) correlation between the blink rate response and VBR. Our results support the hypothesized inverse relationship between dopamine activity and cerebral atrophy and draw attention to the fact that the blink rate response to neuroleptic test dose may be useful clinical predictor of short-term therapeutic outcome in schizophrenic patients.

NR225 **Tuesday May 15, 12 noon - 2:00 p.m.**

LEUKOENCEPHALOPATHY IN LATE ONSET SCHIZOPHRENIA

John C.S. Breitner, M.D., Psychiatry, Duke University, Box 3925 DUMC, Durham, NC 27710; Mustafa M. Husain, M.D., K. Ranga R. Krishnan, M.D., Gary S. Figiel, M.D., Orest B. Boyko, M.D.

Summary:

Vascular or other organic change has long been suspected as a cause of late onset psychosis, and evidence of occult white matter disease on magnetic resonance (MR) imaging has been recently associated with late onset affective illness. We therefore examined the MR scans of the heads of a series of eight patients with late onset psychosis, as contrasted with eight aged controls. Although some patients had mild cognitive impairment, none had depression or a history or examination suggesting focal brain disease. Thus, all patients met *DSM-III-R* criteria for late onset schizophrenia. All eight patients showed significant leukoencephalopathy or evidence of vascular pathology on the MR image. Such lesions were minimal or absent in the controls. Temporoparietal and occipital white matter lesions were especially prominent in the cases, occurring in seven out of the eight. Seven of the patients also showed small vascular changes in the pons or basal ganglia. These results suggest that focal brain disease, probably of vascular origin, may be associated with late onset psychosis - as it appears to be with late onset depression - and that MR scanning of such cases may provide important clues to pathogenesis.

NR226 **Tuesday May 15, 12 noon - 2:00 p.m.**

SCHIZOPHRENIA: BRAIN STEM CHOLINERGIC NUCLEI

Craig N. Karson, M.D., Psychiatry, VAMC-116A-NLR, 4300 W. 7th Street, Little Rock, AR 72205; Sue W. Griffin, Ph.D., Muhammad Husain, M.D., Robert Mrak, M.D., Jason A. Smith, Edgar Garcia-Rill, M.D.

Summary:

The pendunculopontine (PPN) and lateral dorsal tegmental (LDT) nuclei located in the pons are cholinergic, assist in regulating sleep and locomotion[1], and project to substantia nigra. Cholinomimetics produce sleep patterns and affective disturbances similar to schizophrenia and a role for cholinergic hyperactivity has been proposed[2]. We examined these nuclei in schizophrenia. *METHODS:* Human brain tissue was obtained post mortem from two control subjects, ages 37 and 61 and three subjects with the diagnosis of schizophrenia ranging in age from 64 to 70. The interval between death and autopsy was generally five to seven hours. The right half of the brain stem was placed in a special fixative and sectioned in 10 micron slices thereafter. NADH diaphorase stained the cholinergic neurons whereas cathecholaminergic neurons of the locus ceruleus (LC) were stained with an antibody to tyrosine hydroxylase. *RESULTS:* The number of neurons in each nuclei is presented in Table 1. Changes in the size of PPN and LDT were also apparent.

TABLE 1

Dx	PPN	LDT	LC
Control	13452 ± 5787	4704 ± 4157	15738 ± 908
Schizophrenics	22040 ± 6638	12616 ± 5980	15008 ± 3935

DISCUSSION: An increase in the number of neurons in PPN and LDT in schizophrenia was found and is consistent with the hypothesis of cholinergic hyperactivity in this disorder.

NR227 **Tuesday May 15, 12 noon - 2:00 p.m.**

POOR NEUROLEPTIC RESPONSE: DO WE NEED MANY DRUGS?

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Summary:

Poor neuroleptic response (PNR) is a major clinical problem which is still unresolved. As of today no pharmacological strategy has been found superior to others in overcoming PNR. Moreover, the existence of a large number of neuroleptic drugs in the market, which partially results from PNR, has never been found as having an additional effect on this problem. The rational for such abundance is, thus, questionable. This study evaluates the proportion of acutely exacerbated schizophrenics who would remain unimproved after consecutive administration of three neuroleptic drugs. Sixty patients were treated by haloperidol, perphenazine and levopromazine, administered in randomly determined order, one after the other. Each drug was given for four weeks, during which, the patient either improved or, was shifted to the next drug. The overall improvement rate was 95%. Interestingly - the frequency of good responses to the first, second and third drug did not differ significantly: (66%, 55%, and 66% respectively). Four independent variables (age, BPRS' anxiety/depression, family support scores and concurrent biological abnormalities) were associated with PNR. These findings suggest that a small number of neuroleptics can adequately cover the treatment needs of most schizophrenic patients. The relevance of the findings to understand PNR is discussed.

NR228 **Tuesday May 15, 12 noon - 2:00 p.m.**

NMR SPECTROSCOPY OF PSYCHOTROPIC DRUGS IN THE BRAIN

Joseph E.O. Newton, M.D., VA Medical Ctr. 116A-NRL, 4300 W. 7th Street, Little Rock, AR 72205; Richard A. Komoroski, Ph.D., P. Mohanakrishnan, Ph.D., Jay Sprigg, M.S., Dave Cardwell, B.S., Craig N. Karson, M.D.

Summary:

We are developing NMR spectroscopy methods to determine concentrations of brain Lithium-7 (^{7}Li) and Fluorine-19 (^{19}F, a component of several neuroleptics and other psychotropics) using 15-cm, single-loop, transmit-receive surface coils positioned over the prefrontal area of the head. *RESULTS:* In three subjects maintained at a steady state, there is delayed lithium influx to and efflux from the brain relative to serum levels. The brain concentrations approximate 50% those of serum. Preliminary results employing localized ^{7}Li concentrations may be obtainable in *localized areas* of brain as small as 4 x 4 x 4 cm. The brain concentrations of ^{19}F have been examined in three subjects receiving trifluoperazine and a single subject receiving fluoxetine. It appears that it may require increased sensitivity of the technique to determine brain neuroleptic concentrations via ^{19}F NMR spectroscopy.

NR229 **Tuesday May 15, 12 noon - 2:00 p.m.**

SYMPTOM CORRELATES OF VENTRICLE SIZE IN SCHIZOPHRENIA

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Summary:

Ventricular enlargement has been consistently replicated in neuroimaging studies of schizophrenia, but previous studies have not established clear relationships between symptoms of the disorder and changes in specific brain regions. We measured the brains of 40 schizophrenics and 25 controls with magnetic resonance (MR) using a T1 weighted 3D gradient echo pulse sequence (FLASH) which yielded 3.1 mm thick contiguous sections of the entire brain in the coronal orientation. Measurements were performed with a semi-automatic computerized mensuration system. We determined the volume of the frontal, occipital, and central portions of the lateral ventricle, temporal horns (subdivided into anterior and posterior portions), and the third and fourth ventricle. Patients were in their first episode before receiving substantial neuroleptic treatment.

All components of the ventricles were larger in patients (2 percent to 40 percent) than controls. There was a predominant enlargement of the left hemisphere volumes in patients which approached statistical significance ($p = .08$ MANOVA). Measures of hallucinations, bizarre behavior, sum of positive symptoms, affective flattening attentional dysfunction, and anhedonia had robust correlations with temporal horn volumes ($r = .39$ to $.67$ $p < .05$ - $p < .001$). Volumes of ventricular segments on the left consistently correlated with symptoms to a greater degree than the right. These findings and additional analyses will be presented and discussed.

NR230 **Tuesday May 15, 12 noon - 2:00 p.m.**

MILACEMIDE TREATMENT OF SCHIZOPHRENIA

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Summary:

Drugs (eg. PCP) which interfere with glutamatergic transmission at the N-methyl-D-aspartate (NMDA) subclass of glutamate receptor precipitate both positive and negative symptoms of psychosis in humans. Based on a proposed "glutamatergic deficiency" in schizophrenia, pharmacologic facilitation of NMDA-mediated neural transmission by direct stimulation of the strychnine-insensitive glycine binding site was attempted. Milacemide is an acylated "prodrug" of glycine that readily crosses the blood brain barrier and is converted to glycine in the brain. To study the potential utility of milacemide in the treatment of schizophrenia, 5 male patients with DSM-III-R chronic schizophrenia were treated up to 28 days with milacemide (1200mg) QAM after completing a 4-7 day drug-free placebo lead-in. Efficacy measures included a weekly BPRS, SANS, CGI and NOSIE. No subject demonstrated improvement on any measure. Three patients received the WCST at baseline, while on milacemide, and within two weeks of going off milacemide; patients on milacemide either showed no improvement or deterioration while on milacemide. One study patient experienced a skin rash, another clinically significant liver enzyme elevations. In this open-label, pilot study, the 1200mg/day milacemide dose was not effective or well tolerated.

NR231 **Tuesday May 15, 12 noon - 2:00 p.m.**

NORADRENERGIC FUNCTION IN CHRONIC SCHIZOPHRENIA

Alan Breier, M.D., Psychiatry, MD Psych Res Center, P.O. Box 21247, Baltimore, MD 21228; Owen M. Wolkowitz, M.D., Alec Roy, M.D., William Z. Potter, David Pickar, M.D.

Summary:

Several lines of evidence from postmortem, CSF, plasma and pharmacologic studies support a role for altered noradrenergic function in schizophrenia. The significance of these data for the pathophysiology of schizophrenia remain unclear. In the present study, we examined resting, standing and change (standing minus resting) plasma norepinephrine levels in drug-free chronic schizophrenic patients ($N = 14$) and age and sex matched healthy volunteers ($N = 33$). Schizophrenic patients in comparison to volunteers had significant elevations in resting ($p < .0001$), standing ($p < .0001$), and change ($p < .005$) plasma norepinephrine levels. In addition resting and standing norepinephrine levels were significantly related to positive and negative schizophrenic symptoms. Also, there was a significant positive correlation between resting plasma norepinephrine levels and CSF norepinephrine levels ($r = .59$, $p = .03$). Moreover, there was a significant negative correlation between CSF homovanillic acid and resting ($r = -.64$, $p = .02$), standing ($r = -.70$, $p = .009$), and change ($r = -.50$, $p = .05$) plasma norepinephrine levels. The significance of these data for the pathophysiology of schizophrenia and a model interrelating dopamine and noradrenergic function is discussed.

NR232 **Tuesday May 15, 12 noon - 2:00 p.m.**

NIMH LONGITUDINAL STUDY OF CHRONIC SCHIZOPHRENIA

Alan Breier, M.D., Psychiatry, MD Psych Res Center, P.O. Box 21247, Baltimore, MD 21228; Judith L. Schreiber, M.S.W., Janyce Dyer, M.S.N., David Pickar, M.D.

Summary:

In order to examine the course of illness of chronic schizophrenia, we examined the outcome and predictor indices of 58 young chronic schizophrenic patients who had a research hospitalization at the NIMH in the 1970s and early 1980s. At followup, which was up to 12 years subsequent to the index NIMH hospitalization, the sample showed substantial functional impairment and levels of symptoms with only about 20 percent of the sample demonstrating good outcomes. In addition, there was strong intercorrelation among the symptom and functioning indices at follow-up. Moreover, neuropsychological tests of frontal cortical functioning were significantly correlated with outcome levels of negative symptoms and social functioning but not with levels of positive symptoms. During the period from index to the follow-up assessment, 78 percent of the sample relapsed, 38 percent had suicide attempts, and 24 percent had episodes of major affective illness. Further, positive and negative symptoms ascertained when patients received optimal neuroleptic treatment during the index hospitalization significantly predicted outcome levels of symptoms and functioning and time spent hospitalized during the followup period. In contrast, index positive and negative symptoms ascertained during the drug-free state did not predict outcome symptoms or functioning. CT scan morphologic parameters were not predictive of any course or outcome measure. The implication of these data for the course of illness of schizophrenia are discussed.

NR233 **Tuesday May 15, 12 noon - 2:00 p.m.**

LONGITUDINAL PLASMA HVA IN PSYCHIATRIC PATIENTS

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Summary:

The dopamine hypothesis (DA) for schizophrenia postulates a functionally hyperactive central dopaminergic system in schizophrenic patients. Recent studies have suggested that changes in CNS DA activity may be reflected in plasma HVA (pHVA). Here we report the results of pHVA measured longitudinally in 40 inpatients (25 schizophrenics and 15 non-schizophrenics). After giving informed consent, all patients underwent up to three-week drug washout period followed by four-week treatment period. Patients were diagnosed by RDC and DSM-III with the discharge diagnosis considered definitive. During the washout and treatment phases weekly blood samples were drawn and BPRS and GAS were administered by two trained raters who were blind to medication status and pHVA measurements. pHVA showed a trend towards increase during the washout period and was highest at week three. There was a decrease in pHVA values during the treatment phase. Initial data analysis showed no correlation between baseline BPRS and pHVA either during the washout or treatment phases. In schizophrenic patients the baseline pHVA did not predict response to neuroleptic treatment. Although other studies have reported a positive correlation between pHVA and psychotic symptoms, results of this study suggest that further research is needed to establish the validity of pHVA as an indicator of psychotic severity in schizophrenic patients.

NR234 **Tuesday May 15, 12 noon - 2:00 p.m.**

HALOPERIDOL PLASMA LEVELS: STEADY-STATE PREDICTION

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Summary:

Large interindividual differences in steady-state plasma levels (Css) of antipsychotics, including haloperidol (HPDL), may result in response variabilities in psychotic patients. Further, the relationship between Css of antipsychotics and therapeutic response remains controversial. We are presently conducting a large project which "targets" patients to randomly preassigned HPDL Css (low, medium or high). As part of this study we examined the relationship between the 24 h HPDL plasma level after a single 15 mg dose, the targeted HPDL Css and the dose required to achieve this. Acutely psychotic, hospitalized patients who consented to participate in the study underwent up to 2 weeks of drug washout. Each patient then received a 15 mg "test" dose (PO) of HPDL and blood was drawn 24 and 48 h after the dose. They were then randomly assigned to a dose (2, 5 or 10 mg bid) to achieve a "targeted" low [<5 ng/ml], medium [10-20 ng/ml] or high [>25 ng/ml] Css of HPDL within 5 days. If Css was not in the "targeted" range the dose was adjusted to achieve the assigned Css. The data were analyzed by a linear regression model. The log Css in terms of the log dose revealed a strong linear relationship ($R^2 = 0.78$, $n = 29$), which was further improved by the addition of the 24 hour log plasma level ($R^2 = .087$). Based upon the final dose required and the initial 24 h plasma level we then estimated the 95% prediction interval for the Css. In subsequent patients this interval can be used to choose the dose required to achieve a "targeted" Css, once the initial 24 h plasma level is obtained.

NR235 **Tuesday May 15, 12 noon - 2:00 p.m.**

SEROTONERGIC RESPONSIVITY IN SCHIZOPHRENIA

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Summary:

Several lines of evidence suggest a role for serotonin in the pathophysiology of schizophrenia. Many antipsychotic agents are potent serotonin antagonist, notably the atypical neuroleptic, clozapine. Metachlorophenylpiperazine (mCPP), a serotonin agonist, has been used to study serotonin function in psychiatric disorders. We are investigating the effects of intravenous mCPP (0.075 to 0.1 mg/kg) in schizophrenic patients when drug-free and during treatment with clozapine and/or the typical neuroleptic, fluphenazine. In this preliminary study, although mCPP did not significantly alter BPRS total scores, three of eight drug-free schizophrenic patients experienced exacerbation of symptomatology (greater than 25% increase in BPRS total scores). Clozapine treatment blocked mCPP-induced behavioral disturbances in these patients. mCPP increased plasma cortisol levels ($F = 7.53$, p 0.05, $n = 5$), a marker of serotonin stimulation. Treatment with clozapine blocked this response. In patients who were also studied during fluphenazine treatment, fluphenazine attenuated, but did not block, this effect. These data suggest that the serotonin agonist mCPP induces behavioral responses in some, but not all, schizophrenic patients. Their cortisol response to mCPP appears similar to responses reported in other diagnostic groups. The important component of chronic clozapine treatment.

NR236 **Tuesday May 15, 12 noon - 2:00 p.m.**

DISTURBED WATER METABOLISM IN SCHIZOPHRENIA

William B. Lawson, M.D., Psychiatry, Vanderbilt Medical Center, MCNA 2215, Nashville, TN 37232; Dennis E. Schmidt, Ph.D., Eric Morales, B.S.

Summary:

Excessive fluid intake, often with polydipsia has been reported in otherwise healthy schizophrenic patients for over half a century. The etiology remains unknown, although recent findings suggest multifactorial determinants. Our efforts to determine etiology(s) lead us to do a series of studies on DSM IIIR schizophrenic patients recruited from a state psychiatric facility and through the local AMI chapter. (1) Fourteen patients, four with a history of hyponatremia, had diurnal determinations made of plasma nicotine and cotinine (by HPLC with electrochemical detection), plasma electrolytes, and urine output. Preliminary findings showed a significant negative correlation ($-0.7, p < .05$) between AM nicotine levels and plasma sodium. While nicotine levels were higher in the AM, in the PM, plasma sodium was lower, and both estimated urine output and bodyweight were higher in the PM. (2) In an ongoing study, additional patients and normal controls were given fluid challenges of 20cc/kg H_2O followed 90 minutes later by slow infusion of hypertonic saline. Response of plasma and urine electrolytes and urine output will be presented. Preliminary findings indicate slower return to baseline of plasma osmolality, and smaller cumulative urine output in hyponatremia patients. Plasma vasopressin, atrial natriuretic peptide, and angiotensin II were also determined.

NR237 **Tuesday May 15, 12 noon - 2:00 p.m.**

CLOZAPINE EFFECTS ON POSITIVE VERSUS NEGATIVE SYMPTOMS

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Summary:

Clozapine is a novel atypical antipsychotic with a possible specific effect on negative symptoms. This study examined clozapine's differential effect on negative and positive syndromes in a group of chronic state hospital schizophrenics, characterized by long-term neuroleptic non-response, and significant negative symptoms. Twelve DSM-III chronic schizophrenics (mean age 32.5 years, mean duration of illness 14.2 years) were treated in an open label fashion on clozapine. They were evaluated at baseline and, thereafter, on a weekly basis while undergoing 15 weeks of clozapine. They were evaluated at baseline and, thereafter, on a weekly basis while undergoing 15 weeks of clozapine treatment. The assessment battery included the Positive and Negative Syndrome Scale (PANSS), Clinical Global Impressions Scale (CGI), Abnormal Involuntary Movement Scale (AIMS), and medical evaluations. Analysis of trends and mean differences from baseline indicated that clozapine produced significant improvements in both positive and negative syndromes, with decidedly more pronounced change on the positive symptoms. Major improvements were noted on the "though disorganization" and "paranoid/belligerence" symptoms clusters, while more modest but significant improvement was also obtained on "angergia," "activation," and "depression". Improvements were found as early as week 4 of clozapine and continued through the fifteenth week which emphasizes the advantage of long-term clozapine treatment. Four patients who had been undischargeable were able to be discharged after study. The nature, sequence, and timing of specific clinical changes with clozapine are discussed in relation to the indications for this compound as the treatment of choice.

NR238 **Tuesday May 15, 12 noon - 2:00 p.m.**

VISUAL SELECTIVE ATTENTION IN SCHIZOPHRENIA

Paul G. Nestor, Ph.D., Psychiatry, Harvard Medical School, VAMC-116A 940 Belmont Street, Brockton, MA 02401; Steven F. Faux, Ph.D., Robert W. McCarley, M.D., Virginia Penhune, B.A., Stephen Sands, Ph.D.

Summary:

Platelet serotonin (5-HT) uptake was measured in 19 premenstrual syndrome (PMS) subjects meeting *DSM-III-R* criteria during a double-blind, placebo-controlled buspirone study. Two buspirone cycles (40.6 $\pm$ 12.2 mg.day) were significantly more effective than two placebo cycles on the Premenstrual Syndrome Tension (PMTS) Scale. There were no differences in 5-HT uptake between subjects and controls or between subject treatment groups. When subgrouped by mean control 5-HT uptake, the K_m in the group below the mean (low group, $n = 9$) was significantly decreased during the luteal compared to the follicular phase, whereas the V_{max} in the group above the mean (high group, $n = 10$) was significantly higher in the luteal compared to the follicular phase. The low group was significantly more symptomatic than the high group on baseline PMTS and Profile of Mood State (POMS) scores. Buspirone significantly improved POMS, PMTS, HAM-A, and Premenstrual Assessment Form (PAF) scores in the low group whereas the high group showed no improvement or worsened. Our results suggest that serotonergic dysfunction may be present in PMS and that buspirone's efficacy in part may be due to its effect on serotonin uptake during the luteal phase.

NR239 **Tuesday May 15, 12 noon - 2:00 p.m.**

VISUAL P300 ERPS IN SCHIZOPHRENIA

Steven F. Faux, Ph.D., Psychiatry, Harvard Medical School, VAMC-116A 940 Belmont Street, Brockton, MA 02401; Paul G. Nestor, Ph.D., Robert W. McCarley, M.D., Martha E. Shenton, Ph.D., Virginia Penhune, B.A., Seth D. Pollak, M.Ed.

Summary:

Evaluation of schizophrenics (SZ) shows a L < R voltage asymmetry of the auditory "oddball" P300 not present in normals ($N = 50$ SZ, 3 studies, medicated and unmedicated; age-matched normals). To determine if the asymmetry is modality-specific we are now testing SZ who show L < R auditory P300 asymmetries on an analogous visual detection task. Subjects viewed a series of digits presented singly for 100 msec, and responded to infrequent targets under perceptually degraded (blurred) conditions. Visual P300 ERPs to the target stimulus from the SZ (current $N = 5$, neuroleptic-medicated, DSM-III-R diagnosed) were compared with 9 age-matched normal controls. No differences in P300 peak latency were observed (SZ = 509 msec; NL = 494 msec) at Cz (see fig.) Although N's are currently too small to use our MANOVA test for topographic asymmetries, planned comparisons of integrated P300 amplitudes (400-500 msec) at specific electrode sites showed much greater statistical group separation at left temporal electrode sites than at right temporal sites (Mann-Whitney non-parametric test: T3 [$p < .04$], C3 [$p < .02$], Cz[$p < .03$], C4 [not sig.], T4 [not sig.]). These initial data indicate that P300 asymmetries in SZ may be apparent across modalities. The visual L < R asymmetry is compatible with other data pointing to the hippocampus as an important P300 source generator for several modalities and to the involvement of this structure and/or its inputs in pathological processes in at least some schizophrenics.

NR240 **Tuesday May 15, 12 noon - 2:00 p.m.**

THE ENTORHINAL CORTEX IN SCHIZOPHRENIA

Manuel F. Casanova, M.D., CBDB, NIMH, 2700 Martin L. King Jr. Ave SE, Washington, DC 20032; Richard Saunders, Ph.D., Lori Altshuler, M.D., Terry E. Goldberg, Ph.D., Este Armstrong, Ph.D., Daniel R. Weinberger, M.D., Joel E. Kleinman, M.D.

Summary:

The purpose of the present study was to examine the entorhinal cortex of schizophrenic (SC) patients for neuronomorphometric abnormalities and to elucidate whether these cytoarchitectural peculiarities, if present, were specific to the schizophrenic process. Serial Nissl stained whole brain sections were obtained from 8 leukotomized SC patients (mean age of 59.8 years), 5 patients leukotomized for various affective disorders (mean age 64.6 years), 5 patients leukotomized for reasons other than schizophrenia (i.e., intractable pain) (mean age 53.6 years) and 8 normal nonleukotomized patients (mean age of 61.7 years). Morphometric parameters studied from photomicrographic enlargements or by interfacing a computerized image analysis system (LOATS) with a microscope included neuronal cell number, shape, orientation and area. The results indicated neuronal cell loss in the entorhinal cortex of both SC patients and affective controls. No significant differences between groups was detected for any other neuronomorphometric parameters examined. Revision of the literature suggests that the lesion responsible for the neuronal loss occurs during development. Since the entorhinal cortex acts as a funnel for sensory information going into the hippocampus, the findings reported in the present study provide an important pathological correlate to the symptoms observed in both schizophrenia and primary affective disorder.

NR241 **Tuesday May 15, 12 noon - 2:00 p.m.**

PATHOLOGY OF COGNITIVE IMPAIRMENT IN SCHIZOPHRENIA

Manuel F. Casanova, M.D., CBDB, NIMH, 2700 Martin L. King Jr. Ave SE, Washington, DC 20032; Nicholas Carosella, M.D., James M. Gold, Ph.D., Richard E. Powers, M.D., Daniel R. Weinberger, M.D., Joel E. Kleinman, M.D.

Summary:

Neuropsychological testing of elderly schizophrenic (SC) patients reveals that a significant portion of this patient population exhibit varying degrees of cognitive impairment. Since Alzheimer's disease (AD) is the most common cause of dementia in geriatric patients, we decided to investigate whether the cognitive decline observed in schizophrenia is the result of AD-like degenerative changes. For this purpose the number and distribution of senile plaques (SP) and neurofibrillary tangles (NFTs) were mapped in the hippocampus of 10 elderly cognitively impaired SC patients, 10 AD patients and 10 subjects with cognitive impairment were not attributed to either SC or Alzheimer's disease. Our results indicated that in AD degenerative changes invariable predominate in the CA1 subfield, subiculum, and proisocortex. Alternatively, Alzheimer's-like changes virtually spared the hippocampi of our SC and other cognitively impaired patients. Furthermore, the presence of SPs in the molecular layer of the dentate gyrus of AD patients corroborated the existence of an entorhinal cortex lesion in this illness. No similar changes were reported in our schizophrenic patients. The authors conclude that cognitive impairment in schizophrenia is not the result of AD-like degenerative changes.

NR242 **Tuesday May 15, 12 noon - 2:00 p.m.**

IMPACT OF CLOZAPINE ON COGNITION IN SCHIZOPHRENIA

Richard Greenberg, M.D., CBDB, NIMH, 2700 Martin L. King Jr. Ave SE, Washington, DC 20032; Terry E. Goldberg, Ph.D., Suzanne J. Griffin, M.D.

Summary:

Patients with schizophrenia who were refractory to treatment with conventional neuroleptic medications received the atypical neuroleptic antipsychotic clozapine. Changes in patient clinical status were assessed in an "off" (but receiving typical neuroleptic) - "on" (receiving clozapine) design. Immediately prior to the introduction of clozapine, psychiatric symptomatology was assessed by the Brief Psychiatric Rating Scale and cognitive functions by a neurophysiological test battery comprised of the WAIS-R, Wechsler Memory Scale , Trails B, Line Orientation Face Recognition, WRAT, Category Test, and Wisconsin Card Sorting Test. Four to 25 months after clozapine therapy commenced, patients were reassessed. Both so-called positive and negative psychiatric ratings improved considerably. However, some cognitive functions, notably those in visual memory, declined. The latter results may be due to clozapine's potent anticholinergic properties. Associations among psychiatric and cognitive change scores were not significant.

NR243 **Tuesday May 15, 12 noon - 2:00 p.m.**

A STRATEGY FOR LINKAGE IN TYPICAL SCHIZOPHRENIA

Jeremy M. Silverman, Ph.D., Psychiatry, Bronx VA Med Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Richard C. Mohs, Ph.D., David A. Greenberg, Ph.D., Larry J. Siever, M.D., William Wallace, Ph.D., Kenneth L. Davis, M.D.

Summary:

The phenotype for a schizophrenia-related gene remains unclear, but adoption and family studies of schizophrenia suggest that phenotypic expression frequently includes the milder schizophrenia-like personality characteristics found in schizotypal personality disorder. Subtle psychophysiological deficits, such as smooth pursuit eye movement abnormalities and poor performance on the continuous performance task, may also help to identify relatives carrying a predisposing gene(s) for schizophrenia. Our strategy to pursue the localization of schizophrenia-related gene though linkage analysis therefore involves collecting a comprehensive psychiatric, behavioral, personality, cognitive and psychophysiological profile of all 1° relatives of schizophrenic probands participating in biological studies at one of our affiliate centers. This approach thus allows for the identification of "affected cases" as currently understood, as well as independent re-evaluations of relatives, as the phenotype is further clarified. To date, we have studied 79 relatives of 13 schizophrenic proband families having at least 1 additional member with a schizophrenia related disorder (SRD). Preliminary linkage analysis for chromosome 5 markers will be presented in a subset of our sample - the 1° relatives (n=54) of 7 families with schizophrenia (n=13) and SRD (n=9).

NR244 **Tuesday May 15, 12 noon - 2:00 p.m.**

PLATELETS, EOSINOPHILS AND PSYCHIATRIC SYMPTOMS

Murray A. Cowen, M.D., Natha S. Kline Inst., Orangeburg, NY 10962 Maurice Green, M.D.

Summary:

The "Trophic Base" model proposes that trophic interactions among neurons, glia, and capillaries, in the CNS are modulated by the bases histamine, bradykinin, and the polyamines(1). These local actions are then integrated globally by monoaminergic and cholinergic networks. Eosinophils are increased by histamine and bradykinin while platelets modulate monoamines. A double-blind placebo-controlled study, with eight week trials and four-week washout period, using acetozolamine plus thiamine as an enhancing agent (2), was done on 13 chronic schizophrenic patients with weekly psychiatric (S.A.P.S. and S.A.N.S), eosinophile, and platelet determinations. Increases in eosinophils correlated with Inattention (–0.70) and Avolition (–0.53) negative symptoms and with worsened Bizarre Behavior (0.54) positive symptoms. Increases in platelets correlated strongly with improved total SAPS (–0.71), Hallucinations (–0.63), Delusions (–0.62), and Though Disorder (–0.69), but not Bizarre Behavior positive symptoms. It also correlated with improved total SANS (–0.55), Inappropriate Affect (–0.52), and Alogia (–0.53), but not with Inattentivity or Avolition negative symptoms. Hence the eosinophile and platelet correlations were mutually exclusive. The acetazolamide plus thiamine did not significantly influence overall platelet or eosinophile counts.

NR245 **Tuesday May 15, 12 noon - 2:00 p.m.**

ALKALINE PHOSPHATES AND PSYCHIATRIC SYMPTOMS

Murray A. Cowen, M.D., Natha S. Kline Inst., Orangeburg, NY 10962 Maurice Green, M.D.

Summary:

The "Trophic Base" Model proposes that trophic interactions among neurons, glia, and capillaries, in the CNS are modulated by the bases histamine, bradykinin, and the polyamines. These local actions are then integrated globally by monoaminergic and cholinergic networks. Alkaline phosphates, "AP" inhibits polyamine synthesis (1). A double-blind placebo-controlled study, with eight-week trials and a four-week washout period, using acetazolamide plus thiamine as an enhancing agent (2), was done on 13 chronic schizophrenic patients with weekly psychiatric (S.A.P.S. and S.A.N.S.) and AP determinations. Increases in AP correlated strongly with worsened total SAPS (0.68), Hallucinations (0.73), Bizarre Behavior (0.53), and Thought Disorder (0.55) subtests. It did not correlate significantly with Delusions (0.47), and was completely unrelated to any negative symptom alteration. The acetazolamide plus thiamine did not significantly influence overall AP concentrations.

NR246 **Tuesday May 15, 12 noon - 2:00 p.m.**

FAMILY, COGNITION AND SCHIZOPHRENIA OUTCOME

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Summary:

In a cross-sectional investigation of clinical, social and cognitive correlates of outcome in chronic schizophrenia, we studied 26 patients hospitalized at a state psychiatric facility continuously for 18 months or longer, and 26 patients missing for at least three years without rehospitalization. Patients met RDC for chronic schizophrenia based on the SADS, were maintained on neuroleptic medication and were matched for sex, age, ethnicity, SES and chronicity.

Patients were rated on the BPRS, AIMS and EPS scales and given a two-hour neurophysiological test battery. Family members' reports of patients' problematic behaviors, family distress and available social supports were assessed using the Social Behavior Assessment Schedule.

Stepwise discriminant function analysis found family members' reports of patients' behavior was the most important predictor of prolonged inpatient status. A composite measure of neuropsychological functioning was the second highest predictor and social support to the family ranked third. The BPRS was a significant but less powerful predictor than family reports of patient behaviors. The total function had an eigenvalue of .92 and correctly classified 85% of cases.

The findings highlight the contribution of family perceptions, available social supports and cognitive functioning to the long-term outcome of schizophrenia.

NR247 **Tuesday May 15, 12 noon - 2:00 p.m.**

NEUROCOGNITIVE CORRELATES OF SCHIZOPHRENIA OUTCOME

Deborah A. Perlick, Ph.D., Psychiatry, Montefiore Hospital, 111 E 210th Street, Bronx, NY 10467; Peter Stastny, M.D., Steven Mattis, Ph.D., Jeanne Teresi, Ph.D., Ira R. Katz, M.D.

Summary:

This study is part of a larger investigation of socioclinical correlates of outcome in schizophrenia (Statsny, et.al., in preparation) which found that a composite neurophysiological variable correlated significantly with outcome. Here we investigate specific cognitive functions correlating with outcome and relevant covariates.

Subject were 26 patients hospitalized at a state psychiatric facility continuously for 18 months or longer, and 26 patients treated as outpatients for at least three years without rehospitalization. Patients met RDC for chronic schizophrenia based on the SADS, were maintained on neuroleptic medication and matched for sex, age, ethnicity, SES and chronicity.

Patients were rated on the BPRS, AIMS and EPS scales and given a two-hour neurophysiological test battery. Blood specimens were obtained for determination of neuroleptic and anticholinergic serum levels, using the radioreceptor methods described by Tune et.al., 1982.

Stepwise discriminant function analysis found that interhemispheric fine motor integration discriminated between patient groups most strongly, with measures of perseveration, attention, construction, memory and facial recognition discriminating further. When effects of medication, BPRS, AIMS and EPS were partialled out, neuropsychological variables remained significant discriminators.

These data underscore the importance of cognitive dimensions in schizophrenia outcome research and are consistent with an interhemispheric integration defect model of schizophrenia.

NR248 **Tuesday May 15, 12 noon - 2:00 p.m.**

SCHIZOPHRENIC DEPRESSION: RESPONSE TO NEUROLEPTICS

Menahem Krakowsky, M.D., Psychiatry, New York University, Nathan Kline Institute Bldg 35, Orangeburg NY 10962; Pal Czobar, Ph.D., Jan Volavka, M.D.

Summary:

Depression is common in acute schizophrenic patients but its etiology is disputed with some authors implicating neuroleptic treatment, while others consider depression an integral part of schizophrenic process. Sixty-nine depressed and 79 nondepressed newly admitted schizophrenic patients were randomized to high, low or intermediate plasma levels of haloperidol and followed for several weeks. While depressive symptoms decreased significantly over time, the difference between the two groups persisted throughout treatment (ANOVA $F=30.0$, $df=1,101$, $p<.001$ at the end of 3 weeks). The depressed patients evidenced more vegetative signs including sleep ($F=9.3$, $df=1,106$, $p<.01$) and appetite disturbances ($F=3.9$, $df=1,106$, $p<.05$). Neither depression, nor extent of improvement was correlated to haloperidol plasma level. A positive correlation (Pearson's $r=.33$, $p>.001$) between depression and neurological side effects (as measured by Simpson-Angus scale) emerged at the end of three weeks of treatment. It reflects greater sensitivity to neuroleptic side effects in the depressed group rather than a direct depressogenic effect of medication. The depressed patients evidenced more positive symptoms (e.g. ANOVA $F=6.7$, $df=1,133$ $p<.01$ for total SAPS score, $F=6.0$, $p<.05$ for hallucinations and $F=11.3$, $p<.001$ for delusions subscales scores). A neurological examination (administered to 109 patients) revealed more frontal lobe impairment in the nondepressed patients.

NR249 **Tuesday May 15, 12 noon - 2:00 p.m.**

COGNITIVE DEFICITS IN EARLY SCHIZOPHRENIA

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Summary:

Recent evidence indicates that brain structural abnormalities may exist close to the onset of schizophrenic symptoms. These findings raise the following questions about cognitive deficits in schizophrenia: 1) Do they likewise exist early on in the illness? 2) Are they progressive? and 3) Are they associated with specific abnormalities in brain morphology? In order to address these questions, we administered a neuropsychological battery to 32 consecutively admitted first episode patients with diagnoses of schizophreniform illness and compared their performances to 26 patients with *DSM-III-R* chronic schizophrenia (mean duration of illness = 10.1 $\pm$ 6.6) and to 16 normal controls. In addition, MRI measurements of frontal and temporal lobes, ventricular system, and medial limbic structures (hippocampus, parahippocampus) of 34 patients (25 first episode, 9 chronic) were obtained. Duration of illness was calculated from the time of onset of behavior change from reliable family informants.

A multivariate analyses of variance was performed on neuropsychological test variables, yielding an overall significant multivariate F (Wilk's lambda = 1.63, $p < .03$). Post-hoc tests revealed that first episode patients did not differ from chronic patients on any measure and both groups were more significantly impaired compared to normals on most measures. Duration of illness was associated with significantly poorer performances on measures of verbal memory and mental processing speed. In addition, smaller parahippocampal volume was associated with lower verbal IQ and reductions in verbal memory, while other correlations of structure to cognitive function were not significant.

NR250 **Tuesday May 15, 12 noon - 2:00 p.m.**

PREFRONTAL CORTEX AND COGNITION: A PET STUDY

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Summary:

Hypofunction of the prefrontal cortex, particularly during conditions that result in increased activity of this brain area in normal individuals, has been the most consistent cerebral functional abnormality to emerge from positron emission tomography (PET) and xenon-133 regional cerebral blood flow (rCBF) studies of schizophrenia. However, there is insufficient information about the role of the PFC in normal higher cognitive operations to allow full understanding of the implications of cognitively-related "hypofrontality" in disease states. To pursue this line of inquiry, we used a method for computer-driving administration of neuropsychological tests that allows rapid, repeated measurements of rCBF during supine PET scanning. This technique allows the neurophysiological response to a number of different testing conditions to be compared in the same subject. Six healthy, male subjects (ages 23-38) each underwent six PET rCBF measurements in a single session during a battery of neuropsychological tasks keyed to various cognitive operations which have been putatively linked to the dorsolateral prefrontal cortex (DLPFC). The battery consisted of three DLPFC tasks plus a sensorimotor control task matched to each. The DLPFC tasks included the Wisconsin Card Sorting Test (WCS), a version of the Delayed Alternating Task (DA), and a spatial Delayed Response Task (DR). Studies were performed on a Scanditronix PC2048-15B brain tomograph which produces 15 slices 6.5 mm think with in plane image resolution of 6.5 mm. Forty mCi of $H_2{}^{15}O$ were injected for each rCBF measurement. For data analysis, rCBF images were normalized to the mean CBF value. Magnetic resonance images obtained in planes parallel to the PET images guided neuroanatomic localization. Each of the three tasks produced activation in the left and right inferior DLPFC (percent increase above the sensorimotor control task on the left: WCS = 10 percent, DA = 7 percent, DR = 5 percent; right: WCS = 8 percent, DA = 4 percent, DR = 5 percent). Percent activations in the left superior DLPFC were; WCS = 7 percent, DA = 6 percent, DR = -2 percent; and in the right: WCS = 11 percent, DA = 6 percent, DR = 0.5 percent. These data suggest that the cognitive operations subserving these tasks have in common that they involve the DLPFC. However, the magnitude and locale of the activations produced may differ. Implications for cognitive neuroscience and the application of this method to the study of neuropsychiatric diseases will be discussed.

NR251 **Tuesday May 15, 12 noon - 2:00 p.m.**

CHANGE IN SELF-DESTRUCTIVENESS OF BORDERLINE PATIENTS

Alex N. Sabo, M.D., Psychosocial, McLean Hospital, 115 Mill Street, Belmont MA 02178; Deborah Chauncey, A.B., John G. Gunderson, M.D.

Summary:

Clinicians must regularly decide whether self-destructive behavior indicates that a patient is (A) suicidal or (B) non-suicidal, i.e., indicating non-lethal motivations. The authors review the relevant literature and offer a framework for differentiating these kinds of self-destructive acts. The current study examines the change in both kinds of self-destructive behavior in 17 DIB-defined, initially hospitalized borderline patients who were beginning psychotherapy and then followed for a period of two years. Patients were assessed using the DIB, the Suicidal Behaviors Questionnaire, the Action Scale, and a Global Suicidality Scale at baseline, six months, one-year, and two-year follow-up.

The number of patients reporting Type B (non-suicidal), self-destructive ideation or acts, did not change significantly over the two-year period: 59% at baseline and 47% at two-year follow-up. The average number of Type B acts did decline from 19/person in the six months prior to baseline to 6/person at two years. There was also a trend towards these acts becoming less destructive over the two-year interval. In contrast, though Type A (suicidal) ideation persisted, there was a striking decline in suicidal acts. 41% of the patients reported suicide attempts at baseline, 24% at six months, and only 6% reported a suicide attempt at two years ($P = .003$).

NR252 **Tuesday May 15, 12 noon - 2:00 p.m.**

ANTIPSYCHOTIC DRUGS: LIABILITY TO AFFECT SEIZURES

Bruce I. Diamond, Ph.D., Psychiatry, Medical College of GA., 1515 Pope Avenue, Augusta, GA 30912; Bonnie Van-Schooneveld, M.D., Richard L. Borison, M.D.

Summary:

Occurrence of antipsychotic drug-induced seizures range from 0.5% to 10% in nonepileptic patients. The type and dose of antipsychotic drugs are thought to be critical characteristics for seizure production. It was the aim of this study to characterize antipsychotic drug-induced seizure production. Male Swiss mice were used in generalized tonic-clinic maximal electroshock (MES) and pentylenetrazol (PTZ) absence seizure models, whereas male Sprague Dawley rats were studied in the Kainic acid (KA) temporal lobe epilepsy (TLE) model. Animals were pretreated with either 10 or 30 mg/kg of chlorpromazine (CPZ), thioridazine (TDZ) or 0.1 and 1 mg/kg of haloperidol (HAL). Latency to tonic seizures (MES, clonic seizures (PTZ 85 mg/kg) and limbic seizure stage (KA, 15 mg/kg) were measured. Only high dose CPZ had a significant effect (anticonvulsant) on the MES test. In the PTZ test CPZ and TDZ at high dose displayed anticonvulsant properties, whereas low dose CPZ facilitated seizures. Limbic seizures induced by KA were prevented by CPZ. In contrast, high dose of HAL potentiated these seizures. These data demonstrate that the type and dose of neuroleptic is important in seizure production as well as on the kind of seizure produced.

NR253 **Tuesday May 15, 12 noon - 2:00 p.m.**

MEMORY IN MONOZYGOTIC TWINS DISCORDANT FOR SCHIZOPHRENIA

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Summary:

Recent studies on amnesic disorders have proposed the independence of the declarative and procedural memory systems. We investigated these dimensions of memory in 13 pairs of SCID diagnosed monozygotic twins discordant for schizophrenia (nine pairs), schizoaffective disorder (two pairs), and delusional disorder (two pairs). Subjects received the WAIS-R Vocabulary subtest, FAS, and three trials on a 20-word list with an immediate recognition test (declarative memory measures), and 15 pursuit rotor trials at 30 and 60 rpm (to assess procedural memory). The twins did not differ on vocabulary but did differ on FAS, suggesting that the basic semantic system was intact but access to this information is deficient. The groups did not differ on motor learning rate, but the ill twins performed slightly worse overall. The groups differed on measures of verbal recall and recognition. The ill twins learned over repeated trials but at a significantly reduced rate. The data suggest that declarative memory is impaired in schizophrenia while the procedural system remains relatively intact. This nonamnesic form of memory impairment is consistent with neuroimaging and neuropathological findings of temporal and frontal lobe abnormalities in schizophrenia.

NR254 **Tuesday May 15, 12 noon - 2:00 p.m.**

LITHIUM RESPONSE, VBR, BRAIN DENSITY AND SCHIZOPHRENIA

Surendra Kelwala, M.D., WNSSTU, Northville Reg. Hospital, 41001 W. Seven Mile Road, Northville, MI 48167; Anil K. Jain, M.D., Ibrahim Youssef, M.D., L.J. Bronn, M.D., Pramila Baddigam, M.D., Suresh Yerasi

Summary:

In a study to evaluate Lithium's efficacy in schizophrenia, 31 inpatient veterans completed the Li trial and consented for brain CAT-Scans. CAT-Scans were also obtained on 14 matched controls (C). Li was given without any concomitant medication, in an open trial for 2-6 weeks (X=29 days) at levels 0.8-1.4 (X=0.96) mEq/L. 5 patients showed good therapeutic response (R) (>40% decrease on the BPRS of New Haven Schizophrenia Index (NHSI) discharge from hospital on Li alone), 13 patients responded partially (PR) (>20% decrease on the BPRS or NHSI) and 13 showed poor response (NR) (<20% decrease on the BPRS/NHSI with at least 2 weeks of Li trial). The table summarizes the Ventricular Brain Ratio (VBR) and brain densities measurements of the anterior and posterior quadrants of the three Li groups and the controls.

Parameter	R	PR	NR	C
VBR	10.83±0.39	8.09±2.87	8.74±3.22	6.70±1.96
Ant Lt Hemisphere	34.36±3.30	38.39±2.95	40.09±2.97	42.28±4.67
Post Lt Hemisphere	39.55±4.14	44.52±4.98	48.10±4.64	44.75±5.79
Ant Rt Hemisphere	35.64±2.99	38.84±2.54	40.19±2.24	42.39±4.80
Post Rt Hemisphere	38.04±3.99	44.36±4.84	47.56±4.36	43.98±5.84

ANOVA with post hoc Scheffe showed that patients differed significantly from controls in their VBR ($p<.02$) and brain densities (on many quadrants) and Li responsive patients had significantly higher VBR ($p<.05$) and lower brain densities (on many quadrants) than Li non-responsive and partially responsive patients.

NR255 **Tuesday May 15, 12 noon - 2:00 p.m.**

EFFECT OF DOMPERIDONE ON PLASMA HVA IN SCHIZOPHRENIA

P. Eric Konicki, M.D., NSB, NIMH, NIH Bldg 10 RM 4N214, Bethesda, MD 20982; William Z. Potter, Richard E. Scott, B.A., David Pickar, M.D.

Summary:

Among the initial effects of neuroleptics administration in animal models in an increased rate of CNS dopamine turnover, resulting in increased levels of plasma HVA. We and others have shown that plasma HVA levels increase during the first few days of fluphenazine administration in previously unmedicated schizophrenic patients. Domperidone is a butyrophenone dopamine antagonist which does not cross the blood-brain barrier. In order to investigate the contribution of peripheral dopamine receptor blockade to increased plasma HVA levels, we administered domperidone acutely to a group of medication-free patients with schizophrenia. Method: Twelve patients with schizophrenia who were medication-free for at least three weeks were administered domperidone (80 mg/day) orally for two days. Plasma was collected at baseline and eight, 24, and 48 hours after the start of domperidone administration. Sample collection and biochemical analysis were performed according to previously reported methods. Results: Plasma HVA levels were unchanged from baseline at all observation points. Significant elevations in plasma prolactin levels were observed at eight, 24, and 48 hours after the initiation of domperidone administration consistent with known effects on the dopaminergic tuberoinfundibular system. These data suggest that the neuroleptic-induced increase in plasma HVA levels are dependent upon interaction with CNS dopaminergic systems rather than the result of peripheral dopamine receptor blockade.

NR256 **Tuesday May 15, 12 noon - 2:00 p.m.**

JOB CLUB FOR PSYCHIATRIC PATIENTS: TRAINING JOB FINDING SKILLS

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Summary:

Two hundred nineteen persons with a variety of psychiatric disorders participated in a structured, behaviorally-oriented Job Finding Club in which they learned job seeking skills (e.g., soliciting job leads, completing job interviews). Daily participating for 6 hours/5 days per week was supervised by rehabilitation counselors (2 counselors per 40 patients). Research quality diagnoses were established with the PSE and assessments were made of symptom severity (BPRS), work history, social functioning, and quality of performance in the Job Club. Twelve month follow-ups documented employment outcomes. Overall 41% of patients obtained employment or paid job training; 10% were deemed to symptomatic to participate in the Club; 12% dropped out during the Job Club training phase and 37% dropped out during the job search phase. Patients with SSI were significantly less likely to become employed but those on SSdi obtained jobs as frequently as non-disabled persons. Diagnosis was a significant factor in determining outcomes with 20% of schizophrenics and bipolars vs. 50% of depressives and substance abusers getting jobs. Severity of symptoms, previous work history, and performance on a role play job interview also predicted vocational outcomes. The Job Club was cost-effective as a rehabilitation intervention as the average duration leading to employment was 4 weeks at $400 per job placement.

NR257 **Tuesday May 15, 12 noon - 2:00 p.m.**

SCHIZOPHRENIA, MANIA AND ATTENTIONAL DYSFUNCTIONS

Barbara Cornblatt, Ph.D., Psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; Michael Obuchowski, M.A., Paul Fergeson, B.A., Sukhdeb Mukherjee, M.D.

Summary:

The association between schizophrenia and dysfunctions in attention and information processing (AIP) has been solidly documented throughout literature. However, the extent to which these deficits are involved in the etiology and pathogenesis of the illness is still unclear. One critical issue is whether the dysfunctions are traits independent of clinical state. Another issue, important from a genetic perspective, is whether such traits are specific to schizophrenia.

AIP dysfunctions were measured on a multidimensional version of the Continuous Performance Test (CPT-IP; Cornblatt et al, 1989) in sixteen schizophrenic and nine manic patients. Eight schizophrenics were tested in off-on-on medication design, to assess the fluctuations in performance due to changes in medication. The remaining eight schizophrenics were tested on an on-on-on medication schedule to control for practice effects. Manics were tested twice, first when in florid episode and then when in remission (with most subjects medicated on both occasions). No differences in performance curves across session were found among the three groups. In addition, no differences in level of performance were found between the control schizophrenics and the manics, either in pattern or severity of dysfunction.

These findings indicate that performance does not covary with changes in clinical state (whether due to shifts in medication or remission), suggesting that AIP dysfunctions are invariant traits. Furthermore, the lack of specificity supports faulty processing of information to be critically involved in both schizophrenia and bipolar disorder.

NR258 **Tuesday May 15, 12 noon - 2:00 p.m.**

PLATELET MAO IN SCHIZOPHRENIA AND AFFECTIVE SUBTYPE

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Summary:

It has been suggested that schizophrenics have low levels of platelet monoamine oxidase (MAO). However, neuroleptics can lower these levels and some studies find that drug-free schizophrenics have similar MAO levels to normal controls. We report on 688 subjects: 205 schizophrenics, 149 depressives, 58 manics, 76 other diagnoses, and 200 normal controls, whose platelet MAO levels were measured after a washout period averaging 3 weeks, using tryramine, and/or benzylamine and/or tryptamine as substrates. The subjects were assayed on two different days. In examining schizophrenic subtypes, we found no difference in MAO levels between paranoid versus non paranoid, hallucinating versus non-hallucinating, chronic versus acute or those with or without affective features. In affective patients, we found no differences in MAO levels between RDC subtypes, or mania vs. depression. There were no differences between affectively ill patients and schizophrenics. All patients subgroups had slightly lower levels with tyramine as substrate than did normal controls. For benzylamine and tryptamine, all patient subgroups had normal MAO levels.

NR259 **Tuesday May 15, 12 noon - 2:00 p.m.**

REFINING THE CONCEPT OF NEGATIVE SYMPTOMS

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Summary:

The discrimination between primary and secondary "negative" symptoms is a major unresolved challenge of the negative symptoms research. Recently, some investigators have attempted to resolve this issue by including a duration criterion in the operational definition of negative symptoms (Carpenter et al. 1988). They predicted that 'true' or primary symptoms should persist over time and be associated with chronicity in schizophrenia.

This study examined the validity of this proposed refinement. The prognostic importance of negative symptoms defined cross-sectionally (without a duration criterion) versus that of symptoms defined longitudinally (with a duration criterion) was compared in a sample of 74, "first-episode" DSM-III schizophrenic patients. Of the 74, 37 (50% had 2 or more negative symptoms at study intake or cross-sectionally; but, only 10 (13.5%) had 2 or more persistent symptoms (i.e., symptoms present at intake and during the follow-up period). As predicted, levels of persistent negative symptoms were significantly associated with most aspects of poor 18-month outcome ($rs > .30$); whereas, cross-sectional levels of negative symptoms were not. The implications of our findings for the definition and measurement of negative symptoms will be discussed.

NR260 **Tuesday May 15, 12 noon - 2:00 p.m.**

LOW AMINE METABOLITE EXCRETION IN SCHIZOPHRENIA

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Summary:

Psychotic symptoms of schizophrenia have been attributed to an excess of dopamine (Carlsson, 1978) or phenylethylamine (Fischer et al. 1972; Potkin et al, 1980) and the negative symptoms to a deficit in catecholamines (Stein, 1971) or phenylethylamine (Sabelli, et al, 1989). However, clozapine does not block dopamine receptors. Previous investigations of the CSF levels of the dopamine metabolite homovanillic acid (HVA) have been controversial; plasma levels have been found low (Javaid, 1988), but data could be explained by untimely sampling. Total daily excretion of HVA could overcome such objection if complete collections were guaranteed. We have now obtained repeated samples from 18 schizophrenic subjects (DSMIII-R diagnosis) during a period of acute psychosis, under close supervision by nursing and research staff, catheterizing some subjects as required, and monitoring volume and creatinine. Total urinary excretion of HVA, phenylacetic acid (PAA, phenylethylamine metabolite) and methoxy-hydroxy-phenylglycol (MHPG, norepinephrine metabolite) were measured by chromatographic methods. HVA (813 ± 452 mcg/d) and PAA (73 ± 48 mg/d) excretions were decreased in comparison to controls. These results are at variance with the dopamine hypothesis. The observed decrease in dopamine and phenylethylamine turnover may explain the anhedonia and other negative symptoms of schizophrenia.

NR261 **Tuesday May 15, 12 noon - 2:00 p.m.**

SLEEP IN SCHIZOPHRENICS ON AND OFF NEUROLEPTICS

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Summary:

Sleep research in schizophrenia has shown deficits in slow wave sleep (SWS) as well as variability of rapid eye movement sleep (REM) measures such as REM latency. We examined the state-dependent contribution of neuroleptic withdrawal and psychotic relapse in influencing individual sleep parameters. Clinically stable male schizophrenic (DSM-III-R) patients on haloperidol were studied with three nights of polysomnography for baseline measures and again after neuroleptic withdrawal. Sleep measures were obtained at the point of relapse (REL) or after a six-week drug-free period if the patient remained clinically stable (i.e. nonrelapser in NonREL). *RESULTS:* REM latency and SWS appear to decrease modestly following neuroleptic withdrawal. There were no significant differences in baseline sleep in those who relapsed ($N = 7$) and those who remained clinically stable ($N = 7$). Sleep changed significantly in those patients who relapsed: sleep latency increased and sleep continuity deteriorated with decreases in both NonREM and REM sleep. Delta sleep decreased at a trend level. The mean REM latency shortened from a baseline of 86 ± 47 min. to 53 ± 21 min. at relapse ($p = .06$). In NonRELs, sleep also changed significantly following haloperidol withdrawal: sleep latency increased and total sleep and total NonREM sleep decreased. Stages 3 and 4 and REM latency decreased moderately without reaching statistical significance. RELs differed from NonRELs in that they had significantly decreased total sleep time, sleep efficiency, total Non-REM sleep, and stage 2. Total REM time and REM % decreased in relapsers at a trend level. The change in SWS and REM latency did not significantly differ between the two groups.

NR262 **Tuesday May 15, 12 noon - 2:00 p.m.**

CLOZAPINE RESPONSE IN TREATMENT RESISTANT PATIENTS

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Summary:

Clozapine was given to 22 chronic patients (mean BPRS Total = 55) on a specialized inpatient unit for treatment refractory schizophrenics. They were optimized on conventional antipsychotics and adjunctive medications such as lithium. Neuroleptic was then discontinued for at least one week. Subjects were started openly on clozapine and followed for a minimum of 5 weeks, holding all other medications constant. Patients were rated weekly on the BPRS. Weekly and 24 hourly time-sampled behavioral data were also recorded. Data were analyzed by MANOVA of repeated measures and linear trend analysis.

For the group as a whole, clozapine showed a modest improvement of 4 points in BPRS Total over conventional neuroleptics ($F = 7.4$, $p = .002$) at 5 weeks. This improvement was seen in the areas of motor tension, hostility, hallucinations and points earned in the unit's token economy. A subgroup of 16 patients who were followed up for 9 weeks was analyzed separately. The additional 4 weeks yielded significant further improvement as measured by BPRS Total, idiosyncratic behavior and level achieved in the token economy. 14 clozapine responders were also analyzed separately. In these patients, the changes at 5 weeks were greater, with a drop of 7.3 points in the BPRS Total and a decrease in autistic withdrawal. BPRS measures of negative symptoms were not consistently improved in any of the analyses.

An analysis of predictors of response will be presented, as well as case vignettes.

NR263 **Tuesday May 15, 12 noon - 2:00 p.m.**

THE EFFECT OF TARGET CHARACTERISTICS ON THE SPECIFICITY OF SMOOTH PURSUIT EYE TRACKING DYSFUNCTION

Xavier F. Amador, Ph.D., Psychiatry, Columbia University, 722 West 168th Street Box 2, New York, NY 10032; Harold A. Sackeim, Ph.D., Sukdeb Mukherjee, M.D.

Summary:

Conflicting reports regarding the specificity of SPEM dysfunction to schizophrenia when comparisons to bipolar disorder have been made have been interpreted as due to the effects of treatment with lithium or because it is a marker of psychosis. This study investigates these issues and also assesses the effect of attentional and target motion manipulations on rates of SPEM dysfunction. SPEM was assessed in 30 chronic schizophrenic patients, 17 bipolar manic patients, and 20 normal controls. Manic patients were tested both while receiving lithium and when lithium-withdrawn. The manic group was unusual in that it consisted of patients with significant inter-episode psychosocial impairment, a high representation of psychosis, and a long-term decline in functioning. Four types of target conditions were presented. In all groups variation in the nature of the tracking task resulted in variability in rates of SPEM abnormality. Depending on the task condition, 47 to 77% of the schizophrenic group, 8 to 58% of the manic group and 5 to 25% of the normal sample were rated as abnormal. This variability in rates of SPEM abnormality contingent on task may be critical in interpreting divergent figures in the literature.

NR264 **Tuesday May 15, 12 noon - 2:00 p.m.**

CEREBRAL SPECT IN DRUG FREE SCHIZOPHRENIC PATIENTS

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Summary:

In the last decade, there have been numerous reports of altered regional cerebral blood flow (rCBF) and metabolism in schizophrenia but the results obtained are still controversial.

A Single Photon Emission CT (SPECT) study was conducted on 16 patients (12 men, 4 women; mean age 23 ± 7 years) diagnosed as schizophrenic according to the DSM-III-R criteria, who were not taking any drug for at least one month. SPECT was performed with a rotating gammacamera on patients in resting condition, eyes open, 30 minutes after the intravenous injection of TC-99m-HM-PAO (hesamethylpropilene-amino-oxime) as tracer.

Two scanning levels were considered (level A passing through centrum-semiovale; level B through the basal ganglia) and the radioactive emittence of computer derived cerebral regions (frontal, parietal, temporal, occipital) normalized by area and divided by the radioemittence of a reference region (cerebellum) was calculated. The CSF spaces were traced and subtracted from the B level slice calculations.

As compared to 14 age- and sex-matched healthy controls, schizophrenic patients showed a diffuse cerebral hypoperfusion, significant in the left frontal (level A: $p = .04$; B: $p = .005$), and left temporal ($p = .011$) areas. Antero-posterior gradient of CBF was tendentially reduced in schizophrenic patients as compared to controls. These results confirm previous observations of reduced rCBF and metabolism in schizophrenia and indicate a left prevalence of hypoflow in drug-free patients.

NR265 **Tuesday May 15, 12 noon - 2:00 p.m.**

TARDIVE DYSKINESIA IN NEUROLEPTIC-TREATED DIABETICS

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Summary:

Each of 38 neuroleptic-treated diabetics (ND) was matched to a neuroleptic-treated nondiabetic control (NC) on 5 parameters: age, sex, psychiatric diagnosis, neuroleptic dose, and time on neuroleptics. All were on stable doses of neuroleptics. A rater blind to all diagnoses and medications assessed each subject for tardive dyskinesia (TD), parkinsonism and cognitive deficits with the Abnormal Involuntary Movement Scale (AIMS), Sct Hans Dyskinesia Scale (SHDS), Sct. Hans Parkinsonism Scale (SHPS), and the Mini-mental State Exam (MMSE).

The group was predominantly older (mean 62.7 yrs.), treated long-term with neuroleptics (mean 18.1 yrs.) and treated with low-moderate doses of neuroleptics (mean 303 chlorpromazine equivalents/day). Of the ND group, 79% met Schooler-Kane criteria for TD as compared to 53% of the NC group ($p = .02$). Mean AIMS score for ND was 7.6 as compared to 5.2 for NC ($p < .004$), mean SHDS summed score was ND = 7.6, NC = 4.1 ($p < .001$), and mean SHDS global score was ND = 2.8 compared to NC = 2.1 ($p < .005$). There were no statistical differences in severity of parkinsonism (SHPS mean ND = 11.1, NC = 11.3), MMSE score (mean ND = 24.3, NC = 25.2), use of anticholinergic or other psychotropic drugs including antidepressants and lithium, or CNS disease including strokes.

Based on data from this retrospective cohort study, we propose that diabetics may be a risk factor for increased prevalence and severity of TD. Possible mechanisms for this predisposition will be discussed.

NR266 **Tuesday May 15, 12 noon - 2:00 p.m.**

DIAGNOSIS OF DYSPHAGIA IN PSYCHIATRIC INPATIENTS

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Summary:

Study of 31 choking incidents involving 27 psychiatric patients in a state psychiatric hospital over a one-year period revealed three major types of dysphagia: (1) bradykinetic and dyskinetic neuroleptic-induced dysphagia (Craig et al, 1982, Weiden and Harrigan, 1986); (2) festinating dysphagia, characterized by hasty consumption of meals and food gorging and: (3) paralytic dysphagia due to pervious CVA or other neurologic cause.

Twenty-one of the 27 patients were studied by videofluoroscopy. Eight of the 21 patients showed clinically unsuspected aspiration and/or penetration and two of these eight patients required placement of gastrostomy tubes. In several cases, findings included esophageal webs or strictures. Videoflouroscopy findings correlated with the severity of dysphagia, but not necessarily with the clinical type of dysphagia.

NR267 **Tuesday May 15, 12 noon - 2:00 p.m.**

DILTIAZEM SUPPRESSES QUINPIROLE-INDUCED STEREOTYPY

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Summary:

Tardive dyskinesia (TD) is one of the most serious untoward effects of chronic neuroleptic therapy. Dopaminergic receptor sensitization is assumed to be involved in its pathogenesis. Treatment with calcium channel blockers can suppress neuroleptic-induced behavioral supersensitivity to apomorphine in rats (climbing or aggression)(Grebb Et al., 1987; Pucilowski & Kostowski, 1988). We present the evidence that TD-like symptoms (oral stereotypy), elicited in haloperidol-withdrawn rats with a selective D2 dopaminergic agonist quinpirole, is suppressed by prolonged concurrent treatment with the calcium channel blocker diltiazem. Male Wistar rats were administered (b.i.d.) intragastrically haloperidol (2 mg/kg), diltiazem (5 mg/kg), diltiazem plus haloperidol, and water (controls) for 21 days. Forty-eight hours after withdrawal, the rats were injected ip with 0.3 mg/kg of quinpirole and observed for stereotypic behaviors (rearing, grooming, licking, tongue protrusions). There was significant overall between-group difference in the duration of grooming and the number of tongue protrusions. The haloperidol withdrawn rats scored markedly higher than control and diltiazem alone treated rats. Concurrent treatment with diltiazem and haloperidol prevented the increase of tongue protrusion episodes. We conclude that concurrent diltiazem and haloperidol administration can prevent the occurrence of some behavioral manifestations of dopaminergic receptor supersensitivity, including a lingual dyskinesia.

*Supported by Fogerty International Research Fellowship 1FO5 TWO4191 to O. Pucilowksi.

NR268 **Tuesday May 15, 12 noon - 2:00 p.m.**

DO NEUROLEPTICS CAUSE PAIN?

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Summary:

It is well documented that some patients with idiopathic or postencephalitic parkinsonism experience primary sensory symptoms, i.e., pain and paresthesias of presumed central dopaminergic origin. To preliminary test the hypothesis that neuroleptic-induced parkinsonism (NIP) is likewise associated with primary sensory symptoms, we prospectively interviewed and examined a consecutive sample of 60 acute inpatients on neuroleptics and 47 controls on psychotropic drugs other than neuroleptics. NIP and primary symptoms were operationally defined on the bases of structured interviews (derived from the McGill Pain Questionnaire) and standardized neurological examinations (derived from the Unified Parkinson's Disease Rating scale), independently conducted by two blind raters. The neuroleptic treated patients had significantly more complaints of pain than controls (23% vs 2; $p < .01$), but not of paresthesias (8% vs 9%). Eleven of the 21 patients with NIP complained about pain, compared with 3 of 36 patients without NIP (52% vs 8%; $p < .001$). The intensity of pain did not correlate with the severity of Parkinsonism score ($r = .07$). Pain was usually described as a poorly localized, intermittent, aching sensation mostly involving the four limbs and sparing the ventral torso. The results suggest that NIP may present primary sensory symptoms - mostly pain-, and generally support the desirability of extending studies of extrapyramidal side-effects of neuroleptics to include sensory complaints.

NR269 **Tuesday May 15, 12 noon - 2:00 p.m.**

HIGH DOSE BUSPIRONE IN TARDIVE DYSKINESIA

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Summary:

Tardive dyskinesia has become the major management problem of chronic psychoses. Theoretically, drugs which modulate dopamine supersensitivity but which will not exhibit up or down regulation of receptors are ideal for management of this condition. Buspirone theoretically appears to be the ideal such drug. It has mild "Intrinsic dopaminergic activity" (IC50 = 150/260nM) (1) and its dopamine agonist effect is at least partly mediated via non-dopamine mechanisms as depletion of dopamine stores does not block the reversal of phenothiazine-induced catalepsy. This is most likely through its partial agonism of the serotonin 1A receptor (IC50-15-20nM). (1),(2).

This paper reports an ongoing open pilot study of the successful usage of high doses of buspirone in tardive dyskinesia. Long standing TD patients off neuroleptics for greater than one month were evaluated by SCT HANS and AIMS scales. Early results are extremely promising. Severe TD requires doses of 100-160 mg/day; mild 40-60. Like the anxiolytic effect, the TD improvement takes several weeks to occur. Withdrawal of the buspirone takes several weeks to occur. Withdrawal of the buspirone exacerbates the TD but to a lesser extent than originally and reinitiation improves it.

The effects are blocked by giving cyproheptadine, suggesting that the mechanism is mediated by the serotonin receptor.

NR270 **Tuesday May 15, 12 noon - 2:00 p.m.**

DELAYED ONSET OF HYDROPHILIC B-BLOCKERS IN AKATHISIA

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Summary:

Improvement in neuroleptic-induced akathisia (NIA) is usually seen within 1-3 days of the initiation of treatment with relatively lipophilic -blockers (eg. propranolol)(1,2). The time course of the response to hydrophilic -blockers (eg. nadolol) has not been well established. Lipinski et al. (1) observed that nadolol was ineffective acute treatment of NIA. Rate (3) reported three patients who responded after 2 weeks of treatment with nadolol. We now report further data as to this time course of the improvement in 5 patients treated with nadolol 60-80 mg/day. Akathisia ratings were done at baseline and then every 1-3 days during treatment.

In four patients improvement was seen only after 12-14 days of nadolol treatment. Repeated measure ANOVA showed a significant overall effect on akathisia ratings; post-hoc planned comparisons (Scheffe F-tests) indicated that this was due improvement in ratings at day 12-14 of nadolol treatment. Thus, this investigation verifies both Lipinski's and Ratey's findings of a subacute, but not an acute, onset of action of nadolol, in that effect was not seen until two weeks.

We also treated a fifth patient with NIA, who had active neurosyphilis. This patient responded within one day of initiation of nadolol treatment. The rapid response of this patient suggests a central mechanism of action of -blockers in NIA, as the CNS syphilis infection presumably lead to a more permeable blood-brain barrier and more rapid penetration of nadolol. This is an ongoing investigation and additional data will be included at the time of presentation.

NR271 **Tuesday May 15, 12 noon - 2:00 p.m.**

SENSITIZATION TO NEUROLEPTIC TREATMENT

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Summary:

The importance of treatment schedule of neuroleptics in the development of tardive dyskinesia (TD) is of clinical relevance. The kindling phenomenon represents an example of the effect of multiplicity on neuronal plasticity. It bears resemblance to pharmacological sensitization. We have treated 85 rats discontinuously (DIS) or continuously (CON) with haloperidol (HAL) or zuclopenthixol (ZU) for 15 weeks. During and after treatment, we observed vacuous chewing movement (VCM) and tongue protrusions (TP). All HAL-treated animals showed an early rise in VCM. The rise during medication was less pronounced in ZU-treated rats. The change disappeared a few days after termination of CON medication. Remarkably, the significant change in DIS treated rats persisted 11 weeks after withdrawal. Only DIS treated animals developed a rise in the number of TP. After termination of medication HAL-treated rats were electrically kindled in amygdala. The results suggest a cross-sensitivity between DIS HAL-treatment and amygdala-kindling. The reversible increase in VCM seen from the first week of HAL-treatment might result from D1-receptor preponderance according to blockade of D2-receptors; this may be a model of acute dyskinesia. The persisting rise in VCM and TP observed only in DIS treated rats is suggested to be an animal model of TD. This is reconcilable with the hypothesis of a kindling-like sensitization to the dyskinetic side-effects of neuroleptic drugs.

NR272 **Tuesday May 15, 12 noon - 2:00 p.m.**

NEGATIVE SYMPTOMS AND AWARENESS OF DYSKINESIAS

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Summary:

We examined subjective awareness of abnormal involuntary movements (AIMs) and SANS ratings of negative symptoms in 57 schizophrenic (SCHZ) and 17 bipolar (BP) patients, all manifesting AIMs of at least mild severity. Negative symptoms were significantly higher in SCHZ than in BP patients. Otherwise, the groups did not differ in age at onset, years of education, or AIMs severity. Lack of awareness of AIMS was noted in 45 SCHZ and 8 BP patients ($X^2 = 6.6$; $p = .01$). Across the diagnostic groups, such unawareness was significantly associated with greater affective blunting ($p < .001$), alogia ($p < .001$), and anhedonia ($p < .001$), and orofaciolingual dyskinesia severity ($p < .05$). Affective blunting was associated with unawareness in both SCHZ and BP patients ($p = .02$ and .05, respectively). Unawareness of AIMs was not associated with age, age at onset, duration of illness, years of formal education, avolition, or attentional impairment, or limb-axial dyskinesia score. The findings suggests that subjective lack of awareness of AIMs may be a component of the "defect state." Its implications for issues of informed consent in patients receiving long-term neuroleptic treatment will also be discussed.

NR273 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

COST OF CAPITATED CARE FOR CHRONIC MENTAL ILLNESS

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Summary:

In 1987, a capitation program for the chronically mentally ill began in Rochester, New York, designed to allow seriously and persistently mentally ill patients to be discharged from the local State hospital. Aims included providing superior care, investigating the capitation model, and examining different administrative and clinical approaches to providing this care. Each of four CMHCs contracted to care for a similar set of chronic patients. Patients were divided into: group A, those who had spent the preceding three years in the State psychiatric hospital; group B, those intermittently hospitalized over three years before enrollment; and group C, those not hospitalized during the prior three years.

Costs of providing care varied significantly among providers; for group A, average per month costs ranged from $1,545 for the least costly CMHC to $2,646 for the most costly; for group B, $1,014 to $1,521; and group C, $475 to $1,762.

Across all four CMHCs, the percentage of total expenses, across all patient groups, were:

Hospitalization	4%	Emergency Department	0%	Medications	5%
Housing	11%	Case Management	11%	Treatment for Somatic Illness	1%
Clinic	21%	Psychosocial Clubs	5%	Spending Money	1%
Partial Hospitalization	22%	Transportation	1%	Miscellaneous	5%

While the clinical success of the demonstration will be reported elsewhere, this is reflected in the minimal cost of hospitalization and negligible use of emergency services.

NR274 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

CARBAMAZEPINE AND ACTH/CORTISOL RESPONSES TO CORTICOTROPIN-RELEASING HORMONE

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Summary:

Carbamazepine (CBZ) is an effective agent in the acute and the long-term management of major affective disorder, including rapid-cycling bipolar illness. Although mechanisms of action of CBZ have been delineated for seizure and pain disorders, relatively little is known about effects which may be important in recurrent affective illness.

Hypercortisolism is frequent in the depressed phase of major affective disorder. Previous data from our group and others implicate hypersecretion of corticotropin-releasing hormone (CRH) as the mechanism of hypercortisolism in major depression; this finding may be relevant not only to acute episodes but also to the pathophysiology and longitudinal course of affective illness, as CRH can alter behavioral and physiologic reactivity in a long-lasting fashion. We report here a study of pituitary-adrenal responses to exogenous ovine CRH (1 ug/kg, i.v.) from 8-10 pm in 25 patients with *DSM-III* major affective disorder (19 bipolar, 6 unipolar) studied both drug-free and during CBZ treatment. Seventeen patients were depressed prior to CBZ treatment (Hamilton score >16); two were manic; and six were euthymic or only mildly depressed. Five of the bipolar patients had ongoing or recent (within six months of study) rapid cycling. Responses to CRH were compared to a group of 43 healthy volunteers studied with CRH stimulation testing under identical conditions.

Basal plasma cortisol (F) levels were elevated in most depressed patients in the drug-free state; however, a subgroup ($n=7$) had low basal F levels. Euthymic and manic patients had normal basal F levels. While most depressed patients had blunted plasma ACTH responses to CRH prior to treatment, the subgroup of rapid-cycling patients had exaggerated ACTH responses (peak ACTH >25 pg/ml). Basal F, when elevated prior to treatment, significantly decreased on CBZ ($p<0.05$), while when initially low or normal tended to increase on CBZ. Plasma ACTH responses were variably affected by CBZ.

These findings suggest that the effects of CBZ on hypothalamic-pituitary-adrenal (HPA) function are dependent upon pretreatment HPA activity. They are particularly intriguing in the light of *in vitro* data showing that CBZ potently inhibits stimulated hypothalamic CRH secretion, while directly stimulating pituitary ACTH secretion. Hence, central CRH secretion would be normalized when initially elevated, but reduced when initially normal or low. These findings may have relevance, not only to the nosology of depression based on differences in baseline HPA activity, but also to mechanisms of CBZ's therapeutic actions in affective illness.

NR275 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

PTSD: RISKS FOR EVENT EXPOSURE AND SYNDROME

Naomi Breslau, Ph.D., Psychiatry, Henry Ford Hospital, 2799 West Grant Blvd., Detroit, MI 48202; Glenn C. Davis, M.D., Patricia Andreski, M.A.

Summary:

Studies of PTSD among civilians have focused mostly on victims of disasters. Little is known about the prevalence of traumatic events in the general population or on the risk for PTSD in persons exposed to trauma. We report on an epidemiologic survey of a random sample of 1,007 young adults (20-30 years of age) from a large HMO serving the Detroit, Michigan area. The NIMH DIS, revised according to *DSM-III-R*, was used. The sample was 60 percent female, 80 percent white.

Results: Thirty-nine percent reported traumatic events in their lifetime, chiefly physical attack or rape, serious accidents or injury, threat to life, seeing others or hearing about relatives seriously injured or killed. Lifetime prevalence of PTSD in the sample was 9.2 percent, 24 percent in those with traumatic events.

Multivariate analysis showed that low education, early conduct problems, use of drugs or alcohol, high extraversion, and family history of psychiatric disorder increased the risk of exposure to trauma. Neuroticism,, early separation from parents, and family history of anxiety increased the risk for PTSD in those exposed to trauma. In sum, PTSD risk factors are of two classes: (1) lifestyle factors that affect the risk of exposure to trauma, and (2) psychologic predispositions that affect individuals' response to trauma.

NR276 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

GENERALIZED ANXIETY DISORDER AND DYSTHYMIA: THE DETROIT EPIDEMIOLOGIC STUDY

Naomi Breslau, Ph.D., Psychiatry, Henry Ford Hospital, 2799 West Grand Blvd., Detroit, MI 48202; Glenn C. Davis, M.D.

Summary:

DSM-III-R defines generalized anxiety disorder (GAD) as chronic (six months) anxiety. GAD thus resembles dysthymia, a chronic (two years) affective distress with depressed rather than anxious mood. Despite differences in duration and symptom criteria, the distinctiveness of these disorders in the population is unknown. We report data from the Detroit Epidemiologic Study of 1,007 young adults, in which the Revised NIMH-DIS was used. The sample was 60 percent females, 80 percent whites, all 20 to 30 years old.

Lifetime prevalence of GAD was 3 percent and dysthymia, 3.2 percent. Both were more common in women and in the divorced or separated. The relative risk of dysthymia in persons with GAD was 11.3 and that of GAD conditional on dysthymia, 11.5. Anxiety and affective disorders were present in 80 percent of persons with GAD and 90 percent of dysthymics. Family history of depression and anxiety increased the risk for dysthymia but not for GAD. ANOVAs across four groups - GAD, dysthymia, Neither, Both - on scales of anxiety and depression showed greater general distress in dysthymia than in GAD. In persons with a history of generalized worry, duration of episodes was associated with increased anxiety and depression. The data suggest that persons with GAD or dysthymia suffer non-specific distress and that the more pervasive symptoms in dysthymia might be a function of its longer duration criterion.

NR277 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

DSM-III-R GENERALIZED ANXIETY DISORDER: THE DETROIT EPIDEMIOLOGIC STUDY

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Summary:

The revised definition of Generalized Anxiety Disorder (GAD) is more stringent than in DSM-III on two counts: it requires (1) 6 month duration and (2) that the worry be unrealistic or excessive. We previously reported that the longer duration markedly reduced the prevalence of GAD but increased its overlap with MDD. The effect of the second revision is unknown. We report on a recent epidemiologic study of 1000 young adults in Detroit, MI, in which the NIMH-DIS, revised according to DSM-III-R, was used.

The sample was 60% women, 80% whites, and ranged in age between 20 and 30. Lifetime prevalence of DSM-III-R GAD was 3%. If the "unrealistic or excessive" criterion were not applied, the prevalence would have increased twofold. DSM-III-R GAD was more common in females than in males (4.2% vs. 1.1%) and in the divorced or separated than the married (9.3% vs. 3%). Of persons with GAD, 50% had major depression (MDD) and 80% had an affective or another anxiety diagnosis. The strongest associations (in descending order) were with Mania, Dysthymia, OCD, MDD, and Panic. In 41%, the onset of GAD coincided with MDD or Dysthymia. Family history of anxiety did not increase the risk for GAD. The data do not support the diagnostic validity of the newly defined GAD.

NR278 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

FOLLOW-UP OF SOFT-SIGNS AND ANXIETY INTO ADULTHOOD

Eric Hollander, M.D., Psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; Concetta DeCaria, M.S., Bonnie Aronowitz, M.A., Michael R. Liebowitz, M.D., Donald F. Klein, M.D., David Shaffer, M.D.

Summary:

We have demonstrated that adult patients with obsessive-compulsive disorder have significantly more signs of central nervous system dysfunction than do matched controls (Hollander et al, 1990). A previous prospective follow-up study demonstrated that early soft-signs at age 7 were associated with the development of anxiety disorders in adolescence (Shaffer et al, 1985). Eight of these subjects with early soft-signs were restudied in early adulthood. The four with early soft-signs and adolescent anxiety disorders continued to have increased soft-signs and adult anxiety or affective disorders, including obsessive-compulsive disorder. The four with soft-signs and no adolescent anxiety disorder had only minimal soft-signs and no adult anxiety or affective disorders at follow-up, although obsessive-compulsive tendencies were present. The implications of these findings will be discussed.

NR279 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

PANIC ACUITY AFFECTS ANXIOGENIC VULNERABILITY

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Summary:

Reactivity to two anxiogenic challenges was examined relative to panic acuity in order to evaluate the importance of current "conditioned" state on the vulnerability to these stimuli.

IV lactate infusion and 60 mg oral fenfluramine were given to 26 patients meeting DSM-III-R criteria for PD. Using a Panic Acuity Index scale of 1-4, patients with more recent and more frequent spontaneous attacks scored higher reflecting a higher panic acuity.

There was a significant positive correlation between panic acuity and responses to lactate ($r = 0.6$; $p = 0.000$) and fenfluramine ($r = 0.5$; $p = 0.02$). Nine of 12 patients (75%) with high acuity (defined as having one or more panic attacks per week) reacted positively to both challenges in contrast to none of 14 PD patients with low acuity (1 attack or less per month) ($X2 = 12.9$; $p = 0.0003$).

There was no correlation noted between anxiogenic responses to lactate and fenfluramine in the same patient ($r = 0.2$; $p = ns$). Further, there was no association noted between positive anxiogenic responses to lactate and positive responses to fenfluramine in the same patient ($X2 = 0.72$; $p = ns$).

These findings demonstrate that anxiogenic reactivity to lactate or fenfluramine is exacerbated by high panic acuity in PD patients. The findings suggest that the "conditioned" state of the patient rather than putative underlying trait factors predominates in the evocation of experimentally induced panic-like reactions.

NR280 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

PREVALENCE OF PANIC ATTACKS IN ADOLESCENTS

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Summary:

Several studies have suggested that sudden episodes of severe anxiety, i.e. panic attacks (PA) occur in non-clinical subjects as well as in patients who respond to DSM-III-R criteria for panic disorders. A recent epidemiological survey (NIMH-ECA program) has also shown that in subjects reporting a history of PA, age of onset was found to peak at 15-19 years. In order to assess the frequency of panic attacks we undertook a survey in a population of high school students ($n = 608$; mean age 18.4 ± 1.3), by means of a self-rated structured questionnaire using DSM-III-R criteria. Trait-anxiety was also assessed in these subjects using the Spielberger scale. The results of this survey demonstrate a high frequency of panic attacks in high school students: 30% ($n = 181$) reported sudden episodes of acute anxiety accompanied by at least 4 of the DSM-III-R panic attack symptoms in their lifetime. This prevalence increased to 43% of the subjects if only 2 symptoms were required to define a panic attack. The mean age of onset of panic attacks was 14.8 ± 3.2 years. In the group of students reporting a history of panic attacks 35.8% reported one or two episodes in their lifetime and 12% reported more than four episodes during the month preceding the survey. These students included a significantly higher proportion of girls ($p < 0.002$), with higher scores of trait-anxiety ($p < 0.001$) and more frequent anxiety-associated symptoms, e.g. insomnia. Cigarette smoking was more frequent in the group of subjects with panic attacks ($p < 0.006$) but not alcohol nor coffee consumption. In most cases, the occurrence of a PA was preceded by a period of stressful lifetime events. The relevance of PA occurring in a non-clinical population will be discussed in relation to the psychopathological factors involved in the evolution of panic disorders. The preliminary results of a study assessing the reliability of the questionnaire used in this survey will also be presented.

NR281 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

COMORBIDITY OF SOCIAL PHOBIA WITH PSYCHIATRIC ILLNESS

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Summary:

Fifty-seven consecutively evaluated patients meeting the DSM-III-R criteria for social phobia were studied. Patients were referred to two Anxiety Disorder Clinics at McMaster University affiliated hospitals. All patients were interviewed using the Structured Clinical Interview for DSM-III-R (SCID). 82.5% of this sample of social phobic patients had a life-time diagnosis of mood disorder and 70% had had a major depression in their life-time. 33.3% of these patients had suffered from another anxiety disorder in their life-time while 28% had a life-time diagnosis of two other anxiety disorders. In these patients, the life-time diagnosis of panic disorder or panic disorder with agoraphobia occurred 49% of the time. A further 28% of these patients had suffered from alcohol dependence or abuse and 14% had suffered from substance abuse or dependence in their life-time. Social phobia predated the onset of any episode of a mood disorder 84% of the time and predated the onset of another anxiety disorder 63% of the time. Social phobia is associated with a number of psychiatric disorders. The fact that social phobia often predates these other disorders may demonstrate an etiologic role or may suggest that the diagnosis of social phobia predisposes individuals to other psychiatric illnesses.

NR282 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

CCK-4 VERSUS CO2 PANIC ATTACKS IN PANIC DISORDER

Jacques Bradwejn, M.D., Psychiatry, Mc Gill University, 3830 Lacombe Avenue, Montreal Quebec, Canada H3T 1M5; Diana Koszycki, M.A., Christian L. Shriqui, M.D.

Summary:

Inhalation of 35% carbon dioxide and I.V. injection of cholecystokinin-tetrapeptide (CCK-4) have both been reported to induce panic attacks in panic-disordered patients and healthy volunteers. Their seemingly unrelated neurochemical properties raises the question of whether these two agents induce panic attacks which are comparable with respect to symptomatology and severity. The present study compared the action of 25 micrograms I.V. of CCK-4 and inhalation of 35% CO_2 in 22 patients with panic disorder. DSM-III-R criteria, including anxiety of at least moderate intensity, plus patients' self-report that the induced attack was identical to or very similar to natural panic attacks were used to judge the occurrence of a panic attack. There was a trend for panic attacks to occur at a higher rate in the CCK-4 group than the CO_2 group (ten of eleven patients versus five of eleven) ($p = .06$, Fisher's Exact). Among patients who panicked with either CCK-4 or CO_2, there were no statistically-significant differences for the number of symptoms reported (mean $\pm$ SEM) {13.1 ± 1.4 (CCK-4) versus 10.6 ± 1.2 ($C0_2$)}, sum intensity rating of symptoms {33.9 ± 4.4 (CCK-4) versus 25.4 ± 3.9 (CO_2)}, and symptom profile. A common site of action or a multisystem pathophysiology with a common final pathway could explain these findings.

NR283 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

CHOLECYSTOKININ PANIC: PANIC DISORDER VERSUS AGORAPHOBIA

Jacques Bradwejn, M.D., Psychiatry, Mc Gill University, 3830 Lacombe Avenue, Montreal Quebec, Canada H3T 1M5; Diana Koszycki, M.A., Christian L. Shriqui, M.D.

Summary:

Patients with panic disorder (PD) or PD with agoraphobia (PDAG) experience similar rates of panic during biological challenges. In the majority of studies, response profiles of panic disorder subtypes have not been differentiated and it is unknown whether the panic attacks of PD or PDAG share a common pathophysiology. This study compared the responses of panic disorder subtypes to I.V. injections of 25 micrograms of cholecystokinin-tetrapeptide (CCK-4). A double-blind placebo (saline) controlled design with a randomized sequence of injection was used. The incidence of CCK-4 induced panic was similar for the two groups: 91% (10/11) for PD and 92% (11/12) for PDAG. PD and PDAG did not significantly differ with respect to onset of symptoms (seconds) (mean $\pm$ SEM) (PD = 27.6 ± 2.7 versus PDAG = 26.5 ± 2.4), duration of symptoms (minutes) (PD = 9.45 ± 2.0 versus PDAG = 10.92 ± 1.2), number of symptoms reported (PD = 12.1 ± 1.5 versus PDAG = 12.7 ± 0.6), and sum intensity rating of symptoms (PD = 31.1 ± 4.9 versus PDAG = 38.2 ± 1.9). The comparable sensitivity of PD and PDAG to 25 ug of CCK-4 might support a symptom (panic attack) rather than a syndrome specific pathophysiology. However, a CCK-4 specific mechanism unrelated to the pathophysiology of both PD and PDAG cannot be ruled out.

NR284 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

DOSE RANGING STUDY OF CCK-4 IN HEALTHY VOLUNTEERS

Jacques Bradwejn, M.D., Psychiatry, Mc Gill University, 3830 Lacombe Avenue, Montreal Quebec, Canada H3T 1M5; Diana Koszycki, M.A., Christian L. Shriqui, M.D.

Summary:

Cholecystokinin-tetrapeptide (CCK-4) is found in the mammalian CNS and binds preferentially to CNS CCK receptors. We reported that CCK-4 induced panic attacks in patients with panic disorders. The aim of the present investigation was to study the effect of three I.V. doses of CCK-4 (9, 25, and 50 micrograms {ug}) in healthy volunteers. A double-blind placebo (saline) controlled design with a randomized sequence of injection was used. DSM-III-R criteria, including moderate to severe anxiety, was used to define the occurrence of a panic attack. The percent of subjects who panicked with 9, 25, and 50 ug of CCK-4 was 11 (1/9), 17 (2/12), and 47 (7/15) percent, respectively. Oneway ANOVAs revealed significant dose-related differences for the number of symptoms ($p < .05$), sum intensity of symptoms ($p < .05$), and onset of symptoms ($p < .01$). Post hoc comparisons revealed significant ($p < .05$) differences between 50 and 9 ug of CCK-4 for the number of symptoms reported and sum intensity rating of symptoms. Subjects receiving 50 ug of CCK-4 also reported a more rapid onset of symptoms than those receiving either 9 or 25 ug. Although these findings do not elucidate the site and mechanism of action of CCK-4, they support a dose-related panicogenic effect.

NR285 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

PSYCHOLOGICAL CORRELATES OF RESPONSE TO INHALATION OF THIRTY-FIVE PERCENT CO2

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Summary:

This investigation examined the relationship between the psychological constructs of anxiety sensitivity and coping resourcefulness and response to inhalation of 35% CO_2. Reiss et al's Anxiety Sensitivity Index and Rosenbaum's Self-Control Schedule were completed by subjects with panic disorder (PD, $n = 15$), panic disorder with agoraphobia (PDAG, $n = 15$), and normal controls ($n = 15$) prior to CO_2 inhalation. $C0_2$ response measures included: number of somatic symptoms reported, number of somatic symptoms feared, number of DSM-III-R cognitions (e.g. fear of dying), and psychic anxiety (STAI, Speilberger et al). Pearson correlations failed to detect any significant ($p < .01$) relationships between anxiety sensitivity and coping resourcefulness and responses to CO_2 in either PD or PDAG. Anxiety sensitivity was not significantly correlated with responses to CO_2 in normal controls, however, a strong negative association between coping resourcefulness and the number of somatic symptoms reported was found ($r = -.76$, $p < .001$). On the whole, the results from the present study cast doubt on the belief that responses to biological challenges are largely influenced by psychological variables.

NR286 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

PLATELET ALPHA2-RECEPTOR BINDING IN PTSD, GENERALIZED ANXIETY DISORDER AND MAJOR DEPRESSIVE DISORDER

Rachel Yehuda, Ph.D., Psychiatry, University of Conn., 263 Farmington Avenue, Farmington, CT 06032; Bruce D. Perry, M.D., Steven M. Southwick, M.D., Earl L. Giller, Jr., M.D.

Summary:

Our previous work has suggested distinct neuroendocrinological differences in patients with post-traumatic stress disorder (PTSD) compared to patients with major depressive disorder (MDD) despite a large degree of symptom overlap between these two disorders. Patients with PTSD appear to be distinguishable from major depressed patients with respect to the 24-hour urinary excretion of several hormones, including cortisol, norepinephrine and epinephrine, and also in the regulation of glucocorticoid and alpha2-adrenergic receptors as measured in blood elements. These biological differences are found even in PTSD patients who present with a concurrent major depressive syndrome. In the present study, we compared platelet alpha2-adrenergic binding characteristics in hospitalized veterans with PTSD to patients with Generalized Anxiety Disorder (GAD) in order to determine the relationship between the anxiety syndrome as it occurs in PTSD compared to GAD. Platelet alpha2-adrenergic binding was also examined in veterans with endogenous MDD and in a group of normal controls. The results showed that patients with PTSD had significantly fewer alpha2-adrenergic binding sites than patients with either MDD or GAD, and normal controls. Patients with MDD or GAD were not significantly different on any receptor measure, but had significantly more binding sites than both PTSD and normal control groups.

NR287 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

CSF OPIOID ACTIVITY IN PANIC PATIENTS AND CONTROLS

R. Bruce Lydiard, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; Kathleen T. Brady, M.D., James C. Ballenger, M.D., Michele T. Laraia, R.N., Jenny Shook, Ph.D., Mark D. Fossey, M.D.

Summary:

The role of the endogenous opioids in the affective and anxiety disorders has been an area of considerable interest and investigation. Naloxone, a specific opioid receptor antagonist, for example, has been shown to be anxiogenic. Stress and phobic exposure have been shown to increase plasma beta-endorphin levels, although lactate infusion in panic disorder patients has not been associated with significant increases. Recently, two investigators have reported the cerebrospinal fluid (CSF) beta-endorphin levels in panic disorder patients (Eriksson et al, 1989), and in panic disorder patients recently detoxified from alcohol (George et al, 1989) were increased relative to normal controls. To further investigate these interesting findings, we assessed opioid activity in the CSF of panic disorder patients and normal controls. *METHODS*: After 4 days of a low monoamine diet and 9 hours of bedrest, CSF was obtained (15-26th cc) from 25 panic disorder patients (5 males and 20 females, ages 35.6 ± 8.8 yrs., mean ± SD) and 14 normal controls (7 males and 7 females, ages 30.7 ± 7 yrs., mean ± SD), frozen on dry ice and stored at -70 degrees centigrade until assay. CSF samples were assayed for beta-endorphin and dynorphin by radioimmunoassay. *RESULTS*: No significant age or sex differences were noted. We found no difference in beta-endorphin or dynorphin in panic disorder patients vs. normal controls. Using height as a covariate did not affect this finding. Positive correlation was found between beta-endorphin levels and depression ratings in patients with Hamilton Depression scores of less than 18 and between Hamilton Anxiety ratings and beta-endorphin levels in normals, but not in panic disorder patients. These findings suggest that there may be abnormal regulation of endogenous opioid activity in panic patients.

NR288 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

CSF MONOAMINE METABOLITES IN OBSESSIVE COMPULSIVE DISORDER

R. Bruce Lydiard, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; James C. Ballenger, M.D., Everett H. Ellinwood, Jr., M.D., Michele T. Laraia, R.N., Linda S. Austin, M.D., Mark D. Fossey, M.D.

Summary:

Abnormalities in serotonin function in patients with OCD have been observed in a variety of studies. Evidence from treatment studies suggests that specific serotonin uptake inhibitors are more effective than less selective agents in treating OCD. Challenge studies indicate that these patients are more sensitive to compounds which stimulate serotonin receptors than other anxious patients or normal controls. CSF 5-hydroxyindoleacetic acid (5-HIAA) levels have been reported to be higher in patients with OCD than in normal controls. We report here the results of our studies of CSF metabolites in patients with OCD. *METHODS*: After 9 hours bedrest and 4 days of a low monoamine diet, lumbar punctures were performed on fasting patients between 9 and 10 a.m. CSF samples were frozen on dry ice and stored at -70 degrees Centigrade until assay. Subjects included 25 nondepressed patients with OCD and 17 normal controls. CSF concentrations for 5-HIAA, the dopamine metabolite homovanillic acid (HVA) and the norepinephrine metabolite 3 methoxy-4hydroxy-phenylethyleneglycol (MHPG) were determined in the laboratory of W.Z. Potter, M.D., Ph.D. *RESULTS*: No significant differences were found between patients and normal controls in demographic characteristics. The levels of these amine metabolites were not different between patients and controls. This study failed to support the previous findings of higher 5-HIAA. Practical and theoretical implications will be discussed.

NR289 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

NORADRENERGIC FUNCTION IN PANIC: NEW CSF FINDINGS

R. Bruce Lydiard, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; James C. Ballenger, M.D., Michele T. Laraia, R.N., Mark D. Fossey, M.D.

Summary:

There has been considerable speculation and investigation of potential abnormalities of noradrenergic function in patients with panic disorder. Measures of plasma and urinary catecholamine (CA) levels in panic disorder patients have not been consistently different from normal controls. We previously reported that levels of the monoamine metabolites MHPG, HVA, and 5-HIAA in the cerebrospinal fluid (CSF) of panic disorder patients were substantially different than normals. Investigations into the relationship of these monoamine metabolites to each other in healthy controls and various patient groups have shown, in general, high correlations between HVA and 5-HIAA. MHPG has been found to correlate with HVA and (in women) 5-HIAA. We report the findings of such an analysis of the CSF from panic disorder patients and normal controls. *METHOD*: After 4 days of a low monamine diet and 9 hours of bedrest, CSF (15th-26th cc) was obtained from 25 panic disorder patients and 14 normal controls, frozen on dry ice immediately, and stored at -70 degrees centigrade until assay. Pearson or Spearman's correlation was performed as indicated. *RESULTS*: Significant correlations were found in controls between HVA and 5-HIAA (p 0.0001), MHPG and 5-HIAA ($r = 0.70$; p 0.03), and MHPG and HVA (p 0.03). In panic disorder patients HVA and 5-HIAA were highly correlated (p 0.0001), but MHPG did not significantly correlate with either 5-HIAA ($r = -0.04$; p 0.84) or HVA ($r = 0.172$; p 0.41).

These data indicate that abnormal noradrenergic regulation in panic patients may exist. Theoretical and practical implications will be discussed.

NR290 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

IMIPRAMINE BINDING PREDICTS RESPONSE IN PANIC DISORDER

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Summary:

Alprazolam has been found to be an effective treatment of panic disorder and agoraphobia in comparison to placebo; however there was a considerable placebo response. We have reported (Pecknold et al, 1989) that alprazolam-treated patients with panic disorder have an increase in the number of high affinity platelet tritiated imipramine binding sites which significantly correlated with improvement in symptoms of anxiety, depression and a decrease in the number of panic attacks. 43 patients with DSM III panic disorder were treated over an 8 week period with either alprazolam (22 patients) or placebo (21 patients). Prior to the onset of treatment, these patients had determination of 3H-imipramine binding obtained from platelet rich plasma. Patients were divided into responders, nonresponders on the basis of response to the HAM-A scale; the 31 responders had imipramine binding BMax of 812 and the 12 non-responders BMax of 943 ($p < .09$). When the groups are analyzed according to alprazolam-placebo, the 16 alprazolam responders' BMax was 808 and the non-responders 1063 ($p < .03$). For the placebo group, the differences were not significant. The same pattern was observed for the response on the HAM-D scale but no significant findings were obtained when response/non-response was analyzed on the panic attack nor phobic scales.

Our findings are that alprazolam-treated patients who respond to treatment as measured by the HAM-A have a significantly lower BMax than those who do not respond or are treated with placebo. These observations correlate with our findings on a smaller number of patients who had BMax determined before and at the end of treatment.

NR291 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

PANIC DISORDER COMPARING DRUG AND PSYCHOTHERAPY

M. Katherine Shear, M.D., Psychiatry, Payne Whitney Clinic, 525 East 68th Street, New York, NY 10021; Andy Leon, Ph.D., Laura Portera, B.A., Gerald L. Klerman, M.D.

Summary:

Imipramine (Imi) is widely recognized as an effective antipanic agent. Recent studies indicate that cognitive behavioral treatment (CBT) alone is also effective in blocking panic. A prospective controlled study is needed to provide definitive data comparing the two approaches, and will shortly be underway. However, this study will take more than five years to complete. We have conducted two prospective randomized treatment trials with panic disorder patients, one using medication alone and the other psychotherapy alone. Although patients were not randomly assigned to these protocols, the two studies overlapped in time and enrolled patients who are roughly comparable. Several outcome measures were identical. We present here a comparison of the outcome of the two studies. *Methods*: Group 1 consists of 14 patients who received Imi in a 16-week placebo controlled randomized trial. Dose was increased to a maximum of 300 mg unless full symptom remission or unacceptable side effects occurred before this dosage was achieved. Group 2 consists of 20 patients randomly assigned to receive 15 weeks of CBT or a psychoeducation, reflective listening treatment. Both groups completed weekly diaries reporting panic and anticipatory anxiety and the SCL-90 symptom checklist pre- and post-treatment. Each group also completed ratings of depression and phobic avoidance. *Data Analysis*: Two way repeated measures analysis of variance was done testing the effects of treatment and time.

Results: 1) There were no significant differences in responder rate defined as panic free or as greater than 50 percent reduction in weekly panic. Using the latter criteria both treatments achieved a 90 percent response rate. 2) There was a highly significant time effect on each subscale of the SCL-90. There were no significant group differences on any scale, but there was a trend suggesting greater decrease in the drug group which was related to slightly higher pretreatment scores. 3) The drug group had significantly higher mean pretreatment 4) symptom panic episodes than the psychotherapy group (7.9 vs 2.2/week) and, therefore, had a significantly greater reduction in panic ($p<01$).

NR292 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

TRICHOTILLOMANIA AND OBSESSIVE COMPULSIVE DISORDER

Melinda A. Stanley, PH.D., Psychiatry, Univ of TX Medical School, 1300 Moursund Street, Houston, TX 77030; Theron C. Bowers, M.D., Alan C. Swann, M.D.

Summary:

Trichotillomania has been viewed as a variant of obsessive-compulsive disorder (OCD), with apparent similarities in the nature of symptoms and efficacy of treatment with clomipramine. Here we compare psychopathology and treatment response to fluoxetine in these two groups. Three patients with trichotillomania and three patients with OCD were treated with fluoxetine for 12 weeks. All trichotillomania patients had noticeable hair loss, and pulled an average of *51* hairs daily. OCD patients spent approximately 2-3 hours per day with obsessions and rituals.

The Yale-Brown Obsessive-Compulsive Inventory (YBOC) and Hamilton Depression and Anxiety Scales (HAMD, HAMA) were administered, and all patients kept daily records of obsessions and rituals. In trichotillomania, these measures estimated thoughts and behaviors surrounding hair-pulling. At pretreatment, trichotillomania patients were less anxious (HAMA = 8 vs 15), less depressed (HAMD = 9 vs 16), and spent less time obsessing (Ms = 136 vs 204 minutes/day). Time spent ritualizing (Ms = 202 vs 211 minutes/day) and YBOC scores (Ms = 16 vs 19) were similar.

Fluoxetine was increased from 20 to 80 mg/day by the end of week 2. All trichotillomania patients showed decreases in number of hairs pulled, with two reporting over 50% improvement during the first week. Two trichotillomania patients reported exacerbation of symptoms between weeks 6 and 12. OCD patients demonstrated initial improvement more gradually, but were more likely to maintain gains throughout treatment.

NR293 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

PLASMA VASOPRESSIN ELEVATED BY STRESSFUL INTERVIEW

James L. Meyerhoff, M.D., Med Neuroscience, WRAIR/WRAMC, Washington, D.C. 20307; Marvin Oleshansky, M.D., K. Kalogeras, M.D., Edward H. Mougey, M.D., George P. Chrousos, M.D., Larry Granger

Summary:

A stressful 30 min interview increased plasma levels of vasopressin (VP), ACTH, β -endorphin (β-EP), β-lipotropin (β-LPH), plasma renin activity (PRA) and heart rate in healthy male volunteer subjects. These elevations occurred within 7 min of beginning the interview: VP (39%), ACTH (59%), β-EP (79%), β-LPH (42%), PRA (123%) and heart rate (27%). Plasma glucose levels and osmolality were unchanged at this time, therefore, neither hypoglycemia nor hyperosmolality contributed to the VP response. By twenty-two min after the end of the interview, all values had returned to baseline levels, except PRA which remained elevated. Levels of atrial natriuretic peptide did not change. We believe this to be the first report that psychological stress elevates VP in normal subjects. Given the effects of VP on blood pressure and water retention, coupled with the effects of PRA on blood pressure (via angiotensin II) and sodium retention (via aldosterone), this model would appear to be useful for the study of the effects of psychological stress on blood pressure. VP can also stimulate ACTH release and thus might augment the pituitary-adrenal response to stress, thereby accentuating stress-induced hypercortisolemia. Finally, these data are of interest because of the reported behavioral effects of VP.

NR294 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

EFFECT OF IV PROCAINE ON ALCOHOLICS WITH PANIC

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Summary:

Symptoms of paroxysmal tachycardia, sweating and trembling provide strong evidence for autonomic dysfunction in patients with panic disorder. However, studies on peripheral measures of sympathetic nervous system activity have not demonstrated consistent differences between panic patients compared to control populations. To explore the role of the parasympathetic nervous system in panic disorder, we administered procaine HCL (1.8mg/kg IV over 30 sec) to controls ($n = 10$), alcoholics ($n = 17$), and alcoholics with panic disorder ($n = 7$). We quantitated behavioral changes and heart rate and vagal tone. Procaine is a local anesthetic which has anecdotally been reported to induce panic attacks and is thought to selectively activate the limbic system. All subjects were medication and alcohol free for 3 weeks prior to the study. Parasympathetic activity was measured using a vagal tone monitor which quantified the amplitude of respiratory sinus arrhythmia from beat by beat heart rate variability. The results show a difference between groups (2/15 alcoholics, 5/7 alcoholics with panic disorder, 2/10 controls) for the induction of a panic attack ($\text{chi sq} = 9.59$, $df = 2$ $p < .01$). Panic patients showed a greater increase in heart rate per change in vagal tone compared to the other groups. These preliminary results suggest procaine may be a useful probe to study panic disorder. Secondly, alcoholics with panic disorder appear to be more automatically reactive than control populations. Additional panic patients with and without alcoholism are needed to confirm and further elucidate these findings.

NR295 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

A PILOT STUDY OF FLUOXETINE FOR TRICHOTILLOMANIA

Ronald M. Winchel, M.D., Neurochemistry, NYS Psych. Inst., 722 West 168th Street, New York, NY 10032; Barbara Stanley, Ph.D., Jeannine Guido, M.A., J. Sidney Jones, M.D., Kelly Posner, B.A., Michael Stanley, Ph.D.

Summary:

Trichotillomania (compulsive hair-pulling) has been generally refractory (or poorly responsive) to traditional treatments, including dynamic psychotherapy, behavioral therapy, hypnosis and anxiolytic agents. Recently, Swedo et al (NEJM 321(8); 497-501, 1989) have reported improvement in symptoms of trichotillomania in patients treated with clomipramine, a 5-HT uptake blocker.

We have investigated the clinical efficacy of fluoxetine in the treatment of this disorder. Thirteen patients have been enrolled in an open pilot study. Fluoxetine (up to 80 mg/day) was administered for 16 weeks. Data analysis at this time has shown that fluoxetine is effective in reducing the symptoms of trichotillomania. The mean onset of response to fluoxetine was 4.1 weeks from initiation of treatment.

Our results indicate that patients with this disorder can be distinguished from patients with obsessive-compulsive disorder by low scores on other measures of obsessional behavior. They also do not demonstrate an unusual incidence of impulsive behaviors and therefore, cannot be easily categorized as being at either end of the compulsive/impulsive spectrum.

NR296 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

EARLY ONSET PHOBIAS AND LATER MAJOR DEPRESSION

Alan F. Schatzberg, M.D., Psychiatry, MMHC, 74 Fenwood Road, Boston, MA 02115; Jacqueline A. Samson, Ph.D., Anthony J. Rothschild, M.D., Rachel Bruno, B.A., Monica Luciana, B.S., Sandra Cole, M.S.

Summary:

Several recent studies suggest that early onset phobic disorder may lead to later major depression (MD) in childhood or adulthood. For example, Kovacs et al (*Arch Gen Psychiatry* 46:776-782, 1989) reported that some two-thirds of children with MD had a history of antecedent anxiety, particularly separation anxiety. We report on the possible role early phobic disorders may play in the development of MD. Data presented are derived from the McLean Hospital Depression Research Facility Study begun in 1985 to explore the relationships between psychosocial and biochemical measures in drug-free depressed patients at baseline as well as at one, three, and five years of follow-up. Diagnostic assessment is performed using SCID-P and SCID-II instruments. These data are complemented by any other historical information to derive a *DSM-III-R* diagnosis by two experienced clinicians/investigators. Baseline data are presented on the initial 69 depressed patients (32 men and 37 women, mean ± SD age = 34 ± 10 years). The mean ± SD HDRS score was 21 ± 5. Of the 69 patients, 62 percent experienced a *DSM-III-R* anxiety disorder at some time in their lives and 52 percent met criteria for a current anxiety disorder. Social phobia was the most common disorder (28 percent lifetime prevalence), followed by obsessive-compulsive disorder (22 percent), panic (16 percent), and simple phobia (10 percent). In 15 of the 28 unipolar MD patients with a history of anxiety, the initial MD episode occurred at least two years after the onset of the anxiety disorder. In this group, the mean ± SD age of onset of anxiety disorder of 11 ± 5 years was significantly lower than the mean ± SD age of onset of the initial episode of MD (24 ± 9). Eleven of these 15 patients with MD secondary anxiety experienced onset of social (N = 8) or simple phobia (N = 4) before age 14.

NR297 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

LYMPHOCYTE BETA-ADRENORECEPTORS IN PANIC DISORDER

Richard J. Maddock, M.D., Psychiatry, Univ of Calif. Davis, 4430 V. Street, Sacramento, CA 95817; Cameron S. Carter, M.B., Joseph R. Magliozzi, M.D., Dorothy Gietzen, Ph.D.

Summary:

Considerable evidence suggests that alteration of noradrenergic functioning is an important feature of panic disorder. The density of beta-adrenoreceptors on lymphocyte membranes has been shown to correspond to the sensitivity to beta receptor medicated responses in other peripheral systems. Many studies have demonstrated down regulation of lymphocyte beta adrenoreceptors in major depression. Two recent studies reported similar findings in panic disorder. We now report on 20 patients with panic disorder who participated in a clinical trial of adinazolam. Prior to treatment, patients had significantly lower beta-receptor density (iodine-125-labeled cyanopindolol binding) than 20 control subjects (X = 41.1 Fmol/mg protein vs X = 73.5 Fmol/mg, p = .01). There was no difference in receptor affinity. Patients who responded with ≥50% decrease in symptoms after 5 weeks of treatment (n = 10) had significantly lower pretreatment beta-receptor density that nonresponders (X = 30.1 Fmol/mg vs X = 52.1 Fmol/mg, p = .03).

Down regulation of beta-adrenoreceptors in panic disorder may represent an adaptive, homeostatic response to the illness. These preliminary findings support the hypothesis that greater down regulation prior to treatment is associated with a better treatment response. Data on functional sensitivity of the lymphocyte beta-adrenoreceptor (isoproterenol stimulated CAMP production) will also be presented.

NR298 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

EFFECTS OF FLUVOXAMINE ON YOHIMBINE ANXIETY

Andrew W. Goddard, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Dennis S. Charney, M.D., George R. Heninger, M.D., Scott W. Woods, M.D.

Summary:

The alpha-2 adrenergic receptor antagonist yohimbine (YOH) produces robust anxiogenic effects, in panic disorder (PD) patients presumably via a noradrenergic mechanism. The aim of this study was to investigate the effects of chronic effective treatment with the specific 5HT reuptake inhibitor fluvoxamine on YOH-induced anxiety. Methods: Fifteen patients (37 ± 10 years, 7M, 8F) with DSM III-R PD completed a double-blind placebo controlled study of fluvoxamine (FLUV). YOH (0.4 mg/kg IV) and placebo challenges were performed during a three week drug-free period preceding randomization and again after nine weeks of treatment. Within challenge measurements included visual analog scale (VAS) anxiety, DSM III-R somatic panic symptoms, and plasma cortisol (CORT) and MHPG. Results: Six of 8 patients met response criteria on FLUV, as compared to 2 of 7 completing placebo treatment. In the FLUV group, the net YOH VAS anxiety response was reduced from 48.8 ± 47.9 mm at baseline to 11.8 ± 44.8 ($p < .06$). In the placebo group, the net response was reduced only from 41.9 ± 20.9 to 40.7 ± 26.3, NS. The difference between FLUV and placebo effects on the net YOH anxiety response was statistically significant ($p < .04$, Mann-Whitney U-test). FLUV but not placebo reduced DSM III-R somatic panic symptoms after YOH (breathlessness, faintness, and fear of loss of control). CORT levels in both FLUV and placebo groups rose significantly after YOH as expected but there was no significant effect of treatment in either group. MHPG data will be reported. Conclusions: Effective chronic treatment with FLUV appears to reduce YOH-induced anxiety and somatic symptoms as compared to relatively ineffective chronic placebo treatment. Possible mechanisms for this effect, including interactions between serotonergic and noradrenergic systems, will be discussed.

NR299 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

POSTPARTUM ONSET OF PANIC DISORDER

Diane E. Sholomskas, Ph.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Scott W. Woods, M.D., Lisa Dogolo, B.A., Deborah W. O'Brien, R.N.

Summary:

Recent case reports have documented that the onset of panic disorder in the postpartum period has rarely been reported. The extent to which these may be coincidental events is the focus of this investigation.

Method: Forty-seven childbearing women treated at the Yale Anxiety Research Clinic between 1982 and 1989 were interviewed by telephone and their charts reviewed. Panic disorder in the postpartum period was defined as the first panic occurring within 12 weeks of the woman's first childbirth.

Results: Most women had panic with agoraphobia. Four women met criteria for postpartum onset which occurred a mean of 9.7 weeks post delivery. Forty-three reported the first onset of panic at a time other than the postpartum period. The expected percentage of postpartum onsets in the sample (1.4 percent) was calculated as the number weeks of risk for panic in the first postpartum period divided by the total number of weeks of risk for a first postpartum times 47 times 100 percent. The finding of 8.5 percent postpartum onsets is significantly greater than the expected rate, $X^2 (1) = 15.51$, $p < .001$.

Discussion: This investigation's data indicate that first onset of panic in the postpartum period is not a coincidental event. Further consideration of postpartum panic as a discrete entity and suggestions for further research will be discussed.

NR300 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

DRUG/BEHAVIOR TREATMENT OF PANIC: STUDY DESIGN

Diane E. Sholomskas, Ph.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; David H. Barlow, Ph.D., Jacob Cohen, Ph.D., Jack M. Gorman, M.D., Karla Moras, Ph.D., Laszlo A. Papp, M.D., M. Katherine Shear, M.D., Scott W. Woods, M.D.,

Summary:

Existing studies document the efficacy of both pharmacological and behavioral treatments for agoraphobia. Behavioral treatment for agoraphobia differs from newly developed cognitive behavioral treatments for Panic Disorder and few studies have investigated the pharmacological treatments for Panic Disorder without agoraphobia. This NIMH supported multicenter comparative treatment study will investigate the relative efficacy of Panic Control Therapy (PCT), (a cognitive behavioral treatment), Imipramine, and the combination in panic disorder with minimal or no avoidance.

METHOD: Four sites (SUNY Albany, Cornell, Hillside/Columbia, and Yale) will enroll 480 patients over four years in randomized clinical treatment trial for DSM-III-R Panic Disorder with or without mild Agoraphobia. The three active treatments are Panic Control Therapy (PCT), Imipramine plus medical management (IMI), and the combination (PCT & IMI). Two control conditions are pill placebo plus medical management (PLA) and PCT plus placebo (PCT & PLA) for a total of five treatment conditions. A four by five factorial design will compare treatments in a 12 week acute phase, a 6 month maintenance and a 6 month follow-up.

DISCUSSION: The total sample size and the distribution of the sample within treatment conditions were derived from extensive power analyses to optimize the chance of detecting a difference of one panic attack per week between the three active treatment conditions. A description of manual-guided therapies, quality control procedures, cross-site coordination procedures and the data management plan will be presented.

NR301 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

AN OPEN TRIAL OF FLUOXETINE IN PTSD

Christopher J. McDougle, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Steven M. Southwick, M.D., Ronald L. St. James, A.C.S.W., Dennis S. Charney, M.D.

Summary:

Post-traumatic stress disorder (PTSD) (*DSM-III-R*) is characterized by reexperiencing, avoidance, and hyperarousal. To date, only four controlled pharmacological trials have been reported in PTSD. This open trial examined the efficacy of fluoxetine in Vietnam war veterans with chronic PTSD. *METHODS*: 20 consecutive male Vietnam war veterans with PTSD (mean $\pm$ SD age, 41.2 $\pm$ 2.2 years), referred to an outpatient medication clinic, completed 4-48 weeks (mean $\pm$ SD duration, 26.9 $\pm$ 13.9 weeks) of treatment with fluoxetine (mean $\pm$ SD dose, 35.0 $\pm$ 20.4 mg/day). Global clinical response was assessed on the 7-point CGI scale (7 = "very much worse," 1 = "very much improved"; responder = 2 or 1). Response in the three primary PTSD symptom clusters was assessed using the same scale. Response of comorbid major depression was assessed. *RESULTS*: Thirteen of the 20 patients (65 percent) responded to treatment with fluoxetine. There were highly significant differences on the CGI in responders as compared to nonresponders: (Clinician-Global, 1.9 $\pm$ 0.3 vs 3.6 $\pm$ 0.8, $p < 0.0001$), (Reexperiencing, 2.3 $\pm$ 0.6 vs 3.7 $\pm$ 0.8, $p < 0.0001$), (Avoidance, 1.9 $\pm$ 0.8 vs 4.0 $\pm$ 0.0, $p < 0.0001$), and (Hyperarousal, 2.6 $\pm$ 0.7 vs 3.7 $\pm$ 0.8, $p < 0.003$). A significant symptom cluster effect was found in responders (One-Way ANOVA: $F = 4.0$, $df = 2$, $p < 0.03$). Tukey's Studentized range test indicated a significant difference between avoidance and hyperarousal scores ($p < 0.05$), suggesting that reduction of avoidance symptoms contributed substantially to global improvement in responders. Comorbid major depression ($p = 0.52$, Fisher's exact test) was not associated with response. *CONCLUSION*: This study suggests that fluoxetine may be an effective treatment for some patients with chronic combat-related PTSD. In fact, all 13 responders continued to be maintained on fluoxetine. The data suggest that improvement resulted from a reduction in core symptoms of PTSD, rather than an antidepressant effect. Unlike previously reported controlled trials with tricyclic antidepressants and/or phenelzine, fluoxetine reduced symptoms of avoidance. A controlled comparison with placebo is necessary to definitely answer questions of efficacy.

NR302 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

LITHIUM AUGMENTATION IN FLUVOXAMINE REFRACTORY OBSESSIVE COMPULSIVE DISORDER

Christopher J. McDougle, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Lawrence H. Price, M.D., Wayne K. Goodman, M.D., Dennis S. Charney, M.D., George R. Heninger, M.D.

Summary:

Despite success with inhibitors of serotonin (5-HT) reuptake (e.g. fluvoxamine (FVX)) in OCD, many patients are unimproved with these agents. This double-blind placebo-controlled study examined the efficacy of adding lithium carbonate to an ongoing treatment trial in 24 patients with primary OCD who had failed to respond to FVX. METHODS: 24 patients (12 inpatients, 12 outpatients) with OCD (*DSM-III-R*) were randomized to two weeks of treatment with active (N = 12) or placebo (N = 12) lithium augmentation of ongoing FVX treatment. Outcome was assessed with Y-BOCS scores before and after the addition of lithium to FVX. Global clinical response was assessed on the CGI. RESULTS: Two of 12 (17 percent) patients met criteria for meaningful clinical response (one marked, one partial) to active lithium, whereas no patients demonstrated a response to placebo. Active lithium augmentation of FVX was associated with a significant improvement in scores on the Y-BOCS (-4.1 ± 5.0, $p < .02$, paired t-test, two-tailed), and on the HAM-D (-6.3 ± 8.7, $p < .03$). There were no significant changes on these measures in the placebo lithium-treated group. There were also significant between-group differences as measured by the Y-BOCS ($p < .03$, student's t-test). An analysis of all patients treated subsequently with 3-5 weeks of open active lithium augmentation (N = 20) found a significant improvement in Y-BOCS scores (-4.4 ± 5.4, $p < .002$), 7/20 (35%) patients showed a qualitative response (one marked, six partial). Neither a comorbid diagnosis of major depression nor severity of baseline depression were associated with treatment response. CONCLUSION: In this double-blind placebo-controlled study lithium produced a small but statistically significant reduction in obsessive-compulsive symptoms in comparison to placebo. Although the 35 percent response rate of open lithium augmentation in this sample of OCD patients on FVX is close to a previously reported 44 percent response rate of treatment-resistent depressed patients on FVX, the depressed patients had a larger symptom reduction. This may reflect different mechanisms of action of lithium augmentation in OCD and depression, and/or pathophysiological differences between the two disorders.

NR303 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

ON THE AGORAPHOBIA/SIMPLE PHOBIA BOUNDARY

George C. Curtis, M.D., University of Michigan, Med Inn 444/0840, 1500 East Medical Center, Ann Arbor, MI 48109; Joseph A. Himle, M.S.W., Julie A. Lewis, B.A., Yue-Joe Lee, M.D.

Summary:

In *DSM-III-R*, "situational" phobias, such as heights (acrophobia), enclosures (claustrophobia), driving, or flying may be diagnosed as simple phobias if they occur alone, or as part of agoraphobia if they occur in the context of an agoraphobic syndrome. Review of the literature suggests that "simple" "situational" phobias have ages of onset, manners of onset, and family histories more like agoraphobia than like other simple phobias. The Epidemiologic Catchment Area (ECA) study provides demographic and clinical information on a representative community sample of roughly 18,000 people, including 2,025 people reporting some type of phobia. In re-analyses of these data, subjects with acrophobia or claustrophobia had ages of onset, patterns of co-occurrence with other phobias, and lifetime histories of panic attacks or depression which differed significantly on most variables from subjects with animal phobias, and were closer to subjects with agoraphobia. On most of the same variables, claustrophobia differed significantly from acrophobia, having an earlier age of onset, more co-occurring phobias, a higher proportion of women, and a more frequent lifetime history of panic attacks and major depression. Acrophobia and especially claustrophobia, even when occurring as the only phobia, appear to be more closely related to agoraphobia than to other simple phobias.

NR304 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

MAINTENANCE DRUG THERAPY OF PANIC DISORDER

George C. Curtis, M.D., University of Michigan, Med Inn 444/0840, 1500 East Medical Center, Ann Arbor, MI 48109; Juan Massana, M.D., Claudio Udina, M.D., Jose L. Ayuso-Gutierrez, M.D.

Summary:

This study attempted to address a shortage of information on maintenance drug therapy of Panic Disorder with or without Agoraphobia. 1168 such patients were entered into a multicenter, flexible dose trial comparing alprazolam, imipramine and placebo. In the first 8 weeks the active treatments were about equally effective. Alprazolam had a more rapid onset of action, fewer side effects and fewer dropouts. Consenting patients at four sites then entered a 6 month maintenance phase on the same double blind treatment. There were 78 patients on alprazolam, 65 on imipramine, and 38 on placebo, or 58.2%, 47.1%, and 27.3% of the initial samples. Continuing patients had improved more than noncontinuers. Otherwise, on most measures, continuers proved representative of the initial samples, and the 3 maintenance groups were comparable to each other. During the maintenance phase average dose remained stable for all groups. All groups retained most of their initial improvement. On most measures, including dropout rates, there was a very slight, gradual shift of advantage away from alprazolam and toward imipramine. Despite differential dropout rates and nonrandomized samples in the maintenance phase, the results probably give a fair estimate of expectations for patients who remain on each treatment.

NR305 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

COMORBIDITY OF ANXIETY DISORDERS IN OBSESSIVE COMPULSIVE DISORDER PATIENTS

Linda S. Austin, M.D., Psychiatry, MUSC, 171 Ashley Avenue, Charleston, SC 29494; R. Bruce Lydiard, M.D., Mark D. Fossey, M.D., Michele T. Laraia, R.N., James C. Ballenger, M.D.

Summary:

Obsessive-compulsive disorder (OCD) shares numerous clinical features with other anxiety disorders. In order to study the relationships between OCD and other anxiety disorders, 36 OCD patients were administered the Structured Clinical Interview for DSM III (modified for DSM III-R). Fourteen of 36 (38%) had experienced panic attacks at some point in their lives, four of whom reported panic attacks before the onset of OCD. Five of 36 patients (14%) met DSM-III-R criteria for panic disorder at the time of the interview. This is significantly greater than the six-month prevalence at three sites of 0.6%, 1.0% and 0.9%, in the normal population as reported in the ECA study. Seven of 36 patients (20%) met DSM-III-R criteria for one or more simple phobias, and five of 36 patients (14%) reported social phobias. Eighteen patients were treated with clomipramine in doses of at least 100 mg/day for three months. Eight of 11 patients (73%) with other anxiety disorders responded to clomipramine with moderate to marked improvement, while only 1 of 7 patients without other anxiety disorders responded, a difference which is statistically significant (p 0.05). The data are consistent with other studies that suggest that OCD patients should be carefully screened for the presence of other anxiety disorders.

NR306 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

DIAGNOSIS OF ANXIETY DISORDER: INSIGHTS FROM SCL-90

Cary L. Hamlin, M.D., 500 Route 24 Suite 2B, Chester, NJ 07930

Summary:

Because of symptom overlap among disorders in DSM-3R, differential diagnosis may be difficult. To examine these overlaps, similar patient groups meeting criteria for panic disorder (PD,49), social phobia (PD,49), social phobia (SP,14), obsessive-compulsive disorder (OCD,16) dysthymia (DYS,18) filled out the SCL-90. Mood items (55) were selected for study. Predictions were made based upon expected differences in responses. As expected, PD patients had significantly greater panic scores than OCD patients, but unexpectedly not greater than SP or DYS (one tailed student's T, $p < .05$). As expected, self-consciousness, feeling inferior were higher in SP than PD, but not higher in DYS than SP. In PD vs SP, crying easily, thoughts of death, fear of fainting, feeling weak, hypochondriasis, guilt were higher, but feeling trapped, fearful, avoiding places were lower. In PD vs DYS, dizzyness, hypochondriasis were greater, but anxiety to be left alone wasn't. Self-blame, loneliness were higher in DYS vs PD. In PD vs OCD, agoraphobia, fear of fainting, dyspnea, chest pain were greater. There are 78 significant differences between group means, and these comparative data are examined as a possible aid to clinical diagnosis.

NR307 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

POST-EARTHQUAKE FEARS IN GIRLS WITH PANIC ATTACKS

Chris R. Hayward, M.D., Psychiatry, Stanford University, Behavioral Medicine Program, Stanford, CA 94305; Joel D. Killen, Ph.D., Ruthven D. Patrick, M.A., C. Barr Taylor, M.D.

Summary:

The October 17th earthquake in the Bay Area occurred between two assessment phases of a longitudinal psychiatric study of bulimia, depression, and panic attacks in sixth and seventh grade girls. We hypothesized that students who had previously experienced a panic attack would be most vulnerable to having a fearful and subsequently avoidant response to the earthquake, compared to those with different psychiatric symptoms or those without psychiatric symptoms. To assess post-earthquake avoidance, we developed a questionnaire which asked about fear of bridges, freeways, going to school, and being left alone since the earthquake. The questionnaire was administered two weeks after the earthquake to a sample of 286 seventh grade girls. For analysis the sample was divided into three groups: those with a previous history of panic attacks ($N = 11$); those previously reporting symptoms of either bulimia or depression ($N = 57$); and those without psychiatric symptoms ($N = 218$). Comparing mean scores on the post-earthquake avoidance questionnaire the panic group scored higher than either those with psychiatric symptoms or those without symptoms ($F = 3.8$, $df = 2,252$, $p = 0.005$). These results indicate that seventh grade girls with a history of panic attacks are at risk for having avoidant responses to frightening unexpected events, such as an earthquake.

NR308 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

URINE PH IN PANIC: A SIMPLE SCREENING DEVICE

Laszlo A. Papp, M.D., Psychiatry, Columbia Univ. LIJ, 722 West 168th Street, New York, NY 10032; Jack M. Gorman, M.D., Jeremy D. Coplan, M.D., Eric Hollander, M.D., Donald F. Klein, M.D.

Summary:

Research suggests that complex respiratory changes may be etiologically and clinically significant in the development of panic. The exact nature of these changes, however, is still unclear. Venous blood gasses in panic disorder patients (PD) are consistent with a baseline state of mixed chronic and acute respiratory alkalosis, while arterial blood gasses are only consistent with baseline acute respiratory alkalosis.

While traditionally overlooked, renal compensatory mechanisms are significantly different during chronic and acute hyperventilation. Acute respiratory alkalosis is accompanied by alkalotic urine production, chronic respiratory alkalosis produces normal urine pH.

We found that 14 untreated PD patients had significantly higher urine pH($\pm$ SD) than 13 age- and sex-matched controls (7.0 ± 0.7 vs 5.5 ± 0.5; $T = 6.69$, $p < 0.001$). This finding suggests that patients with panic disorder may suffer from a series of discreet hyperventilatory episodes perhaps superimposed on chronic hyperventilation.

Since acute hyperventilation in response to stress is most likely to normalize following breathing retraining and it is the only type accompanied by abnormal urine pH, if these findings hold up, screening urine pH may be a simple test of respiratory status, and the success of breathing retraining in patients with PD.

NR309 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

CRF AND TRH IN THE CSF OF PANIC PATIENTS

Mark D. Fossey, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; R. Bruce Lydiard, M.D., Michele T. Laraia, R.N., Garth Bissette, Ph.D., Charles B. Nemeroff, M.D., James C. Ballenger, M.D.

Summary:

The purpose of this study was to examine the CSF of patients with panic disorder for evidence of dysregulation of CRF and TRH. Both have been reported to be high in patients with major depression. Lumbar punctures were performed on 23 patients with panic disorder and 14 normal controls to measure levels of CRF and TRH. Levels of CRF did not differ significantly between panic patients and normal controls (44.50 pg/ml vs 46.10 pg/ml). Neither did levels of TRH differ significantly between the two groups (1.85 ± 0.86 pg/ml vs 2.35 ± 0.84 pg/ml). No correlation between CRF and TRH was noted. There was a trend for HAM-D scores to be directly proportional to levels of TRH ($p = .13$) however, no relationship was noted between HAM-D scores and CRF. These results do not support the hypothesis of dysregulation of CRF and TRH in patients with panic disorder. Larger samples are needed to explore the suggestion that TRH is associated with depression in panic patients.

NR310 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

EXPERIMENTS WITH THE BUSPIRONE METABOLITE 1-PP

Marc L. Leavitt, Ph.D., Psychiatry, Allegheny General Hosp., 320 East North Avenue, Pittsburgh, PA 15212; Trevor R.P. Price, M.D., Joseph C. Maroon, M.D.

Summary:

Our previous work indicates that subcutaneous unlike intracerebroventricular (IVT) infusion of the anxiolytic buspirone reduces aggressive behavior in rats (1). Buspirone is metabolised to a number of metabolites including 1-pyrimidinyl-piperazine or 1-PP. The presence of higher brain concentrations of 1-PP than its parent following injection of buspirone suggests that 1-PP may contribute to buspirone's effects (2). The present study examined whether the ineffectiveness of IVT-buspirone in our previous study was due to insufficient brain levels of 1-PP. This was tested by measuring the effects of IVT 1-PP infusion in rats previously treated with 6-OHDA (200ug, IVT) to enhance mild footshock-induced attack behavior or SIA (3). SIA was measured prior to infusion of either 1-PP (5 or 7mg/kg/day, N = 7) or sterile water (0.5ul/hr, N = 9) via indwelling osmotic minipumps which were connected to a lateral ventricular cannula. Rats were monitored every 2-3 days over the 2 week infusion. Neither treatment reduced SIA. The mean ($\pm$ SEM) number of attacks for the 1-PP group was 28.8 $\pm$ 2.0 before, versus 32.6 $\pm$ 2.4 and 35.6 $\pm$ 1.1 on the first and second weeks of infusion respectively. Control rats attacked 34.2 $\pm$ 1.3 times before versus 34.5 $\pm$ 1.4 and 32.6 $\pm$ 1.7 times during the first and second weeks of water infusion respectively. These results suggest that brain 1-PP is not responsible for the antiaggressive actions of systemically infused buspirone thus further indicating a peripheral site of action.

Supported by Allegheny-Singer Research Institute.

NR311 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

VERTICALITY PERCEPTION IN AGORAPHOBIC PATIENTS

Jean-Claude Bisserbe, M.D., Inerm U320, Centre Esquirol, Chu Cote De Nacre, Caen 14033, France; Jean-Philippe Boulenger, M.D., Bernadette Laverdure, Edouard Zarifian, M.D.

Summary:

Dizziness and unsteadiness are among the most frequent symptoms reported by panic disorder patients (PD). Distortion of space and floating sensations have also been reported. In recent works it has been suggested that abnormal vestibular function could play a role in the occurrence of PD (Jacobs et al.; Stein et al.). We present here the first results from an investigation of the verticality perception in anxious patients using the Rod and Frame Test (RFT). RFT enables the exploration of the relative contribution of different sensory systems involved in the perception of verticality. 24 anxious patients, 16 PD (13 with agoraphobia, 3 without) and 8 other anxious patients were compared to 24 control subjects matched for age and sex in two RFT conditions, head straight (standard) and head tilted. Patients were diagnosed according to DSM-III-R criteria and anxiety was assessed using the Speilberger State and Trait Inventory, the Hamilton Anxiety Rating Scale and COVI anxiety scale. Perception of verticality as obtained with the RFT in standard conditions (head straight) was significantly less accurate in anxious patients than in controls. Modification of the experimental conditions (tilting the head), changing the relative contribution of the different sensory systems involved in the perception of verticality, induced a relative improvement in agoraphobic patients compared with non-agoraphobic anxious patients and controls. The results obtained with the two experimental conditions will be discussed in relation to the clinical characteristics of the patients. The possible involvement of the different sensory systems participating in the perception of space in the expression of different types of anxious disorders will be considered.

NR312 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

A PLACEBO-CONTROLLED STUDY OF VALPROATE IN MANIA

Susan L. McElroy, M.D., McLean Hospital, 115 Mill Street, Belmont, MA 02178; Harrison G. Pope, Jr., M.D., Paul E. Keck, Jr., M.D., James I. Hudson, M.D.

Summary:

A growing number of studies over the past 15 years, mostly uncontrolled, suggest that the antiepileptic valproate may be effective in the treatment of the manic phase of bipolar disorder. We performed a placebo-controlled double-blind study of valproate in 36 patients with acute mania. All were either resistant to or intolerant of treatment with lithium. Treatment duration ranged from 7-21 days. No other psychotropic medications were allowed, with the exception of lorazepam given up to 4 mg per day as needed for agitation during the first ten days of treatment. Valproate plasma concentrations were reported three times weekly to an unblinded investigator, who adjusted dosage to produce plasma concentrations between 50-100 mcg/ml.

Valproate was superior to placebo in reducing manic symptoms. Nine of 17 (53 percent) patients receiving valproate demonstrated a 50 percent or greater improvement on the Young Mania Rating Scale (MRS), as compared to two of 19 (11 percent) patients receiving placebo ($p = .010$). Patients assigned to active drug demonstrated a median 54.3 percent decrease in scores on the MRS as compared to a median 5.0 percent decrease among patients receiving placebo ($p = .003$). Valproate-treated patients also displayed significantly reduced scores on the Global Assessment Scale and the Brief Psychiatric Rating Scale, and required significantly fewer doses of lorazepam. Valproate's clinical effect appeared rapidly; responders, those with 50 percent or greater improvement on the MRS, demonstrated a median 58 percent improvement within seven days of treatment. Adverse effects were infrequent, with no adverse effect occurring significantly more frequently with valproate than with placebo.

NR313 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

MODE OF ONSET SIMPLE PHOBIA SUBTYPES

Joseph A. Himle, M.S.W. Psychiatry, Univ of Michigan, 1500 E. Medical Center Drive, Ann Arbor, MI 48109; David Crystal, M.S.W., George C. Curtis, M.D., Thomas E. Fluent, M.D.

Summary:

Previous research has demonstrated heterogeneity of the simple phobic diagnostic category. Differences in age of onset, sex ratio, family history and co-morbidity have been demonstrated in clinical samples. It has been proposed that circumscribed situational phobias of heights, enclosures, driving, flying, bridges, etc., resemble more closely the agoraphobic syndrome than other Simple Phobias such as animal or insect phobias. As a further test of the notion of heterogeneity of the DSM-III-R Simple Phobia diagnostic category, the mode of onset was examined in a sample of 84 Simple Phobic outpatients. In keeping with a prior study using nearly the same sample of phobic patients (Himle, et al., 1989), patients were separated into one of four subtypes: animal or insect ($n = 23$); blood and injury ($n = 10$); "situational" (heights, enclosures, driving, flying, etc.)($n = 41$); and choking-vomit phobias ($n = 10$). Careful study yielded five distinct mode of onset categories. Two researchers independently determined the mode of onset for the patients studied: Direct Trauma ($n = 38$); Spontaneous ($n = 20$); Vicarious Learning ($n = 9$); Gradual (no specific event)($n = 6$); Lifelong (no recalled specific event)($n = 5$). Significant mode of onset differences were observed ($p < .0002$) across groups. Mode of onset differed between the situational group and the animal group ($p < .0011$) with situational phobics accounting for 18 of the 20 spontaneous modes of onset found in this study, while the animal phobics reported a predonderance of direct trauma and vicarious learning modes of onset with no reported spontaneous onset. Spontaneous onset among situational phobics was also mainly responsible for significant mode of onset differences between the situational and B1 groups ($p < .0047$) and the situational and choking-vomit group ($p < .0461$), with onset mode among the B1 and the choking-vomit groups again mainly characterized by direct trauma or vicarious learning. These results offer further evidence of the heterogeneity of the Simple Phobia diagnostic category and also support the contention of "situational" Simple Phobias being closely related to Agoraphobia.

NR314 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

PANIC ANXIETY: DIAZEPAM/CLOMIPRAMINE COMPARISON

Sergio Gloger, M.D., Psychiatry, University of Chile, Bucarest 118-B, Santiago, Chile; Francisco O'Ryan, M.D., Danica Gladic, Alexei Franulic, M.D., Mario Barahona, R.N.

Summary:

Few studies have compared tricyclics to classic benzodiazepines in panic anxiety. Clomipramine has been reported to be effective in small doses, in open trials. This study compares the treatment outcome of clomipramine and diazepam, in an 8 week double-blind design, and six months of follow-up. Sixty nine outpatients were accepted (D.S.M.-III 300.01, 300.21); After two washout weeks, two groups of 25 patients, assigned randomly, completed the trial. Seven rating scales were administered, including a daily panic-attack inventory, and the Clinical Global Impressions (C.G.I.).

Clomipramine dosage was 10-100 mg (mean 61.3; 12 patients 50 mg or less), and diazepam 5-50 mg. (mean 28.8). Most clomipramine patients (23/25), showed very much or much improvement (C.G.I.). Significant differences (t test) were found in favor of clomipramine in mean number of major panic attacks ($p < .05$), C.G.I. improvement and therapeutic effect ($p < .01$), and G.H.Q. ($p < .025$).

Seventeen patients treated with clomipramine completed 24 weeks of follow-up; further improvement was observed. Eight patients completed the diazepam treatment; twelve were changed to other tricyclics and five dropped out.

These findings support a better outcome of panic disorder treated with tricyclic over diazepam; and the effectiveness of relatively small doses of clomipramine in a controlled study.

Supported by FONDECYT grant 472-89).

NR315 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

SEASONAL BIAS IN THE ONSET OF FIRST PANIC ATTACK

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Summary:

The lifetime prevalence of panic disorder is about 1.5 per cent in the general population. Recently, two new findings detained our attention. In one hand, Weissman et al. (1989), in a general population study, have described that panic disorder and attacks are associated with an increased risk of suicidal ideation and suicide attempts. In other hand, Leliott et al. found that most of agoraphobic patients with panic disorder (1.0) experienced their first panic rather in late spring and summer (May through August) than in fall and winter.

In an ongoing study of comorbidity of anxiety disorders, we assessed the month of first panic in 101 outpatients with Panic Disorder with or without Agoraphobia consecutively seen at the Anxiety Clinic (Hopital Bichat-Paris). Among them, 75 could recall the month or the precise date of their first attack. All the patients were assessed with a semi-structured diagnostic interview: the S.A.D.S.-S.A.

In this population, 30 were agoraphobics and 45 suffered from P.D. without agoraphobia. We replicated the findings of Lelliot Et al. (1989) and extended them to patients with P.D. In fact, 52 subjects out of 75 had their first panic in late spring or summer and 23 experienced their initial attack in fall or winter (p.01). Furthermore patients who experienced their first panic in spring or summer had an increased risk of suicide attempt than other. The occurrence of the first panic was not related to agoraphobia neither to social phobia, or sociodemographic characteristics.

The results are discussed according in an integrative perspective where neurobiological and cognitive factors may interract.

NR316 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

EFFICACY OF SHORT-TERM INPATIENT TREATMENT: A 6 TO 18 MONTH FOLLOW-UP STUDY

Jeffrey M. Jonas, M.D., Cape Psych Centers, Cape Code Hospital P.O. Box 640, Hyannis, MA 02601; Jeff Eagle, Ph.D., Allyson McClave, B.S., Nancy Smith, M.S., Alice Zimmerman, M.Ed.

Summary:

Although there is a growing interest in short-term inpatient treatment of psychiatric patients, there are few controlled follow-up studies documenting the efficacy of this approach. We conducted a blind follow-up study of 68 patients hospitalized on a short-term inpatient psychiatric unit. Follow-up after discharge was obtained for 6-18 months, using a structured telephone interview conducted by a blind rater using a methodology we have described elsewhere (Ref.1). Statistical analysis was performed using probit regression and chi-square. The mean age for the sample was 36.2 years (range 13-76). The mean length of stay was 16 days with a bimodal distribution of 10 and 15 days (range 1-88 days). We found that 75% of our patients were not re-hospitalized by the end of the study, a re-hospitalization rate of 25%, which compares favorably with rates seen in longer-term hospitalization. Factors significantly related to avoiding re-hospitalization included living with family ($P < .05$), having regular interactions with friends and family ($P < .006$), and the patient's admission diagnosis ($P < .007$). Global occupational and social functioning were found to be significantly related to diagnosis ($P < .002$), the type of medications prescribed ($P < .05$) and having interactions with friends and family ($P < .04$). Of the 17 patients who were re-hospitalized, 6 stated the reason for this was stopping recommended treatments, 5 stated that they did not follow through with aftercare plans, and 6 stated that they had new problems which necessitated re-hospitalization. We conclude that short-term inpatient hospitalization is an effective means of psychiatric treatment, but that most re-hospitalization results from a failure of compliance with after-care plans. Short-term hospitalization may be more effective when closely coupled with outpatient providers.

NR317 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

REDUCTION IN MATERNAL DEPRESSIVE SYMPTOMS FOLLOWING MISCARRIAGE: THE EFFECT OF RESEARCH INTERVIEWS

Richard Neugebauer, Ph.D., Sergievsky Ct., Columbia University, 630 West 168th Street, New York, NY 10032; Jennie Kline, Ph.D., Patricia O'Connor, Ph.D., Pat Shrout, Ph.D., Jim Johnson, Ph.D., Andrew E. Skodol, M.D., Judith Wicks, B.A., Mervyn Susser, B.Ch.

Summary:

In a prospective study designed to assess effects of spontaneous abortion on depressive symptoms in the 6 months following loss, we observed a substantial reduction in symptom levels at the time of women's second or later study interview. 382 miscarrying women were first interviewed at 2 weeks, 6 weeks or 6 months after loss. At their first contact subjects were questioned on current psychiatric symptoms, and physical and psychosocial aspects of the pregnancy including warning signs, anticipation and circumstances of the loss. Interviews were administered by telephone by lay personnel. 318 community women, not pregnant in the preceding year, comprised one comparison cohort interviewed once. Depressive symptoms were measured with the Center for Epidemiologic Studies-Depression scale (CES-D); symptom levels are expressed in terms of proportions of women with pronounced symptomatology (scores of 30 +). the women interviewed at 6 weeks and 6 months after loss comprised two groups: those women being interviewed for the first time at that point and women being reinterviewed.

At 2 weeks after loss, 36% of miscarrying women scored 30 + on the CES-D, as compared to 10% of community women. At 6 weeks and at 6 months after loss, 20 to 30% of miscarrying women, being interviewed for the first time, scored 30 + . At each point, these miscarrying women were significantly and substantially more depressed than the community women. However, at 6 weeks and 6 months after loss, the CES-D scores of reinterviewed women were no different from those in the community. These findings persist in analyses adjusted for potentially confounding variables. Possible explanations include selection bias or a possible test or therapeutic effect of study interviews. Our interpretation is that a 1-2 hour structured telephone interview by nonprofessionals, conducted within 6 weeks of loss, may produce substantial reduction in depressive symptomatology.

NR318 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

PSYCHIATRIC SYMPTOMS AND THE CAPACITY FOR WORK

Robert P. Liberman, M.D., Psychiatry, UCLA & Brentwood VA, Wilshire & Sawtelle Blvds, Los Angeles, CA 90073; Jim Mintz, Ph.D., Mary Jane Arruda, M.S., H. Keith Massell, Ph.D., Harvey E. Jacobs, Ph.D., Carol Giannini, M.S.

Summary:

Four hundred and ninety patients with various *DSM-IIIR* psychiatric disorders plus 79 normal controls participated in either a three-day or 15-day work evaluation in which they engaged in a spectrum of basic work activities (e.g., filing, assembling, electronics). They completed a comprehensive psychiatric evaluation (Present State Exam, BPRS, Target Symptom Scales), assessment of social and independent living skills, and were followed for 12 months for their psychiatric, social, and vocational status. Multivariate analyses and late structure analysis was carried out on the data and revealed that psychiatric symptom severity—independent of diagnosis—was the main determinant of vocational disability. Other factors contributed to disability during the follow-up period--restrictions in social activities, poor daily living skills, and poor performance on the work capacity evaluation—but these were primarily related to subjects' severity of symptoms. Comorbidity with substance abuse did not increase disability during the follow-up period. Quality of life as perceived by the subjects was highly correlated with vocational status. This study validated elements of the current Social Security Administration criteria for adjudicating psychiatric disability.

NR319 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

REDUCING DISABILITY IN SSDI APPLICANTS

Samuel O. Okpaku, M.D., Psychiatry, Vanderbilt University, School of Medicine, Nashville, TN 37232; Leonard Bickman, Ph.D., Kathryn H. Anderson, Ph.D., J.S. Butler, Ph.D.

Summary:

The mentally ill represent a large proportion of the disabled population. For example, in 1987, 19.9% of Social Security Disability Insurance (SSDI) new awards and 25.3% of those on the rolls were disabled as a result of mental illness. The corresponding payments were $18.0 billion. Therefore, interest in innovative programs to increase the exit rates of these individuals is increasing. Other salient trends have resulted in a greater emphasis in rehabilitation of the mentally ill. Among these is the shift in philosophies concerning the capability of the mentally ill to work and the increasing advocacy for these individuals to gain access to a better quality of life.

The paper describes the preliminary results of a project that randomly assigns SSDI mentally impaired individuals into an experimental and a control group prior to knowledge of the results of their applications. The experimental group receives the joint services of an interdisciplinary case management team and the front line services of specially trained, specific task (work) vocational rehabilitation specialists. The outcome variables are length of time until finding a job, type of mental health and vocational services received, mental health status, and the characteristics of the successful SSDI applicants.

NR320 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

EVALUATION OF PSYCHIATRIC PROBLEMS AMONG IRANIAN IMMIGRANTS IN CANADA

Aghdas A. Bagheri, M.D., Psychiatry, Queen St. Mental Hlth Ctr, 99 Avenue Road Suite 701, Toronto Ontario, Canada M5R 2G5

Summary:

Since 1979, the number of Iranian immigrants in Canada has continued to grow from 4000 to approximately 30000 in 1988. This study is the result of a review of 111 charts of Iranian patients who were referred for psychiatric treatment during the period of July 1985 through March 1988. 98% of these patients arrived in Canada after the Iranian revolution which started in 1979 and the Iran-Iraq war of 1980. 10% of these patients were experiencing trauma as a result of their involvement with the revolutionary government or the war. The symptoms presented were in accordance with the DSM III criteria for post traumatic stress disorder. 60% met the criteria of adjustment disorder with depressed or anxious mood. 6% had been subjected to physical and psychological torture and confinement. Symptoms were worse for these people and, except for one, all received in-patient treatment. Of both post traumatic stress disorder and adjustment disorder patients, 56% responded to a combination of chemotherapy and psychotherapy and the rest to psychotherapy alone. This is the first study that looks at the prevalence of psychiatric illness among Iranians and illustrates the effect of migration and displacement in the integrity of the psychic life of this ever-growing population. The study also demonstrates the cultural variation in the presentation of mental illness in this population.

NR321 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

BEHAVIOR THERAPY FOR IMMIGRANT HISPANIC FAMILIES

Cynthia A. Telles, Ph.D., Psychology, Univ of Southern Calif., Seeley G. Mudd Bldg, Los Angeles, CA 90089; Steven R. Lopez, Ph.D., Rosario H. Mendrano, M.S.W., Gloria de la Cruz, M.S.W.

Summary:

We present how behavior family therapy was adapted for use with low income immigrant Hispanics who have a family member with schizophrenia. The modifications were made to address the central incompatibilities between the therapy as originally conceived and the sociocultural reality of this population. As part of a longitudinal treatment outcome study, 17 primarily Spanish-speaking families have been treated with this therapy. Adjustments have been made in all the treatment components: education, communication skills, and problem solving. For example, some exercises in communicating feelings, such as looking the parent directly in the eyes, may reflect a lack of respect for the parent. Therefore, one treatment modification allows the therapist to make adjustments with regard to this communication exercise. In general, the modifications primarily concern the treatment process, from the manner in which the therapist engages the patient and their family, to how family problems are resolved. Based on this experience, we propose guidelines that can be used to adapt therapies for special populations, particularly for cultural minorities.

NR322 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

RELIGIOUS VARIABLES IN DRUG AND ALCOHOLIC OUTPATIENTS

Shimon Waldfogel, M.D., Psychiatry, Jefferson Med'l College, 1651 Thompson Bldg. 11 Walnut, Philadelphia, PA 19107; Paul R. Wolpe, Ph.D., Ronald Serota, M.D., Brenda Byrne, Ph.D.

Summary:

Though religious variables have been correlated with mental illness rates in general, little work has been done on patients with substance abuse problems. Understanding a patient's religious beliefs may be particularly important in this population due to the spiritually oriented programs of many drug and alcohol self-help groups such as AA, CA and NA. This study is an initial attempt to determine the distribution of religious affiliations and subjective religious attitude among a population appearing for outpatient treatment for substance abuse. Of 141 patients agreeing to fill out the questionnaire in an urban, downtown, university affiliated outpatient clinic, religious affiliation was 34.4% Protestant, 37.5% Catholic, 5.5% Muslim and 2.3% Jewish. 20.3% were unaffiliated. 76.6% reported moderate to strong religious belief, and 83.2% reported that God made a daily difference in their lives. Despite the fact that 40% reported attending religious services at least once a month, only 13.9% reported having spoken to their clergyman about the problem that brought them to treatment. Neither religious affiliation nor strength of belief was correlated with length of stay in treatment or tendency to actually show up for an initial visit. However, those who had seen a clergyman about their problems did have a greater tendency to enter and remain in treatment. Clearly religious variables have a correlation to important factors in treatment planning for drug and alcohol patients. More work is needed to help the clinician evaluate the patient and the best avenues for outpatient communication between clergy and clinicians also seems important for those patients who are strongly connected to their church as a source of social support.

NR323 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

THE DETERMINANTS OF DISABILITY

Bruce M. Smoller, M.D., Psych Medicine Group, Chevy Chase, 5530 Wisconsin Avenue Ste. 806, Chevy Chase, MD 20815; Virginia Leone, C.R.C.

Summary:

The *purpose* of this on-going study is to investigate the relationship between certain workplace and personality-based factors and the incidence/duration of disability.

The *method* of the study involved three phases. I. A data base from the Columbia Graduate School of Business was used to correlate the incidence of lost-time disability and variety of workplace factors. II. Site studies at IBM and Mt. Sinai Hospital were developed to validate these factors. III. In cooperation with the NIH pain studies unit, a study of personality factors most highly correlated with lost-time disability is being conducted via the use of a personality survey form.

The *results* of the studies so far (data base and IBM) indicate that the work factors most important in the genesis of disability are: access to management, participation in grievance process, management style, and company involvement/follow-up post-injury or illness. The Mt. Sinai and NIH studies are still on-going.

The *importance* of the research lies in the fact that time lost from work and disability affect 31.4% of the American workforce and costs over 120 billion a year in lost-time, indemnity and lowered productivity. With a better understanding of the precursors of disability, treatment can be made more precise and thus effective. In the future, "at risk" employees may be identified and appropriate interventions developed.

NR324 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

MANAGED MENTAL HEALTH CARE AND MEDICAL COST OFFSET

Bernard S. Rappaport, M.D., American Biodyne, 400 Oyster Point Blvd Ste 218, S. San Francisco, CA 94080; Michael S. Pallak, Ph.D., Nicholas A. Cummings, Ph.D.

Summary:

A large HCFA-sponsored randomized prospective research study investigated the effects of outpatient mental health treatment services in 10,279 continuously eligible Medicaid recipients in Honolulu, Hawaii. Changes in costs of medical services following mental health intervention showed statistically significant decreases for those patients treated in the managed care setting ($n = 337$), as compared with those receiving other mental health treatment ($n = 1,1993$) or no treatment at all. The medical cost offset effect was especially apparent in the subset of patients with chronic medical diagnoses (CMD). The data were analyzed to differentiate new and continuing mental health treatment (MHT) subjects, with at least 18 months of utilization data pre- and post the six month mental health treatment period. Medical utilization costs for new MHT-CMD patients receiving managed mental health care services declined by $1,074, while new patients receiving MHT from other providers increased by $704 ($t = 3.11$, $p < .01$). For continuing MHT-CMD patients the figures were -$1,154 for managed care versus +$117 for non-managed care ($t = 2.73$, $p < .01$). Implications for evaluating and valuing emerging forms of quality, cost-effective mental health treatment delivery models (unrestricted but managed mental health care benefits) will be discussed as a research alliance on the road to clinical excellence.

NR325 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

EFFECTS OF INVOLUNTARY PATIENTS' RIGHT TO REFUSE PSYCHOTROPICS

Yvette I. Sheline, M.D., Psychiatry, Valley Medical Center, 820 Enborg Court, San Jose, CA 95128; Martha C. Beattie, Ph.D

Summary:

In June 1989 California Supreme Court decision - "Riese" gives psychiatric patients on involuntary holds the right to refuse psychotropic medication. The only exceptions are a life threatening emergency or judicial determination of incapacity to make treatment decisions. To assess the effect of the Riese ruling a prospective sample of 272 psychiatric evaluations was studied in a large county emergency psychiatric service which primarily treats involuntary patients. Patients who "successfully" refused medication were compared to those who refused but were given medication under emergency provisions and to patients who consented to medication. 150 patients were prescribed medication. Of these, thirteen patients (9%) were refusers, 23 (15%) were emergencies, 38 (25%) had legal guardians, and 76 (51%) were voluntary consenters. Although emergencies had the highest acuity on Axis V scores (24.0 vs 34.7 refusers; 36.0 conserved; 38.8 voluntary, $p = .01$), refusers fared the worst on two outcome indices: longest length of stay (p .05) and number hospitalized (refusers 85%; conserved 63%; emergencies 52%; and consenters 33% (p .001). However, the number of refusers was small: retrospective analysis failed to show statistically significant differences before and after Riese in total number of emergency evaluations and total number of involuntary hospital admissions.

NR326 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

RECENT NONVERBAL MEMORY DEFICIT IN OBSESSIVE COMPULSIVE DISORDER

Kathy J. Christensen, Ph.D., Grecc Program, Minneapolis VA Hospital, One Veterans Drive, Minneapolis, MN 55417; Suck-Won Kim, M.D., Maurice W. Dysken, M.D., Kathy T. Maxwell, B.A.

Summary:

Neuropsychological functioning was examined in a group of 18 nondepressed patients with obsessive-compulsive disorder (OCD) and 18 age-, education-, and gender-matched normal controls. Multivariate analysis of variance with follow-up univariate tests revealed a mild recent nonverbal memory deficit ($p < 0.01$) as measured by the Visual Reproduction subtest of the Wechsler Memory Scale (30 ' recall). Performance on this task showed significant correlation ($p < 0.05$) with severity of OCD symptoms as measured by the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). Deficits in verbal abilities, including recent verbal memory, were not identified. Results were equivocal for executive function (Category Test, Controlled Oral Word Recognition, Design Fluency, Porteus Mazes, and Wisconsin Card Sort) and visual-spatial abilities (WAIS Block Design and Object Assembly). From performance on timed and untimed measures of the same construct (subtests of the Multidimensional Aptitude Batter and WAIS), it appears that patients with OCD score more poorly than controls when speed is a factor. Although performance on timed tactual-spatial motor test (Tactual Performance Test) was also impaired ($p < 0.01$), it is unclear whether this deficit is attributable to the nonverbal memory and/or speed deficits. The previously established association of recent nonverbal memory abilities with functioning of the right mesial temporal area is discussed in the context of current hypotheses about the neuroanatomic substrate of OCD.

NR327 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

TRICHOTILLOMANIA SYMPTOMS AND FLUOXETINE RESPONSE

Cesar L. Benarroche, M.D., Fair Oaks Hospital, 5440 Linton Blvd., Delray Beach, FL 33484

Summary:

Eighteen consecutive outpatient admissions, (2 males, 16 females), with a presenting complaint of hair pulling were assessed with a semistructured interview, (Trichotillomania Assessment Scale), and enrolled in a three-month open trial with fluoxetine 80 mg./day. Peak age of onset, (11-13), correlated closely with menarchy in 50 percent of female patients associated oral behaviors were present in 69 percent of the subjects, (38 percent admitted to Trichophagia). Prevalent coexisting diagnoses included OCP (25 percent), OCD (18 percent), PD (11 percent), and nail biting (11 percent). Thirty-three percent of the subjects pulled from multiple areas of their bodies - a set of identical twins were discordant for the disorder. First-degree relatives' diagnoses included basal ganglia disorders (11 percent), "picking at skin/biting habits" (22 percent), and OCP (33 percent). Ten of the 18 patients completed a three-month trial of fluoxetine of 80 mg./day - By month 2, 80 percent of the subjects had a >60 percent reduction of hair pulling behavior. Six subjects have remained totally asymptomatic for 6 months - further data on subsequent subjects will be presented.

The effectiveness of serotonine reuptake blockers, the time lag of response, the effect of lithium augmentation, and the family and individual psychiatric comorbidity support the notion of Trichotillomania as an "OCD spectrum" anxiety disorder.

NR328 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

SEROTONERGIC, APLHA2-ADRENERGIC TREATMENT COMPARISON IN OBSESSIVE COMPULSIVE DISORDER

William W. Hewlett, Ph.D., Psychiatry, Stanford University, Room TD114, Stanford, CA 94305; Sophia Vinogradov, M.D., W. Stuart Agras, M.D.

Summary:

Serotonergic reuptake inhibitors have been shown to be successful in the treatment of obsessive-compulsive disorder (OCD). In this study we compare the efficacy of clomipramine, a serotonergic reuptake inhibitor, to that of clonazepam, a benzodiazepine with serotonergic effects, clonidine, an alpha-two adrenergic agent with putative efficacy in OCD; and diphenhydramine, a histamine-1 antagonist with non-specific sedative effects. Twenty-eight patients with *DSM-III-R* diagnosis of OCD entered a randomized, double-blind multiple crossover study comparing the efficacy of these medications.

All medications improved the symptoms of OCD. The order of efficacy over all trials was clomipramine > clonazepam > diphenhydramine > clonidine. Clomipramine and clonazepam were significantly more effective than clonidine in treatment of OCD. There was no significant difference in efficacy between clomipramine and clonazepam.

These results are consistent with a serotonergic mechanism in the treatment of OCD and suggest that the clonazepam may be a useful alternative in the treatment of patients with OCD who cannot tolerate serotonergic reuptake inhibitors.

NR329 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

SPECT AND MRI IN OBSESSIVE COMPULSIVE DISORDER

Steven R. Machlin, M.D., Psychiatry, Johns Hopkins, 600 N. Wolfe St. Meyer 3-166, Baltimore, MD 21205; Gordon J. Harris, M.S., Godfrey D. Pearlson, M.D., Rudolf Hoehn-Saric, M.D., Edwaldo E. Camargo, M.D., Jonathan M. Links, Ph.D.

Summary:

Neuroimaging studies have shown that OCD may be associated with increased cerebral glucose metabolism in the front cortex and decreased size of the caudate. We used SPECT to measure cerebral blood flow and MRI for volumetric analysis in patients with obsessive compulsive disorder. SPECT images were obtained using Tc-99mm HmPAO in 11 DSM-3R OCD patients (18-49 yrs.) and 9 normal volunteers (20-29 yrs.), under resting conditions with minimal sensory stimulation. Data were generated from transverse images at the level of the basal ganglia using a locally developed computer program. Average counts/pixel were calculated automatically for the frontal pole (bilateral medial prefrontal cortex) and normalized to mean cortical values. Preliminary analysis on a subset of OCD pts found a significantly higher mean ratio of frontal pole to cortical mean ($p < .05$).

We used locally developed software to measure volumes from MRI of caudate, putamen and globus pallidus in 21 OCD patients and 15 controls. Also measured were distance between heads of caudate, brain area at level of basal ganglia, and distance between anterior tips of the frontal horns of the lateral ventricles. No significant between-group differences were found on any of the measures. This study supports reports increased blood flow in frontal cortex in patients with OCD but challenges the finding of decreased size of basal ganglia.

NR330 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

CSF ARGININE VASOPRESSIN AND OXYTOCIN IN OBSESSIVE COMPULSIVE AND EATING DISORDERS

Margaret Altemus, M.D., DIRP/CNE, NIMH Bldg 10 RM 3S231, 9000 Rockville Pike, Bethesda, MD 20892; Teresa A. Pigott, M.D., Mark A. Demitrack, M.D., Samuel J. Listwak, B.Sc., Dennis L. Murphy, M.D., Philip W. Gold, M.D.

Summary:

The central administration of arginine vasopressin (AVP) and oxytocin (OT) delay and enhance respectively the extinction of behaviors acquired during aversive conditioning. We have previously reported that patients with eating disorders show increased AVP and decreased OT secretion into the CSF, and have suggested that these abnormalities contribute to their obsessional, perseverative preoccupation with the aversive consequences of eating and weight gain. In the present study, we wished to explore whether hypersecretion of CSF AVP and/or hyposecretion of CSF oxytocin is present in patients with obsessive-compulsive disorder (OCD), which would suggest that abnormal AVP and OT secretion are a generalized phenomenon in illnesses characterized by obsessive behaviors.

CSF AVP and OT levels at 9AM were compared in controls (N = 21) and drug-free patients with OCD (N = 9), bulimia (N = 25), and anorexia nervosa (N = 13). Compared to controls (.65 ± 21 pg/ml), CSF AVP levels were significantly elevated in patients with OCD (.93 ± .25pg/ml), p = .003), anorexia nervosa (.69 ± .24pg/ml, p = .10), and bulimia (.80 ± .20pg/ml, p = .02). While CSF OT levels were normal in all three patient subgroups, the ratio of CSF AVP/OT was significantly higher in OCD patients compared to controls (.15 ± .03 vs. .11 ± .06, p = .04).

These data are compatible with our recent finding in a large series of patients that the eating disorders and OCD show significant overlap in symptomatology. The occurrence of a relatively increased AVP/OT ratio in the CSF of patients with OCD may contribute to the severity of obsessional symptoms in OCD patients.

NR331 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

IMBALANCE BETWEEN THE CEREBRAL HEMISPHERES IN OBSESSIVE COMPULSIVE DISORDER

Bruce E. Wexler, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Wayne K. Goodman, M.D.

Summary:

Five different language-related dichotic listening tests were used to compare cerebral laterality in right-handed OCD patients (N = 22) and healthy controls (N = 62). In all tests two different words or nonsense syllables were presented simultaneously, one to each ear. Healthy subjects more often reported the stimulus presented to their right ear, since information from this ear goes directly to the language specialized left hemisphere. Information from the left ear is first processed in the right hemisphere and then transferred to the left. The magnitude of this right ear advantage (REA) reflects the relative efficiency of all neural components along the different pathways from each ear to the left hemisphere, as well as the degree of left hemisphere activation resulting from the test stimuli themselves. The five dichotic tests different with respect to the meaningfulness and emotional valence of the stimuli. These differences led to the differences in magnitude of the REA on the different tests in the healthy subjects, presumably reflecting differences among the tests in the particular set of neural processing systems engaged. OCD patients, however, had significantly lower REAs than healthy controls on all tests (p = .001). Moreover, those patients with lower REAs scores had more severe symptoms than did those patients with higher REAs (p = .02). These data provide evidence of dysfunction in some neural component common to all the tests, such as increased right hemisphere function, decreased left hemisphere function, or increased flow of information from the right to the left hemisphere.

NR332 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

WITHDRAWN

NR333 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

SEX OFFENDER TREATED WITH FLUOXETINE: PRELIMINARY RESULTS

Kenneth Kashkin, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06508; David D'Amora, M.A., Ronald Anderson, Ph.D.

Summary:

The medical treatment of deviant sexual behavior has been limited to the use of anti-androgen medications and it has been equated with "medical castration." Since serotonin has been implicated as a mediator of neurohormonal events underlying sexual aggression and behavior, and serotonin-enhancing agents have been used to treat aggressive, addictive, and obsessive-compulsive behaviors (with the documented side effect of anorgasmia), we piloted an open trial of fluoxetine, a serotonin-uptake inhibitor, in ten sex offenders at high risk of re-offending despite behavioral therapies. Diagnoses in subjects included pedophilia, exhibitionism, voyeurism, sexual sadism/masochism, and frotteurism. Objective measures of sexual obsessions and compulsions, craving for the sexually aberrant act, and aberrant sexual arousal and behavior, decreased in all subjects and increased again in three subjects who stopped or decreased fluoxetine intake. These changes were associated with increased latency or failure to reach orgasm, but not impotence. This is the first report of the use of serotonin-uptake inhibitors in the control of illegal sexual behaviors, and we discuss its possible implications for the neurobiology of sexual behavior and its treatment.

NR334 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

NEUROANATOMICAL ABNORMALITIES IN OBSESSIVE COMPULSIVE DISORDER

Frederick G. Moeller, M.D., Department of Psychiatry, VA Medical Ctr. (116A), 3350 La Jolla Village Dr., San Diego, CA 92161; Renee M. Dupont, M.D., Terry L. Jernigan, Ph.D., Nelson Butters, Ph.D., J. Christian Gillin, M.D., Stephen M. Stahl, M.D.

Summary:

Obsessive-compulsive disorder (OCD) has been linked to neuroanatomical abnormalities. Other studies have produced mixed results, possibly due to the heterogeneous etiologies of this disorder. Ten prospectively selected male patients with a DSM-III-R diagnosis of OCD (mean age 25.2 years, SD 7.03; education 15.83 years, SD 1.95) and twelve male controls (mean age 40.3 years, SD 8.03; education 15.83, SD 2.5) were screened using a structured psychiatric interview and medical history. All subjects underwent MR imaging using a standard protocol and a three hour neuropsychological test battery. Preliminary MRI results of six patients and twelve controls demonstrated abnormalities in 5/6 OCD patients using blind evaluation by a senior neuroradiologist. (One tail Fisher's Exact Test $p = 0.004$). 2/6 demonstrated subcortical signal hyperintensities, 3/6 demonstrated cortical atrophy, and 1/6 was diagnosed as having a 5X4mm cystic lesion within the left temporal lobe. 1/12 controls demonstrated cortical atrophy. Initial neuropsychological test results demonstrated mild impairment on letter fluency, speed and attention (DSSS, Trails A and B). Structural abnormalities and quantitative MRI analysis will be presented in the context of their clinical and neuropsychological significance.

NR335 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

SIGNIFICANT ISSUES OF THE SECOND SEXUAL REVOLUTION

Samuel S. Janus, Ph.D., Psychiatry, NY Medical College, P.O. Box 2247, Charlottesville, VA 22902; Cynthia Janus, M.D.

Summary:

This paper, part of a long-term study of American sexuality, documents changes that are manifest in America's sexuality today. Americans have experienced more sexual change in the past two decades than in the prior two centuries. The reality today is that we have launched into the era of The Second Sexual Revolution. The First Sexual Revolution began with "the" pill in the 1950's and ended in the late '80s. AIDS and great social pressures resulted in its ending. The Second Sexual Revolution is not a product of the young as was the First Sexual Revolution, rather it is led by women, and the mature segment of the population. Middle-age and post-middle-age Americans have rediscovered sex and decided that it is legitimate for them. New sexual changes affect all of American society.

POPULATION: The population for this study consisted of 4,500 Americans surveyed between 1983 and 1985, and a follow-up group of an additional 2,655 between 1988-1990.

METHOD: Respondents were surveyed with a specially developed 172-item questionnaire, and 200 in-depth interviews were conducted. Results were analyzed in all major areas of sexual function.

RESULTS: In addition to the practice of "safe sex," many Americans are utilizing personal coping mechanisms and avoiding panic. This study documents an increase in sexual activity and shows where the crucial changes have been made in definition of "normalcy."

NR336 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

ARE MENTAL HOSPITAL EPISODE RATES GOING UP OR DOWN?

Alex Richman, M.D., Psychiatry, Dalhousie University, 5849 University Avenue, Halifax NS, Canada B3H 4H7; Rodney Riley, B.A.

Summary:

Despite research advances, there has been little evidence of lowered rates of psychiatric hospitalization. US admission rates to specialized hospitals have been stable (NIMH). When general hospitals with psychiatric units are included, admission rates have increased (Kiresuk and Sibulkin). This is the first paper to show large scale decreases in psychiatric admission rates. We analyzed Canadian admission rates (per 100,000 population) between 1971 and 1985 for mental hospitals and all general hospitals (including hospitals without psychiatric units). The trends outlined below were consistent during the 15 year period.

Schizophrenia and affective psychoses: The episode rates are stable under age 65.

Other disorders (excluding organic psychoses, mental retardation, alcohol and drug abuse): There has been a 39% decrease overall, more marked in women (-43%) than for men.

Elderly: The admission rates for non-organic disorders increased 23%.

The admission trends for the functional psychoses do not support the general belief in an accelerating "revolving-door". Women have far fewer admissions in recent years. Decreased hospitalizations for the functional disorders demonstrate the results of clinical advances in medication, management and community care.

NR337 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

A CAUSAL MODEL OF COMMUNITY TENURE

Suzanne King, Ph.D., Psychosocial, Douglas Research Center, 6875 LaSalle Blvd, Verdun PQ, Canada H4H 1R3; Celine Mercier, Ph.D.

Summary:

A statistical "causal model" reflects the researcher's beliefs about the relationships among a given set of variables. Frequently, however, the researcher realizes that several variables in such a model belong together in that they reflect a more global, underlying construct. In such cases, one can use the LISREL statistical program to create these underlying, "latent" variables from two or more "manifest" variables, and then test the plausibility of causal relationships among them.

We describe the use of LISREL, with recently collected and coded data, in testing a model of the tenure in the community and perceived quality of life of 250 schizophrenic and affective psychotic outpatients. Using 15 manifest variables, the model illustrates the hypothesis that quality of life is a function of service utilization, the illness, the living situation, daily activities, and interpersonal life. Tenure in the community, or the percentage of time the patient remains out of the hospital, is a function of all of these variables plus the quality of life dimension. The results will offer insight into the processes involved in keeping a psychiatric outpatient in the community and will suggest which areas are the most important for intervention.

NR338 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

STRESS SYMPTOMS AND EPINEPHRINE

Oliver G. Cameron, M.D., Psychiatry, University of Michigan, 900 Wall Street, Ann Arbor, MI 48109; Sharon Gunsher, B.S., M. Hariharan, Ph.D.

Summary:

There is little empirical support for the widely-held belief that the adrenergic symptoms of stress are largely due to the effects of epinephrine (E; adrenaline) released from the adrenal medulla. Typically, plasma E increases only to 300 pg/ml or less in response to mental stress. The hypothesis of this study is that subjective awareness of E's effects occur only at levels greater than 300 pg/ml. Twelve healthy subjects (6 males and 6 females; mean age = 28.6 years) were each studied in one experimental session. Subjects received continuous infusions of either E (1.25, 2.5, and 5.0 μg/min, order completely counterbalanced across subjects) or saline in alternating 15-minute epochs. Blood pressure, pulse, plasma E, subjective choice response (whether E or saline was infused), and 15 symptoms, rated "none" to "most ever," were determined at the end of each epoch. Mean E levels were 114, 359, 435, and 848 pg/ml, for the saline and the three ascending E doses, respectively. Significant increases in response to E infusion occurred for plasma E, pulse, choice response, and the symptoms "fast or hard/irregular heartbeat, breathing changes, trembling, and tingling sensations"; choice favored "saline" at E levels below 300 pg/ml and only favored "epinephrine" above 500 pg/ml. By multiple regression, only fast or hard/irregular heartbeat, tingling, and plasma E contributed significantly to choice. Thus, systemic release of E plays at most a small role in producing the symptoms of mental stress.

NR339 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

EMOTION AND PHYSICAL ACTIVITY IN HEALTHY WOMEN

Thomas F. Flynn, M.D., Psychiatry, Univ of Nevada, School of Medicine, Reno, NV 89557; Grant D. Miller, M.D., Lisa A. Hill, B.S., Barbara J. Scott, M.P.H., Sachiko T. St. Jeor, Ph.D.

Summary:

Positive relationships have been reported between psychological well-being and physical activity. However, measures of physical activity have been based largely on subjective self-report. The purpose of this study was to examine the relationship between selected measures of emotional well-being and improved measures of physical actively estimated by a portable accelerometer, as well as by responses on a two-item questionnaire asking subjects how often exercise was an important part of their current recreation and work. Measures of well-being included the General Well-Being Schedule, Center for Epidemiologic Studies Depression Scale, and the Derogatis Revised Symptom Checklist anxiety, depression, and general severity index subtest scores. Subjects were 81 women (mean weight = 153, %IBW = 118) ages 40-60 (mean = 49) participating in the Reno Diet-Heart Study. Total energy expenditure (TEE) was estimated in kcal/day using 7-day mean accelerometer readings. Resting energy expenditure (REE) was measured via indirect calorimetry using a metabolic cart, and activity calories (AC) were derived by subtracting TEE from REE. Pearson correlations between physical activity (AC) and emotional well-being were insignificant, but in the predicted direction. ANOVA between subjective measures of physical activity and well-being were also insignificant. This study does not support the popular notion of a positive relationship between psychological well-being and physical activity in healthy women.

NR340 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

TREATMENT OF TYPE-A BEHAVIOR IN CARDIAC PATIENTS WITH BUSPIRONE

Andrew B. Littman, M.D., Psychiatry, Mass General Hospital, 32 Fruit Street ACC 221, Boston, MA 02114; Maurizio Fava, M.D., Stefania Lamon-Fava, M.D., Kathleen McKool, R.N.

Summary:

The efficacy of buspirone in reducing Type A behavior (TAB) and hostility was evaluated with an open 8-week trial in 10 male, middle-aged cardiac patients. In order to enter the study, patients had to have a score of greater than 30 on the Videotaped Structured Interview (VSI) for TAB at screening and four weeks later at the baseline visit. Treatment with buspirone 5 mg tid was initiated at the baseline visit and was gradually titrated up to 20 mg tid if necessary. Subjects who had been recently treated with centrally active drugs, or had a history of or active psychiatric illness, substance abuse, affective, or anxiety disorder were excluded with the use of the SCID. Efficacy of treatment was determined with the use of the VSI, the Kellner's Symptom Questionnaire, the Perceived Stress Scale, and the Cook-Medley hostility scale.

No significant differences between baseline and screening measures were found, except for an increase in the Kellner subscale ($p(0.05)$. After treatment, the Kellner total scale decreased ($p(0.02)$, as did the anxiety subscale ($p(0.05)$, depression subscale ($p(0.07)$, and hostility subscale ($p(0.001)$. The VSI total score decreased ($p(0.001)$, as did the time urgency subscale ($p(0.001)$, and hostility subscale ($p(0.01)$. The Perceived Stress Scale also decreased ($p(0.01)$. The Cook-Medley score was unchanged. This study suggests that TAB, hostility, and perceived stress observed in cardiac patients may be lessened over an eight-week period with the use of buspirone, an anxiolytic agent relatively free of side effects and abuse potential.

NR341 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

THE LONG-TERM EFFECTS OF CHILDHOOD SEXUAL ABUSE

Geoffrey M. Margo, M.D., Psychiatry, Suny Health Sci Center, 750 East Adams Street, Syracuse, NY 13210; Elvera M. Weld, M.A.

Summary:

Persons who have been sexually abused as children may continue to experience the negative effects of this abuse into adulthood. As part of a current research project, standard measures of psychological distress were administered to 38 female patients on the inpatient psychiatry unit at University Hospital. Historical data was also collected which included information about the occurrence of childhood sexual abuse. It was hypothesized that women who were sexually abused as children would report more severe symptoms of psychological distress than women who were not abused. As predicted, the sexually abused women scored significantly higher on measures of anxiety, hostility, somatization and overall feelings of distress. These results suggest that even with a highly distressed population (psychiatric inpatients), a history of childhood sexual abuse contributed to more severe psychological symptomatology in adult women.

NR342 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

PTSD IN ALSATIAN WORLD WAR II VETERANS

Marc-Antoine Crocq, M.D., Psychiatry, C.H. Specialise, Secteur 8, Rouffach 68250, France; Jean-Paul Macher, M.D., Fabrice Duval, M.D., Jorge Barros-Beck, M.D., John C. Kluznik, M.D., Stewart J. Rosenberg, M.D.

Summary:

We applied *DSM-III-R* criteria for post-traumatic stress disorder to a group of 525 French Alsatian men who had been forcibly drafted into the German army during World War II, then captured and imprisoned by the Russians. All had catastrophic psychosocial stressors according to Axis IV of *DSM-III-R*.

The following symptoms, which indicate the recurrent reexperiencing of the traumatic events (group B symptoms in *DSM-III-R* diagnostic criteria for PTSD), were found to be significantly associated with a longer duration of captivity: nightmares ($p < .05$), sudden reexperiencing of the traumatic events ($p < .005$), and intense anxiety triggered by exposure to stimuli reminiscent of war or captivity ($p < .005$).

Enduring personality changes after catastrophic experience, which constitute a new specific diagnostic category in the draft of *I.C.D.-10*, such as an increased dependence on love and support from others and the feeling of being different from others, were similarly associated (all $p < .05$) with a longer captivity. Enduring personality changes, notably the paradoxical association of constant anxious apprehension and feelings of detachment and lack of ambitions, seem to be a prominent feature in this population.

NR343 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

COMBAT STRESS AMONG HOMELESS VIETNAM VETERANS

Robert Rosenheck, M.D., Psychiatry, Yale University, VAMC 950 Campbell Avenue, West Haven, CT 06516; Peggy Gallup, M.P.H., Catherine A. Leda, M.P.H.

Summary:

Introduction and Methods: In 1987 the VA established a national outreach program for homeless veterans. Of 10,524 veterans screened by this program, a high proportion, 51%, were Vietnam Era Veterans, compared to only 28% in the non-homeless veteran population. This study reviews assessment data to understand the reasons for the predominance of Vietnam Era Veterans among homeless veterans.

Results: 1) A total of 37.3% of all homeless veterans were 35-44 years old, considerably more than the 20.3% in the general veterans population. Within this specific age cohort, Vietnam era veterans were *not* over-represented. 2) A total of 44.8% of homeless Vietnam Era Veterans served in Vietnam and 40.4% were exposed to combat fire, similar to non-homeless veterans. 3) Almost half (44.9%) of the homeless veterans who served in Vietnam report symptoms of combat-related stress, considerably more than the 25.3% reported in the National Vietnam Veterans Readjustment Study.

Conclusions: 1) The over-representation of Vietnam veterans among the homeless principally reflects the large cohort of 35-44 years-olds among homeless veterans. 2) Homeless Vietnam Era veterans are not more likely to have served in combat in Vietnam than their non-homeless peers. However, 3) among homeless veterans who served in Vietnam, a high percentage report symptoms of combat-related stress. Service in Vietnam does not appear to be a major cause of homelessness but the stresses of homelessness appear to augment combat-related symptomatology among Vietnam combat veterans.

NR344 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

CYCLIC AMP SIGNAL TRANSDUCTION IN PTSD

Bernard Lerer, M.D., Herzog Research Center, P.O. Box 140, Jerusalem 91001, Israel; Avraham Bleich, M.D., Richard P. Ebstein, Ph.D.

Summary:

Peripheral blood cells provide an accessible model for studying transmembrane signal transduction. By means of this approach, abnormal second messenger (adenylate cyclase) activity has been demonstrated in major depression and alcoholism. In the case of alcoholism, molecular techniques have pinpointed an abnormality of messenger RNA coding for the alpha subunit of Gs, the stimulator G protein which couples receptors to the catalytic unit (C) of adenylate cyclase. Since comorbidity with depression and/or alcoholism is frequently observed, cyclic AMP signal transduction in PTSD is of considerable interest. We have demonstrated abnormally low responsiveness of adenylate cyclase in platelets from two independent samples ($N = 29$) of male patients with PTSD compared to matched controls. Neither depression nor alcoholism were prominent features of either sample. While our first study demonstrated an abnormality at the level of Gs as well as distal to it, our subsequent findings reflected lower responsiveness of the C unit or dysfunction G-C coupling. Further studies should a) Determine whether abnormal cyclic AMP signal transduction is an intrinsic characteristic of PTSD b) Pinpoint the molecular basis of the abnormality and c) Examine its relationship to similar findings in depression and alcoholism. Biochemical as well as clinical overlap would have important implications for the pathogenesis of all three disorders.

NR345 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

ANIMAL MODELS FOR PTSD

Bruce I. Diamond, Ph.D., Psychiatry, Medical College of GA., 1515 Pope Avenue, Augusta, GA 30912; Mark B. Hamner, M.D., Thomas L. Chalker, B.S., Richard L. Borison, M.D.

Summary:

A number of animal models have been proposed for the study of depression. These generally involve exposure of laboratory animals to a variety of stressors and are essentially learned helplessness models. It has been hypothesized that exposure to inescapable and variable stress may provide a model for post-traumatic stress disorder (PTSD) in humans. Changes in noradrenergic function may occur in both learned helplessness and in PTSD. In order to study this, male Sprague Dawley rats (160 g) underwent three different stress paradigms and were subsequently challenged with yohimbine or clonidine to stimulate or inhibit, respectively, central norepinephrine release. The effect of these drugs on immobilization after stress was investigated in animals exposed to either: (A) chronic intermittent and heterogeneous stress, (B) chronic intermittent homogeneous stress, or (C) no stress. The immobilization percentages for each drug were statistically analyzed. There was no difference in immobilization scores after heterogeneous or homogeneous stress. However, yohimbine improved the heterogeneous chronic stress group only. In contrast, clonidine significantly improved both chronic stress groups. Moreover, there was a significant weight loss in all groups chronically stressed. Results of this study demonstrate a differential effect of heterogeneous versus homogeneous chronic stress in response to noradrenergic stimulation.

NR346 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

ELEVATED PLASMA DOPAMINE LEVELS IN PTSD

Mark B. Hamner, M.D., Psychiatry, Medical College of GA., 1515 Pope Avenue, Augusta, GA 30912; Bruce I. Diamond, Ph.D.

Summary:

Increased peripheral autonomic nervous system activity in post-traumatic stress disorder (PTSD) has been suggested by psychophysiologic investigations and recent neuroendocrine studies. Abnormalities of catecholamine function may be present in PTSD and have long been hypothesized in mood disorders. Mood disorders, including depression, are relevant in both the differential diagnosis of PTSD and as potential comorbidity. In the present study investigating catecholamine function in PTSD, resting plasma dopamine and norepinephrine levels were measured in four subject groups using HPLC with electrochemical detection: (1) male Vietnam combat veterans meeting *DSM-III-R* criteria for PTSD (n = 12), (2) male veterans meeting *DSM-III-R* criteria for major depressive episode (n = 8). Resting plasma norepinephrine was comparable between all groups. Resting plasma dopamine was higher in PTSD (1.53 $\pm$ 0.5 ng/ml, mean $\pm$ SEM) versus both depressed patients (0.33 $\pm$ 0.1 ng/ml) and controls (0.52 $\pm$ 0.3 ng/ml). In the two subjects with combined diagnoses of PTSD and depression, resting plasma dopamine levels were elevated and comparable to resting dopamine levels in the PTSD group. The data suggest that resting plasma DA levels may differentiate PTSD from major depression and controls perhaps due to autonomic nervous system hyperactivity or other mechanisms. These preliminary findings support the hypothesis that abnormalities of catecholamine function, in this case dopamine activity, are present in PTSD.

NR347 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

ALEXITHYMIA PREDICTS IN PTSD TREATMENT RESPONSE

Thomas R. Kosten, M.D., Psychiatry, Yale University, 27 Sylvan Avenue, New Haven, CT 06519; Earl L. Giller, Jr., M.D., Julia B. Frank, M.D., Elisheva Dan, P.A., John H. Krystal, M.D.

Summary:

Alexithymia was assessed using the Alexithymia Provoked Response Questionnaire (APRQ) in 57 Vietnam combat veterans with post traumatic stress disorder (PTSD). The APRQ uses 17 questions such as "How would you feel if someone insulted you?" to reliably (retest r = 0.8) assess alexithymia (no or few affective terms such as angry, fearful, or sad). Lower scores (range 0-17) indicating more alexithymia were hypothesized to reduce treatment response in this 8 week randomized clinical trial comparing imipramine or phenelzine to placebo. Treatment response was measured by avoidance (AVD) and intrusion (INT) subscales of the 15 item Impact of Events scale. At intake the mean APRQ was 9.2 (sd = 4.2) and the INT and AVD were 1.63 (sd = 9.8) and 17.4 (sd = 8.3), and at termination mean INT and AVD were 11.2 (sd = 10.5) and 12.8 (sd = 7.5). The APRQ significantly ($P < 0.05$) predicted both the terminal AVD (r = -0.30) and change from baseline AVD (r = -0.26), but did not predict either the terminal INT (r = 0.06) or change in INT (r = -0.01). The prediction of change in AVD by APRQ held for placebo (n = 16)(r = 0.62, $P < 0.01$), but not phenelzine (r = 0.1)(n = 19) or imipramine (r = -0.01)(n = 23) groups. Since severity of war atrocities, as assessed on a 6 item scale scored 0 to 18 (mean = 8.4 +/− 4.0), also predicted treatment response - terminal AVD (r = 0.38) and INT (r = 0.30), we adjusted for atrocity score, but this did not affect the prediction of AVD by the APRQ (r = 0.27, $P < 0.05$). Thus, alexithymia predicts a poor response of PTSD avoidance, but not intrusion, symptoms to treatment, independent of severity of war trauma, and particularly when treated without medications.

NR348 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**
WITHDRAWN

NR349 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**
SUBTYPES OF SEXUALLY ABUSED WOMEN

Nicholas G. Ward, M.D., Psychiatry, Univ of Washington, 1959 NE Pacific RP-10, Seattle, WA 98195; Albert S. Carlin, Ph.D.

Summary:

The relationships of childhood sexual abuse with MMPI subtypes and DSM-III diagnoses were examined in 171 women admitted to an acute psychiatric unit. A cluster analysis on all MMPI's revealed 4 relevant clusters. While 47.6% of the group acknowledge sexual abuse, 75% of the most disturbed cluster and 30.4% of the least disturbed cluster were sexually abused ($p < .02$). Childhood forced intercourse showed a similar distribution but casual fondling was not overrepresented in any cluster. Cluster membership was not associated with age of onset, relationship to the perpetrator or to duration and frequency of abuse. When compared to other diagnoses sexual abuse was overrepresented only with adjustment disorder (58% vs. 41%, $p < .05$). Thus, sexual abuse in these women, most of whom already had serious psychiatric disorders, appears to increase the likelihood of coexisting personality dysfunction, but does not guarantee it. This data suggests that differences among subtypes of abused women may be a function less of specific abuse experiences than of differences in response to abuse.

NR350 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**
REM SLEEP DISTURBANCE AS THE HALLMARK OF PTSD

Richard J. Ross, M.D., Research 151, Phila. VA Medical Center, University & Woodland Avenues, Philadelphia, PA 19104; William A. Ball, M.D., David F. Dinges, Ph.D., Nancy B. Kribbs, Ph.D., Adrian R. Morrison, D.V.M., Steven M. Silver, Ph.D.

Summary:

The recurrent anxiety dream may be relatively specific to posttraumatic stress disorder (PTSD) and might therefore be its clinical hallmark. Many aspects of the phenomenology of the PTSD anxiety dream suggest its emergence from REM sleep, leading to the view that PTSD represents fundamentally a disorder of REM sleep mechanisms. Yet no consensus exists regarding REM sleep architecture in PTSD.

Polysomnographic studies were carried out in 11 physically healthy, male Vietnam veterans (mean age 41.1 $\pm$ 3.5, S.D.) who met DSM-III-R criteria for current PTSD and in 8 normal control veterans (43.9 $\pm$ 2.8). Five PTSD patients also had past and/or current major depression. No participant had abused any substance during the preceding 6 weeks or taken a psychotropic drug over the prior 2 weeks.

After 1 adaptational night, the PTSD group had a higher REM sleep percent (26.1 vs. 19.4, $p < 0.01$, 2-tail), a longer mean REM sleep period duration (29.4 vs. 21.9 min., $p < 0.02$, 2-tail), a higher REM density (rapid eye movements/REM sleep time) (6.3 vs. 3.5, $p < 0.051$, 2-tail), and a greater variance of REM latency ($F = 34.3$, $p < 0.001$). One PTSD patient reported a single anxiety dream, directly following a spontaneous awakening from the first REM sleep period (REM period time 25 min., REM density 17.6).

Thus, PTSD might involve a problem in the timely recruitment of the ensemble of CNS processes that define REM sleep as well as a disorder of specific events within REM sleep, including rapid eye movement generation. Supported by V.A. Med. Res., MH-42903, and F32-MH-09584-01.

NR351 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

CHILDHOOD ABUSE AND PERSONALITY DISORDERS

Stanley W. Raczek, M.D., Psychiatry, U.S. Naval Hospital, Box 19-4714, FPO New York, NY 09521

Summary:

The hypothesis that childhood abuse is associated with specific personality disorders was tested by comparing the personalities of two groups of psychiatric outpatients: (A) 13 patients who admitted having been physically and/or sexually abused as children, and (B) 29 patients without history of childhood abuse. The history of abuse was obtained using a structured research questionnaire and clinical interview. The personality profile of all patients was evaluated using the Personality Disorder Examination (PDE), a structured diagnostic interview developed by Loranger et al. The "abused" patients were found to have much higher number of various personality disorders than "nonabused" patients (2.5 and 1.2 personality disorders per patient respectively). In the "abused" group the most common personality disorders were borderline (54%), histrionic (39%), and antisocial (31%), while in the "nonabused" group the most common disorders were borderline (24%), avoidant (24%) and passive-aggressive (14%). The "dramatic" cluster (Cluster B) of personality disorder (antisocial, borderline, histrionic and narcissistic) was represented in the "abused" group three times more frequently than in the "nonabused" group (1.4 and 0.4 diagnoses per patient respectively). The results of this study suggest that abuse in childhood may be associated with the development of specific cluster of personality disorders.

NR352 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

PSYCHOPATHOLOGICAL SEQUELAE OF CHILDHOOD TRAUMA

Stanley W. Raczek, M.D., Psychiatry, U.S. Naval Hospital, Box 19-4714, FPO New York, NY 09521

Summary:

42 subjects referred for psychiatric evaluation to the Mental Health Clinic at the military hospital were studied. They were divided into two groups. The first group consisted of 13 subjects with self-reported history of physical and/or sexual abuse in childhood. The second group consisted of 29 subjects without history of abuse. The relevant clinical data were obtained from the research psychiatric questionnaire and from the clinical interview. The personality profile of all subjects was evaluated using the Personality Disorder Examination (PDE), a structured diagnostic interview developed by Loranger et al. The subjects from the "abused" group endorsed much higher number of pathological personality traits, particularly from cluster B personality disorders (antisocial, borderline, histrionic and narcissistic). They reported more behavioral problems in school and were generally less educated than "nonabused" subjects. They had more difficulties adjusting to military life and abused alcohol more frequently. They more often complained of depressed and hopeless feelings during the interview and admitted to frequent suicidal ideations in the past. The results of this study support the findings of other researchers that childhood trauma may result in severe psychopathology. This project is ongoing and the results will be updated at the time of presentation.

NR353 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

PSYCHIATRISTS INJURED BY PATIENT ATTACKS

Harold A. Carmel, M.D., Psychiatry, UCLA, Box 7001, Atascadero, CA 93423; Mel Hunter, M.P.A.

Summary:

The seven staff psychiatrists injured by patient attack in a large state hospital in five years were compared to the 47 psychiatrists who were not injured by attack. In this period, 54 different psychiatrists were employed in the hospital for 128.5 person-years. 13% of the staff psychiatrists were injured by patient attack in the five years (2.6% per year); 5.5 injuries per hundred person-years occurred.

Psychiatrists under 36 years of age were more likely to be injured (22.6 injuries per hundred person-years vs. 3.5 injuries for psychiatrists more than 37 years old, Fisher exact test = .0290). Psychiatrists less than ten years out of residency were more likely to be injured (13.9 injuries per hundred person-years vs. 3.1 injuries for psychiatrists more than ten years post-residency, Fisher exact test = .05). Graduates of university-affiliated residencies were 3 times as likely to be injured by patient attack as graduates of public-sector residencies (8.7 injuries per hundred person-years vs. 2.9). Male psychiatrists were injured at a rate approximately 50% higher (5.9 per hundred-person years) than female psychiatrists (3.8). Board-certification, length of service in the hospital and graduation from a foreign vs. North American medical school were not related to being injured by patient attack.

NR354 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

CAFFEINE INGESTION: DIAGNOSIS AND VIOLENCE

Harold A. Carmel, M.D., Psychiatry, UCLA, Box 7001, Atascadero, CA 93423; Mel Hunter, M.P.A.

Summary:

(1) Estimates of daily caffeine intake, (2) rates of violent behavior, and (3) primary DSM-III-R diagnosis were obtained for the 682 patients hospitalized 90 days or more in a large California state hospital. The correlation between estimated caffeine intake and rate of patient violence was +.375 in patients with primary diagnosis of bipolar disorder ($N = 37$, $df = 35$, $p < .05$, r-squared = .141). In patients with a primary diagnosis of schizophrenia, the correlation was +.253 ($N = 320$, $df = 318$, $p < .001$), r-squared = .064). The correlation was not statistically significant in patients with primary diagnoses of organic brain syndrome ($r = .023$, $N = 70$, $df = 68$), or non-psychotic disorders.

These data suggest that in inpatients with psychiatric disorders related to neurotransmitter dysfunction, ingestion of caffeine (which affects several neurotransmitter systems) is associated with behavior toxicity, such as aggression.

NR355 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

PATIENT CENSUS AND PATIENT AGGRESSION

Harold A. Carmel, M.D., Psychiatry, UCLA, Box 7001, Atascadero, CA 93423; Mel Hunter, M.P.A.

Summary:

In 29 months between January 1985 and May 1987, the square footage available to patients in a large California state hospital was constant. Therefore, Average Daily Census (ADC) (which ranged between 864 and 989, a variation of 14.5%) was a direct measure of patient density. During this time, the hospital's census was far below its historical highs and was not overcrowded. In this period, the hospital recorded 828,374 patient-days (2268 patient-years), 3864 incidents of patient violence (including 2089 incidents of physical aggression and 1775 incidents of non-physical aggression) and 655 incidents of self-injurious behavior. The correlation between Average Daily Census and rate of physical aggression was negative ($r = -.4543$, $df = 27$, $p < .05$, r-squared = .206). The correlations between Average Daily Census and rates of non-physical aggression ($r = .0065$, $df = 27$) and of self-injurious behavior ($r = -.1453$, $df = 27$) were not significant. This is evidence that increased patient density in a hospital which is not overcrowded is correlated with lower rates of physical aggression by patients. This study does not support policies of overcrowding in public psychiatric hospitals.

NR356 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

VIOLENCE TOWARD PSYCHIATRIC RESIDENTS

Marian Fireman, M.D., Psychiatry, Oregon Health Sci. Univ., 3181 SW Sam Jackson Park Road, Portland, OR 97201; Joseph D. Bloom, M.D., Larry R. Faulkner, M.D.

Summary:

In recent years, psychiatric residents have expressed increasing concerns about their own safety and the safety of the settings they work in. We investigated the issue of threats and assaults toward psychiatric residents by surveying, by questionnaire, all current residents in three university programs located in three large western cities. Approximately seventy-nine percent of the respondents reported threats of violence toward them and twenty-eight percent reported actual assaults during their training. Most of these events occurred during the first two years of residency training, and all except one occurred in an inpatient or emergency room setting. Only fifty percent of the respondents considered these settings safe or secure. Thirty-one percent of residents had threats made on their lives; in one-third of these threats, the patient either had or said they had a gun. In seven percent of incidents a knife was brandished, but the resident was not injured. The typical violent or threatening patient was a young to middle-aged male. The majority of these patients carried primary diagnoses of psychotic disorder, substance abuse or personality disorder. Sixty-one percent had known alcohol or other substance abuse and forty-one percent had a known history of violence.

NR357 **Tuesday, May 15, 3:00 p.m. - 5:00 p.m.**

BUSPIRONE RESPONSE IN PMS AND PLATELET 5-HT UPTAKE

Candace S. Brown, Pharm.D., Pharmacy, University of Tenn., 26 South Dunlap Room 210B, Memphis, TN 38163; Carolyn M. Chesney, M.D., Frank W. Ling, M.D., Barbara G. Wells, Pharm. D., Abbas E. Kitabchi, M.D.

Summary:

Platelet serotonin (5-HT) uptake was measured in 19 premenstrual syndrome (PMS) subjects meeting DSM-III-R criteria during a double-blind, placebo-controlled buspirone study. Two buspirone cycles (40.6 mg $\pm$ 12.2 mg.day) were significantly more effective than two placebo cycles on the Premenstrual Syndrome Tension (PMTS) Scale. There were no differences in 5-HT uptake between subjects and controls or between subject treatment groups. When subgrouped by mean control 5-HT uptake, the K_m in the group below the mean (low group, n = 9) was significantly decreased during the luteal compared to the follicular phase, whereas the V_{max} in the group above the mean (high group, n = 10) was significantly higher in the luteal compared to the follicular phase. The low group was significantly more symptomatic than the high group on baseline PMTS and Profile of Mood State (POMS) scores. Buspirone significantly improved POMS, PMTS, HAM-A and Premenstrual Assessment Form (PAF) scores in the low group whereas the high group showed no improvement or worsened. Our results suggest that serotonergic dysfunction may be present in PMS and that buspirone's efficacy in part may be due to its effect on serotonin uptake during the luteal phase.

NR358 **Wednesday, May 16, 9:00 a.m. - 10:30 a.m.**

DEPRESSIVE SYMPTOMS IN THE SIX MONTHS FOLLOWING MISCARRIAGE

Richard Neugebauer, Ph.D., Sergievsky Ct., Columbia University, 630 West 168th Street, New York, NY 10032; Jeannie Kline, Ph.D., Patricia O'Connor, Ph.D., Pat Shrout, Ph.D., Jim Johnson, Ph.D., Andrew E. Skodol, M.D., Judith Wicks, B.A., Mervyn Susser, B.Ch.

Educational Objectives:

To examine the effect of reproductive loss on maternal depressive symptoms using a research design that includes subjects unexposed to this potentially traumatic event.

Summary:

Twelve to 15 percent of clinically recognized pregnancies end in spontaneous abortion. This study tests the a priori hypothesis that miscarriage increases maternal depressive symptoms up to 6 months following loss and that number of living children, advanced maternal age, and prior reproductive loss affect risk. Miscarrying women (N = 382), entering the study in stages, were interviewed at 2 weeks, 6 weeks, and 6 months after loss. Two hundred eighty-three *1 pregnant women and 318 community women, not pregnant in the preceding year, comprised comparison cohorts. Pregnant women served as a comparison cohort for the 2-week assessment only. Symptoms were measured with the Center for Epidemiologic Studies-Depression scale (CES-D); symptom levels were calculated in terms of proportions of women with pronounced symptomatology (scores of 30 +). At 2 weeks after loss the proportion of miscarrying women scoring 30 + was 3.5 fold that in pregnant women (95 percent confidence limits[CI] 2.1-5.3); 4.2 fold in that community women (95 percent CI 2.9-5.6). Among miscarrying women first interviewed at 6 weeks and 6 months, but not among those interviewed previously, the proportion scoring 30 + was significantly elevated, 2.6 to 3 fold, respectively. Lower scores among reinterviewed women at 6 weeks and 6 months were attributed to therapeutic or test effects of study interviews. At 2 weeks after loss the proportion of childless miscarrying women scoring 30 + was 5.7 and 11.0 fold that in childless pregnant and community women, respectively. At 6 weeks and 6 months, the childless miscarrying women remained significantly more depressed than childless community women, 3.3 and 5.1 fold, respectively. For women with children, the effects of miscarriage were largely confined to the 2-week time point. Prior reproductive loss and advanced maternal age (35 + years) did not affect symptom levels. This study, the first controlled investigation of the psychiatric effects of miscarriage, demonstrates that early reproductive loss is associated with substantial symptom elevation. This elevation is most pronounced and prolonged for childless women.

References:

Clarke M, Williams AJ. Depression in women after perinatal death. *Lancet* II:916-17, 1979.

Kennell JH, Slyter H, Klaus MH. The mourning response of parents to the death of a newborn infant. *N Engl J Med* 283:344-49, 1970.

NR359 **Wednesday, May 16, 9:00 a.m. - 10:30 a.m.**

SLEEP ABNORMALITIES IN REMITTED DEPRESSIVES

Michael E. Thase, M.D., Psychiatry, WPIC, 3811 O'Hara Street, Pittsburgh, PA 15212; Anne D. Simons, Ph.D.

Educational Objectives:

To become familiar with the basic EEG sleep changes of depression, their relation to state- and trait-like abnormalities, and their value for prediction of relapse.

Summary:

Although the electroencephalographic (EEG) sleep features of depression are well-described, much less is known about the resolution of these abnormalities across the recovery process. We now report the EEG sleep findings for 50 outpatient remitted, unmedicated RDC endogenous depressives, studied before and after 16 weeks of treatment with Becks's cognitive therapy. Results strikingly demonstrated the persistence of EEG sleep disturbances: none of 22 sleep measures showed evidence of normalization and 60 percent of remitted patients continued to manifest multiple EEG sleep abnormalities, including reduced REM latency and diminished slow wave sleep. Results of follow-up studies obtained in 8 patients after one year of sustained remission also revealed little evidence of normalization. The findings indicate that prominent aspects of the EEG sleep profiles of depressives may be more trait-like than previously suspected. Ongoing longitudinal study of our sample will evaluate whether such "traits" may be vulnerability markers for relapse or recurrence.

References:

Thase ME, Kupfer DJ: Current status of EEG sleep in the assessment and treatment of depression. In Burrows GD, Werry JS (eds): Advances in Human Psychopharmacology, Volume4. Greenwich, CT:JAI Press, 93-148, 1987.

Rush AJ, Erman MK, Giles DE, et al: Polysomnographic findings in recently drug-free and clinically remitted depressed patients. *Arch Gen Psychiatry,* 43:878-884, 1986.

NR360 **Wednesday, May 16, 9:00 a.m. - 10:30 a.m.**

LINKAGE STRATEGIES FOR BIPOLAR AFFECTIVE DISORDER

Sylvia G. Simpson, M.D., Psychiatry, Johns Hopkins Univ, Meyer 3-181 Johns Hospital, Baltimore, MD 21205; Susan E. Folstein, M.D., J. Raymond DePaulo, Jr., M.D.

Educational Objectives:

To discuss strategies of overcoming the problems of heterogeneity and bilineality in linkage studies of bipolar affective disorder.

Summary:

Most genetic linkage studies have used one or a few very large families to try to deal with the issue of genetic heterogeneity. However, recent reports have failed to confirm the linkage of bipolar disorder to markers on chromosome 11p and have raised concerns about using such large pedigrees in linkage studies of bipolar disorder. An alternative approach, which we are using to study bipolar affective disorders, is to use a DNA marker (RFLP) map, improved linkage methods, and a set of small families with multiple affected sibs. Families with more than one disease gene for affective disorder (called bilineal families) present a substantial problem for current linkage analyses which are efficient at detecting only one disease locus per family. In our initial screening of approximately 1,000 bipolar pedigrees, we ruled out many families where both parents were obviously affected and identified 45 families with bipolar type I proband and two or more sibs affected with either bipolar or recurrent unipolar disorders. Further evaluation revealed that only 12 of those families were clearly unilineal. We will discuss strategies for dealing with bilineal families, as well as the genetic implications of the high prevalence of bilineality in multiply-affected families, and will present the results of our linkage analyses to date.

References:

(1) Lander, E. and Botstein, D.: "Strategies for studying heterogeneous genetic traits in humans by using a linkage map of restriction fragment length polymorphisms." Proc. Natl. Acad. Sci. 83:7353-7357, 1986.

(2) Merikangas, K. and Spiker, D: "Assortative mating among in-patients with primary affective disorder." *Psychological Medicine.* 12:753-764, 1982.

NR361 **Wednesday, May 16, 9:00 a.m. - 10:30 a.m.**

QUANTITATIVE SPECT CHANGES WITH TREATMENT OF DEPRESSION

Anand Kumar, M.D., Psychiatry, Univ of Pennsylvania, 3615 Chestnut St Ralst. Pen., Philadelphia, PA 19014; P. David Mozley, M.D., Michel V. Velchik, M.D., Chris Dunham, M.D., John Reilley, CNMT, Abass Alavi, M.D

Educational Objectives:

This is the first study to demonstrate consistent changes in the cerebral/cerebellar functional relationship with treatment of depression.

Summary:

Major depressive disorder (MDD) is one of the most common mental health problems in the elderly. We set out to examine the relationship of clinical improvement of MDD with somatic treatment (antidepressants or electroconvulsive therapy) to I-123-IMP uptake in the brain using SPECT. Four subjects (mean age $\pm$ SD = 79 $\pm$ 8) who met *DSM-III-R* criteria for MDD with the first depressive episode occurring after age 60 (LOD) were studied before and after treatment. Clinical improvement was associated with a drop in the mean Hamilton rating scale score for depression (HRSD) from 20 pretreatment to 7 post-treatment. Thirty minutes after injecting 5 mci of IMP, subjects were scanned in the resting state with their eyes open and ears unoccluded and saggital images were used in this analysis. ROI's were generated and both absolute counts/pixel and ratios were obtained using the cerebellum as the reference. Clinical improvement was associated with a significant increase ($p < 0.05$, paired t test) in the mean cerebrum/cerebellum ratio of radioactivity (0.824 $\pm$ 0.030 pre to 0.878 $\pm$ 0.026 post). This was associated with a decrease in the absolute counts of radioactivity/pixel in both the cerebellum (1586 $\pm$ 275 pre vs 1171 $\pm$ 148 post) and cerebrum (1309 $\pm$ 219 pre vs 1029 $\pm$ 130 post) with the cerebellum consistently showing more striking decrements after treatment. There was significant correlation ($r = 0.74$, $P < 0.05$, Spearman rank correlation) between HRSD scores and absolute radioactivity in the cerebellum both before and after treatment. These preliminary data suggest that there is a significant change in the cerebrum/cerebellum functional relationship, as determined by IMP SPECT, with successful treatment of MDD. These findings may have important implications with regard to both the pathophysiology and treatment of LOD.

References:

1) G.S. Alexopoulas, R.C. Young, B.S. Meyers et al. Late Onset depression. (1988) Psychiatr Clin N Am Vol 1:101-115

2) L.R. Baxter, M.E. Phelps, J.C. Mazziotta et al. Cerebral metabolic rates for glucose in mood disorders *Arch Gen Psychiatry* 42:441-447, 1985.

NR362 **Wednesday, May 16, 9:00 a.m. - 10:30 a.m.**

LITHIUM-7 NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY OF THE HUMAN BRAIN

Laslo Gyulai, M.D., Psychiatry, Hosp. Univ. Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104; Steven W. Wicklund, B.S., Robert Greenstein, M.D., Mark S. Bauer, M.D., Patrick Ciccione, M.D., Peter Whybrow, M.D.

Educational Objectives:

At the end of the presentation the learner should be familiar with the basic concepts of 7-lithium magnetic resonance spectroscopy, it's potential use in the management of bipolar disorder and the pharmacodynamics of lithium in the brain and muscle of patients with bipolar disorder.

Summary:

Measurements of the lithium concentration in the occipital pole of the head and calf muscle of nine patients with bipolar disorder in remission were performed using *in vivo* lithium-7 nuclear magnetic resonance spectroscopy (^{7}Li-NMR)(1,2). ^{7}Li-NMR measurements were performed on one-meter bore, 1.85 Tesla, superconducting magnet supplemented with a multinuclear spectrometer, using 11.5 cm diameter surface coils.

The average lithium concentration in the occipital pole was 0.36 $\pm$ 0.03 mEq/L, while in the muscle it was 0.50 $\pm$ 0.06 mEq/L, both lower than the average serum lithium concentration (0.79 $\pm$ 0.08mEq/L). The average brain/serum lithium concentration ratio was 0.47 $\pm$ 0.04 while the average muscle/serum lithium concentration ratio was 0.66 $\pm$ 0.07. There was a positive correlation between the brain vs. serum and brain vs. muscle lithium concentrations. The calculated average brain intracellular/extracellular lithium concentration ratio was 1.65. Hypotheses are advanced that:

1) human brain tissue may accumulate lithium against concentration gradient

2) the minimal effective concentration of brain lithium concentration for maintenance treatment of bipolar disorder is around 0.2-0.3 mEq/L.

References:

1) Renshaw PF, Wiclund S: In Vivo Measurement of Lithium in Humans by Nuclear Magnetic Resonance Spectroscopy. *Biol. Psychiatry* 23:465-475, 1988.

2) Komorosky RA, Newton J, Walker E, Cardwell D, Chang C: Lithium-7 In Vivo NMR Spectroscopy of Rats and Humans. Abstr. Soc. Magn. Reson. Med.:57, 1988

NR363 **Wednesday, May 16, 9:00 a.m. - 10:30 a.m.**

IMIPRAMINE IS EFFECTIVE TREATMENT FOR COGNITIVE THERAPY NONRESPONDERS

Jonathan W. Stewart, M.D., Psychiatry, New York State Psych Inst, 722 West 168th Street, New York, NY 10032; Frederic M. Quitkin, M.D., Mary Ann Mercier, Ph.D.

Educational Objectives:

To inform the clinician of the likelihood of imipramine response in patients who have not benefitted from short-term cognitive therapy.

Summary:

Studies comparing cognitive therapy to tricyclic antidepressants report similar rates of efficacy, usually in the range of 50-70 percent. These rates compare favorably to usual rates of placebo response, although few comparative studies included a placebo control group. If cognitive therapy and imipramine are effective for the same subpopulation of depressed patients, imipramine should not be effective when cognitive therapy is not, and vice versa.

We sought to test this hypothesis by first treating depressed outpatients with 16 weeks of cognitive therapy, then randomly assigning nonresponders to imipramine or placebo for six weeks. Of 16 patients judged not to have benefitted from cognitive therapy, 12 completed the subsequent imipramine/placebo trial. All six patients randomized to imipramine responded, while there were no placebo responders (chi square = 12.000, p = .0005).

These results suggest that cognitive therapy and imipramine may be effective for different populations of depressed patients. Although equally effective for large groups of patients, they may be differentially effective for individual depressives. If corroborated by a larger sample, cognitive therapy may effectively remove potential placebo responders, as well as imipramine nonresponders from the pool of depressed patients, leaving a population most of whom will benefit from imipramine. Thus, imipramine may be a highly effective treatment for depressed patients who do not benefit from short-term cognitive therapy.

NR364 **Wednesday May 16, 9:00 a.m. - 10:30 a.m.**

PERSONALITY DISORDER STRUCTURE IN TWO SAMPLES

W. John Livesley, M.D., Psychiatry, University of B.C., 2211 Wesbrook Mall, Vancouver BC, Canada V6T 2B5; Marsha L. Schroeder, Ph.D.

Educational Objectives:

To present recent research on the classification of personality disorder that is especially relevant to the question of whether personality disorders should be classified by using a dimensional or categorical model.

Summary:

The question of whether personality disorder should be classified using a categorical or dimensional model has received considerable discussion without resolution. The question can be investigated empirically. If personality disorders are best represented using a categorical system, the distribution of personality characteristics should be discontinuous across clinical and nonclinical samples. Furthermore, correlations between characteristics should differ in the two samples resulting in different factorial structures (Eysenck, 1987). This hypothesis was tested on a sample of personality disorder patients (N = 158) and a general population sample (N = 274). Subjects completed a structured personality questionnaire assessing the traits defining *DSM-III-R* personality disorders. The questionnaire possesses satisfactory psychometric properties (Livesley, Jackson, and Schroeder, 1989). Principal component analyses were performed on the two data sets; 15 components were extracted. The Varimax rotated clinical pattern matrix was used as the target for an orthogonal Procrustes rotation of the general population pattern. Congruence coefficients were computed to examine the degree of factor correspondence. The results indicate substantial similarity in the organization of personality disorder features in the two samples. Congruence coefficients were high for most factors (Range 0.98 - 0.62). The factorial structure underlying the personality traits in the combined sample will also be described. The results support a dimensional classification of personality disorders.

References:

Eysenck, HJ. The definition of personality disorders and the criteria appropriate to their definition. *Journal of Personality Disorders* 1:211-219, 1987.

Livesley WJ, Jackson DN, Schroeder ML. A study of the factorial structure of personality pathology. *Journal of Personality Disorders,* 3:292-306, 1989.

NR365 **Wednesday May 16, 9:00 a.m. - 10:30 a.m.**

EYE MOVEMENT DYSFUNCTION IN SCHIZOTYPAL PERSONALITY DISORDER

David P. Bernstein, Ph.D., Psychiatry, Bronx VA Medical Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Richard S.E. Keefe, M.A., Emil F. Coccaro, M.D., Jeremy M. Silverman, Ph.D., Richard C. Mohs, Ph.D., Larry J. Siever, M.D.

Educational Objectives:

To familiarize attendees with new research on attentional/psychophysiological impairment in schizophrenia-related disorders.

Summary:

In order to investigate the relationship between eye movement dysfunction (EMD) and schizotypal personality disorder, 26 schizotypal patients were compared to 17 patients with non-schizophrenia-related personality disorders, 44 schizophrenic patients, and 29 normal controls. Patients were diagnosed with the SADS and SIDP, and kept medication free for at least two weeks prior to study. Eye tracking was measured electroculographically, with tracings rated by two independent, blind raters ($r = .93$). Both schizophrenic and schizotypal patient groups evidenced significantly worse eye tracking than the normals by Scheffe contrasts ($p < .05$), while the other personality disorder patients did not significantly differ from the controls. Only one of the schizotypal criteria, social isolation, significantly predicted EMD (stepwise regression: $F = 4.40$, $p < .05$). Preliminary results of a second study using infrared assessment suggest that EMD in both schizotypal patients and "odd cluster" relatives of schizophrenics was intermediate between schizophrenics and control groups (other personality disorder patients, screened relatives of schizophrenic patients, and normals). These results support the existence of a "schizophrenia spectrum" characterized by attentional/psychophysiologic impairment and social isolation.

References:

1) Siever LJ, et al: Eyetracking impairment in clinically identified schizotypal personality disorder patients. *American Journal of Psychiatry* (in press).

2) Siever LJ, et al: Smooth pursuit eye movement impairment: A vulnerability marker for schizotypal personality disorder in a volunteer population, *American J. Psychiatry,* 141:1560-1566, 1986.

NR366 **Wednesday May 16, 9:00 a.m. - 10:30 a.m.**

TESTING A SCALE FOR OUTCOME PREDICTION IN BPD

Jonathan R. Aronoff, Ph.D., Austen Riggs Center, Main Street, Stockbridge, MA 01262; Eric M. Plakun, M.D., Thomas H. McGlashan, M.D., George S. Patrick, M.D.

Educational Objectives:

After reviewing these data the learner should understand the state of knowledge of outcome prediction in BPD and the predictive value of McGlashan's prognostic scale for borderlines in the Austen Riggs sample and be able to list new predictors proposed for further development of a prognostic scale for borderlines.

Summary:

McGlashan, Plakun, Stone, and Paris have all published longitudinal studies of borderline personality disorder (BPD) demonstrating outcome heterogeneity. McGlashan and Plakun have reported outcome predictor variables. McGlashan has developed two prognostic scales for BPD patients derived from the Chestnut Lodge follow-up sample: one derived from a pure sample of non-comorbid inpatients females and the second from a combined group of pure and comorbid male and female inpatients. The current study tests both McGlashan prognostic scales, applied by two raters with established reliability, on the Austen Riggs Center sample of 31 pure, non-comorbid BPD patients at mean 14-year follow-up. Correlation coefficients are reported on the predictive power of each scale and each of the 11 items composing them against seven dimensions of outcome at long-term follow-up. Neither scale was significantly predictive of outcome alone. When both scales were combined there was a significant correlation with the Strauss-Carpenter Social Scale at follow-up ($r = 0.36$, $p = < .05$). Item by item correlations showed three achieving statistical significance (affective instability, depressed thinking, and highest maximum IQ). When used as a scale these three items had significant predictive capacity. The authors propose additional predictors extracted from the Austen Riggs Center sample to advance development of a prognostic scale for borderlines based on samples from two different hospitals.

References:

McGlashan TH: The borderline syndrome. I. Testing three diagnostic systems. II. Is it a variant of schizophrenia or affective disorder? *Arch Gen Psychiatry* 40:1311-1323, 1983

Plakun EM, Burkhardt PE, Muller JP: 14-year follow-up of borderline and schizotypal personality disorders. *Compr Psychiatry* 26:448-455, 1985.

NR367 **Wednesday May 16, 9:00 a.m. - 10:30 a.m.**

A NEW LOOK AT THERAPEUTIC ALLIANCE AND OUTCOME

Marianne Kardos, M.D., Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139; J. Christopher Perry, M.D., Jon Perry, Ph.D.

Educational Objectives:

This presentation reviews aspects of therapeutic alliance which are important to attend to because they promote a positive treatment outcome. The study suggests that deterioration of the alliance within a single session may be a better predictor of outcome than its overall level. This parallels the concept of regression, which in certain patients may predict poorer outcome in therapy.

Summary:

In psychotherapy studies, therapeutic alliance in early sessions has predicted later symptomatic improvement. This pilot study explores the potential value of assessing therapeutic alliance at three different junctures in therapy: at intake, and in early and later sessions. The Therapeutic Alliance Analogue Scales (TAAS), adapted from the Vanderbilt Psychotherapy Process Scales, can assess both non-therapy intake interviews as well as therapy sessions. Seven patients with personality disorders or significant traits entering individual dynamic therapy participated. Patient alliance was assessed by raters using the 17-item patient alliance TAAS scale on the following: 1) each of two videotaped intake interviews, 2) four early and 3) four late therapy sessions at one year. Each intake interview was rated as a whole, while each therapy session was divided into thirds, and rated after the segments had been presented in random order by patient, time (early vs. late session), and segment order within the sessions (beginning, middle, end). Outcome at one year was measured by change descriptively on the GAS and dynamically on the Psychodynamic Conflict Rating Scales.

At one year, all patients improved dynamically, while three improved descriptively. Mean patient alliance scores from the intake interviews and early sessions both predicted descriptive but not dynamic improvement. The mean trend toward a deterioration in alliance within a session (negative slope across segments) predicted poorer dynamic improvement. This finding suggests that patients whose alliance regresses within therapy sessions despite an overall positive alliance have poorer dynamic outcomes. Future research should examine both the overall level and regressive trends in therapeutic alliance as more powerful predictors of subsequent change.

References:

(1) Strupp HH, Suh CS, O'Malley SS. The Vanderbilt Process Measures: the Psychotherapy Process Scale (VPPS) and the Negative Indicators Scale (VNIS). In: Greenberg LS and Pinsof WM, eds. The Psychotherapeutic Process—A Research Handbook, New York, NY: the Guildford Press, 285-313, 1986.

(2) Luborsky LL, McLellan AT, Woody CE, O'Brien CP, Auerbach A. Therapist Success and Its Determinants. *Arch Gen Psychiatry. 42: 602-611, 1985.*

NR368 **Wednesday May 16, 9:00 a.m. - 10:30 a.m.**

BROMOCRIPTINE AND REACTIVITY TO COCAINE CUES

Henry R. Kranzler, M.D., Psychiatry, Univ of Conn Hlth. Ctr., 263 Farmington Avenue, Farmington, CT 06032 Lance Bauer, Ph.D.

Educational Objectives:

To clarify the relationship between cue exposure and subjective and autonomic reactivity in cocaine dependence. To clarify the effects of bromocriptine on the reactivity.

Summary:

Prior studies have indicated that abstinent cocaine-dependent patients report an increased desire to use cocaine and exhibit signs of increased autonomic nervous system (ANS) arousal when exposed to cocaine-associated stimuli. The present study tested the ability of bromocriptine to dampen these stimulus-evoked increases within a controlled laboratory setting. Twenty cocaine-dependent patients viewed videotapes of cocaine-associated and neutral stimuli in two laboratory sessions, scheduled one week apart. Measures of ANS activity and subjective ratings of the desire for cocaine and of the intensity of cocaine intoxication and withdrawal symptoms were recorded during both sessions. Between sessions, patients received either bromocriptine (1.25 mg) or placebo, administered b.i.d. in double-blind fashion. The results indicated that during the first laboratory session the cocaine film evoked significant changes in desire for cocaine, in respiratory sinus arrhythmia (RSA), and in the intensity of several symptoms of cocaine intoxification. During the second laboratory session, many of these effects either diminished or disappeared. Yet this decrease in reactivity was not attributable to bromocriptine: the drug had no significant effect on the desire for cocaine, RSA, or cocaine intoxication symptom severity. Bromocriptine did increase self-rated hostility, fear, and paranoia. It also produced increases in heart rate and decreases in pulse transit time in response to the cocaine film which were not detectable in patients who received placebo. The implications of these findings will be discussed in terms of current theories of conditioning, approach-avoidance, and ANS response specificity.

References:

Childress AR, McLellan AT, Ehrman R, O'Brien CP: Classically conditioned responses in opioid and cocaine dependence: A role in relapse? *Learning Factors in Substance Abuse.* National Institute on Drug Abuse Research Monograph 84. DHHS Pub. No. (ADM) 88-1576. Washington, D.C.: Supt of Docs., U.S. Gov't Print. Office, 1988, pp. 25-43.

NR369 **Wednesday May 16, 9:00 a.m. - 10:30 a.m.**

LONG-TERM MORTALITY OF ANOREXIA NERVOSA

L.K. George Hsu, M.D., Psychiatry, WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213; Arthur H. Crisp, M.D., John S. Callender, M.B., Walter H. Kaye, M.D.

Educational Objectives:

At the end of the program, the learner should be able to know the long-term (20 year) mortality and causes of death of anorexia nervosa in Aberdeen and St. George's Hospital, London, and how they compare with findings in other studies.

Summary:

Two female anorectic cohorts, one from the Aberdeen Case Register (1965 to 1973, N = 63) and the other under Professor Crisp at St. George's Hospital Medical School in London (1968 to 1973, N = 105), were followed after a mean duration of 24 (range 17 to 44) years from onset of illness. All the Aberdeen patients had some refeeding in a psychiatric or medical ward but received minimal psychotherapy, while 75 percent of the St. George's patients had medical and psychotherapeutic intervention. The two cohorts were comparable in terms of age at presentation, age at follow-up, and duration of follow-up. However, the Aberdeen cohort, while significantly older at onset of illness (19.1 ± 5.3 vs. 16.8 ± 3.8, $t = 3.27$, $df = 166$, $p < 0.01$), had a shorter duration of illness at initial presentation (2.0 ± 2.4 vs. 3.7 ± 4.1, $t = 3.0$, $df = 166$, $p < 0.01$). Two Aberdeen and four St. George's patients were untraced, although not recorded as dead at the National Health Service Central Register. The crude mortality was 12.7 percent (8/63) in Aberdeen and 3.8 percent (4/105) at St. George's. Complications of malnutrition and suicide were the most common causes of death. Based on expected mortality calculated from sex specific mortality rates for the respective populations in 1981 (mid-point of follow-up period) the standardized mortality ratio (SMR) was 471 (8/1.70) for Aberdeen, and 136 (4/2.95) for St. George's. The difference in SMR between the two cohorts is unlikely to be related entirely to patient selection, and, compared with other long-term studies, the low mortality of the St. George's cohort is unexpected. To us, the finding indicates that comprehensive treatment of this disorder may at least reduce its mortality.

References:

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NR370 **Wednesday, May 16, 12 noon - 2:00 p.m.**

THE ROLE OF QUANTITATIVE EEG IN NEUROPSYCHIATRIC LUPUS

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Summary:

Neuro-psychiatric manifestations of systemic lupus erythematosus (NP-SLE) are quite common with a prevalence of between 24 to 75%. This disparity is contributed to by the lack of diagnostic criteria for determining neuro-psychiatric involvement and inherent difficulties in distinguishing neuro/psychiatric symptoms which arise from CNS involvement from those which are secondary in nature. A diagnostic test for NP-SLE must be highly sensitive, specific, and capable of quantifying the severity and chronology of the event. The neurometric approach to quantitative EEG (QEEG) compares QEEG features from individual patients to an age appropriate normative data base. QEEG profiles express the degree to which each EEG feature deviates from normal. This approach is culture free and capable of distinguishing patients with cognitive, psychiatric and neurological dysfunctions from normals and from one another. In the present study we examined the sensitivity and specificity of this approach in SLE patients including; (a) patients with objective signs of NP-SLE, (b) patients with no objective signs but with subjective complaints, (c) patients with no current symptoms but with a prior history of NP-SLE, and (d) SLE control patients. QEEG sensitivity was 87% with a specificity of 84% for patients in groups a and d respectively. The putative role of the QEEG as an index of the severity and chronology of NP-SLE will also be presented.

NR371 **Wednesday, May 16, 12 noon - 2:00 p.m.**

KINDLING: SOMATOSTATIN AND ENKEPHALIN IMMUNOREACTIVITY

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Summary:

Characteristics of the kindling phenomenon have led to hypotheses concerning clinically totally unrelated conditions such as psychiatric manifestations of epilepsy, alcoholism, affective disorder and tardive dyskinesia. The mechanisms underlying kindling are still unclear, but GABA systems and neuropeptides seem involved in the process.

We studied somatostatin (SS) met-enkephalin and cholecystokinin (CCK) using immunochemistry in rats 24 hours following full hippocampal kindling (three stage 5 seizures). Sham-kindled rats, unoperated rats and rats given a single electroconvulsive seizure (ECS) served as controls.

The important findings were that following kindling there was, as compared to unoperated controls, 1) a hitherto undescribed marked increase of SS immunoreactivity in cell bodies in the dentate hilus and their presumed projections area in the outer parts of the dentate molecular layer, - and 2) a marked increased of met-enkephalin immunoreactivity in hippocampal mossy fiber terminals. There was no increased growth of mossy fibers and no change in CCK.

As the increase of SS immunoreactivity was absent after a single ECS it is not explained by the seizures *per se*, and therefore it seems likely that somatostatin may play a role in the induction and maintenance of the kindling process.

NR372 **Wednesday, May 16, 12 noon - 2:00 p.m.**

DECREASED CHOLESTEROL IN MANIA

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Summary:

On admission, the group of all 107 patients with acute mania admitted to a teaching university hospital over a four-year period showed serum cholesterol levels 10% lower (186.2, SD 45.2 mg/dL, $p < .0025$, $F = 9.42$) than 83 controls (207.0, SD 47.3 mg/dL). The average cholesterol of all 132 admitted depressives was still higher (214.0, SD 42.6 mg/dL). Controls were all admissions for elective cartilage surgery, with history of no psychiatric illness. Height-to-weight ratio, a measure of nutritional status, was not a significant covariant ($F = 0.44$, $p = .51$) of the cholesterol difference. Inclusion of sex as a covariant increased significance ($F = 12.9$, $p = .0004$); cholesterol was separately lower among both male manics (176.1, SD 37.3 mg/dL) vs. male controls (201.5, SD 45.0 mg/dL, $F = 8.06$, $p = .005$), and female manics (193.9, SD 49.2 mg/dL) vs. female controls (225.1 SD 51.0, $F = 5.44$, $p = .02$). Age was covaried with every comparison. These cholesterol differences are clinically meaningful; dietary aberration is the most straightforward rationalization. Perhaps it is coincidence that cholesterol comprises about 4% of brain white matter and 0.7% of gray matter, but the organic lesion of mania remains unidentified.

NR373 **Wednesday, May 16, 12 noon - 2:00 p.m.**

COMBINED BUSPIRONE-FLUOXETINE IN SEVERE DEPRESSION

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Summary:

Ten patients with severe treatment resistant major depression were treated with a combination of buspirone and fluoxetine. Buspirone was dosed 40-60 mg/day and fluoxetine 20-40 mg/day. All patients had previously responded to fluoxetine alone, but had lost antidepression efficacy over time regardless of fluoxetine dose. Addition of buspirone restored antidepressant activity when buspirone doses of 40-50 mg/day were reached. In four patients fluoxetine was discontinued. The patients continued to do well on buspirone 40-50 mg per day for one to two months and then efficacy decreased. When fluoxetine was reintroduced efficacy was restored. The combination of buspirone and fluoxetine is more potent in antidepressant activity than either drug alone. Side effects of the combined treatment were minimal. Since both compounds affect serotonergic transmission, buspirone by a direct agonist effect, and fluoxetine by serotonin reuptake inhibition, it is postulated that the combined therapy more fully utilizes the serotonergic system to achieve antidepressant activity. The combined therapy has continued to be efficacious for over 6 months. While this study is not placebo controlled, it provides early evidence that severely depressed patients who initially showed some efficacy to fluoxetine but lost efficacy with time, may benefit from the addition of buspirone at 40-60 mg/day doses.

NR374 **Wednesday, May 16, 12 noon - 2:00 p.m.**

PURE VERSUS COMPOUNDED DEPRESSION: OUTCOME AT 12 MONTHS

Gabor I. Keitner, M.D., Butler Hospital, 345 Blackstone Blvd., Providence, RI 02906; Christine Ryan, Ph.D., Ivan W. Miller, Ph.D.

Summary:

Patients with DSM-III major depression only (pure depressed) were compared to depressed patients with a coexistent Axis I, II or II illness (compounded depression) at the acute stage of a depressive episode and at monthly intervals throughout a one-year follow-up period. Over 1/2 of the patients (52.6%) had a concurrent psychiatric or medical condition, with no particular Axis I, II or III disorder predominating. At 12 months post-hospitalization, twice as many of the pure depressed were recovered compared to those with compounded depression (65% vs. 33%, $X^2 = 6.79$, $p < .01$). No differences were found in pharmacotherapy at discharge of 12-month follow-up, nor in the percentage receiving family therapy. The compounded depressed, however, were significantly more likely than the pure depressed to receive individual psychotherapy (95% vs. 64%, $X^2 = 9.07$, $p < .01$). An interaction effect between gender and depression type was noted; while recovery rates for male and female patients did not differ for the compounded depressed, all of the males with pure depression recovered compared to only one-half of the females ($X^2 = 7.17$, $p < .01$). Throughout the follow-up period patients with pure depression had significantly better social adjustment ratings than did those with compounded depression. Overall, the study provides evidence that comorbidity in depression is a common phenomenon; it also suggests that a compounded depression, irrespective of the accompanying diagnosis, adversely affects the course of the illness and outcome, necessitating the development of more comprehensive and effective treatments for this subgroup of depressed patients.

NR375 **Wednesday, May 16, 12 noon - 2:00 p.m.**

RECOVERY AND MAJOR DEPRESSION

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

Summary:

During hospitalization for a depressive episode 78 patients with a DSM-III diagnosis of major depression were assessed on a variety of clinical, psychosocial, and family functioning measures. Of the 70 patients who were followed throughout the one-year study period, 49% were recovered at least 12 months. Recovery status at 12 months was then used to determine which factors differentiated recovered patients from those who did not recover. Patients who recovered were significantly less likely to have a coexistent medical and/or psychiatric condition. Recovered patients had a significantly shorter length of hospitalization, later age of onset of the depression, and lower levels of neuroticism. Further, those who recovered were less likely to have had two or more previous hospitalizations, reported fewer life events, had better family functioning, and better post-hospitalization social adjustment ratings than those not recovered. Gender was marginally significant, with 64% of the males recovered vs. only 40% of the females. No differences were found in treatments received, severity of the illness at hospitalization, number of previous depressive episodes, length of longest depressive episode, suicidality, social support, marital status, or socioeconomic status. Improvement in depressive symptomatology and social functioning as early as one month post-discharge predicts favorable long-term outcome. Additionally, improvement in family functioning is very strongly associated with recovery from the depression.

NR376 **Wednesday, May 16, 12 noon - 2:00 p.m.**

THE COMORBIDITY OF ANXIETY AND DEPRESSION IN DAILY LIFE

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Summary:

Anxiety patients who consulted a specialty CMHC clinic for anxiety were studied using the Experience Sampling method. Subjects were randomly signaled 10 times a day for 6 days to fill out self-report forms assessing their mental state and the situation in which they occurred. The compliance with the method and construct validity were high. Matched on demographic variables, subjects were divided into 4 groups ranging from low anxiety and low depression to high anxiety and high depression, based on their scores on the state trait anxiety inventory and the ZUNG scale for depression. No differences were found between these groups on the frequency of co-occurrence of anxiety and depression. The occurrence of anxiety and depression was not related to major environmental factors such as place, activity and social situation when a log-linear model was fitted to the data. The occurrence of anxiety and depression was however linked to the moment of the day with depressive events having a higher frequency during the morning period. Moreover, the covariation of anxiety and depression did not differentiate the 4 comorbid groups instead of a range of individual variations were found in each group. These data suggest that the impact of cross-sectionally defined comorbid conditions on the experience of psychopathology should be interpreted cautiously. Cross-sectional assessments of comorbidity may reflect other factors than their occurrence or co-occurrence in daily life. These data further suggest that the impact of comorbidity is more directly related to an increase in severity than to a specific aspect of the comorbid process.

NR377 **Wednesday, May 16, 12 noon - 2:00 p.m.**

LIFE EVENTS AND SEVERE MOOD DISORDERS

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Summary:

The aim of this study was to assess the contribution of stressful life events (SLE) during various periods of the patient's life, to the development and course of severe mood disorders. Two experimental groups of 50 unipolars and 50 bipolars and two matched control groups of 50 normals and 50 borderline patients were asked to record SLE for their whole lifetime on revised PERI and Coddington life events scales. The subjective components of SLE were assessed by a semi-structured interview. Life events and attributions towards them were compared among groups by ANOVAs and Duncan tests. The experimental groups reported more losses in childhood and an increased frequency of life events, especially negative events, losses and uncontrolled events only during the year preceding the first episode. The investigators contend that loss events during childhood contribute to the formation of a "depression node." An aggregation of SLE during the year preceding the first affective episode may spur the activation of a mechanism of pathological reactivity, linked to the "depression node." Such a mechanism, once established, will be reactivated in the future even by less numerous and less severe stressors.

NR378 **Wednesday, May 16, 12 noon - 2:00 p.m.**

ENDOCRINE EFFECTS OF SDZ HDC-912 IN SCHIZOPHRENIA

Fabrice Duval, M.D., Psychiatry, C.H. Specialise, Service Du Dr Macher, Rouffach 68250, France; M-Claude Mokrani, Ph.D., Jean-Paul Macher, M.D., Jean-Marc Moeglen, B.Psych, Paul Bailey, M.B.

Summary:

The ergoline derivative SDZ HDC-912 exhibits simultaneously dopamine (DA) agonist and antagonist activity, the latter being predominant within the CNS. Based on this dual pharmacological activity, this compound may be considered as a potential antipsychotic agent (DA-antagonist properties) without producing neurological adverse effects (DA-agonist component). In order to evaluate SDZ HDC-912 activity we investigated neuroendocrine effects during treatment in 11 inpatients (7M, 4F ; mean 28.6 ± 5.8 SD yrs) who met DSM III criteria for schizophrenia. Circadian secretion of prolactin (PRL) and hormonal responses to apomorphine hydrochloride (APO 0.75 mg subcutaneously), a short acting dopamine receptor agonist, were studied after a minimum 10 day wash-out and after a four-week treatment period. The neuroendocrine changes produced by SDZ HDC-912 were : 1) A significant decrease in plasma circadian variations of PRL (i.e. mesor : $p<0.01$; amplitude : $p<0.01$; percent of rhythm : $p<0.05$). 2) A significant blunting of PRL suppression to APO (measured by percentage of change from baseline obtained by area under the curve (AUC) ($p<0.02$). 3) A significant decrease in growth hormone (GH) stimulation (measured by GH-AUC) ($p<0.04$). The strong prolactin suppression differentiates SDZ HDC-912 from typical antipsychotic drugs. Moreover the blunting of PRL and GH responses to APO is in accordance with the AD-agonist/antagonist properties of this agent.

NR379 **Wednesday, May 16, 12 noon - 2:00 p.m.**

TRH-TSH TEST, DST AND ANTIDEPRESSANT TREATMENT

Fabrice Duval, M.D., Psychiatry, C.H. Specialise, Service Du Dr Macher, Rouffach 68250, France; Jean-Paul Macher, M.D., M-Claude Mokrani, Ph.D., Jaurez Oliveira Castro, M.D., Marc-Antoine Crocq, M.D.

Summary:

We studied TSH response after TRH injection (200 ug I.V.) at 8 AM and 11 PM, and cortisol suppression after dexamethasone ingestion (1mg) on the same day at midnight in 47 drug-free inpatients with DSM-III-R Major Depressive Episode (MDE) (19M/28F, mean 39.8 ± 10.8 SD yrs), and 23 hospitalized controls (11M/12F, mean 35.5 + 9.2 SD yrs). In both groups, ΔTSH (TSH increment above baseline) was significantly greater at 11 PM than 8 AM ($p < .00001$). The difference between 11 PM- ΔTSH minus 8 AM- ΔTSH (ΔΔTSH) was significantly lower in patients than in controls ($p < .00001$). Thirty-five MDEs (74%) showed a blunted ΔΔTSH (i.e. less than 3 uU/ml) ; 17 (36%) were DST non-suppressors (i.e. plasma cortisol above 140 nmol/l). Twelve patients (25%) had both abnormal DST and ΔΔTSH ; 7 patients (15%) showed no abnormality. Subsequently, patients were treated with tricyclic antidepressants (23 with amitriptyline, 10 with clomipramine) or selective inhibitors of serotonin reuptake (9 with fluoxetine, 5 with fluvoxamine). After 4 weeks, 34 patients (72%) responded to treatment. The association of blunted ΔΔTSH and DST nonsuppression correlated with positive treatment response ($p < .04$, two-tailed Fisher's exact test), whereas neither TRH challenge nor DST alone were found to predict a positive outcome.

NR380 **Wednesday, May 16, 12 noon - 2:00 p.m.**

PRL RESPONSES TO TRH AND APOMORPHINE IN DEPRESSION

Fabrice Duval, M.D., Psychiatry, C.H. Specialise, Service Du Dr Macher, Rouffach 68250, France; M-Claude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Jaurez Oliveira Castro, M.D., Jean-Paul Macher, M.D.

Summary:

Prolactin (PRL) responses to thyrotropin-releasing hormone (TRH) challenge (200 ug I.V.) and to apomorphine (APO) (0.75 mg subcutaneously), a short acting dopamine receptor agonist, were studied after a minimum ten day Washout in 17 inpatients with a Major Depressive Episode (MDE) (11M/6F, mean 34.9 ± 7.7 SD yrs) and in 10 hospitalized controls (6M/4F, mean 36.6 ± 8.9 SD yrs). Both PRL stimulation by TRH (ΔPRL) and PRL suppression by APO (percentage of change from baseline obtained from area under curve) in MDEs did not differ from controls. In the whole population, there was a negative correlation between PRL response to TRH and the intensity of PRL suppression by APO ($rho = -0.57$, $n = 27$, $p < 0.007$). The latter finding underlines the pituitary interaction of dopamine (DA) and TRH and suggests that DA and TRH play mutually antagonistic roles.

NR381 **Wednesday, May 16, 12 noon - 2:00 p.m.**

CIRCADIAN VARIATIONS IN RESPONSE TO TRH CHALLENGE

Fabrice Duval, M.D., Psychiatry, C.H. Specialise, Service Du Dr Macher, Rouffach 68250, France; M-Claude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Jaurez Oliveira Castro, M.D., Jean-Paul Macher, M.D.

Summary:

We studied circadian TSH and prolactin (PRL) responses to TRH infusion (200 g I.V.) at 8 AM and 11 PM in 35 drug-free inpatients with DSM-III-R Major Depressive Episode (MD) (14M/21F, mean 34.8 ± 8.0 SD yrs) and 22 hospitalized controls (11M/11F, mean 35.2 ± 9.1 SD yrs). In each group, maximum TSH and PRL responses were lower at 8 AM than at 11 PM ($p < .0005$ and $p < .05$ respectively). The difference between 11 PM-ΔTSH minus 8 AM-ΔTSH (ΔΔTSH) was significantly lower in MDEs compared with controls ($p < .00001$). No such blunting was observed in PRL responses to the TRH in MDEs. In the overall population, there were significant correlations between TSH responses to TRH and TSH circadian parameters, i.e. mesor and amplitude (all $p < .0001$). These correlations were also observed with PRL. TSH mesor and amplitude were lower in MDEs than in controls ($p < .0001$). In controls PRL mesor and amplitude were not significantly different between diagnostic groups, matched for sex. Thus, ΔΔTSH seems to offer a chronobiological refinement to the mesure of thyroid axis dysfunction in major depression. However, the lack of concomitant alternations of PRL response to TRH suggests that the abnormal TSH response cannot be solely explained by a hyposensitivity of pituitary TRH receptors.

NR382 **Wednesday, May 16, 12 noon - 2:00 p.m.**

REFRACTORY DEPRESSION: A CONTROLLED CLINICAL TRIAL

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Summary:

This study reports the treatment outcome of 68 outpatients who were refractory to an adequate double-blind trial of either imipramine or phenelzine and completed crossover to the other drug under continuing double-blind conditions. All patients met Research Diagnostic Criteria for Major, Minor or Intermittent depression and exhibited mood reactivity to favorable events. The majority also met criteria for definite or probable atypical depression by Columbia criteria. Of patients refractory to phenelzine, 41% (9 of 22) responded to imipramine. Of patients refractory to imipramine, 67% (31 of 46) responded to phenelzine ($X^2 = 4.3$, $p < .05$). This is in agreement with open clinical trial data as well as with a controlled trial reported in the literature. The significance of these data to the clinician is that MAO inhibitor antidepressants are often elective in tricyclic unresponsive patients and should be used more frequently in these cases.

NR383 **Wednesday, May 16, 12 noon - 2:00 p.m.**

CHRONIC DEPRESSIVE DISORDER (DYSTHYMIA) RESPONDS TO A 5HT2 RECEPTOR ANTAGONIST, RITANSERIN

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Summary:

The aims of this study were to (i) undertake a prevalence study of dysthymia in an emergency service (ii) to test the validity of Akiskals' subclassification of dysthymic disorders and (iii) to seek to confirm an earlier report that dysthymia responds to treatment with 5HT2 antagonist ritanserin.

All consecutive referrals to the Maudsley Hospital Emergency clinic were screened for depression. Dysthymics were subdivided into late onset, variable onset, and early onset using Akiskals' criteria. Patients were entered into a double-blind, placebo-controlled parallel group trial of ritanserin for a four-week period. Sleep EEG data were obtained and repeated at the end of treatment.

Significant differences were found between patients categorized as major affective episode and dysthymia with regard to anxiety, age at onset of condition, family psychiatric history, and number of past affective episodes. No significant differences were found between patients with sub-affective dysthymic disorder and characterological dysthymic disorder.

Seventeen patients entered the treatment study. Analysis of covariance for the depression scores at week 4 (Hamilton Depression Rating Scale) showed a treatment effect. Ritanserin produced a significantly larger reduction in total scores than placebo ($P = 0.04$)

This study demonstrates that 5HT2 receptor blockade by ritanserin reduces the severity of depression in a patient population suffering from a chronic depressive disorder (dysthymia). The proposed subclassification of dysthymia (Akiskal 83) is not supported.

NR384 **Wednesday, May 16, 12 noon - 2:00 p.m.**

THE IMPORTANCE OF THE PLASMA DEXAMETHASONE WINDOW: A DOSE RESPONSE STUDY IN DEPRESSED PATIENTS

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Summary:

Cortisol escape following dexamethasone administration may reflect central disinhibition of the hypothalamic pituitary adrenal (HPA) axis or it may result from inappropriately low levels of plasma dexamethasone (O'Sullivan et al., 1989). In some patients, the 1mg dose of dexamethasone produces too high a level resulting in cortisol suppression irrespective of HPA axis function. To more accurately define the range of plasma dexamethasone levels that would allow reliable interpretation of HPA axis disinhibition, a dose response study using 2 doses of dexamethasone is reported. Patients were given 0.5 mg and either 1.0 or 1.5mg dexamethasone at 11pm in a randomized cross-over design. Blood for cortisol and plasma dexamethasone determination was collected at 8am and 4pm the following day. All 90 subjects were drug free at the time of testing. Satisfactory suppression of plasma cortisol was achieved in 19 healthy subjects and in 17 psychiatric controls when dexamethasone reached 2.0 nmol/l or more at 4pm. Controlling for plasma dexamethasone concentrations by selecting the dose that produced plasma levels that fell within a 4pm "window" (2-4nmol/l) in 54 patients with major depression resulted in a sensitivity of 55%. The importance of the plasma dexamethasone window is highlighted in patients that changed DST status over the dose-responsive curve. Eight of the 10 depressed patients who were suppressors with high dexamethasone levels (4.0 nmol/l) after 1.0 or 1.5mg became nonsuppressors within the window when re-tested with 0.5mg dexamethasone. This is in contrast to eight nondepressed controls who remained suppressors after the lower dose of dexamethasone.

NR385 **Wednesday, May 16, 12 noon - 2:00 p.m.**

EFFECTS OF LITHIUM ON NEUTROPHIL FUNCTION IN VIVO

Michael H. Kronig, M.D., Psychiatry, Hillside LIJ Med Center, 75-59 263 Street, Glen Oaks, NY 11004; Susan A. Moak, M.S., Robert A. Greenwald, M.D.

Summary:

Lithium treatment of affective disorders may be complicated by induction or exacerbation of psoriasis. Since the lithium is known to affect neutrophils (PMNs), and since "activation" of PMN function is known to occur in psoriasis, we studied several parameters in PMN function before and after lithium treatment of 6 patients (2M, 4F, age range 25-67). Cells were harvested from peripheral blood and assayed blindly without knowledge of lithium treatment status for chemotactic index, superoxide generation, and modulation of the extracellular conversion of superoxide to hydroxyl radical at varying time points (from 15-60 min). A mild leukocytosis was noted in 5/6 cases. In 4 or 5/6 cases, post-lithium PMNs showed moderate to marked enhancement of the PMN function measurements, in the same direction as can be observed in natural psoriatics. Similar results for other markers have been reported in vitro exposure of normal and psoriatic PMNs to lithium; we now demonstrate an in vivo effect in patients with affective disorders. The cutaneous toxicity of lithium may be mediated by direct effect on PMN function, and the lithium model may help elucidate the pathogenesis of natural psoriasis.

NR386 **Wednesday, May 16, 12 noon - 2:00 p.m.**

PARADOXICAL EFFECTS OF REWARD IN DEPRESSION

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Summary:

Depression can produce a number of information processing deficits including difficulty with effort-demanding tasks and abnormal decision-making manifested in part by poor discrimination (accuracy of distinguishing between old and novel stimuli) and abnormally conservative response bias (how subjects respond when uncertain). We examined the effects of differential reward contingencies on memory performance in depression hypothesizing that the response bias of depressed subjects would be reward-insensitive. We administered a verbal recognition memory task to 22 subjects (mean age 53.0 $\pm$ 17.4) with *DSM-III-R* major depression (mean HAM-Dep score = 26.0 $\pm$ 6.8) and nine normal volunteers (49.8 $\pm$ 11.6) under three different reward matrices (neutral, liberal, and conservative). In the depressed patients, discrimination showed a significant ($p < .05$) decline under liberal matrix conditions compared to the neutral matrix and the liberal matrix produced a paradoxical but significant ($p < .05$) conservative shift in response bias compared to the neutral matrix condition. Normal controls did not show these effects. These results suggest that one explanation of reward-insensitive behavior seen in depression is that the increased cognitive demand produced by the imposition of differential reward conditions (notably the affectively incongruent liberal condition) exceeds the reduced cognitive capacity produced by the illness. This supports the cognitive demand hypothesis as an explanation of memory and decision dysfunction in depression.

NR387 **Wednesday, May 16, 12 noon - 2:00 p.m.**

CATECHOL-CORTISOL CORRELATIONS: FACT OR ARTIFACT?

Jacqueline A. Samson, Ph.D., Psychiatry, Harvard Medical Shool, Psych Chem Lab 74 Fenwood Road, Boston, MA 02115; Russell G. Vasile, M.D., Kerry L. Bloomingdale, M.D., John J. Mooney, M.D., Edison Miyawaki, M.D., Joseph J. Schildkraut, M.D.

Summary:

While some studies report significant positive correlations between urinary free cortisol (UFC) levels and various measures of urinary catecholamines (CA) and metabolites in depressed patients, not all agree. Maes et al. (1986) suggest that the correlation between UFC and one CA metabolite, MHPG, is a statistical artifact resulting from the common relationship of urinary MHPG and UFC with creatinine and volume. The effects of creatinine and volume on the intercorrelations among other urinary CA measures remain to be examined. In a sample of 25 inpatients with DSM-III-R unipolar nonpsychotic major depressive disorders (12 males and 13 females) studied prior to treatment, we initially found significant positive correlations among urinary NE, NMN, E (but not MN), VMA, MHPG and UFC. Creatinine correlated significantly with MHPG ($r = .62$, $p = .01$), E ($r = .42$, $p < .05$), and UFC ($r = .45$, $p < .05$). After partialling for the effects of age, sex, creatinine, and volume: 1) a significant correlation remained for UFC:NE ($r = .72$, $p < .01$); 2) sizeable correlations remained for UFC:VMA ($r = .49$, $p = .06$), UFC:MHPG ($r = .48$, $p = .06$), UFC:E ($r = .44$, $p = .10$), and UFC:NMN ($r = .43$, $p = .10$); and 3) among CA measures, significant correlations remained for NE:E ($r = .66$, $p = .001$), NE:MHPG ($r = .68$, $p = .001$, NE:VMA ($r = .80$, $p < .001$, NE:NMN ($r = .66$, $p = .001$, VMA:NMN ($r = .68$, $p = .001$), MHPG:NMN ($r = .66$, $p = .001$) and VMA:MHPG ($r = .81$, $p < .001$). Using identical methods, results were replicated in an independent sample of 35 unipolar nonpsychotic depressed patients. These findings suggest that correlations between UFC and CA measures do not result solely from the common relationship with creatinine and that differences in methods and sample heterogeneity are responsible for inconsistent findings in the literature.

NR388 **Wednesday, May 16, 12 noon - 2:00 p.m.**

DEPRESSION IN COMBAT PTSD

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Summary:

Depressive symptoms are commonly seen in veterans suffering from war-related post-traumatic stress disorder (PTSD). Yet, information concerning similarities and differences between depressive symptoms and syndromes as they co-exist in PTSD compared to other disorders is minimal. In the present study, several aspects of the depressive phenomenology, including ratings of current symptoms, as well as more enduring dimensions characteristic of the depressive experience, were assessed in combat veteran inpatients with PTSD ($n = 28$) compared to patients with major depressive disorder ($n = 17$) (MDD). Current state symptoms were measured using the Hamilton Depression Rating Scale (HDRS). Dependency, self-criticism, and self-efficacy were determined using the Depressive Experiences Questionnaire (DEQ). The results suggest that veterans with PTSD are similar to patients with MDD with respect to overall severity of depressive symptoms as assessed by HDRS scores, but are significantly more symptomatic on some specific symptoms including insomnia, diurnal variation and somatic anxiety. PTSD patients additionally show more self-criticism than MDD subjects as measured by the DEQ. The introjective versus analytic subtyping of depression in veterans with PTSD was supported by a significant negative correlation between dependency and self-criticism in the PTSD group. In addition, we have found this subtyping to be useful clinically.

NR389 **Wednesday, May 16, 12 noon - 2:00 p.m.**

CARDIOVASCULAR EFFECTS OF BUPROPION

Steven P. Roose, M.D., Clinical Psychiatry, NYS Psychiatric Inst., 722 West 168th Street, New York, NY 10032; Gregory W. Dalack, M.D., Alexander H. Glassman, M.D., Sally Woodring, R.N., B. Timothy Walsh, M.D., Elsa G.V. Giardina, M.D.

Summary:

Bupropion, a new antidepressant structurally unrelated to tricyclics, has been demonstrated to be relatively free of cardiovascular effects in healthy, depressed patients. However, it remained unknown whether bupropion would be safe in a population with significant pre-existing cardiac disease. Therefore, we prospectively studied the cardiovascular effects of bupropion in depressed patients with left ventricular impairment, ventricular arrhythmias, and/or conduction disease.

Thirty-six patients, mean age 69 $\pm$ 9 years with *DSM-III* major depressive episode, were treated with a mean dose of 442 mg of bupropion. Mean 24-hour pulse was unchanged on drug. Mean supine systolic pressure increased from 140 mmHg to 145 mmHg on drug ($p < .01$) and systolic orthostatic drop increased from 4 to 8 mmHg ($p < .02$). Left ventricular function as measured by ejection fraction was unchanged (34 percent baseline vs. 32 percent on drug) and there was no significant widening of the PR or QRS intervals indicating the drug had no effect on cardiac conduction. Of note is that in the 15 patients with arrhythmia the mean rate/hour of ventricular premature depolarizations decreased from 172 $\pm$ 134 baseline to 32 $\pm$ 40 on drug ($p < .005$). However, bupropion was discontinued because of cardiovascular effects in four patients: two had a significant increase in systolic pressure, one orthostatic hypotension, and one an increase in angina.

Nonetheless, over a three-year period we have encountered five patients who could not tolerate tricylics due to cardiovascular side effects and who were treated and maintained on bupropion. These cases indicate that from the cardiovascular perspective bupropion may be a clinically useful addition to the antidepressant armamentarium.

NR390 **Wednesday, May 16, 12 noon - 2:00 p.m.**

IS DOXEPIN A SAFE TRICYCLIC FOR THE HEART?

Steven P. Roose, M.D., Clinical Psychiatry, NYS Psychiatric Inst., 722 West 168th Street, New York, NY 10032; Alexander H. Glassman, M.D., Sally Woodring, R.N., Jeffrey K. Halpern, M.D., Elsa G.V. Giardina, M.D.

Summary:

There is a long standing belief that doxepin is the most benign tricyclic in terms of cardiovascular effects. A critical review of the literature reveals that this legend is based on limited data from two methodologically flawed studies from the 1960's. We undertook a prospective study of the cardiovascular effects of doxepin in depressed patients with pre-existing left ventricular impairment, ventricular arrhythmia, and/or conduction disease.

Thirty-two depressed patients (mean age 69 ± 9) were treated with doxepin (mean dose 221 ± 58 mg., mean plasma level 230 ± 113 ng/ml). Neither pulse, lying systolic, or diastolic blood pressure was significantly affected; however, doxepin did cause a significant increase in the orthostatic drop from 4 mmHg baseline to 12 mmHg on drug ($p < .003$). Doxepin slowed conduction as evidenced by a significant increase in the PR interval (baseline 168 msec. vs. on drug 176 msec., $p < .02$) and a trend toward an increased QRS interval (baseline 107 msec. vs. on drug 110 msec., $p < .1$). In patients with arrhythmia doxepin decreased the rate of VPDs from 134 ± 109/hour baseline to 53 ± 74/hour on drug, $p < .02$. As previously documented for nortriptyline and imipramine, doxepin does not have a deleterious effect on left ventricular function as measured by ejection fraction even in patients with pre-existing left ventricular impairment. However, 17 of 32 patients (53 percent) treated with doxepin were forced to discontinue the drug because of intolerable side effects including six patients with orthostatic hypotension and three patients with marked anticholinergic phenomena. Thus, the belief that doxepin is a more benign tricyclic in patients with heart disease is not substantiated by these data: on the contrary, the drug was poorly tolerated by this group of patients.

NR391 **Wednesday, May 16, 12 noon - 2:00 p.m.**

IMPLICIT MEMORY IS IMPAIRED IN MAJOR DEPRESSION

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Summary:

Major depression is often associated with selective cognitive impairments. For example, explicit cognitive operations requiring sustained attention are disrupted while automatic memory processes and those involved in searching knowledge memory are spared. We now report that depressed patients demonstrate particularly profound impairments in memory functions not requiring conscious awareness (implicit memory).

Eight patients meeting *DSM-III* criteria for a major depressive episode and 10 healthy control subjects were studied. Subjects were presented with pictures that had been degraded into eight progressive levels of completeness. Patients were shown each card for 10 seconds. If unable to identify the object, the subsequent card was presented. Time to respond was recorded. Patients were re-tested 24 hrs later, using 10 new pictures and the 10 previously presented items.

Although initial response times were slower than in normals (49.2 ± 3.5 vs 42.7 ± 1.5 sec., $p < .05$), depressed patients were able to identify all objects without seeing the completed picture, suggesting that access to knowledge memory was unimpaired. In contrast, implicit memory, as measured by percent savings (time to solve on Day 2, relative to Day 1) (23.7 ± 3.5 vs 43.0 ± 2.8 percent, $p < .001$) was dramatically disrupted.

These results are especially striking given that even densely amnesic patients demonstrate intact implicit memory functions, despite failures in explicit memory. These findings suggest that experiences stored in implicit memory do not influence how depressed patients respond to relevant, ongoing events.

NR392 **Wednesday, May 16, 12 noon - 2:00 p.m.**

ACUTE STIMULANT RESPONSES PREDICT TRAZADONE EFFECT

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Summary:

The effects of acute methylphenidate (MPH) or d-amphetamine (d-AMP) on depressive symptoms may correlate with eventual tricyclic antidepressant-induced improvement. Although both drugs markedly increase synaptic catecholamine concentrations, in rats they demonstrate serotonergic effects as well. Both MPH and d-AMP acutely increase frontal and striatal 5-HIAA, while MPH decrease and d-AMP increases 5-HT levels. In this study, we examined the relationship between acute d-AMP and acute MPH response and eventual antidepressant response to trazadone, a weak serotonin uptake inhibitor and precursor of m-CPP, a serotonin receptor agonist. Twenty-two inpatients meeting DSM-III criteria for major depression participated. (Mean baseline Hamilton Score: 21, mean age: 35.) All subjects orally received a 40 mg MPH challenge, blind and in random order with either a 20 mg d-AMP challenge (N = 16) or placebo challenge (N = 6) on a sequential day. Subjects completed a test battery at baseline, +90, and +150 minutes. They were then begun on trazadone and rated for three weeks on the Hamilton and CGI by a psychiatrist blind to the stimulant challenge results.

There were no day order effects found. Overall, subjects on trazadone experienced a 40% decrease in Hamilton scores. MPH-induced improvement on both Hamilton ($r = .47$, $p = .03$) and global improvement line scale ($r = .48$, $p = .02$) correlated with eventual improvement on trazadone. However d-AMP responses were not related to trazadone effects.

NR393 **Wednesday, May 16, 12 noon - 2:00 p.m.**

VALPROATE IN MANIA: A DOUBLE-BLIND STUDY

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Summary:

With informed consent, 27 (m = 6, f = 21) acutely manic patients were randomly assigned in a double-blind fashion to either lithium or VPA treatment groups. Patients assigned to the lithium group (n = 13) were begun at dose of 0.5meq/kg/d. The VPA treated group (n = 14) received 1500mg/d for the first week. The dosage for weeks 2 and 3 were 2250 mg/d and 3000mg/d, respectively. Symptoms were quantitated using the SADS-C and BPRS rating scales. The ratings were repeated on a weekly basis prior to dose changes. Plasma level monitoring was done through an unblinded pharmacist. Rescue medications with lorezepam and thiothixene were allowed in extreme circumstances.

The lithium and VPA groups did not differ in age, initial mania, depression, or BPRS scores. Response was characterized as favorable or unfavorable based on the final SADS-C mania and GAS scores as described in the NIMH collaborative study. Twelve of the 13 lithium and nine of the 14 VPA responded favorably. The presence of mixed features in the form of higher depression factor scores predicted response to VPA. The results suggest that although lithium continues to be the treatment of choice for many manic patients, VPA may be particularly useful in patients with dysphoric mania.

NR394 **Wednesday, May 16, 12 noon - 2:00 p.m.**

DECREASED NATURAL KILLER CELLS IN MAJOR DEPRESSION

Dwight L. Evans, M.D., Psychiatry, Univ of North Carolina, South Wing CB#7160, Chapel Hill, NC 27599; James D. Folds, Ph.D., Cort A. Pederson, M.D., Robert N. Golden, M.D., John J. Haggarty, Jr., M.D., Mark H.N. Corrigan, M.D., Howard Ozer, M.D.

Summary:

Although the specific relationship between depression and cellular immunity has not been established, several research groups have found an association between severity of depression and decreases in immune function as measured by mitogen stimulation assays and natural killer cell assays (NKA). In preliminary studies we found a decrease in natural killer cell populations in patients with major depression compared to psychiatric control subjects with depressive symptoms. We have now studied an additional 84 age- and sex-matched, drug free subjects (major depressed, N = 35; normal controls, N = 49), using the Leu series of monoclonal antibodies (Becton Dickinson). Natural killer cell populations (Leu 7 and Leu 11) were significantly lower in the major depressed subjects compared to the normal controls, and the decreases in Leu 11 cells were related to the severity of depression as measured by the Hamilton Rating Scale for depression. Preliminary analyses suggest a similar finding for NKA. These results confirm our previous findings, and are consistent with immune function studies showing decreases in immune measures as a function of severity of depression. Neither the mechanisms nor the clinical relevance of depression-related immune changes are known; the relationship between these immune alterations and the endocrine state, as well as the possible significance of these findings for patients with cancer and HIV infection, will be discussed.

NR395 **Wednesday, May 16, 12 noon - 2:00 p.m.**

NUMBER OF REM PERIODS AND WEIGHT CHANGE IN MAJOR DEPRESSION

Timothy Hsu, M.D., Psychiatry, Univ of Michigan, 900 Wall Street, Ann Arbor, MI 48109; James E. Shipley, M.D., Alan S. Eiser, Ph.D., Roger F. Haskett, M.D., Leon J. Grunhaus, M.D., Atul C. Pande, M.D.

Summary:

In a previous study, we reported that depressed patients with comparable depressive severity differed with respect to a number of measures of EEG sleep, depending on whether they reported loss or gain of weight during their depressive episode. Because of recent reports linking REM sleep with metabolic function, we examined the association between self-reported weight change and the number of REM periods per night in a sample of patients with MDD. All 107 patients in the study had MDD by RDC. Subjects were divided into three groups according to 1) whether they had 1-2, 3-4, or 5-6 mean REM periods per night, and 2) whether they reported a loss or gain of weight during their current depressive episode. These groupings were similar with respect to age, sex, in- vs. out-patient status, HDRS, and MDD subtype. All recordings of EEG sleep were made after two weeks drug-free, and the data from two consecutive nights were averaged. The three REM-period groups differed significantly with respect to their distribution within the three weight-change groups ($p < .02$ by Chi-square); weight losers exhibited significant variation, while weight-gainers had very little variation. Weight maintainers displayed intermediate values. Comparison of the REM-period groups with respect to selected measures of EEG sleep by multiple ANOVAs did not reveal any significant differences. These results suggest that further metabolic characterization of depressive patients may be of value in defining depressive subtypes.

NR396 **Wednesday, May 16, 12 noon - 2:00 p.m.**

ALEXITHYMIA IN DIVERSE PATIENT GROUPS

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Summary:

The ability to identify one's feelings, to differentiate among feelings, and to describe one's feelings to another person are important to any form of psychotherapy. Apart from psychotherapy, the self-reporting of affect states is essential for accurate evaluation on patient scales such as the Beck Depression Inventory Rating Scale. Dysfunction in this area has been linked to alexithymia as either a personality trait or reactive state. Alexithymia, defined as a lack of words for moods, has been cited as the single most common cause for failure of psychoanalytic psychotherapy (Krystal 1988). This study reports on the incidence of alexithymia, as measured by the Toronto Alexithymia Scale (Taylor, Bagby, Ryan, Parker, Doody & Keefe 1988) in several patient populations: in a typical neuropsychiatric practice ($N = 40$); in research study groups for panic disorders ($N = 15$), depression ($n = 15$), and pain ($N = 10$). Results indicate that alexithymia is present in all populations studied to a greater degree than found in a non-patient population, but with intergroup differences. Overall, results and specific variations in incidences are interpreted in light of subscales from the Toronto Alexithymia Scale and subgroups within the studied populations. Alternate methods for assessing abilities to identify and discuss affect states are suggested and illustrated with clinical case examples.

NR397 **Wednesday, May 16, 12 noon - 2:00 p.m.**

IMIPRAMINE FOR ALCOHOLICS WITH DEPRESSION OR PANIC

Edward V. Nunes, M.D., Therapeutics, NYS Psychiatric Inst., 722 West 168th Street, New York, NY 10032; Jonathan W. Stewart, M.D., Patrick J. McGrath, M.D., Frederic M. Quitkin, M.D., Wilma Harrison, M.D., Steven Wager, M.D.

Summary:

We pursued the hypothesis that a small subgroup of alcoholics may be "self-medicating" depression or panic disorder by performing an open label trial of imipramine. Patients were selected by lifetime history for depression or panic disorder which was primary or had persisted during periods of sobriety. Seventy-nine outpatient alcoholic patients entered and 59 completed a minimum of six weeks of imipramine in conjunction with counseling. Sixty-one percent (34/56) achieved a favorable response, defined as both a "much improved" global rating in mood, and either abstinence or minimal social drinking. Twenty-two of the 35 responders were randomized, double-blind, to either taper to placebo or continue on imipramine and followed for six months. A total of 6/9 (67 percent) who tapered to placebo relapsed compared to 5/13 (38 percent) on imipramine (NS). The survival time (weeks without relapse) on placebo was $12 +/- 10$ compared to $18 +/- 8$ on imipramine ($T = 1.76$, 20 d.f., $p < .05$). This tentatively supports our hypothesis. Although the mood disordered subgroup is probably small (approximately 5 percent to 15 percent of alcoholics), its identification is worthwhile if specific antidepressant treatment is indicated. Replication is underway.

NR398 **Wednesday, May 16, 12 noon - 2:00 p.m.**

LITHIUM FOR BIPOLAR SPECTRUM COCAINE ABUSERS

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Summary:

An open trial of lithium carbonate in 10 cocaine abusers with primary bipolar spectrum disorders, led to disappointing results. In addition to pharmacotherapy all patients received weekly counseling. Only one patient achieved prolonged cocaine abstinence despite adequate trial lengths and lithium blood levels in 8 of 10 patients. Hypomania and cyclothymia have shown poor reliability. This suggests the importance of establishing diagnostic reliability for comorbid psychiatric disorders targeted in drug abuse treatment trials. Interestingly past alcoholism (5/10), and family history of alcoholism (5/10) were frequent in this sample, while family history of depression or bipolar disorder was absent. These patients may actually have had familial alcoholic rather than affective diatheses. This suggests the usefulness of family history data in validating comorbid psychiatric disorders in drug abuse. Finally several patients with persistent depression on lithium did well when switched to antidepressants (imipramine or prozac), suggesting that in the absence of clear bipolar I disorder, antidepressants may be more appropriate than lithium for the treatment of comorbid mood disorders in cocaine abusers.

NR399 **Wednesday, May 16, 12 noon - 2:00 p.m.**

THE SEX CHROMOSOMES AND PSYCHOLOGICAL DEVELOPMENT

Bruce G. Bender, Ph.D., Pediatrics, National Jewish Center, 1400 Jackson Street, Denver, CO 80206; Arthur Robinson, M.D., Mary G. Linden, M.S.

Summary:

The psychosocial prognosis of children with sex chromosome abnormalities (SCA) has become a vital concern of parents facing a termination decision following prenatal diagnosis of an SCA fetus. Such prognostic information is provided by the Denver Study, which includes 46 SCA children (14 with 47,XXY, 4 with 47, XYY, 11 with 47,XXX, 9 with 45,X and 8 mosaics) identified in the chromosome screening of 40,000 consecutive newborns. The propositi and 25 sibling controls have been followed prospectively since birth in a study now in its 25th year. With the exception of Turner syndrome girls, the propositi were not phenotypically distinguished, and their development in infancy was generally unremarkable. By four years of age, delayed language development was documented in the 47,XXY and 47,XXX groups. At school age, increased language and motor deficits occurred in all four groups of nonmosaic propositi and were associated with learning difficulties and problematic psychosocial adaption. Nonmosaic female propositi were generally more severely affected than males. In adolescence and early adulthood, ratings of psychological adaption based upon blind psychiatric interviews were significantly reduced in the 47,XXX group, with trends suggesting similar but milder impairment in the 45,X, 47,XXY, and 47,XYY groups. The mosaic females were indistinguishable from controls on any measure of development. Successful adaption has been observed in some adolescents and adults and is correlated with absence of early developmental deficits, stronger language skills, and greater family stability.

NR400 **Wednesday, May 16, 12 noon - 2:00 p.m.**

LANGUAGE AND MEMORY DEFICITS IN PSEUDODEMENTIA

V. Olga Emery, Ph.D., Darthmouth Medical, School 9 Maynard Street, Hanover, NH 03756; Charles Solow, M.D.

Summary:

The construct of pseudodementia is examined; subtypes defined. A methodological approach is described for cognitive assessment of pseudodementia. Study results are reported pertaining to language and memory processing in depressive pseudodementia (n = 18), SDAT (n = 20), major depression/unipolar (n = 20), and normal aging (n = 20). Variables of age, sex, race, education, occupation, native birth, and native language were controlled. Participants were administered eight measures of memory (WMS-R; KTDM) and eleven measures of language (WAB; TSC; CTS). Significance was determined by ANOVA, followed by Scheffe's test. The Omega Squared statistic was calculated to determine effect size of tests. Results indicate there are significant differences in patterns of deficits characterizing the research groups. Greatest discrimination between depressive pseudodementia and major depression/unipolar on measures of memory occurs on tasks of information and orientation. Greatest discrimination between depressive pseudodementia and SDAT results from story recall. Results from language assessment suggest depressive pseudodementia is best discriminated from major depression/unipolar by the most complex measures, i.e., semantic, syntactic, or meta-naming. In contrast, depressive pseudodementia is best differentiated from SDAT by two simple naming tasks requiring implicit interpretation. Issues of nosological validity and construct utility of pseudodementia are discussed on the basis of data presented.

NR401 **Wednesday, May 16, 12 noon - 2:00 p.m.**

EFFECTS OF LIGHT ON MOOD AFTER SIMULATED JET LAG

Margaret L. Moline, Ph.D., Psychiatry, New York Hospital, 21 Bloomingdale Road, White Plains, NY 10605; Charles P. Pollak, M.D., Daniel R. Wagner, M.D., Steven M. Zendell, Laurie S. Lester, Ph.D., Charles A. Salter, Ph.D., Edward Hirsch, Ph.D.

Summary:

Bright light is used to treat seasonal affective disorder, and may be applicable to other disorders of biological rhythms, such as jet lag. We simulated jet lag in our time isolation laboratory to test light as a countermeasure. Fifteen healthy men (7 controls, 8 light; ages 18-25) were studied for 15 days. Subjects slept on their usual schedules for six nights. During the seventh night, subjects awoke six hours earlier. Thereafter, six-hour phase advanced schedule was maintained for the remaining eight days. The light group was exposed to 2500 lux for four hours on the four days after the shift. Data collected included temperature, polysomnography, alertness, mood, and performance.

Sleep, mood, temperature, and performance parameters did not differ between groups before the shift. After the shift, however, the light group slept less efficiently than controls, had less compensatory deep sleep. However, light subject reported being more alert than before the phase shift. They were also significantly happier than controls and when compared to their baseline. Light treatment did not hasten adjustment of the temperature rhythm to the new schedule. These data suggest that light may affect mood and alertness independently of its effect on the biological clock.

NR402 **Wednesday, May 16, 12 noon - 2:00 p.m.**

ACOUSTIC ANALYSIS IN MAJOR DEPRESSION AND PARKINSON'S DISEASE

Alastair J. Flint, M.D., Psychiatry, Toronto Hospital, 399 Bathurst Street, Toronto Ontario, Canada M5T 2S8; Sandra E. Black, M.D., Irene Campbell-Taylor, Ph.D., Gillian F. Gailey, MHSc, Irene Tamas, MHSc

Summary:

In its early stages Parkinsons Disease (P.D) may be difficult to distinguish from Major Depression (M.D) leading to inappropriate management. Both illnesses are characterised by psychomotor retardation. The neurovegetative symptoms used to diagnose M.D are not specific and in P.D may be due to the physical illness itself. Currently, differentiation of the two conditions relies on subjective clinical observation. Improved diagnostic accuracy based on more objective data is needed. To this end, this study used computerised acoustic analysis to contrast speech patterns in P.D. and M.D. The sample, 60 yrs. of age and over, consisted of 30 P.D patients without depression or dementia, (Hoehn and Yahr stages 2 and 3), 30 patients with uncomplicated M.D (DSM-III-R), and 30 age and sex matched controls. Of the 10 acoustic variables studied, M.D patients had statistically significant reduced rate of speech, increased segment duration, increased speech pause time and percent pause time, and shortened voice onset time, compared with P.D. There were no differences between the two groups on mean fundamental frequency, frequency range, formant transition, when these variables were adjusted for sex, or for spirantisation and voice intrusion errors. The data suggest that acoustic analysis may be a valuable tool in the differentiation of P.D and M.D.

NR403 **Wednesday, May 16, 12 noon - 2:00 p.m.**

EEG AND EVOKED POTENTIALS IN DEPRESSION

Stephen L. Stern, M.D., Psychiatry, Ohio State University, 473 W. 12th Avenue, Columbus, OH 43210; Michael W. Torello, Ph.D., Jeffrey A. Coffman, M.D.

Summary:

EEG and evoked potential studies in depression have often employed a limited number of electrodes or examined patients only at baseline. Using a full set of 28 scalp electrodes, we studied 11 medication-free outpatients with DSM-III-R major depressive episode — all of whom had a 17-item HAM-D ≥ 15 — and re-evaluated six after 10 weeks' treatment with antidepressant or mood-stabilizing medications. The patients' mean age was 34.5 years, with a range of 27 to 43; eight were women. We collected resting EEG with eyes open and closed and also examined the auditory "oddball" P300 waveform. Data was analyzed only from subjects who had artifact-free segments totalling ≥ 30 seconds.

We found a significant Pearson correlation between HAM-D scores and theta (slow wave) activity at baseline with eyes open (10 patients, $r = +.72$, $p < .02$), though not with eyes closed (7 patients, $r = +.65$, $p < .12$). No significant correlations were noted between EEG activity in other frequency ranges and HAM-D scores. P300 amplitude increased in all six patients who were studied twice, going from a mean (SD) of 12.8 (3.1) microvolts to 21.5 (4.8), while HAM-D scores decreased from 18.2 (2.2) to 7.8 (4.8). These changes were both significant by two-tailed paired t test, with $p < .001$ and .02, respectively.

The significance of these preliminary findings will be discussed in comparison with results from normal controls matched for age, sex and handedness.

NR404 **Wednesday, May 16, 12 noon - 2:00 p.m.**

SEROTONERGIC FUNCTION IN DEPRESSION

Robert N. Golden, M.D., Psychiatry, Univ of North Carolina, CB 7160 Med School Wing B, Chapel Hill, NC 27599; Robert G. Ruegg, M.D., Mark H. Corrigan, M.D., John H. Gilmore, M.D., Helen L. Miller, M.D., Stanley W. Carson, Pharm.D.

Summary:

We have utilized the neuroendocrine response to clomipramine (CMI), a 5-H uptake inhibitor, as a probe for studying 5-HT systems in depression. Thirty drug free depressed patients and 30 healthy volunteers who were matched for age, sex, and season of study, received an intravenous CMI challenge. The depressed patients demonstrated a blunted prolactin response to CMI, with a mean maximum prolactin increase of 2.4 ± 0.7 ng/ml, compared to 7.1 ± 1.9 in healthy subject ($p < .007$).

Seven depressed patients also received a 500 mcg TRH stimulation test after a minimum three-day washout from the CMI challenge test. While these patients demonstrated a blunted prolactin response to CMI (mean maximum prolactin increase = 1.5 ± 0.7 ng/ml), their prolactin response to TRH was robust (30.4 ± 5.0 ng/ml). This suggests that the blunted prolactin response to CMI reflects dysregulation in central serotonergic systems and is not attributable to diminished hormonal secretory capacity in anterior pituitary lactotrophs.

Ten depressed patients were restudied following four weeks of antidepressant treatment. The change in prolactin response to CMI following treatment differed in five responders vs. five nonresponders ($p < .02$); the former group demonstrated an increased prolactin response compared to their baseline, while the latter had a persistent decline in this measure of 5-HT function. (Supported by PHS grants MH-42145, MH-33127, and RR00046).

NR405 **Wednesday, May 16, 12 noon - 2:00 p.m.**

WITHDRAWN

NR406 **Wednesday, May 16, 12 noon - 2:00 p.m.**

RECOGNITION OF DYSTHYMIA IN A PSYCHIATRIC SETTING

Deborah B. Marin, M.D., Cornell Univ. Med. Col., Payne Whitney Clinic, 525 E. 68th Street, New York, NY 10021; James H. Kocsis, M.D., Winifred Lloyds, John C. Markowitz, M.D., Allen J. Frances, M.D., Gerald L. Klerman, M.D.

Summary:

INTRODUCTION: It was noted prior to the publication of DSM-III that chronic depression was underdiagnosed and mistreated. Yet, a substantial proportion of DD's can be expected to obtain complete recovery from depression with adequate treatment. This study assesses the current rate of recognition of DD as well as comorbid Axis I diagnoses by clinicians.

METHODS: 18 psychiatric outpatients were prescreened for chronic depression and then were assessed by SCID-I by a research psychiatrist at the time of their clinical evaluation. All patients fulfilled DSM-III criteria for DD. A blind rater then reviewed the clinical charts of these patterns.

RESULTS: The clinicians diagnosed DD in 75% of the patients (sensitivity = .66). Clinical interviews and SCID diagnosed comorbid Axis I diagnoses in 28% and 61% of the patients respectively. Sensitivity and specificity of clinicians to diagnose comorbid Axis I diagnoses was .45 and 1.0 respectively.

COMMENT: This study indicates that DD was more frequently recognized by clinicians at Payne Whitney Clinic in 1989 than reported for chronic depression at other centers in 1977 or at our own institution in 1986. We speculate that clinicians are becoming more familiar with the clinical concept and criteria for DD because of definitions in DSM-III and III-R and the educational value of recent research efforts. The higher percentage of comorbid diagnoses noted by SCID underscores the need for systematic evaluation of psychopathology.

NR407 **Wednesday, May 16, 12 noon - 2:00 p.m.**

THE EFFECT OF MEDICAL OVARIECTOMY ON LLPDD

Stephanie D. Jofe, M.D., Psychiatry, Mass General Hospital, REU BHX5 Blossom Street Rear, Boston, MA 02114; Edwin H. Cassem, M.D., David A. Schoenfeld, Ph.D., William F. Crowley, Jr., M.D.

Summary:

This study was designed to investigate whether change in the reproductive hormones across the menstrual cycle are causually related to menstrually related mood disorders (MRMD) or just temporarily coincidental. Fifteen women with prospectively diagnosed menstrually related mood disorders received either a GnRH analogue (D-Trp6-Pro9-NEt-LHRH) in doses sufficient to produce a medical ovariectomy (8ug/kg,sq), or a placebo (an equal volume of normal saline, sq), in a randomized, double-blind, cross-over protocol for each treatment cycle. Weekly bloods were drawn during all four cycles to assure that hormonal suppression was achieved during the drug cycles and that placebo cycles were ovulatory. In the first treatment cycle all 7 subjects who received the analogue improved (6 to within a non-MRMD range) and 5 of the 8 subjects who received the placebo improved (3 to within a non-MRMD range). In the second treatment cycle all 15 subjects improved no matter which treatment they received. The scores of 7 of the 8 subjects receiving GnRHa were within a non-MRMD range as were the scores of 4 of the 7 women on placebo. The improvement with the analogue induced medical castration was significantly greater than that achieved with the placebo ($p = 0.02$) suggesting that the reproductive hormones contribute to the etiology of MRMD. However, the fact that 12 of the 15 women improved during the placebo cycle suggests that other factors are also involved.

NR408 **Wednesday, May 16, 12 noon - 2:00 p.m.**

PROPOSED RESEARCH CRITERIA FOR LLPDD

Stephanie D. Jofe, M.D., Psychiatry, Mass General Hospital, REU BHX5 Blossom Street Rear, Boston, MA 02114; Edwin H. Cassem, M.D., David A. Schoenfeld, Ph.D., William F. Crowley, Jr., M.D.

Summary:

There are no well accepted research criteria for the diagnosis and monitoring of menstrually related mood disorders (MRMD), a source of numerous methodological difficulties. We undertook a prospective study of women with and without self-diagnosed MRMD to empirically derive objective criteria for diagnosing MRMD for future studies. 1030 subjects either complaining of severe MRMD or denying any MRMD were screened by phone to select women ages 18 to 40, with regular cycles, minimal to no dysmenorrhea, on no medication and normal weight. Next, the SADS-L was administered to exclude subjects with current psychiatric disorder. 91 eligible and interested subjects completed the Profile of Mood States (POMS) Scale daily and had midluteal progesterone levels drawn for 2 cycles. 88 cycles from the first 44 subjects who had ovulatory cycles were analyzed. The studentized T test, which produces a z score by calculating the difference between the mean POMS scores on days 5 to 10 and the last 6 days of the cycle and dividing this number by the standard deviation of the POMS scores on days 5 to 10 was used to diagnose the women with MRMD. Women who appeared to have MRMD from the visual inspection of the graphs of their mood changes had z scores <-1.63, representing an increase in negative affect of >1 SD from the mean mood disturbance scores on days 5 to 10, i.e., greater than would be expected by chance. Using these criteria prospectively, 57% of the participants who reported MRMD actually demonstrated these changes. This method has several advantages. The POMS is a well validated, widely used mood scale. The z score considers baseline affective liability when determining whether a premenstrual increase in negative affect is meaningful. Averaging the scores over two cycles minimizes the effect of external events on any one cycle.

NR409 **Wednesday, May 16, 12 noon - 2:00 p.m.**

CORTISOL AND OUTCOME IN DEPRESSION

Anthony J. Rothschild, M.D., McLean Hospital, 115 Mill Street, Belmont, MA 02178; Alan F. Schatzberg, M.D., Jacqueline A. Samson, Ph.D., Joseph J. Schildkraut, M.D., Monica Luciana, Maureen Letson

Summary:

There is no abundant evidence for hyperactivity and hypothalamic-pituitary adrenal (HPA) axis in endogenous or melancholic depression; as well as other specific subtypes, particularly psychotic depression. Several studies have shown that elevated cortisol levels in depressed patients are associated with cognitive disturbances as well as ventricular enlargement. However, few studies have looked at the consequences of *prolonged* elevation of cortisol in depressed patients.

Data will be presented on a one-year follow-up study of 42 rigorously diagnosed unipolar depressed patients (9 psychotic and 33 nonpsychotic). At one-year follow-up, ANOVA revealed that psychotic major depressed (PMD) patients did not differ from nonpsychotic depressed (NPMD) patients on measures of symptoms [Hamilton Depression Rating Scale (HDRS) and Brief Psychiatric Rating Scale], but had significantly ($p < .001$) poorer scores on the measures of functioning (Social Adjustment Scale, SAS). Significant correlations were observed between cortisol levels at one year and measures of functioning at one year. *Higher* urinary free cortisol (UFC) at one year correlated with *poorer* overall functioning at one year as measured by the total SAS score ($r = .57$, $p = .02$). The correlation between *higher* UFC levels at one year and *poorer* overall functioning at one year was even stronger ($r = 0.74$, $p = .005$) when total HDRS score was partialled out. These data suggest an association between elevated levels of cortisol at one year and difficulty in social and occupational functioning that is *independent* of the degree of residual depressive symptomatology.

NR410 **Wednesday, May 16, 12 noon - 2:00 p.m.**

IMP SPECT BRAIN IMAGING IN BIPOLAR DISORDER

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Summary:

This study used I-123 iofetamine (IMP) SPECT imaging to study four patients on lithium monotherapy who met DSM-III-R criteria for bipolar disorder while in depressed, manic/hypomanic, or euthymic states. IMP images of four patients were taken on a GE Starcam system 20 minutes after injection of 5 mCi of I-123 labeled IMP. 64 projection images were obtained over 360 degrees over 45 minutes. After standard reconstruction of the images, regions of interest (ROI) on each tomographic slice were subjected to quantitative, computer assisted analysis. Three out of four patients showed asymmetrically increased IMP activity in the right temporal tip when compared to the left temporal tip either in manic or depressed state. In one patient, three sets of images taken sequentially during depression, euthymia and depression showed temporal lobe asymmetry in the depressed states (right more active than the left in both episodes) but not in the euthymic state. In another patient two sets of images taken sequentially during mania and euthymia revealed temporal lobe asymmetry (right more active than left) in mania which also disappeared in the euthymic state. Furthermore, in two patients an asymmetric uptake of IMP was also observed in the cerebellum. This pilot study suggests that a temporal lobe asymmetry in IMP activity may be present in patients with bipolar disorder in abnormal mood states. This can be indicative of temporal lobe dysfunction in bipolar disorder.

NR411 **Wednesday, May 16, 12 noon - 2:00 p.m.**

NORADRENERGIC/HPA DYSREGULATION IN DEPRESSION

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Summary:

The hypothesis of dysregulated monoamine/neuroendocrine systems in depression implies altered circadian activity and decreased responsiveness to environmental stimuli. Acutely depressed patients, remitted depressed patients, and age- and sex-matched normal controls were studied over an 8 hour or 24 hour period to examine rhythms of cortisol, norepinephrine (NE), and MHPG, and on a separate occasion for response of cortisol or NE to naturalistic challenge. Non-linear multioscillator cosinor analysis revealed hemicircadian and ultradian oscillators for NE and MHPG of increased relative amplitude in depressed patients compared to normal controls, while for plasma cortisol the relative amplitudes of these oscillators were found to be decreased in depressed patients in contrast to normal controls. The response of NE to isometric exertion following orthostatic challenge was reduced in the entire group of remitted depressed and acutely depressed patients ($p < 0.05$) and in acute, but not remitted, patients compared to controls ($p < 0.05$). The plasma cortisol response and placebo-corrected cortisol response to a mental arithmetic task (MAT) was reduced in the entire group of depressed patients compared to controls ($p < 0.05$), but did not differ between acute and remitted patients. These findings suggest that dysregulation of the noradrenergic and cortisol systems in depression are reflected in altered hemicircadian and ultradian rhythms, and that enduring disturbances in task responsiveness may be unmasked by naturalistic challenges.

NR412 **Wednesday, May 16, 12 noon - 2:00 p.m.**

TRYPTOPHAN DEPLETION ALTERS MOOD IN DEPRESSION

Pedro L. Delgado, M.D., Psychiatry, Yale University, West Haven VA Medical Center, West Haven, CT 06516; Dennis S. Charney, M.D., Lawrence H. Price, M.D., George K. Aghajanian, M.D., George R. Heninger, M.D.

Summary:

Brain serotonin (5-HT) content is dependent on plasma levels of the essential amino acid, tryptophan (TRP). We have previously reported on the effects of rapid dietary TRP depletion in psychiatric patients. This study extends those reports and further characterizes the effects of rapid TRP depletion on mood in depressed patients. *METHOD:* 87 depressed (*DSM-III-R*) patients (47 drug free, symptomatic, and 40 in clinical remission on antidepressant) have received tryptophan depletion testing with two two-day tests each involving a 24-hr., 160 mg/day, low-TRP diet followed the next morning by a 16-amino acid drink, in a double-blind, placebo-controlled (TRP depletion (TD) and control testing); crossover fashion. On one test the diet and drink were supplemented with L-TRP (control) and on the other test neither the diet nor drink were supplemented (TD). Behavioral ratings (Hamilton Depression Scale (HDRS)) and plasma (for TRP levels) were obtained prior to, during and after testing. *RESULTS:* Total and free TRP decreased 80 to 90 percent five hrs. after the TRP-free drink (TFD). Thirty-five percent of 47 symptomatic, drug-free depressed patients were unchanged the day of the TFD, but became clinically less depressed (40 percent mean decrease in HDRS, ≥ 9 point decrease in total HDRS score) the day after the TFD. Sixty percent of 40 antidepressant-remitted depressed patients relapsed (300 percent mean HDRS increase) the day of the TFD, with return to remitted state the day after. While 80 percent of monoamine oxidase inhibitor- or fluvoxamine-treated patients relapsed, only 20 percent of desipramine-treated patients relapsed. *Implications:* Rapid depletion of plasma TRP transiently reverses antidepressant response in most remitted depressed patients suggesting that the antidepressant effects of some of these drugs may be dependent on 5HT availability. Clinical characteristics and ultimate treatment response to symptomatic, drug free depressed patients in relation to the behavioral response to TD will be presented.

NR413 **Wednesday, May 16, 12 noon - 2:00 p.m.**

SEROTONERGIC RESPONSIVITY IN MAJOR DEPRESSION

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Summary:

Various lines of evidence link central serotonergic mechanisms to the pathogenesis and treatment of depression. Further support is provided by a neuroendocrine challenge strategy which we used to evaluate serotonergic responsivity in patients with major depressive disorder (MDD) with endogenous features (RDC). Prolactin (PRL) and cortisol (CORT) release as well as mood response were examined in 18 medication-free depressed subjects after a 60mg oral dose of fenfluramine hydrochloride (FF). Responses during the 6 hours following administration of the challenge drug (or placebo) were compared to those observed in 18 closely matched, healthy control subjects in the context of a random assignment, double-blind design. ANOVA with repeated measures revealed no significant effect of FF on CORT release nor on mood response in either group. PRL release was, however, robustly enhanced by FF irrespective of diagnosis but the response was significantly blunted in the MDD subjects as compared to the controls ($p = .01$). Significant enhancement of the PRL response to FF was observed following treatment of MDD subjects with either imipramine or ECT. These findings confirm and extend previous reports and support the classical indoleamine hypothesis which implicates abnormally low brain serotonergic function in the pathogenesis of depression.

(Supported in part by NIMH Grants #40734 and #43873)

NR414 **Wednesday, May 16, 12 noon - 2:00 p.m.**

PHYSIOLOGICAL ASPECTS OF EMOTION IN DEPRESSION

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Summary:

Abnormalities in emotional response are a central clinical feature of depression. Little experimental work has been done, however, to investigate possible abnormalities in physiological response to emotion-evoking stimuli. We conducted two studies for this purpose; each used a different type of emotion-evoking stimuli and measured a different dimension of physiological response. EMG was recorded from muscles that furrow the brow in a frown (corrugators) and curve the mouth in a smile (zygomatics) in 28 patients with MDD (*DSM-III-R*) and 24 healthy controls while they looked at pictures of actors with posed happy, sad, or neutral facial expressions. Healthy subjects showed changes in facial muscle activity mimicking the posed expressions of emotion ($p = .03$). Patients failed to show this automatic emotion-related response. In the second study, 18 patients and 27 controls were presented two different words simultaneously, one to each ear. Each of these dichotic stimulus pairs consisted of one emotionally neutral word and one word with either a positive or negative emotional valence. Because of the high degree of temporal and spectral overlap between the works in each pair (e.g. till-kill) they fuse into a single auditory percept and subjects are unable to identify both words in a pair or to selectively report the word from one ear. Patients heard fewer positive and negative words than did controls ($p = .002$). Both studies suggest that depressed patients have abnormally blunted sensitivity to emotion-related stimuli in general, rather than decreased sensitivity to positive stimuli or increased sensitivity to negative stimuli.

NR415 **Wednesday, May 16, 12 noon - 2:00 p.m.**

INTRAVENOUS VERSUS INTRAMUSCULAR ATROPINE IN ECT

Barry A. Kramer, M.D., Psychiatry, LAC-USC Medical Center, 1934 Hospital Place, Los Angeles, CA 90033; Anoshiravan Afrasiabi, M.D., Vickie E. Pollock, Ph.D.

Summary:

Atropine is frequently administered to patients receiving electroconvulsive therapy (ECT) to decrease secretions and prevent vagal induced bradycardia or asystole. It is given either intramuscularly (IM) 30 minutes or intravenously (IV) 2 minutes prior to the ECT. Twelve patients with a mean age of 52.3 years receiving ECT consented to random assignment of the route of administration of the atropine for ECT #2 - 5 resulting in 24 treatments following IM atropine and 24 treatments following IV atropine. Both IV and IM atropine offered similar protection against secretions and bradycardia. There were no statistically significant differences between groups in heartrate. Although differences in systolic and diastolic blood pressures did not reach statistical significance, trends will be discussed. The IV route eliminates one injection per treatment and the dry mouth and tachycardia that develop in the interval between the IM injection and the ECT. We recommend that when atropine is employed during ECT, the IV route be utilized.

NR416 **Wednesday, May 16, 12 noon - 2:00 p.m.**

DEMORALIZATION PREDICTS NONRESPONSE TO COGNITIVE THERAPY

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Summary:

Demoralization can be defined as a state of "giving up" wherein the demoralized person sees no point in trying since his efforts will lead to naught. Cognitive Therapy is a specialized form of psychotherapy which challenges distorted beliefs. Thus, Cognitive Therapy would seem ideally suited for treating demoralization.

We sought to test this hypothesis by developing a Demoralization Scale from among items on three standard rating scales used in Cognitive Therapy Research, the Beck Depression Inventory, the Hollon Hopelessness Scale, and the Dysfunctional Attitudes Scale. Without knowledge of the patients' responses, the authors chose 20 items from these scales which seemed to reflect an attitude of having "given up" or not wanting to try. Scores for this scale were then calculated for 39 depressed outpatients who had completed 16 Cognitive Therapy sessions.

Demoralization scores for the 21 patients judged by an independent evaluator as much improved or very much improved were significantly lower than were patients rated as minimally improved, unchanged or worse. There was no difference in baseline scores on the Hamilton Rating Scale for Depression or the Beck Depression Inventory between the two groups.

These results suggest that short-term Cognitive Therapy may be most effective for patients with relatively low levels of demoralization. Highly demoralized patients may require other forms of treatment, or longer term Cognitive Therapy.

NR417 **Wednesday, May 16, 12 noon - 2:00 p.m.**

PHOTOTHERAPY, SPECTRAL EEG AND ACTIVITY IN SAD

Martin H. Teicher, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Carol A. Glod, M.S., David Harper, B.S., Eleanor Magnus, B.S., Arlene F. Frank, Ph.D., Gregory Benson, B.A.

Summary:

Seasonal affective disorder (SAD) has recently attracted considerable attention, largely due to the effectiveness of phototherapy. Unfortunately, only about 62 percent of SAD patients fully remit with conventional (2500 lux) phototherapy (Terman et al 1989). We sought to determine whether there were biological factors that could predict response. Thus, patients with Fall-Winter SAD (Rosenthal-NIMH criteria; $n = 12$) were studied using ambulatory motility monitoring (AMM; PCD Actigraph) and computerized-EEG with spectral analysis (C-EEG; QSI-9000), followed by a trial of phototherapy (2 h AM light for at least 2 wk). With AMM, all motions of the nondominant wrist >0.01 g were recorded, and stored in 5 min epochs throughout a 72 h period. Data were analyzed for circadian (24 h) and hemicircadian (12 h) rhythmic properties. At least 5 min of artifact-free C-EEG data (19 channels) were collected in eyes-closed condition. Patients with a good-excellent response to phototherapy ($n = 7$; measured by structured HAM-D) had pretreatment hemicircadian rhythms that were 86 percent greater than nonresponders ($n = 3$; $p < 0.05$), and nocturnal activity levels that were 45 percent lower ($p < .05$). We believe that the hemicircadian rhythm corresponds to the clinical concept of diurnal variation, and can be precisely quanitifed by this procedure. Phototherapy responders also showed a highly significant and widespread reduction in beta frequency (14.0-24.0 Hz) EEG activity following treatment.

NR418 **Wednesday, May 16, 12 noon - 2:00 p.m.**

EFFECTS OF L-DOPA ON MOOD AND EYE FUNCTION IN SAD

Dan A. Oren, M.D., CPB, NIMH Bldg 10 RM 4S239, 9000 Rockville Pike, Bethesda, MD 20892; Douglas E. Moul, M.D., Norman E. Rosenthal, M.D.

Summary:

Although the eye has been implicated in the antidepressant effects of phototherapy in seasonal affective disorder (SAD), the cause of the illness and the mechanism of action of light is unclear. We enter SAD patients into a double-blind medication trial and provide them with placebo. Those who remain depressed are then randomly assigned to continue receiving two weeks of placebo or else to receive two weeks of levodopa at 5-7 mg/kg/day along with carbidopa of 100 mg/day. Mood assessments are performed weekly by trained raters using a modified Hamilton Depression Rating Scale. At various points in the protocol, electroretinograms and visual evoked potentials are obtained as indirect measures of dopaminergic activity in the retina. Although nine patients reporting a history of SAD failed to become significantly depressed while receiving placebo, seven others did not respond and were randomized to continue receiving placebo or levodopa. Two who continued receiving placebo had no change in their mean Hamilton depression scores. Five who were given levodopa improved from a mean Hamilton depression score of 14 to a mean of 6. The study is ongoing and the final results and their implications for the treatment of SAD will be discussed.

NR419 **Wednesday, May 16, 12 noon - 2:00 p.m.**

DOPAMINERGIC FUNCTION, OESTROGEN WITHDRAWAL AND BIPOLAR RELAPSE IN RECENTLY DELIVERED MOTHERS

Dr. Angelika Wieck, Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, United Kingdom; A.D. Hirst, M.N. Marks, T.C. Campbell, S.A. Checkley, R. Kumar

Summary:

Several lines of evidence suggest that the pecipitous fall of plasma and brain oestrogen concentrations after parturition may be responsible for the sharp increase in the incidence of psychosis immediately after childbirth. Of the central neurotransmitter systems the function of the dopaminergic system is particularly influenced by oestrogen. In ovariectomized rats withdrawal from high doses of oestrogen induces an enhanced behavioral response to the dopamine agonist apomorphine (APO).

In this study we measured the growth hormone (GH) responses to APO in 15 women at high risk of relapse (women with a previous history of bipolar depression) and 15 controls on the fourth day after delivery. All women had been free of psychotropic medication for at least two months. The tests were performed according to Corn et al after overnight fasting. Eight high risk subjects subsequently relapsed, six of these within 10 days of childbirth. Patients who later relapsed had a significantly larger GH response to APO than those who remained well and than the normal controls.

We conclude that an enhanced APO-GH response precedes bipolar relapse after childbirth indicating a hypersensitivity of hypothalamic D2 receptors or of some mechanism below the receptor level. Whether oestrogen withdrawal does indeed trigger bipolar illness and whether this effect may be mediated by the dopamine system is being investigated in an ongoing series of experiments.

NR420 **Wednesday, May 16, 12 noon - 2:00 p.m.**

PLASMA TRANYLCYPROMINE LEVELS AND ACUTE MOOD ACTIONS

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Summary:

The MAO-inhibitor antidepressant tranylcypromine (TCP) is structurally similar to amphetamine, and has reputed psychostimulant properties. To investigate acute actions of this agent on mood in relation to plasma levels, we administered 20 mg oral dose to 9 patients who had been receiving ongoing TCP treatment. Over the following 8 hours (hrs), we measured TCP plasma levels, and obtained self-ratings of mood with the Profile of Mood States (POMS) questionnaire. Peak TCP levels in plasma were observed from 1 to 4 hrs post-dose (mean = 1.9 hrs). POMS data were analyzed in relation to the time of the TCP peak for each subject, using two-way ANOVA and Dunnett's test (post-hoc). Despite the reputed psychostimulant properties of TCP, there were no changes in the Fatigue-Inertia ($p > 0.9$) or Vigor-Activity ($p > 0.7$) factors of the POMS. However, Confusion-Bewilderment (a likely measure of cognitive inefficiency) did decrease marginally ($p < 0.055$), with significantly lower mean values on the post-hoc tests at 1 hr ($p < 0.05$) and 3 hrs ($p < 0.05$) post-peak. The Depression-Dejection factor was also marginally decreased after TCP dose administration ($p < 0.07$), with significant post-hoc differences at the TCP peak ($p < 0.05$) and 2 hrs post-peak ($p < 0.05$). Unexpectedly, the most prominent action of TCP was on Tension-Anxiety (a factor mainly descriptive of musculoskeletal tension). This factor decreased significantly following dose administration ($p < 0.01$). Compared to baseline, Tension-Anxiety was significantly lower at the TCP peak ($p < 0.05$), as well as at 2 hrs ($p < 0.01$) and 3 hrs ($p < 0.01$) post-peak. These findings do not support the idea that TCP has acute psychostimulant or amphetamine-like actions. On the contrary, the most prominent observed effect of TCP was a reduction of musculoskeletal tension.

NR421 **Wednesday, May 16, 12 noon - 2:00 p.m.**

DEPRENYL-PHENYLALANINE: FAST RELIEF FOR DEPRESSION

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Summary:

Within 24 to 48 hours, a deprenyl-phenylalanine combination relieved symptomatology in six of 10 patients with drug-resistant major depressive disorder. Subjects included six women and four men, ages 24 to 60, whose depression had not been controlled with tricyclic, heterocyclic, and MAO inhibitor antidepressants. Treatment started with L-deprenyl (selegiline; 5 mg orally in AM); 24 to 48 hours later, L-phenylalanine (1 g orally in AM and early PM) was added, and dosage was increased daily, as needed, up to 6 g/d. These observations indicate that deprenyl-phenylalanine combinations can provide rapid control of depression even in treatment-resistant cases. They may have theoretical significance: low doses of L-deprenyl selectively inhibit monoamine oxidase B, the enzyme that metabolizes dopamine and phenylethylamine (PEA), but not norepinephrine or serotonin, and L-phenylalanine is the aminoacid precursor of PEA. The urinary excretion and plasma levels of the PEA metabolite phenylacetic acid are reduced in 60 percent of depressed patients (Sabelli et al, *Science*, 1983; *J Clin Psychiatry*, 1986). PEA deficit may contribute to the pathogenesis of some forms of depressive illness (Sabelli and Mosnaim, *Amer J Psychiatry*, 1974). Global Assessment Scores (GAS) were 41.5 $\pm$ 2.36 before treatment, and 62.3 $\pm$ 3.87 three days after beginning of phenylalanine treatment. This difference was significant at the 0.01 level, and was maintained six weeks later.

NR422 **Wednesday, May 16, 12 noon - 2:00 p.m.**

SPEAKING RATE PREDICTS ANTIDEPRESSANT RESPONSE

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Summary:

The spontaneous speech of newly admitted depressed patients was timed by computer and compared with rate of counting from 1 to 10 as an indicator of psychomotor retardation, and as a possible predictor of favorable early response to antidepressant medication.

Counting rate, but not spontaneous speaking rate, was found to be significantly related to Hamilton ratings of extant retardation. But it was only spontaneous speech that showed a pattern of slowing prognostic of a positive response to medication during the following six-week regimen, especially among patients that had been diagnosed as bipolars. Bipolars were found to have significantly longer pauses than unipolars in general; patients destined for early response tended to have significantly slower speech rates and shorter vocalizations, but not significantly longer pauses.

Since spontaneous speech requires more cognitive effort than counting from 1 to 10, these results suggest that classical speech retardation in depression is a cognitive speed deficit rather than a slowing of the motor movements required for speech.

NR423 **Wednesday, May 16, 12 noon - 2:00 p.m.**

PLATELET (3H)-IMIPRAMINE BINDING IN FIBROMYALGIA

Douglas H. Finestone, M.D., Psych. Med., East Carolina Univ., ECU School of Medicine, Greenville, NC 27858; David L. Knight, B.S., Charles M. Nemeroff, M.D.

Summary:

This pilot study sought to measure the number and affinity of platelet (^{3}H)-imipramine binding sites in patients with fibromyalgia (FIB). Decreased platelet (^{3}H)-imipramine receptor density (Bmax) previously has been reported in patients with major depression. Some investigators believe patients with FIB are depressed. To our knowledge, only one previous study has examined platelet (^{3}H)-imipramine receptor density in patients with FIB; patients with FIB had a significantly higher mean Bmax than did control subjects.

We compared platelet (^{3}H)-imipramine receptor density in 11 hospitalized patients with FIB to 11 (82% hospitalized) age- and sex-matched patients with DSM III major depression (MD), and to 11 age- and sex-matched normal control (NC) subjects. Patients ranged in age from 29 to 69 years; 82% were female. All patients were drug free for at least 7 days before being studied. Using the Student-Newman-Keuls test, the mean Bmax (1091.74) of the FIB patients did not differ significantly from the mean Bmax (1043.00) of the NC subjects. The mean Bmax of the FIB patients and the NC subjects significantly differed ($p < 0.01$) from the mean Bmax (554.89) of the MD patients. Mean receptor affinity (Kd) of the FIB patients, the NC subjects and the MD patients did not differ.

Our preliminary findings support the reduction in platelet (^{3}H)-imipramine binding sites to be specific to patients with major depression. Our results do not support fibromyalgia to be a variant of major depression.

Supported by NIMH MH-40159.

NR424 **Wednesday, May 16, 12 noon - 2:00 p.m.**

HIDDEN FACTORS IN EMERGENCY DEPARTMENT CHEST PAIN: PANIC DISORDER AND DEPRESSION

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Summary:

Chest pain patients are notoriously high utilizers of medical emergency departments (ED). Acute cardiac ischemia (ACI) and psychiatric disorders, specifically depression (DEP) and panic disorder (PD), may account for a large percentage of ED visits for chest pains. To estimate the relative proportions of ED chest pain pts with ACI vs DEP/PD, and to examine patterns of ED and medication use, we interviewed within 48 hours of their visits 229 (69 percent) of the 334 adults who presented with chest pain to our urban ED over two months. Measures included chest pain history, clinical diagnosis and criteria for ACI, Beck Depression Inventory (cutoff of 19), and *DSM-III-R* criteria for panic disorder. Of the 229, 29 percent (67) had ACI, 23 percent (53) had DEP, and 17 percent (40) had PD. The number with either PD or DEP with 35 percent (80). Of the 67 with ACI, only 19 percent (13) had PD and 15 percent (10) had DEP, suggesting little overlap. The number of pts with one or more ED visits for chest pain in the previous year varied significantly by groups. The ACI + /PD- group contained significantly fewer pts (33 percent) with one or more previous ED chest pain visits than the ACI-/PD + group (59 percent), $p < .05$. Similarly, the ACI + /DEP- group contained fewer (35 percent) than the ACI-/DEP + group (56 percent), p.05. The high ED utilizers also used significantly more anginal ($p = .003$) and psychotropic ($p = .024$) medications. Only 13/229 (5.7 percent) were identified by the ED physician as having a psychosocial contribution to their chest pain syndrome. PD and DEP are as frequently associated with ED chest pain as ACI, they may lead to more frequent ED visits for chest pain, and they are less likely to be recognized by ED physicians than ACI. These findings challenge psychiatrists to help improve the recognition and treatment of PD and DEP in the ED chest pain patient.

NR425 **Wednesday, May 16, 12 noon - 2:00 p.m.**

SYMPATHOADRENAL FUNCTION IN MIXED AND PURE MANIA

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Summary:

Mixed, or dysphoric, mania is a severe form of mania combined with depressive symptoms. Patients with mixed mania may be the largest group of lithium nonresponders. Because of its severity, its poor lithium response, and its combination of depressed and manic states, mixed mania is of both practical and theoretical interest. There is relatively little information about biological correlates of mixed mania. The NIMH Clinical Research Branch Collaborative Program on the Psychobiology of Depression investigated relationships between sympathoadrenal function and the symptoms of mania, and their relationship to the mixed state, in 19 intensively studied manics (RDC criteria). Patients with mania have increased sympathoadrenomedullary (SAM) activity, with increased excretion of NE, E, and their metabolites, and increased adrenocortical function as reflected by am and pm plasma cortisol, urinary free cortisol excretion and CSF cortisol, and a 55% rate of dexamethasone nonsuppression. Relative E, but not NE excretion had robust correlations with rating for mania. Cortisol measures did not correlate with mania. Plasma am cortisol (both pre- and postdexamethasone), and CSF cortisol were significantly higher in mixed than in pure manics. Several measures of cortisol, especially CSF cortisol, correlated significantly with depressed mood. Other than a trend toward increased relative NE excretion, mixed and pure manics did not differ with respect to any measures of catecholamine function and none correlated with depressed mood. These data show that increased SAM activity is associated with the manic state. The mixed state is characterized by combined increases in SAM and adrenal cortical activity.

NR426 **Wednesday, May 16, 12 noon - 2:00 p.m.**

SIDE EFFECTS IN ACUTE TREATMENT OF AFFECTIVE PSYCHOSIS

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Summary:

Hypothesis: Lithium potentiates incidence of serious side effects when combined with anti-psychotic medication: Incidence of side effects associated with combinations of anti-psychotic and anti-manic medication was assessed in radidly stabilizing manic and schizoaffective patients (N = 99) admitted to an acute 5-day inpatient unit over seven month and related to treatment. Of 603 admissions, 59 were diagnosed Bipolar-Manic Phase, 40 as Schizoaffective. Average length of stay was comparable by group; manics averaged eight years older (.002); women outnumbered men both in study sample and as schizoaffective (.01). Patient records were reviewed at 2-7 months post discharge for 1) neuroleptic, lithium, anti-Parkinson, lorazepam medication; 2) daily documentation of encephalopathy, Parkinsonism, mental status changes, various signs/symptoms. All medication dosages were within established ranges for clinical efficacy. Ninety-eight patients received anti-psychotic medication (58 haloperidol); 51 received lithium. Medication combinations were grouped according to nine specific pharmacotherapy regimens, collapsed into two main treatment groups: Anti-Psychotic (TX-1), Anti-Psychotic + Lithium (TX-2). Treatment significantly differed according to diagnosis: 71% Ma received TX-2; 58 SzA received TX-1 (.01). Twenty-nine side effects grouped into serious, moderate or mild/ambiguous, were documented for 77 patients, serious for 37 (38%). Results: Proportions of patients with serious side effects did not differ by treatment (43% TX-2, 30% TX-1; $t = 1.33$, 96 df, $p = .2$), diagnosis, sex or age; 34% SzA, TX-1 and 39% Ma, Tx-2 showed serous side effects. Conclusion: Serious side effects in rapid stabilization of affective psychoses occur in about one-third of patients, with or without lithium.

NR427 **Wednesday, May 16, 12 noon - 2:00 p.m.**

ADOLESCENT BEREAVEMENT: POST-PARENTAL DEATH

Elizabeth B. Weller, M.D., Psychiatry, The Ohio State University, 473 W. 12th Avenue, Columbus, OH 43210; Mary A. Fristad, Ph.D., Ronald A. Weller, M.D.

Summary:

Although 1.2 million children in the United States lose at least one parent by age 15, there has been little systematic research on the impact of parental death on children and adolescents. This study compared psychiatric symptomatology in bereaved versus depressed adolescents. Subjects were 24 bereaved and 10 depressed adolescents aged 13-18. Bereaved families were recruited through obituaries and assessed one month post-parental death. The Grief Interview and Diagnostic Interview for Children and Adolescents-Adolescent and Parent forms were used to assess grief reactions and DSM-III symptoms, respectively. Immediate grief reactions included: sadness (75%), anger (54%), anxiety (33%), relief (21%), and guilt (17%). The bereaved group endorsed fewer overall and specific depressive symptoms than the depressed group: overall ($3.6 \pm .1$ vs 7.3 ± 3.1, $t = 3.13$; $p < .004$), dysphoria ($X^2 = 8.82$, $p < .003$), loss of interest ($X^2 = 6.69$, $p < .01$), guilt/worthlessness ($X^2 = 12.10$, $p < .001$), impaired concentration ($X^2 = 4.87$, $p < .03$), and suicidal ideation ($X^2 = 12.10$, $p < .001$). The bereaved group also reported fewer anxiety symptoms: overall (2.5 ± 3.3 vs 6.4 ± 5.3, $t = 2.13$, $p < .05$), being a "worrier" ($X^2 = 6.24$, $p < .02$), worrying about little things ($X^2 = 14.22$, $p < .0001$), and phobias ($X^2 = 5.89$, $p < .02$). However, nearly three times as many bereaved compared to depressed adolescents worried about their (surviving) parent (36% vs 13%, NS). To reach more definite conclusions about adolescent bereavement, study of a larger sample followed for a longer time period is necessary.

NR428 **Wednesday, May 16, 12 noon - 2:00 p.m.**

DST AND SUICIDALITY IN CHILDREN

Ronald A. Weller, M.D., Psychiatry, The Ohio State University, 473 W. 12th Avenue, Columbus, OH 43210; Elizabeth B. Weller, M.D., Mary A. Fristad, Ph.D., J. Hittner, B.A., Sheldon H. Preskorn, M.D.

Summary:

Suicidality has been associated with dexamethasone suppression test (DST) nonsuppression in adolescents and adults. This study examined the relationship between suicidality, DST results, and post dexamethasone cortisol levels in 121 prepubertal children. Subjects included: 1) 78 consecutively hospitalized inpatients with major depressive disorder (DSM-III criteria) who were moderately to severely depressed; 2) 22 patients consecutively hospitalized for nonaffective psychiatric illness; and 3) 21 nonhospitalized normal volunteers without past/present evidence of psychiatric illness. Suicidality was assessed in all subjects using the Diagnostic Interview for Children & Adolescents (DICA) and the Diagnostic Interview for Depression in Children and Adolescents (DIDCA). Suicidal ideation, intent, plans, and attempts were assessed. Baseline cortisol levels were measured at 8 am and 4 pm. At 11 pm that evening, 0.5 mg of dexamethasone was administered. Cortisol levels were measured at 8 am and 4 pm the following day. Nonsuppressors ($\geq$5 ug/dl) had higher suicide ratings than suppressors ($t = 1.77$, $p < .08$). Higher cortisol levels at 4 pm post-dexamethasone were associated with higher suicide ratings ($r = .23$, $p < .03$). The relationship between suicidal ideation, intent, plans, and actual number of attempts with DST nonsuppression and post-dexamethasone cortisol levels is similar to that previously reported in adolescents and adults.

NR429 **Wednesday, May 16, 12 noon - 2:00 p.m.**

CHILDHOOD ANTECEDENTS OF ADULT DEPRESSION

Richard C. Shelton, M.D., Department of Psychiatry, Vanderbilt University, 394TVC 22nd Ave. So., Nashville, TN 37232; Scot E. Purdon, B.S.

Summary:

Early life experiences, particularly parental loss, have been thought to be associated with adult psychopathology. Breier et al. (1988) discovered that in adults whose parents had died in childhood, depression was related to the quality of parental relationships, not to loss per se. What is less clear is whether or not this is meaningful in a broader population of depressives. *METHOD*: 24 persons (10 men and 14 women, age 40.8 $\pm$ 7.6, 27-56) with major depressive disorder (MDD)(SCID-P) were compared to 10 controls (4 men, 6 women, age 37.3 $\pm$ 8.1, 25-49) free of a history of psychopathology. The subjects were assessed using a modified Quality of Home Life and Personal Adaptation Scale (QHLPAS)(Breier et al. 1988), evaluating life experiences and psychopathology in three age periods: birth to 5, 6-12, and 13-18. *RESULTS*: The QHLPAS was divided into five factors: home environment (HE: i.e. family relationships), physical and sexual abuse (AB), extrafamily relationships (friends: FR), school performance (SP), and depression (DE). A 3 (age) by 2 (group) MANOVA demonstrated differences in HE ($F = 7.10$, $p = 0.01$), FR ($F = 11.39$, $p = 0.002$), and DE ($F = 13.64$, $p = 0.001$), with a trend for AB ($F = 2.89$, $p = 0.10$) and no difference for SP ($F = 0.61$, $p = 0.44$). Within the DE cell there was a positive group by age interaction in the MDD group for DE (i.e. worsening of depression with age). Four MDD (17%) and 3 controls (30%) had lost a parent by death or divorce. *DISCUSSION*: These results support the concept that disturbed relationships in childhood, not loss of parent, are antecedent to depression in adult life. There is also evidence of progressive depression in childhood. Correlations with biological and cognitive data will be presented in order to elucidate mediating influences in adult depression.

NR430 **Wednesday, May 16, 12 noon - 2:00 p.m.**

SLEEP DEPRIVATION AUGMENTATION OF ANTIDEPRESSANTS

Richard C. Shelton, M.D., Department of Psychiatry, Vanderbilt University, 394TVC 22nd Ave. So., Nashville, TN 37232; Peter T. Loosen, M.D.

Summary:

Sleep deprivation (SD) has been shown to produce a rapid but transient improvement in about 60 percent of persons with major depressive disorder (MDD). SD combined with chlorimipramine or lithium, on the other hand, produces a rapid, sustained antidepressant effect in SD responders. SD has not been shown, however, to produce the same response in combination with other drugs. *METHODS*: The subjects were 13 patients (ten men and three women) with a *DSM-III-R* of MDD (with melancholia), a mean age of 49.5 ± 12.5 (range 31-69), and a mean Hamilton Rating Scale for Depression (HRSD) of 20.4 ± 8.8. A 36-hour observed total sleep deprivation was performed. All subjects were rated with a modified version of the HRSD (HRSD-M), at baseline and for a minimum of ten days after SD. After completion of the SD, the subjects were begun on an antidepressant chosen by the treating physician before the SD procedure so that it would be unbiased. *RESULTS*: Nine of 13 subjects (69 percent) showed a minimum of 33 percent reduction in the HRSD-M scores after SD. After initiation of antidepressants, all of the responders showed a sustained antidepressant effect, while the nonresponders continued to exhibit a delayed result. The responders were on : doxepin (1: maximum dose 300 mg/day), fluoxetine (1: 40mg), imipramine (1:150mg), and nortriptyline (6: mean dose 96 mg/day), while the nonresponders were on: fluoxetine (1: 20mg), imipramine (1:150mg), and nortriptyline (2: mean 87.5mg). *DISCUSSION*: This study confirms a 60 percent response rate to SD in MDD and shows that several different antidepressants (both noradrenergic and serotonergic) can be used to sustain the effect. The combination of SD with antidepressants is shown again to be an effective but underused treatment modality.

NR431 **Wednesday, May 16, 12 noon - 2:00 p.m.**

OLD AGE DEPRESSIVE PSEUDODEMENTIA: THREE-TO-FOUR YEAR OUTCOME

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Summary:

Long-term outcome of geriatric depression is unclear. 62 elderly depressives hospitalized for major depression between 1985 and 1987 were followed after a mean 43.30 +/− 4.3 months. 18 patients had met criteria for reversible cognitive impairment at discharge. 77% (48/62) of original patients/caregivers were available for telephone interview. Outcome categories included: group 1 - lasting recovery (31.3%); group 2 - further relapses with complete recovery between episodes (27.1%); group 3 - some residual depressive symptomatology, often with further circumscribed relapses (20.8 %); group 4 - persistently ill with depression (2.1%); group 5 - dementia (via standardized phone questionnaire) (2.1%); group 6 - death (16.7%).

Comparable percentages of patients with and without depression-dependent reversible cognitive impairment were available for follow-up. No differences in distribution of above outcome categories were seen between these groups.

Findings attest to the chronicity of late-life depression. Depression-dependent reversible cognitive impairment at index episode in the elderly was not associated with significantly greater dementia, death, or depressive incapacity at 3-4 year follow-up, challenging the notion that cognitive impairment of depression may be a harbinger of dementia.

Prognostic relevance of demographic (age at index, age at onset of first depression) and clinical (cognitive status, depression severity, physical illness) factors will be reported.

NR432 **Wednesday, May 16, 12 noon - 2:00 p.m.**

IDAZOXAN IN TREATMENT-RESISTANT BIPOLAR DEPRESSION

Ossama T. Osman, M.D., Bldg 10 RM 2D47, National Inst. Men. Hlth, 9000 Rockville Pike, Bethesda, MD 20892; Matthew V. Rudorfer, M.D., Husseini K. Manji, M.D., Fred Grossman, D.O., William Z. Potter, M.D.

Summary:

In spite of the availability of several different types of antidepressant compounds, a significant number of depressed patients (20-30%) fail to show an adequate response. The alpha-2 antagonist idazoxan appears to be especially promising for bipolar patients from this group of non-responders. We are studying the effect of chronic administration of idazoxan in an ongoing placebo-controlled study in patients with a diagnosis of bipolar affective disorder, depressed type. After a washout period of at least 3 weeks, different biochemical and hormonal parameters are measured and patients are subsequently started on idazoxan increasing to a total dose of up to 120 mg daily. In patients studied to date, mean Hamilton score fell from 25 ± 8 to 8 ± 7 after 4-6 weeks on idazoxan ($n = 5$). This antidepressant effect was not accompanied by any significant changes in either systolic or diastolic blood pressure. The only clear side effects were a mild to moderate increase in anxiety and insomnia. Biochemically, idazoxan elevated the norepinephrine levels in CSF, plasma, and urine. The clinical efficacy of idazoxan and the low profile of adverse effects make this novel compound very promising and interesting as an antidepressant agent. Idazoxan treatment was also associated with reductions in ACTH and cortisol. The relationships between biochemical and behavioral changes will be discussed.

NR433 **Wednesday, May 16, 12 noon - 2:00 p.m.**

LIFE EVENTS AND FAMILIAL SUBTYPES OF DEPRESSION

Jose L. Ayuso-Gutierrez, M.D., Psychiatry, Hospital San Carlos, Alcala 152, Madrid 28028, Spain; Rosa Yanez, M.D., Jose Delgado, M.D., Elena Ezquiaga, M.D., Jose L. Ayuso Mateos, M.D.

Summary:

The aim of this study was to validate Winokur's familial classification of unipolar depression using psychosocial variables.

The study sample included 97 patients consecutively admitted to a general hospital with a diagnosis of primary unipolar major depressive disorder according to R.D.C.

The familial subgroups were classified according to data from a structured familial history (FH-RDC) following the criteria of Winokur (1979): Family Pure Depressive Disorder ($N = 42$), Depression Spectrum Disease ($N = 27$) and Sporadic Depressive Disease ($N = 28$). Patients were also given a semistructured interview in order to evaluate whether a given life event would fit into any of the items on the list by Paykel et al. (1971). A subject was considered to have experienced a severe event when any of the top 20 events on the list had occurred within 6 months before onset.

Our results for Winokur's three family subgroups do not significantly differ in the frequency of major life events prior to the index depressive episode. However, we observed a tendency to present fewer precipitants in the Pure Depressive Disorder family subgroup (16%) compared with the other two groups in the sample (S.D.D. 28,6%; D.S.D. 29,6%).

NR434 **Wednesday, May 16, 12 noon - 2:00 p.m.**

FLUOXETINE TEST VERSUS (3H)-IMIPRAMINE BINDING IN DEPRESSION

Jose L. Ayuso-Gutierrez, M.D., Psychiatry, Hospital San Carlos, Alcala 152, Madrid 28028, Spain; Olga Borrego, M.D., Jose V. Baeza, M.D., Ana Barabash, M.D., Jose A. Cabranes, M.D., Maribel B. Cebeira

Summary:

Neuroendocrine tests are being increasingly regarded as a useful method for studying Cerebral MA functions. For example, 5-HT has been found to modulate the secretion of cortisol and prolactin. In a previous report we assessed the effect of fluoxetine on 5-HT functions in humans. Statistically significant differences in plasma cortisol and prolactin secretion between placebo and fluoxetine condition were found after the challenge. In order to determine the relationship between [^{3}H]-I-Binding parameters in platelets and the fluoxetine challenge test, we conducted a study with sixteen depressive women patients meeting DSM-III-R Criteria for M.D.D. All subjects were drug-free for at least 1 week. After an over-night fast [^{3}H]-I-Binding probe was carried out. The following day, responses to fluoxetine were measured in serum plasma of patients.

A significant negative correlation was found between the Bmax and the cortisol secretion following fluoxetine administration. The patients whose cortisol response was blunted and those whose prolactin secretion was lower correlate positively with [^{3}H]-I-Binding parameters. The group with lower prolactin secretion showed significant negative correlation between cortisol secretion and Bmax and Kd. These results suggest fluoxetine's usefulness in assessing serotonergic functions and subtyping depressive illness.

NR435 **Wednesday, May 16, 12 noon - 2:00 p.m.**

PREDICTORS OF RESPONSE TO ECT IN MANIC PATIENTS

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Summary:

The authors present findings on the association between pretreatment symptomatic measures and acute ECT outcome in 20 bipolar manic patients (DSM-IIIR) who had previously failed to respond to lithium or neuroleptic at adequate doses. Clinical ratings using the Modified Mania Scale were conducted by research psychiatrists blind to treatment modality during a 4 to 7 day pretreatment unmedicated baseline. Classification as treatment responder required remission from mania for 7 days following either initial assignment to unilateral or bilateral ECT or, having failed unilateral ECT, following crossover bilateral ECT. Thirteen (65%) of the patients met criteria for classification as a treatment responder. Seven of those had responded to bilateral and 6 to unilateral ECT. Responders were significantly older than nonresponders ($p < .05$). Baseline ratings of irritability, suspiciousness, and anger were significantly higher in ECT nonresponders than responders ($p < .01$, .05, and .05 respectively), but were not correlated with age. Duration of illness, duration of index episode, and baseline ratings of mania severity and psychosis did not differ between responders and nonresponders. Although ECT appears to be effective in lithium nonresponsive manic patients, symptomatic characteristics of ECT nonresponders appear to resemble those reported by some to predict poor lithium treatment outcome.

NR436 **Wednesday, May 16, 12 noon - 2:00 p.m.**

CSF SOMATOSTATIN CRH AND ACTH IN ALCOHOLICS

Alec Roy, M.D., Research, Hillside Hospital, P.O. Box 38, Glen Oaks, NY 11004; Bryon Adinoff, M.D., Philip W. Gold, M.D., Judith DeJong, Ph.D., David R. Rubinow, M.D., Markku I. Linnoila, M.D.

Summary:

Reduced brain and cerebrospinal fluid (CSF) levels of somatostatin, corticotropin releasing hormone (CRH), and corticotropin (ACTH) have been reported among neuropsychiatric patients with cognitive dysfunction. Alcoholism is a disorder in which associated neuropsychiatric disorders occur. Therefore, we compared CSF levels of somatostatin, CRH, and ACTH in alcoholics ($N = 100$) and normal controls (N-29). There were no significant differences between the groups on concentrations of the three peptides. Moreover, there were no significant correlations between concentrations of the peptides in CSF and computed tomographic measures of the size of brain ventricles. There were, however, significant correlations between CSF concentrations CRH and ACTH and between CSF concentrations of CRH and somatostatin in both the alcoholic and control groups. Future studies should extend these observations to patients with alcoholics' dementia and alcoholics during acute withdrawal.

NR437 **Wednesday, May 16, 12 noon - 2:00 p.m.**

ETOMIDATE VERSUS METHOHEXITAL FOR ANESTHESIA IN ECT

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Summary:

Twenty patients were enrolled in a prospective, randomized, open-vial, crossover study. Each patient received glycopyrrolate 0.3 mg IM pre-ECT. Each patient had four ECTs with the following dose schedule: methohexital 1.0 mg/kg for two ECTs and etomidate 0.3 mg/kg for two ECTs. Mean blood pressure (BP) and heart rate (HR) were recorded pre-ECT and at 0.5, 1.5, 3.0 and 5.0 minutes post-ECT. Each drug was evaluated for induction and wake-up times, side effects and seizure duration. There was no significant difference ($p < 0.05$, ANOVA) between the etomidate and methohexital groups concerning BP and HR post-ECT, induction time, or seizure duration. Etomidate had a longer mean wake-up time by 24%. There was no significant difference in dysrhythmias (PAC or PVCs) (Chi-Square Test $p < 0.05$). However, more patients had pain on injection with etomidate (13) than with methohexitol (5). Increased incidence of pain on injection and a longer wake-up time are drawbacks to etomidate. However, etomidate compared favorably to methohexital regarding BP and HR hemodynamics and is an acceptable alternative to methohexital especially when barbiturates may be contraindicated or when the above drawbacks are taken into account.

NR438 **Wednesday, May 16, 12 noon - 2:00 p.m.**

DIAGNOSIS, TREATMENT AND OUTCOME IN REFRACTORY DEPRESSION

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Summary:

Seventy-six depressed patients underwent inpatient diagnostic assessment. Most had previously failed to respond to outpatient treatment with tricyclic antidepressants and were considered treatment refractory. The dexamethasone suppression test (DST) and thyrotropin releasing hormone stimulation test (TRHST) were administered to sixty-seven of these patients. A depressive subtype checklist was administered to all 76 patients. When an accurate subtype diagnosis was established, each patient received somatic treatment custom-tailored to his/her diagnosis. Sixty per cent of the patients had atypical depression and all received monoamine oxidase inhibitor antidepressants, alone or in combination with lithium. Overall, seventy-seven per cent (59/76) had a good response to treatment, documented by rating scale scores below the cutoff for depression at one to twelve months after discharge. The DST and TRHST did not discriminate treatment responders from nonresponders, nor did these tests distinguish endogenous from atypical depressive subtypes. Successful treatment of patients with "refractory" depression appears contingent upon accurate subtype diagnosis and differential pharmacotherapy.

NR439 **Wednesday, May 16, 12 noon - 2:00 p.m.**

TREATMENT OF PSYCHOTIC DEPRESSION SUBTYPES

Raymond F. Anton, M.D., Psychiatry, Med. Univ of SC., 171 Ashley Avenue, Charleston, SC 29425; Earl A. Burch, M.D.

Summary:

We have previously suggested that amoxapine, an antidepressant with possible antipsychotic action was useful in the treatment of major depression with psychotic features (MDPF). In this study, we directly compared amoxapine (AMOX) with a combination of amitriptyline and perphenazine (AMI/PER) in the treatment of MDPF. In addition, we evaluated the efficacy of these medications in patients who had predominantly mood congruent (MC) or mood incongruent (MI) psychotic features.

Thirty-seven inpatients who met DSM-III criteria for MDPF (21 MC and 16 MI) after a placebo washout were randomly given either AMOX 400 mg or AMI/PER 200 mg/32 mg daily. In a double-blind manner, patients were rated at baseline and over four weeks of treatment for depression (HRSD), psychosis (BPRS), and clinical improvement (CGI).

A 2-way ANCOVA showed that both AMOX and AMI/PER showed similar effectiveness in both the MC and MI groups. Both medication groups had similar improvement in the HRSD and BPRS over time, irrespective of the type of psychotic features. 82% of the AMOX group and 86% of the AMI/PER group were rated as "moderate to markedly improved" at termination. This suggests that depressed patients with either mood congruent or incongruent psychotic features respond well to either amoxapine or to a combination of an antidepressant and antipsychotic medication.

NR440 **Wednesday, May 16, 12 noon - 2:00 p.m.**

GH RESPONSE TO CLONIDINE AND INSULIN IN DEPRESSION

Jay D. Amsterdam, M.D., Psychiatry, University of Penna, Res. Unit HUP 3400 Spruce St., Philadelphia, PA 19104; Greg Maislin, M.S., Jennifer Phillips, B.S., Andrew Winokur, M.D.

Summary:

An abnormal growth hormone (GH) response has been observed after a variety of neuroendocrine challenge tests in depression, and this finding is thought to reflect a possible underlying dysfunction in a-adrenoceptor responsiveness. However, little attention has been given to the consistency of GH response abnormalities after different neuroendocrine procedures. We therefore examined GH responses after clonidine and insulin challenges within the same subject to see if consistent GH secretory response patterns were evident.

Methods: We studied 14 patients with DSM-III MDD: 10 with melancholia (MEL) (32 ± 9 yrs), 4 without MEL features (36 ± 10 yrs); and 3 healthy controls (25 ± 3 yrs). Subjects were drug free, and neuroendocrine tests were performed at 08:30 hrs on two separate occasions at least five days apart.

Results: There was a significant reduction in the cumulative GH response after clonidine ($p < 0.0002$). Pair-wise comparisons also showed a blunted GH response in MEL vs non-MEL ($p < 0.003$) and MEL vs control subjects ($p < 0.001$). In contrast, similar differences in cumulative GH responses were not observed after insulin ($p = 0.10$). Furthermore, no apparent within-subject correlation for GH response was seen between clonidine and insulin challenge tests. The present findings indicate a variability in GH secretory response patterns to different neuroendocrine challenge tests within the same subject, and suggest that clonidine may be a more specific neuroendocrine probe for demonstrating possible a-adrenoceptor dysregulation in depression.

NR441 **Wednesday, May 16, 12 noon - 2:00 p.m.**

EFFECT OF LABETALOL ON HEMODYNAMICS AND SEIZURE DURATION DURING ECT

Vaughn W. McCall, M.D., Adult Administration, John Umstead Hospital, 12th Street, Butner, NC 27509; Frank E. Shelp, M.D., Richard D. Weiner, M.D., Shirley Austin, R.N., Audrey Harril, R.N., Eric Moffet, M.D.

Summary:

Recent studies demonstrate that two beta-blockers limit hemodynamic changes during ECT but comprise seizure duration. We present a comparison study with labetalol, a mixed alpha-beta blocking agent.

Ten subjects (2 male, 8 female) aged 39.2 $\pm$ 12.7 received 5 mgs. intravenous labetalol five minutes prior to either the third of fourth ECT in a blind, randomized, and counterbalanced design with a saline control. Subjects received bilateral brief pulse stimulus 50 percent above seizure threshold. Blood pressure and pulse were monitored throughout each treatment. EEG seizure duration was scored by two raters ($r = 0.97$) blind to treatment order, hemodynamic data, and group assignment.

Labetalol reduced maximum pulse by 26 $\pm$ 16.5 beats/minute (18 percent) during the seizure and 9.4 $\pm$ 9.0 beats/minute (12 percent) post-ictally ($p < 0.01$, Wilcoxon signed rank test). Rate-pressure-product, a measure of cardiac work, was similarly reduced by 5540 $\pm$ 4338 (22%, $p < .006$). These findings were independent of treatment order. Labetalol had no effect on blood pressure, resting vital signs, or seizure duration.

These findings substantiate 5 mgs. intravenous labetalol as an effective pre-treatment agent prior to ECT to limit tachycardia without adversely effecting seizure duration. These advantages make it the preferred pre-medication until other agents are better studied.

NR442 **Wednesday, May 16, 12 noon - 2:00 p.m.**

BUSPIRONE AUGMENTATION OF ANTIDEPRESSANT RESPONSE

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Summary:

Buspirone is an anxiolytic having high affinity for 5-HT_{1A} receptors and moderate affinity for brain D2-dopamine receptors. It has been reported that buspirone may augment the effects of fluoxetine in reversing the symptoms of obsessive-compulsive disorder. To explore whether buspirone might also potentiate antidepressant response, seven patients with a primary DSM-III-R diagnosis of major depression who had failed to respond to single trials of antidepressants underwent an open add-on trial of combination therapy with buspirone. Five patients had failed to respond to fluoxetine and two patients had failed to respond to tricyclic antidepressants (imipramine, nortriptyline) with steady state blood levels in the therapeutic range. Following at least three weeks of non-response to the antidepressants, buspirone was added at doses of 2.5-10 mg TID. Six of seven patients reported full resolution of depressive symptoms within two weeks of adding buspirone and one reported partial improvement. Side effects following the addition of buspirone were minimal. In a separate study, five of six patients suffering recurrence of depressive symptoms during the winter while receiving antidepressants showed remission of these symptoms following the addition of buspirone. These results suggest that buspirone may be a useful medication in potentiating antidepressant response. We will relate these findings to the serotonergic hypotheses of depression and anxiety.

NR443 **Wednesday, May 16, 12 noon - 2:00 p.m.**

COMBINED THYROID HORMONE AND ECT TREATMENT

Robert A. Stern, Ph.D., Psychiatry, Univ of North Carolina, CB #7160 Medical School, Chapel Hill, NC 27599; Charles T. Nevels, M.D., Mark E. Shelhourse, M.D., Mark L. Prohaska, Arthur J. Prange, Jr., M.D.

Summary:

Triiodothyronine (T3) has been found to potentiate the antidepressant effects of tricyclics in tricyclic nonresponders. Hypothyroidism, perhaps even in minor degree, can result in memory and other cognitive impairments. Likewise, electroconvulsive therapy (ECT) frequently results in confusion and memory impairment. Results of a retrospective chart review have shown a significant association between low pre-ECT thyroid hormone levels and post-ECT confusion and memory loss.

The above findings led to the hypothesis that T3 may potentiate the antidepressant effects of ECT while diminishing the amnestic sequelae. In a double-blind, placebo-controlled study of combined ECT and T3 treatment, subjects were given 50 ug of T3 or placebo nightly throughout the duration of bilateral ECT. To date we have studied 5 placebo and 6 treatment patients with diagnoses of major depression or schizoaffective disorder. The groups did not differ in age, education, IQ estimate, or pre-ECT Hamilton or BPRS scores. Results indicate that the ECT-T3 group required significantly fewer treatments than the ECT-placebo group (7.7 vs. 12.2, respectively, $t[9] = 3.74$, $p < .01$). Furthermore, although there were no treatment differences in attention or visuospatial learning and memory, there was a significant interaction effect for verbal learning (California Verbal Learning Test)($F[1,10] = 6.59$, $p < .05$). While the ECT-placebo group's verbal learning worsened from pre- to post-ECT, the ECT-T3 group's performance improved.

NR444 **Wednesday, May 16, 12 noon - 2:00 p.m.**

ANTIDEPRESSANTS FOR MILD DEPRESSIVES

Frederic M. Quitkin, M.D., Psychiatry, NYS Psych Institute, 722 West 168th Street, New York, NY 10032; Jonathan W. Stewart, M.D., Wilma Harrison, M.D., Edward V. Nunes, M.D., Steven Wager, M.D., Patrick J. McGrath, M.D.

Summary:

A controlled trial studying the efficacy of placebo, imipramine, and phenelzine was completed in 401 patients. Study design called for a 10-day placebo washout period. Patients who continued to manifest persistently depressed mood were entered into a six-week double-blind trial.

In order to determine minimum degree of severity required to demonstrate drug-placebo differences, all patients who had a Hamilton Depression Scale score of 10 or less at the point of randomization were stratified from the larger sample. Thirty-one patients were treated with placebo, 23 patients with imipramine, and 17 with phenelzine. Twenty-two percent of placebo treated patients, 60 percent of imipramine treated patients, and 82 percent of phenelzine treated patients were rated much improved at the end of six weeks of treatment. These differences are statistically different.

These data have sweeping implications for the treatment of outpatient depressives. They suggest that those who are chronically ill and persistently demonstrate depressed affect should be treated with antidepressants regardless of the severity of their disorder.

At the presentation, predictors of response and lack of response will also be discussed.

NR445 **Wednesday, May 16, 12 noon - 2:00 p.m.**

NEUROLEPTIC ADJUNCTS IN THE EMERGENCY TREATMENT OF SCHIZOPHRENIA

James G. Barbee, M.D., Psychiatry, LSU Medical Center, 1542 Tulane Avenue, New Orleans, LA 70112; Donna M. Mancuso, M.D., Charles R. Freed, M.D.

Summary:

Twenty-eight acutely psychotic schizophrenic patients who presented to the emergency psychiatric service of a general hospital were randomly assigned to treatment with oral preparation of either 5mg of haloperidol and 1mg of alprazolam or 5mg of haloperidol with a matched placebo. Drug was administered every two hours in the first 8 hours of the protocol based upon clinical status; those patients with a score greater than 12 on a short version of the BPRS (consisting of six subscales in the "psychoticism" cluster) were given a repeat dosage upon each evaluation. In the event of sedation, the dosage was held. Results from this procedure were then used to calculate a baseline dosage which was given on Day 2 and 3 of the protocol. Independently rated outcome measures included the BPRS (at 0,24,48 and 72 hours), SAPS and SANS (at 0 and 72 hours), and side effect rating scales (at 72 hours).

Both groups experienced improvement at a similar rate, except in the first 8 hours, when inspection of data reveals that the combination was more effective than haloperidol alone, especially for agitation. Combination-treated patients also required significantly less haloperidol. Implications of these findings will be discussed.

NR446 **Wednesday, May 16, 12 noon - 2:00 p.m.**

GENETIC STUDY OF LITHIUM RESPONSE: ANALYSIS OF THE MODE OF INHERITANCE

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Summary:

The chances of obtaining reproducible findings in psychiatric genetics are enhanced if research focuses on homogeneous groups of families. This homogeneity can be defined not only by a similarity of clinical symptoms but also by similar response to a specific treatment. We studied the mode of genetic transmission in 72 patients suffering from recurrent affective disorders and their families (N = 512). The knowledge of the mode of inheritance is important both for genetic counselling and for further genetic research including linkage analysis. The probands, followed for up to 20 years, were all responders to long term lithium treatment. Based on previous analysis of this sample, the affected phenotype in relatives was defined as having either bipolar, unipolar or schizoaffective disorder (RDC dg). Age-adjusted morbidity risks for these three disorders combined were calculated separately for parents, siblings and children, separately by proband's and relative's sex in each category. The expected morbidity risks were expressed in terms of parameters of genetic models; the parameters were then estimated from the observed risks using maximum-likelihood procedure. The results suggest major-gene effects in the transmission of primary affective disorders in the families studied; the polygenic model with sex-specific thresholds could be rejected. It appears that solutions with relatively frequent recessive allele (q = 0.15) and lower penetrance in males than in females fit the data best, even when the frequency of sporadic cases is fixed to zero. The results do not allow discrimination between the autosomal and X-chromosome transmissions. However, the autosomal model predicts more realistic population frequencies of primary affective disorders than X-chromosome model.

NR447 **Wednesday, May 16, 12 noon - 2:00 p.m.**

ORAL S-ADENOSYLMETHIONINE VERSUS DMI IN DEPRESSION

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Summary:

A double-blind study comparing oral SAMe with desipramine was undertaken. Twenty patients with *DSM-III-R* major depression and a 31-item Hamilton Depression (HAM-D) score >23 were randomly assigned to 28 days of 1600 mg/day SAMe or 250 mg/day desipramine (DMI). The two patient groups were similar in sex, age, family history of alcohol use or depression, precipitating life events, duration of illness, and baseline HAM-D scores (37.6 + 6.9 for SAMe and 40.8 + 7.5 for DMI ($t(1,18) = .3$, n.s.). There was a significant treatment effect over time with final HAM-D scores of 19.1 + 12.8 for the SAMe and 18.9 + 13.5 for the DMI patients ($F(4,64) = 28$, $p < .001$), but no significant difference between treatments (ANOVA, $F(1,16) = .2$, n.s.) and no treatment by day interaction ($F(4,64) = .2$ n.s.). The patients' self-report measure, the BDI, also demonstrated a significant treatment effect over time for both groups (ANOVA, $F(4,64) = 28$, $P < .001$) and no significant difference between treatments. Side effects were not significantly different between groups (ANOVA, $F(1,15) = .4$, n.s.) although minor gastrointestinal complaints were noted in the SAMe patients. When compared to aggressive desipramine treatment, oral SAMe appeared to be an effective antidepressant with minor side effects.

NR448 **Wednesday, May 16, 12 noon - 2:00 p.m.**

NICOTINE POTENTIATES HALOPERIDOL IN TOURETTE CASES

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Summary:

While the drugs of choice for Tourette's disorder are neuroleptics such as haloperidol, some patients show only marginal response. In animals nicotine potentiates the behavioral effects of haloperidol (1), and in a previous open study of 10 children with Tourette's disorder showing partial response to haloperidol, concurrent administration of nicotine polacrilex gum markedly decreased globally assessed tic frequency in eight cases (2). In the present study, 10 additional children and adults whose Tourette's disorder was partially controlled by haloperidol had particular and total tic frequencies rated from videotapes over consecutive two-minute periods (interrater reliability $r = 0.96$). Each patient was rated during an initial baseline period of 30 minutes, during a subsequent 30-minute period of chewing nicotine polacrilex gum (2 mg), and during the two subsequent 30-minute periods. In all cases, during the gum chewing period the tics showed a significant percentage decrement from mean baseline frequency [53.2 ± 6.5 percent; $F = 16.8$ (1,19) $p < .01$]. In 90 percent of cases, this effect lasted for a further hour [56.9 ± 6.3 percent 1st 30 minutes; $F = 6.0$ (1,19) $p < .05$, and 62.4 ± 6.5 percent 2nd 30 minutes; $F = 9.9$ (1,19) $p < .05$]. Nicotine may be a useful adjunct to haloperidol for treating tics in Tourette's disorder.

NR449 **Wednesday, May 16, 12 noon - 2:00 p.m.**
WITHDRAWN

NR450 **Wednesday, May 16, 12 noon - 2:00 p.m.**
COEXISTENCE OF NEUROLEPTIC-INDUCED PARKINSONISM AND ACUTE DYSTONIC REACTION

Patricia I. Rosebush, M.D., Psychiatry, 1200 Main Street West, Hamilton Ontario, Canada L8Z 3Z5; Michael Mazurek, M.D., Wendy Hiscox, R.N.

Summary:

The pathophysiology of neuroleptic-induced parkinsonism and acute dystonic reaction is generally understood in terms of altered dopaminergic neurotransmission in the striatum. According to this scheme, parkinsonism is seen as a deficiency, and acute dystonia as a transient excess, of dopaminergic activity. As such, these 2 drug-induced states ought not to co-exist. We have had an opportunity to examine this issue as part of a prospective study of neuroleptic side effects. Patients being admitted to our 30-bed acute-care general psychiatry ward are entered into the study of they have not previously been exposed to neuroleptic medication and if their clinical condition warrants treatment with neuroleptics. They are scored on a variety of psychiatric (BPRS, Hamilton Depression Scale, Hamilton Anxiety Scale, GAS) and neurological (AIMS, akathisia, dystonia, parkinsonism) rating scales prior to being started on neuroleptics and twice weekly thereafter. The medication used in the great majority of cases has been haloperidol 0.08 mg/day. Of the 41 patients thus far studied, 18 have developed dystonic reactions sufficiently severe to require emergency treatment. In 10 of these 18 patients, the acute dystonia has developed in the context of severe parkinsonism.

These data suggest that our understanding of the pathophysiology of acute dystonic reaction may need to be re-examined.

NR451 **Wednesday, May 16, 12 noon - 2:00 p.m.**
ALPRAZOLAM VERSUS CLONAZEPAM: INTERDOSE REBOUND?

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Summary:

Clinical studies suggest that major limitations in the use of alprazolam as an antipanic agent are: 1) frequent occurrence of interdose rebound anxiety effects and, 2) difficulties in withdrawing from the drug even under gradual tapering regimens. Because of this limitation for alprazolam, clonazepam is being increasingly used as the drug of choice for panic disorder. In order to assess objectively the clinical profile of each of these drugs, alprazolam 1.0 mg at hs and clonazepam 0.5 mg at hs were evaluated in separate sleep laboratory studies each including six insomniac patients. Each study employed a 16-night laboratory protocol: four placebo-baseline nights followed by seven nights of drug administration and five placebo-withdrawal nights. In the clonazepam study on the first three drug nights (5-7), sleep time significantly improved. Additionally, as drug administration continued (9-11) the drug maintained its efficacy with no sign of tolerance. There was little sleep disturbance on the first night following drug withdrawal (nt 12). However, on night 14, sleep was significantly disturbed (rebound insomnia). In the alprazolam study, a significant improvement was also noted with short-term use (nts 5-7) but not with continued use (nts 9-11) as tolerance developed quickly. Following drug withdrawal, there was a significant worsening of sleep on the third withdrawal night (nt 14). Thus, with the similar patterns noted following withdrawal, the major difference in this study between the two drugs was in alprazolam's rapid development of tolerance while clonazepam's efficacy was well maintained. Accordingly, we propose that this rapid development of tolerance is an important factor in alprazolam's reported propensity for producing interdose rebound effects (anxiety) particularly with extended use.

NR452 **Wednesday 16, 12 noon - 2:00 p.m.**

WINTER DEPRESSION RESPONSE TO TRANYLCYPROMINE

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Summary:

Seasonal affective disorder (SAD) is a disturbance of mood bearing a fixed relationship to season. Winter depression is characterized by the onset of a depressive syndrome in the fall or winter and spontaneous remission in the spring. The authors report the results of a study assessing its responsiveness to a standard pharmacological treatment for depression. Fourteen patients (3 men and 11 women) meeting NIMH criteria for winter depression were treated with tranylcypromine. The mean age of the sample was 34.7 ± 7.8 (SD) years. The mean age of onset was 15.2 ± 7.2 years. Eleven (79%) were anhedonic. Thirteen (93%) and 10 (71%) were hypersomnic or hyperphagic, respectively. Twelve patients met the DSM-III-R criteria for melancholia. The mean Carroll Rating Scale for Depression (CRSD) score was 26.5 ± 8.0. All 12 patients responded fully (CRSD score ≤5) and 2 partially (CRSD score 6 - 10). The mean dose of tranylcypromine was 32 mg ± 8 mg and the average time to recovery 23 ± 8 days. The mean CRSD score after 23 days of treatment was 2.6 ± 2.6. All hypersomnic and hyperphagic subjects reported complete remission of these symptoms. The average patient experienced 91% reduction in symptomatology.

NR453 **Wednesday, May 16, 12 noon - 2:00 p.m.**

OPTIMIZING ECT SCHEDULE: A DOUBLE BLIND STUDY

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Summary:

An optimum ECT schedule which maximizes therapeutic benefit and minimizes cognitive morbidity has never been empirically defined. To address this question, patients with major depression (RDC:Endogenous) have been randomly assigned to twice (ECTx2) or three times weekly ECT (ECTx3) administered over a 4-week period. (Treatment parameters: bilateral electrode placement, brief pulse waveform and stimulus intensity titrated to 150 percent above initial seizure threshold). Double-blind conditions have been achieved by the addition of one simulated ECT (anesthesia and muscle relaxant only) per week to the ECTx2 schedule. Long-term effects have been evaluated over a 6-month follow-up period on standardized pharmacotherapy. Data analysis on 40 subjects reveals identical antidepressant outcome after 4 weeks of treatment even though the ECTx3 schedule encompasses 4 additional real ECT's. However, response is significantly more rapid with ECTx3, the data suggesting a rate advantage of a week for this schedule. After 4 weeks of treatment, cognitive adverse effects are significantly more severe with 3x weekly treatment but this difference dissipates by one month follow-up. If cognitive morbidity can be reduced by limiting treatment number, ECTx3 would appear to be the clinically advantageous schedule.

(Supported in part by NIMH Grant #40734)

NR454 **Wednesday, May 16, 12 noon - 2:00 p.m.**

RAPID ANTIDEPRESSANT EFFECT OF DESIPRAMINE PLUS FLUOXTINE

J. Craig Nelson, M.D., Psychiatry, Yale University, 20 York Street MU 10-5, New Haven, CT 06504; Carolyn M. Mazure, Ph.D., Malcolm B. Bowers, M.D., Peter I. Jatlow, M.D.

Summary:

Although there are many effective antidepressant drugs available, all are associated with delayed response. We report here rapid response obtained with desipramine (DMI) combined with fluoxetine. The idea for this trial was based on a recent animal study (Baron, et al, *Eur J Pharamacol* 1988) which reported that combined DMI/fluoxetine treatment resulted in more rapid down regulation of beta adrenergic receptors than occurred with either DMI or fluoxetine alone. We administered fluoxetine with DMI in an open pilot study and compared clinical response with that observed in a prior study of DMI alone. Five patients (three women, two men) mean age 46 (range 25-69) with nonpsychotic unipolar major depression were treated for four weeks with DMI. Fluoxetine 20 mg was added for the first two weeks. Twenty-four hour DMI blood levels were used to rapidly adjust dosage to achieve a target DMI level (Nelson et al, *J Clin Psychopharmacol* 1987) anticipating that fluoxetine would raise DMI levels. Response on a modified 17-item Hamilton Scale (HDRS) in the five augmented patients was compared with similar ratings from a prior study of 52 inpatients treated for four weeks with DMI at a targeted plasma level. Combined DMI/fluoxetine was well tolerated and reasonable DMI plasma levels were quickly attained. Response was substantially and significantly more rapid in patients receiving combined DMI/fluoxetine treatment. At week 1, mean HDRS scores in the combined treatment group improved 47 percent vs 20 percent in the DMI alone group ($t = 2.12$, $p = .02$). Our findings require placebo-controlled, double blind study, but suggest that DMI combined with fluoxetine results in substantially more rapid antidepressant effects.

NR455 **Wednesday, May 16, 12 noon - 2:00 p.m.**

ESTAZOLAM TREATMENT OF INSOMNIA WITH ANXIETY

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Summary:

Estazolam, a triazolo-benzodiazepine with an intermediate elimination half-life, has been previously shown to be an effective and safe hypnotic in insomniacs without concomitant psychiatric illness. To measure its efficacy in insomnia associated with generalized anxiety disorder (GAD), 108 patients meeting criteria for GAD [mean total score of Hamilton Anxiety Scale (HAS) = 22.0 ± 3.1(SD)] and insomnia were given single-blind placebo placebo for seven nights. Nine patients whose anxiety and/or insomnia improved were dropped as placebo responders. The remaining 99 patients were randomly allocated (1:1) to double-blind treatment with either estazolam 2.0 mg or matching placebo for seven nights. Hypnotic efficacy, as determined by patient completed sleep questionnaires, was statistically significant for estazolam 2.0 mg *vs* placebo for all sleep indices, including sleep latency ($p < 0.001$) and total sleep time ($p < .001$). Patients treated with estazolam 2.0 mg showed significantly greater improvement in anxiety than those receiving placebo on the mean total score of HAS [(placebo,-3.4; estazolam,-7.1; $p < .001$) and without the insomnia item (placebo,-2.7; estazolam,-5.5; $p < .001$)]. Anxiety scores on the State-Trait Anxiety Inventory showed greater improvement in the estazolam group, but without statistical significance ($p = 0.329$). Estazolam 2.0 mg is an effective hypnotic in patients with GAD and has a favorable anxiolytic action.

NR456 **Wednesday, May 16, 12 noon - 2:00 p.m.**

PLACEBO SIDE EFFECTS IN DEPRESSION AND OCD

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Summary:

While much has been written on placebo response, the issue of placebo side effects has received little attention. Placebo side effects are of interest for two reasons: 1) Disorder related differences in rates of placebo side effects can inflate true incidence of drug side effects, resulting in more side effects reported for medications prescribed for these disorders and 2) Patients reporting placebo side effects in double-blind trials may be more likely to placebo respond, believing they are on active drug.

We retrospectively examined our data base from several clinical drug trials for the frequency, severity and type of placebo side effects reported during placebo washout for patients with Major Depression (MD) and Obsessive-Compulsive Disorder (OCD). In addition, we compared those reporting placebo side effects with those who did not in terms of response to both active drug and placebo in the subsequent trial. Patients with MD had significantly more ($t = 2.51$, p .013 as well as more severe ($t = 3.02$, p .003) placebo side effects than patients with OCD. No differences were found in type of side effects reported, other than patients with MD had significantly more musculo-skeletal complaints than patients with OCD (X2-8.067, df, 1, p .005). Overall, patients reporting placebo side effects had significantly higher total Hamilton-Depression scores ($t = 1.48$, p .042). Presence of placebo side effects during washout did not predict treatment response in the subsequent trial with either active drug or placebo.

NR457 **Wednesday, May 16, 12 noon - 2:00 p.m.**

USE OF CARBAMAZEPINE IN A STATE HOSPITAL

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Summary:

In order to asses the reasons for a marked increase in the use of carbamazepine (CBZ) in a state hospital a retrospective chart review of chronic patients treated with CBZ was conducted. Response was evaluated in 27 patients (19 males, 8 females) with a mean age of 55 years. Patients had DSM-III diagnoses of schizophrenia(18), organic mental syndromes(7), and bipolar disorder with mania (2). All 27 patients exhibited various manifestations of aggressive behavior. In 23 of the 27 cases the treating psychiatrists judged the response to CBZ as positive with a decrease in aggression. Improvement in other psychotic symptoms were only reported in 7 cases. Side effects included a decrease in WBC to below normal limits in 4 patients, and below normal limits of sodium for 9 patients. Liver enzymes became elevated in 2 cases, requiring discontinuation in one case. Average dosages of CBZ were 900-1000mg/day (range 200-1600mg/day) with an average serum level of 6.6 mg/l (range 3.7-9.8 mg/l). This preliminary review suggests that treatment of aggressive behavior in chronic patients represents a primary reason for the use of CBZ by psychiatrists in a state hospital.

NR458 **Wednesday, May 16, 12 noon - 2:00 p.m.**

DRUG RESPONSIVE SYMPTOMS IN ACUTE PSYCHOSIS

Carolyn M. Mazure, Ph.D., Psychiatry, Yale University, Yale New Haven Hosp MU 10-5, New Haven, CT 06504; J. Craig Nelson, M.D., Peter I. Jatlow, M.D., Malcolm B. Bowers, Jr., M.D.

Summary:

Knowledge of which symptoms respond to neuroleptic drugs and at what rate is essential for monitoring treatment and understanding the pathophysiology of psychosis. We examined resolution of psychotic symptoms in a fixed dose perphenazine treatment study to determine which symptoms improved at ten days in direct relation to perphenazine (PPZ) serum concentrations. Forty-six acutely psychotic inpatients were given 0.5 mg/kg/day of PPZ for 10 days with response rated blind to blood level. Twenty-six of the 46 patients responded, but global response, BPRS total, and the four factors of the BPRS were not related to PPZ levels. However, two individual BPRS items (hallucinations and conceptual disorganization) did improve in direct relation to PPZ serum concentrations. We examined these relationship controlling for pretreatment severity and both items remained significantly related to PPZ drug levels (beta = -.44, p = .0006; -.32, .02, respectively). The correlation between PPZ levels and the combined score of these items was -.36, p = .013. The strongest correlation with the combined score (r = -.56, p = .0001) was obtained if PPZ levels were treated dichotomously (above or below 0.8 ng/ml)—the lower therapeutic threshold suggested by Bolvig Hansen and Larsen (1985). Results indicate that two core positive symptoms of psychosis—hallucinations and conceptual disorganization—may be particularly responsive to drug treatment, as measured by PPZ levels, and useful for assessment of early drug response.

NR459 **Wednesday, May 16, 12 noon - 2:00 p.m.**

EFFECT OF CHRONIC NEUROLEPTIC TREATMENT ON DOPAMINE D2 RECEPTOR MRNA AND BINDING

Patrick J. Rogue, M.D., Neurochemistry, CNRS Center, 5 Rue Blaise Pascal, Strasbourg 67084, France; Jean Zwiller, Ph.D., Emiliana Sassone-Corsi, Ph.D., Andre Hanauer, M.D., Jean-Louis Mandel, M.D., Guy Vincendon, M.D.

Summary:

Long-term treatment with neuroleptic drugs induces a dopamine D2 receptor up-regulation in certain brain regions. The mechanisms underlying receptor regulation are complex. They comprise both short-term phenomena and molecular processes operating over more prolonged periods where both the protein and mRNA are regulated. The recent cloning of the dopamine D2 receptor gene allows a more precise analysis of antipsychotic induced up-regulation. In the present study the effect of prolonged administration of antagonists and agonists on rat striatal dopamine D2 receptor Bmax and mRNA content was examined. Rats were treated during 14 days I.P. with either 1 or 4 mg/kg haloperidol, 12.5 chlorpromazine, 5 mg/kg sulpiride, 10 mg/kg LY171555, mianserin 10mg/kg or vehicule. mRNA was studied by Northern analysis using a mixture of synthetic oligonucleotides with densitometric quantitation of the films. Receptor density was estimated through (3H)spiperone binding. Correlations between the different values were analyzed. Haloperidol determined an up-regulation of D2 Bmax and mRNA. Chlorpromazine did not increase the mRNA content. LY171555 also was without effect. The effect of 5HT-2 receptor antagonists was also studied. The results will be discussed with respect to the influence of dosage, specificity of the drug administered, and mechanism of action of neuroleptics.

NR460 **Wednesday, May 16, 12 noon - 2:00 p.m.**

PINDOLOL TO TREAT AGGRESSION IN THE MENTALLY RETARDED

Karen J. Lindem, B.S., Research, Medfield State Hospital, 45 Hospital Road, Medfield, MA 02052; James Fletcher, M.D., Miriam Blumenkrantz, John J. Ratey, M.D.

Summary:

Aggressive behavior has been estimated to occur in 10-35 percent of institutionalized developmentally disabled. Frequency and severity of destructive behaviors limit individuals to restrictive settings as well as prevent participation in behavioral programming and daily activities. Pharmacotherapies, such as the neuroleptics, are frequently chosen as intervention despite known side effects of cognitive blunting, sedation, and tardive dyskinesia. Alternative medication choices that promote habilitation are currently emphasized, particularly with developmentally disabled patients. Previously we have reported clinical trials of beta blockers treating aggression and self-injury in chronically institutionalized patients. Twenty-two subjects participated in this report of a double-blind, placebo-controlled study of pindolol for destructive behavior in the mentally retarded. Subjects ranged in age from 18-55 and the majority were severely-profoundly retarded. All subjects had a longstanding history of destructive behavior which previous treatment measures had failed to control. Subjects participated for a total of 25 weeks, including four weeks of baseline measurements, four weeks of placebo lead-in, and 16 weeks of blinded treatment. Subjects were randomly assigned to receive either pindolol or placebo. Concomitant medications were held constant. Destructive behaviors were recorded longitudinally with the Modified-Overt Aggression Scale. Comparison of placebo lead-in and the final month of treatment showed that the average weekly frequency of aggressive acts decreased 30 percent for subjects receiving pindolol. Average number of incidents decreased 7 percent for control subjects. Language, communication, and social skills were assessed at baseline and study completion. Receptive language skills on the PPVT improved 62 percent for pindolol treated patients and 14 percent for controls. Furthermore, the Vineland Adaptive Behavior Scale indicated that those patients receiving the beta blocker improved 47 percent in expressive communication and 149 percent in socialization. Improvement of maladaptive behaviors was reflected in these measures of adaptive functioning further supporting beta blockers as an effective and nonsedating pharmacotherapy for aggression and self-injury.

NR461 **Wednesday, May 16, 12 noon - 2:00 p.m.**

BUSPIRONE FOR AGGRESSION IN THE MENTALLY RETARDED

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Summary:

A multiple baseline, placebo controlled study was conducted to evaluate buspirone as an alternative treatment for aggressive and self-injurious behaviors in the mentally retarded. We hypothesize that buspirone decreases aggressive and self injurious behaviors through the reduction of precipitory anxiety. Our subjects were six mild to moderate mentally retarded adults with a history of at least one destructive outburst per week. Subjects participated for 18 weeks including a three week baseline period, four weeks of placebo and 9 weeks of buspirone therapy. Dosages ranged from 5 to 15 mg tid. Subjects' behavior was rated throughout the 18 weeks using the Conners Anxiety Scale and the Modified Overt Aggression Scale. Cognitive testing was administered at baseline and during the final dosage period to evaluate buspirone's possible cognitive enhancing effects. Cognitive testing was videotaped and subjects' on/off task performance was assessed by two independent, blinded raters. Preliminary analysis of four subjects' data shows a 46 percent mean decrease in aggressive outbursts during buspirone therapy, and an 11 percent decrease in agitation, as compared to the placebo period. In addition, two subjects showed improved attention during videotaped testing, one subject's attention decreased and one subject's performance was unchanged. Unlike traditional anti-aggressive agents such as the neuroleptics, buspirone lacks debilitating side effects. This controlled study supports earlier case reports of buspirone's efficacy as an alternative pharmacotherapy for treating aggressive and self-injurious behaviors in developmentally disabled adults.

NR462 **Wednesday, May 16, 12 noon - 2:00 p.m.**

RISK FACTORS FOR ANABOLIC STEROID USE IN MEN

Kirk J. Brower, M.D., Department of Psychiatry, Univ. of Michigan, 1500 E. Med. Ctr. Dr. Box 0116, Ann Arbor, MI 48109; Frederic C. Blow, Ph.D., Elizabeth Hill, Ph.D.

Summary:

The use of anabolic steroids can lead to dependence and other adverse psychiatric effects. In order to prevent steroid use and its negative outcomes, data are needed regarding individuals at risk for use. We conducted an anonymous survey of 404 male weight lifters from community gymnasiums who completed a 20-minute self-administered questionnaire. The sample for this study included all 49 men who admitted to using steroids (users), all 35 men who were considering steroid-taking in the future ("high risk"), and 32 non-using men (randomly chosen from the remaining surveys) who were not considering steroid use ("low risk"). The high-risk group (mean = 20.4 yrs) was younger than both the users (24.4 yrs) and the low risk group (24.0 yrs) ($F = 8.3$, $df = 2$, $p < .001$), which probably accounted for its lower employment rate, income, and married status. There were no differences in race (93% white) and education (mean = 14.6 years). Variables that significantly distinguished the high- from low-risk nonusers were more mean time spent each week lifting weights (9.9 vs. 7.4 hrs), a greater mean number of non-steroidal performance aids tried (3.8 vs. 2.3), greater acquaintance with steroid users (83% vs. 53%), and greater body dissatisfaction. Nearly three-fourths of the high-risk group felt "not big enough" most or all of the time, compared to approximately one-third of each of the steroid users and low-risk group ($p < .05$). Although further analysis will need to control for age, an intriguing interpretation of these data is that dissatisfaction with body size may contribute to the risk of using steroids. Implications for prevention and clinical practice will be discussed.

NR463 **Wednesday, May 16, 12 noon - 2:00 p.m.**

INCIDENCE OF NEUROLEPTIC MALIGNANT SYNDROME

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Summary:

The occurrence of NMS was studied prospectively in two series of 223 consecutive patients from 2 acute wards. Patients in the 1st group ($n = 120$) suffered from schizophrenia and were treated only with haloperidol (HPL) in either 10mg/d or 20mg/d doses. The 2nd group's patients ($n = 103$) were treated with diverse neuroleptics mostly, perphenazine, HPL and levomepromazine (means equivalent chlorpromazine 657 ± 122 mg/d). All patients were on a monoantipsychotic agent with no anticholinergic drug as prophylaxis. Patients who had bipolar affective disorder and those treated with injections were significantly overrepresented in the NMS group (Ps $< .05$, Fisher's exact tests). The incidence of full NMS per admission and first NL exposure was $5/223 = 2.2\%$. This figure is similar to some recent NMS epidemiological studies, but is higher in 1-2 orders of magnitude than others. Possible reasons for this discrepancy will be discussed.

NR464 **Wednesday, May 16, 12 noon - 2:00 p.m.**

PROSPECTIVE LONG-TERM FOLLOW-UP OF DEPRESSIVES WITH AND WITHOUT SUICIDE ATTEMPTS

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Summary:

The results of a 4-6 year prospective follow-up study of 48 patients with the diagnosis of a Brief or Prolonged Depressive Reaction according to ICD-9 who had attempted suicide just before the admission and of 24 inpatients with the same diagnosis but no history of previous suicide attempts are reported. The majority of the patients with a suicide attempt (60%) and of the patients without a suicide attempt (71%) fulfilled the criteria of a Major Depression according DSM-III. Both patient groups were comparable concerning the history of depressive episodes, sociodemographic characteristics, utilization of psychiatric and psychotherapeutic help before and during index treatment. The follow-up assessment of the patients included the use of standardized diagnostic, psychopathological, social, and psychological instruments at index treatment and follow-up. In addition, during follow-up suicide attempts, the utilization of medical services and periods of earning disability were evaluated. The results indicate a favorable course and outcome of both patient groups and a nearly identical course and outcome of the depressed patients with and without suicide attempts in terms of general psychopathology, DSM-III diagnoses, social functioning and social support, personality features, utilization of medical services, and period of earning disabilities.

NR465 **Wednesday, May 16, 12 noon - 2:00 p.m.**

SEROTONIN S2 RECEPTORS IN SCHIZOPHRENIA

Joel E. Kleinman, M.D., CBDB, NIMH Neuroscience, 2700 Martin L. King Jr. Ave SE, Washington, DC 20032; Marc Laruelle, M.D., Manuel F. Casanova, M.D., Daniel R. Weinberger, M.D., Susan Camparini, M.D., Rosanne Toti

Summary:

Functional abnormalities of the dorsolateral prefrontal cortex (DLPFC) of schizophrenics (SCH) have been reported. 1) In postmortem studies of SCH and non-SCH suicides, frontal pole serotonergic S2 density was decreased and increased, respectively. 2) We studied S2 receptors in the DLPFC, the anterior cingulate and the frontal pole of SCH ($n = 11$), non-psychotic suicides (SUI, $n = 10$) and controls (CTR, $n = 13$). In all three regions, there was a significant decrease of S2 receptors in SCH compared to CTR. In the frontal pole, SUI exhibited significantly increased S2 receptor density compared to CTR. The decreased S2 in SCH does not seem to be related to previous neuroleptic treatment, as S2 density was not different between patients on or off neuroleptic treatment at the time of death. SCH suicides showed increased S2 compared to SCH who died from other causes, demonstrating the association between suicide and increased S2 in still another paradigm. D1 receptor was increased in the anterior cingulate of SCH, but not in the DLPFC. The S2 findings replicate other studies while extending them to the DLPFC. They represent the first neurochemical finding in the DLPFC that has been implicated in the pathophysiology of SCH.

NR466 **Wednesday, May 16, 12 noon - 2:00 p.m.**

PREDICTION OF SUICIDE IN 1,906 PSYCHIATRIC INPATIENTS

Donald W. Black, M.D., Psychiatry, University of Iowa, 500 Newton Road Psych Hospital, Iowa City, IA 52242; Rise Goldstein, M.S.W., Amelia Nasrallah, M.A., George Winokur, M.D.

Summary:

Suicide is an important public health problem whose frequency may be increasing among adolescents and young adults. Over the years, researchers have looked at suicide from multiple perspectives in an attempt to learn its risk factors. These efforts have as their ultimate goal the prediction and prevention of suicide. Efforts to date to successfully predict suicide in large samples using statistical models have been disappointing, a fact that may relate to suicide's low base rate. The purpose of the present study was to develop a multiple logistic regression model using demographic, clinical, treatment, and outcome data from the case notes of 1906 affectively ill inpatients in an attempt to predict suicide in a high-risk population.

The set of potential predictors consisted of risk factors described in the literature for which data were available. For a variable to enter our model, as well as to remain, the Chi square statistic had to be significant at the 0.10 level.

From the list of potential predictors, the following met significance level criteria for entry into and retention within the model: Number of suicide attempts prior to index admission; presence of suicidal ideation at index admission, bipolar affective disorder, manic or mixed phase; gender; outcome at discharge; and unipolar depression in persons with family history of mania. The overall Chi square for the model was highly significant (38.66, $p < 0.001$). Based on this model, the classification table for true versus predicted suicides shows that its sensitivity is zero and its specificity is 100%. The model's predictive value is zero. Thus, the model failed to identify a single patient who committed suicide. The results appear to support the contention that, based on present knowledge, it is not possible to predict suicide, even among high-risk affectively ill inpatients.

NR467 **Wednesday, May 16, 12 noon - 2:00 p.m.**

DISTURBED SEROTONERGIC LATERALIZATION IN SUICIDE

Mihaly Arato, M.D., Hamilton Psych Hospital, P.O. Box 585, Hamilton Ontario, Canada L8N 3K7; Kornelia Tekes, Ph.D., Ede Frecska, M.D., Laszlo Tothfalusi, Ph.D., Miklos Palkovits, M.D., Duncan MacCrimmon, M.D.

Summary:

Several lines of evidence—including postmortem neurochemical investigations—indicated an association between altered serotonergic function and suicidal behavior. However, until our studies the possibility of hemispheric asymmetry in the human brain had not been considered or investigated, although lateralized disturbances have been implicated in the pathophysiology of various psychiatric disorders. We have measured serotonergic indices (serotonin and 5-hydroxyindolacetic acid concentrations /5HIAA/, as well as imipramine binding, an indicator of presynaptic serotonin uptake) bilaterally in the frontal cortex of suicide victims and controls. In controls there was significantly higher serotonin metabolism in the right hemisphere than in the left side: significantly increased Bmax of imipramine binding, higher serotonin, and 5HIAA concentrations. Suicide victims showed a reversed asymmetry: they had significantly lower Bmax value in the right hemisphere compared with the controls. The Bmax values were significantly higher in the left side only in the suicide victims who had used violent methods. Lower serotonin turnover in the right frontal cortex may be associated with depression, and increased serotonin turnover in the left hemisphere may be related to violent suicidal behavior. This theoretical model provides a more complex approach to the serotoneric dysfunctions in depression and suicide than the "serotonin deficiency" theory.

NR468 **Wednesday, May 16, 12 noon - 2:00 p.m.**

SEROTONIN-2 RECEPTORS IN DEPRESSION AND SUICIDE

Ghanshyam N. Pandey, Ph.D., Psychiatry, 1601 W. Taylor Street, Chicago, IL 60612; Subash Pandey, Ph.D., Philip G. Janicak, M.D., Robert Marks, M.D., John M. Davis, M.D.

Summary:

Abnormalities in the serotonergic system have been related to the pathophysiology of depression and also to suicidal and/or aggressive behavior. An increased number of serotonin-2 (5HT) receptors in the platelets of depressed patients, and increased 5HT2 receptors in the postmortem brain of suicide victims have been reported. We studied platelet 5HT2 receptor binding sites using ^{125}I-LSD as the ligand in drug-free in-hospital depressed patients and nonhospitalized normal control volunteers. We observe that the mean B_{max} of ^{125}I-LSD binding in depressed patients (67.4 ± 6.1 fmoles/mg/protein) was significantly higher as compared to 20 normal control subjects (46.5 ± 4.8). No differences in the K_D were observed between the depressed patients and normal controls. We then compared the B_{max} of those depressed patients with a recent history of serious suicide attempt or ideation with those of nonsuicidal depressed patients as well as normal controls and observed that the B_{max} in nine suicidal depressed patients (82.4 ± 7.34) was significantly higher as compared to 12 depressives without suicidal history (58.6 ± -8.1), it was also significantly higher than normal control subjects. Our results, therefore, suggest that 5HT2 receptor binding sites in the platelets of depressed patients is significantly increased and that this increase may be partially accounted for by the presence of a subgroup of depressed patients with suicidal history.

NR469 **Wednesday, May 16, 12 noon - 2:00 p.m.**

CAUSES OF REPETITION OF SUICIDE ATTEMPTS

Isaac Sakinofsky, M.D., Psychiatry, St. Michaels Hospital, 30 Bond Street, Toronto Ontario, Canada M5B 1W8; Robin S. Roberts, M.Tech., Yvonne Brown, M.A., Carmen Cumming, B.A., Patricia James, M.A.

Summary:

We present the results of a one-year follow-up of 228 consecutive suicide attempters. The patients were personally interviewed at three monthly intervals and scores on the Beck Depression Inventory (BDI), Dean's Alienation Scale, Rosenberg Self-Esteem Scale, and Weissman and Paykel Social Adjustment Scale (SAS) recorded. At one-year follow-up, 54 (23.7 percent) were known to have repeated at least once and 10 (4.4 percent) repeated on two or more occasions (persistent repeaters). Repetition occurred independently of resolution of problems identified at the index presentation. Stepwise discriminant function analyses were carried out to distinguish repeaters from nonrepeaters. For all repeaters baseline severity of their problems, greater degree of perceived powerlessness, and lower educational levels achieved were predictive of repetition. For the minority group of persistent repeaters only, younger age at first (life-long) episode, higher degree of normlessness (dissonant and confused social values), but lower BDI scores and poorer education attainment were the distinguishing features. In view of the risk of completed suicide with repeated attempts, recurrent deliberate self-harmers constitute a special-high risk group requiring programs tailored to their specific needs.

NR470 **Wednesday, May 16, 12 noon - 2:00 p.m.**

AGGRESSIVE AND SELF-DESTRUCTIVE BEHAVIOR

Harold A. Carmel, M.D., Psychiatry, UCLA, Box 7001, Atascadero, CA 93423; Mel Hunter, M.P.A.

Summary:

The Atascadero 884 is a cohort study of all patients hospitalized on November 4, 1989, in a large California state hospital. The average length of hospitalization in this all-male group was 1.56 years. 2151 incidents of patient aggression and 235 incidents of self-injurious behavior have been recorded since September 1983 (1288 patient-years of experience). We found a strong positive correlation between rate of aggression to others and rate of self-injurious behavior ($r = .395$, $df = 882$, $p < .0001$, r-squared = .156). This finding supports the need for clinicians to be aware of the association between violence against others and self-destructive behavior in state hospital patients.

NR471 **Wednesday, May 16, 12 noon - 2:00 p.m.**

PERSONALITY DISORDERS AND SUICIDAL BEHAVIOR IN THE U.S. NAVY SERVICEMEN

Stanley W. Raczek, M.D., Psychiatry, U.S. Naval Hospital, Box 19-4714, FPO New York, NY 09521

Summary:

42 subjects referred for psychiatric evaluation were admitted for the study. They were divided into two groups. The first group consisted of 30 subjects referred for evaluation of suicidal ideations ("suicidal" group). The second group consisted of 12 subjects who were referred for evaluation for reason other than suicidal thinking ("nonsuicidal" group). The personality structure was evaluated using the Personality Disorder Examination (PDE), a structured diagnostic interview developed by Loranger et al. The personality traits of subjects in two groups were compared. The subjects in both groups endorsed the same number of "pathological" personality traits, however, in the "suicidal" group the most common personality traits were borderline (34.5%), and avoidant (31%), while in "nonsuicidal" group the most common personality traits were borderline (45.5%) and antisocial (27.3%). Chronic feelings of emptiness or boredom (borderline) and inhibition in social situation (avoidant) was the most common combination of personality traits in "suicidal" group, while in "nonsuicidal" group the most common combination was affective instability (borderline) and repeated antisocial acts (antisocial). These results indicate that evaluation of personality structure may have a predictive value in the assessment of the suicide risk and may assist in the development of preventive strategies.

NR472 **Wednesday, May 16, 12 noon - 2:00 p.m.**

CLINICAL CORRELATES OF SUICIDALITY IN SCHIZOPHRENIA

Gretchen L. Haas, Ph.D., Psychiatry, Cornell Univ Med College, 525 East 68th Street, New York, NY 10021; John A. Sweeney, Ph.D., Denise A. Hien, M.S., Dodi Goldman, M.A., J. John Mann, M.D.

Summary:

Suicide is a leading cause of death among patients with schizophrenia, with lifetime risk of suicide estimated at over 15 times that of the general population. *STUDY AIMS*: (1) to assess incidence of serious suicidal behavior in a sample of 80 consecutive admission DSM-III-R schizophrenic disorder inpatients, and (2) to identify clinical correlates of serious suicidal behavior. *RESULTS*: 29% (23/80) reported a history of suicide attempt; 57% (13/23) of the attempts resulted in serious medical damage; 32.5% (26/80) reported ideation only. Attempters had a history of earlier age of onset of psychotic symptoms ($p < .04$), poorer premorbid adjustment ($p < .05$), more frequent hospitalization ($p < .001$), longer lifetime duration of antipsychotic medication ($p < .02$) and higher dosage at discharge ($p < .05$). They also showed better global functioning ($p < .05$), less severe negative symptoms ($p < .05$) and more severe positive symptoms ($p < .05$) at time of discharge from hospital. *SIGNIFICANCE*: History of suicidal behavior was found to be relatively common in a sample of inpatients with DSM-III-R schizophrenia. Among schizophrenics, risk for suicidal behavior may be greater in patients with an early age of onset, poor premorbid adjustment, and evidence of limited neuroleptic responsiveness.

NR473 **Wednesday, May 16, 12 noon - 2:00 p.m.**

BRAIN 3H-PAROXETINE BINDING IN DEPRESSED SUICIDES

Cornelius L. Katona, M.B., Psychiatry, University College, Riding House Street, London W1N 8AA, United Kingdom; Kevin M. Lawrence, M.Sc., Freddy De Paermentier, Ph.D., Sharon C. Cheetham, Ph.D., Rufus M. Crompton, M.D., Roger W. Horton, Ph.D.

Summary:

Brain 5HT uptake sites, labelled with highly selective 5HT uptake inhibitor ^{3}H-paroxetine were measured in brain samples from 22 antidepressant-free suicide victims with a retrospective diagnosis of depression and from 20 controls matched for age and sex. ^{3}H-paroxetine binding was of high affinity and fitted well into a single binding site model in all brain regions studied. B_{max} was highest in substantia nigra, intermediate in caudate, putamen, thalamus and amygdala and lowest in cerebral cortex. K_d values showed little regional variation. No significant difference in B_{max} or K_d values between depressed suicides and controls were found in any of the brain areas studied. B_{max} in putamen was lower in non-violent suicides than in violent suicides or in controls.

NR474 **Wednesday, May 16, 12 noon - 2:00 p.m.**

SUICIDE AND DIAGNOSTIC PRACTICE IN HUNGARY

Cornelius L. Katona, M.B., Psychiatry, University College, Riding House Street, London W1N 8AA, United Kingdom; Toltan Rihmer, M.D., Judit Barsi, M.D., Katlin Veg, M.D.

Summary:

Regional variations in suicide rate and in reported incidence of depression and schizophrenia were examined in the 19 counties of Hungary and the city of Budapest. Regional differences in suicide rate as well as in incidence of psychiatric morbidity were consistent between the three years (1985, 1986 and 1987) examined. Suicide rate showed a significant negative correlation with the incidence of depression in each of the three years (1985: tau = -.374, $p < .05$; 1986: tau = -.663, $p < .001$; 1987: tau = -.479; $p < .01$), as well as correlating positively with perinatal mortality ($p < .01$) and with divorce rate ($p < .05$). No such correlation with incidence of schizophrenia was found. The results suggest that underdiagnosis of depression may contribute to Hungary's very high suicide rate. The implications of this for psychiatric education and practice will be discussed.

NR475 **Wednesday, May 16, 12 noon - 2:00 p.m.**

SUICIDALITY AND FLUOXETINE: IS THERE A RELATIONSHIP?

Maurizio Fava, M.D., Psychiatry, Mass General Hospital, Clin. Psychopharm. Unit ACC815, Boston, MA 02114; Jerrold F. Rosenbaum, M.D.

Summary:

Teicher et al. (1990) have recently reported six cases of depressed patients free of recent serious suicidal ideation who developed intense violent suicidal preoccupation after 2-7 weeks of fluoxetine treatment. Since we had come to know about this case before the article was published, we wanted to evaluate the incidence of this phenomenon (3.5% in Teicher's population) by doing a survey among psychiatrists working in the Clinical Psychopharmacology Unit and the General Psychiatry Practice of the Massachusetts General Hospital who were unaware of the reason of our investigation. Data was gathered retrospectively by chart review using a harvesting form inquiring about depressed patients treated with pharmacotherapy throughout 1989, types of drugs used, and incidence of suicidality during different treatments. If the psychiatrists had noted that suicidality had been reported by the patient only after drug therapy was initiated, we then interviewed the clinicians and obtained further information on each case. Twenty-seven psychiatrists completed our questionnaire and returned it to us. They reported having treated 1017 depressed subjects throughout 1989. Of these, 71 of 294 patients treated with fluoxetine alone (24%), 15 of 73 patients treated with fluoxetine in combination with tricyclic antidepressants (TCA's) (21%), 78 of 458 patients treated with TCA's alone or in combination with lithium (17%), 11 of 74 patients treated with monoamine oxidase inhibitors (MAOI)(15%), and 19 of 118 patients treated with other antidepressants (16%) were reported to have been suicidal sometime during their treatment. Therefore, 194 of 1017 depressed patients treated were also suicidal (19%). Of these 194 depressed suicidal patients, 12 patients had become suicidal only after treatment was initiated: the frequency of suicidality occurring after fluoxetine given alone ($N = 6$) was not significantly different from the rate for either fluoxetine in combination with TCA's ($N = 2$)(chi-square: 0.13; NS) or for TCA's given alone or in combination with lithium ($N = 3$)(chi-square:2.9;NS).

NR476 **Wednesday, May 16, 3:00 p.m - 5:00 p.m.**

ECT EMERGENCE AGITATION AND SUCCINYLCHOLINE DOSE

Conrad M. Swartz, M.D., Psychiatry, Chicago Medical School, 3333 Green Bay Road, North Chicago, IL 60064

Summary:

The syndrome of emergence agitation consists of restless agitation during the half-hour following electroconvulsive therapy (ECT). It has also been called "emergence delirium." It has occurred in about 10 percent of ECT patients at this V.A. medical center and has recurred with every ECT. Management has generally required vigorous restraining actions or intravenous sedatives postictally; without such sedatives, the patients awaken dysphoric and restless.

Five males who had repeatedly shown emergence agitation after each of 21 sessions of ECT with a succinylcholine dose about 0.7 mg/Kg showed no agitation after 13 ECT sessions in which the succinylcholine dose had been increased to about 1.0 mg/Kg and no postictal sedatives had been given. All patients had mesomorphic body habitus. The probability that the pattern of response to higher succinylcholine dose resulted from random processes is 3.0×10^{-6}. These observations suggest that patients predisposed to emergence agitation are sensitive to ECT-induced metabolic changes in skeletal muscle tissue, and that the likelihood of emergence agitation rises with the ratio of skeletal muscle mass to succinylcholine dose. Because ECT-induced serum lactate elevations are blocked by succinylcholine, emergence agitation might be essentially the same phenomenon as lactate-induced panic.

NR477 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

POST-TRAUMATIC DISTRESS AMONG BURN VICTIMS

Robert P. Roca, M.D., Psychiatry, Francis Scott Key, 4940 Eastern Avenue, Baltimore MD 21224; Linda Rice, Ph.D., Elizabeth Eaton.

Summary:

To determine risk factors for post-traumatic stress disorder (PTSD) among burn victims, 45 patients hospitalized in a regional burn center were evaluated using the Structured Clinical Interview for DSM-III-R, the NEO personality inventory, and scales measuring depression and anxiety. 31 (68%) patients were ≤ 40 years of age, and most were male (76%), Caucasian (67%), and had suffered flame or flash injuries (72%). Admission toxicology screens yielded alcohol ($n = 7$), marijuana ($n = 5$), and cocaine ($n = 3$). Hospital stays averaged 22 days. Since the diagnosis of PTSD requires a full month of symptoms, only one patient met all criteria for PTSD; however, many patients had PTSD *symptoms*. 24 (53%) reexperienced the accident persistently (criterion B), 7 (16%) had at least 3 symptoms of avoidance or numbing (criterion C), and 13 (29%) had at least 2 symptoms of hyperarousal (criterion D). Patients meeting criterion B were more likely to have suffered a flame/flash injury than another type of burn ($p < .05$). Those meeting criteria C and D were more anxious and depressed ($p < .02$) and more likely to be alcoholic ($p < .02$) than others. On the NEO, patients meeting criterion B showed low trait "openness" ($p < .01$) while those meeting criterion C showed low trait "extraversion" ($p < .01$). The prognostic importance of these observations is being evaluated in long-term follow-up.

NR478 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

YOHIMBINE IN PTSD

Steven M. Southwick, M.D., Psychiatry, Yale Univ Sch of Med, West Haven VA Medical Center, West Haven CT 06516; John H. Krystal, M.D., Dennis S. Charney, M.D.

Summary:

Previous evidence for noradrenergic (NE) dysregulation in Post Traumatic Stress Disorder includes sympathetic arousal during exposure to reminders of trauma, elevation of 24-hour urine norepinephrine, and decreased alpha-2 receptor number and beta receptor sensitivity in peripheral blood elements. Using a challenge paradigm, this study involved the infusion of yohimbine, an alpha-2 adrenergic antagonist, to further probe NE dysregulation in patients with PTSD. Thirteen male Vietnam veterans (mean age 41.7 ± 5) meeting SCID DSM-III-R criteria for PTSD and 7 healthy controls (mean age 23.6 ± 1.2) on two separate days received either yohimbine (0.4 mg/kg I.V.) or placebo in randomized balanced design under double-blind conditions. Six of the Vietnam veterans met criteria for co-morbid panic disorder. Eight out of 13 (62%) experienced panic attacks and 4 out of 13 (31%) flashbacks during active yohimbine infusion while none had panic attacks and one had a flashback with placebo. No panic attacks or flashbacks were observed in the healthy controls during either active or placebo conditions. PTSD patients also showed increased anxiety and increased PTSD specific symptoms, such as dissociation and intrusive thoughts. Preliminary analysis indicates an increased plasma cortisol after yohimbine infusion in the patients compared to controls. Analysis of MPHG levels are pending. Consistent with a large body of preclinical evidence, these results suggest that trauma can have long-lasting effects on subsequent responsivity to stress and on regulation of brain noradrenergic systems. Further, the response of PTSD patients to yohimbine closely resembles the response seen in panic disorder patients suggesting that PTSD and panic may share certain common biologic abnormalities.

NR479 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

ANTIDEPRESSANT TREATMENT OF PTSD: A META-ANALYSIS

Steven M. Southwick, M.D., Psychiatry 116A, West Haven VAMC, West Haven CT 06516; Rachel Yehuda, Ph.D., Earl L. Giller, Jr., M.D., Dennis S. Charney, M.D.

Summary:

A meta-analysis was performed to synthesize outcome findings across all published reports on the use of antidepressants in the treatment of chronic PTSD. We rated both overall global improvement and improvement in the three primary symptom clusters of DSM-III-R PTSD (reexperiencing, avoidance and hyperarousal) and in the associated symptoms of depression and anxiety. We also assessed the relative efficacies of TCAs and MAOIs and, where possible, determined the extent to which other methodological considerations such as study design and duration of treatment, may have been related to global improvement. Summing across all studies, the total number of subjects was 215. The results of the analysis suggests that antidepressants are useful in the treatment of PTSD. "Reexperiencing symptoms", in particular show a good response to these medications, with MAOIs being generally more efficacious than TCAs. Avoidance and hyperarousal symptoms did not appear to be significantly ameliorated by either class of antidepressants. Surprisingly, adjunctive symptoms of depression and anxiety (including panic) also failed to respond to antidepressants in this group of patients, suggesting that the global improvement in PTSD cannot be attributed to the classic effects of these medications on concurrent major depression or panic disorder. The implications of these finding to the pharmacotherapy of PTSD are discussed.

NR480 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

DSM-III AND DSM-III-R: WHO IS USING THEM AND WHY?

V. Chowdary Jampala, M.B., Psychiatry, UHS Chicago Med School, 3333 Green Bay Road, North Chicago, IL 60064; Mark Zimmerman, B.A., Frederick Sierles, M.D., Michael A. Taylor, M.D.

Summary:

As we await DSM-IV's introduction in 1993, only six years after the publication of DSM-III-R, it would be instructive to learn how DSM-III-R has been received, how it has affected the diagnostic process, and how psychiatrists have adapted to the two recent major changes in our diagnostic nosology. To understand how DSM-III-R is used and perceived by educators, researchers, and practitioners, in the spring of 1989 we surveyed all U.S. psychiatric residency training directors (n = 197), a sample of 337 active psychiatric researchers, and a nationwide random sample of 952 practicing psychiatrists. *Results:* 63.1% of the residency directors, 57.9% of researchers, and 47.7% of practitioners responded to the survey. We found that, two years after the introduction of DSM-III-R, 22.3% of researchers and 30% of practitioners continue to use DSM-III as their diagnostic system. We describe the various factors that influence the choice of the diagnostic manual, as well as the patterns and extent of the use of those manuals. The perceptions of strengths and weaknesses of the DSMs from various perspectives (training, research, and practice) are presented. When the results from the current survey are compared to the results of a similar survey about DSM-III conducted in 1984, there seems to be a modest increase in the acceptance of the DSM system. The implications of these findings for the development of DSM-IV are discussed.

NR481 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

DSM-IV: A NOSOLOGY SOLD BEFORE ITS TIME?

Mark Zimmerman, B.A., Psychiatry, Chicago Medical School, 13000 W. Heiden Circle #3103, Lake Bluff IL 60044; V. Choudary Jampala, M.D., Frederick, Sierles, M.D., Michael A. Taylor, M.D.

Summary:

We conducted a mail survey of psychiatrists' attitudes towards the scheduled publication of *DSM-IV* in the early 1990's. We surveyed 4 groups: 1) a random sample of domestic members of the APA; 2) the directors of all approved psychiatry residency training programs in the US; 3) residents in their third or fourth year of training at these programs; and 4) first authors of articles published in the *Archives of General Psychiatry* and the *American Journal of Psychiatry* who were MD's and to whom reprint requests were directed at a US address. In all four groups the majority believed that *DSM-IV* is being published prematurely. The 3 nonresident samples were consistent in recommending 10 years as a general guideline for separating DSM editions, and that *DSM-IV* should be published in 1996 or 1997. In contrast to respondents who believed that the timing of *DSM-IV* is appropriate, those who indicated that it is being published too soon had more recently completed their residency training, and also believed that *DSM-III-R* was published prematurely. There was no association with theoretical orientation, board certification status, ownership of the DSM manuals, length of time using *DSM-III*, and which diagnostic manual (*DSM-III* or *DSM-III-R*) they were currently using as the primary diagnostic reference.

NR482 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

TWO-TIER DIAGNOSTIC SYSTEM FOR PSYCHOTIC DISORDERS

Stanley R. Kay, Ph.D., Psychiatry, Albert Einstein Col. Med., Bronx Psych 1500 Waters Pl., Bronx NY 10461; Abraham Fiszbein, M.D., Amy Gorelick, M.D., Lewis A. Opler, M.D., Robert L. Spitzer, M.D., Janet B.W. Williams, D.S.W., Miriam Gibbon, M.S.W., Michael B. First, M.D.

Summary:

Psychiatric diagnosis has been advanced in the past 12 years by introduction of strictly operationalized criteria (e.g., RDC, DSM-III-R). The reliability and objectivity of diagnostic judgments have been further improved by structured clinical interviews (e.g., SCID) that standardly secure the pertinent clinical information. There is increasing recognition, however, that categorical diagnosis is of limited value in psychiatry; a dimensional perspective, which profiles a patient's functional impairments, also offers crucial information for treatment and prognostic decisions. We therefore evolved a two-tier diagnostic system (I. categorical, II. functional-dimensional) for more comprehensive assessment of psychotic disorders. Known as the *SCID-PANSS*, it combines the SCID assessment for DSM-III-R with the well operationalized 30-item Positive and Negative Syndrome Scale (PANSS), which has been standardized on 240 psychotic patients. The SCID-PANSS involves a 50-60 minute structured clinical interview that yields diagnostic classification plus dimensional ratings on nine scales, including positive and negative syndromes, depression, and severity of general psychopathology. Field testing by five psychiatrists has shown strong reliability on a sample of 32 psychotic inpatients. The nine dimensional scales yielded interrater correlations in the mid-0.80s to 0.90s, with an *r* of 0.92 for the general psychopathology scale. These data and the clinical and research applications of the SCID-PANSS are described.

NR483 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

AN ARTIFICIAL INTELLIGENCE EMOTION PROFILER

David A. S. Garfield, M.D., Psychiatry, UHS/Chicago Med School, 3333 Green Bay Road, North Chicago IL 60064; Charles Rapp, M.A., Martha Evens, Ph.D.

Summary:

This paper describes the design of a system for the reading of transcripts of physician/patient dialogue and producing a profile of the patient's emotional state. It describes a methodology for identifying emotion in speech content, something that currently exists only in rudimentary form in clinical psychiatry. The emotion profiler is based on previous research in emotion theory, the use of natural language processing in computer science, and emotion representation. Finally, a preliminary design for the emotion profiler, which uses the RUS parser and SNePS knowledge representation system, is described.

NR484 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

SPEECH ANALYSIS IN TURKISH SPEAKING SUBJECTS

Levent Mete, M.D., Psychiatry, Ege University, T1P Fakultesi Bornova, Izmir 35100, Turkey; Paula P. Schnurr, Ph.D., Thomas E. Oxman, M.D., Stanley D. Rosenberg, Ph.D., Inci Doganer, M.D., Soli Sorias, M.D.

Summary:

The purpose of this study is to investigate to what extent computerized speech content analysis differentiates manics and schizophrenics in Turkish speaking subjects.

Eighty subjects were included in this study: 20 schizophrenics, 20 manics, 20 depressives, and 20 healthy controls (10 males and 10 females for each group). After being diagnosed separately by two clinicians through the Turkish version of the SCID, each subject's free speech was tape-recorded in a standardized session. The first 675 words of each sample were analyzed through the use of a computer program and the Turkish version of Harvard-III Psychosocial Dictionary. This dictionary groups 4,500 commonly used words into 83 categories.

The speech content of Turkish subjects exhibited a significant similarity in relation to sex and diagnosis to that previously observed in American subjects. The control group was robustly discriminated from the three psychiatric disorder groups. Manics and depressives were differentiated significantly in 18 of 83 categories from each other. Whereas schizophrenics were differentiated from depressives and manics in ten and six categories, respectively. The relative similarity observed in schizophrenic and manic speech may be due to the fact that mood disturbance is common during schizophrenia.

NR485 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

ONE-THOUSAND BORDERLINES: A STUDY IN COMORBIDITY

Armand W. Loranger, Ph.D., Psychiatry, Cornell University, 21 Bloomingdale Road, White Plains NY 10605

Summary:

DSM-III was the first nomenclature of mental disorders to include the diagnosis of borderline. The new ICD-10 classification will also include borderline as a subtype of emotionally unstable personality disorder. Despite the long awaited official recognition of this condition and its popularity, it remains controversial. Much of the disagreement centers on its relationship with Axis I disorders. For example, one view maintained by some authorities is that borderline is not a personality disorder at all, but merely a variant of affective disorder. The answer to this and other questions awaits the availability of extensive information about the comorbidity of borderline and other mental disorders. The present report is based on the largest sample of borderlines yet studied, 1035 cases admitted to the Westchester Division of The New York Hospital-Cornell Medical Center between 1981-1985. It is 21% male and 79% female and includes 28% of all personality disorder admissions. Borderline patients had significantly more diagnoses of dysthymia, atypical depression, eating disorders, and drug abuse than a sample of 2616 patients with nonborderline types of personality disorders. The borderline sample also had significantly less schizophrenia, bipolar disorder, major depression, and alcohol dependence.

NR486 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

DETECTING DISSOCIATIVE DISORDERS: A COMPARISON OF A SCREENING INSTRUMENT AND A STRUCTURED DIAGNOSTIC INTERVIEW

Marlene Steinberg, M.D., Yale School of Medicine, 100 Whitney Avenue, New Haven CT 06510; Bruce J. Rounsaville, M.D., Domenic V. Cicchetti, Ph.D.

Summary:

Previous investigators have reported that diagnosis and treatment of the dissociative disorders may be delayed for many years due to difficulties in detecting high risk cases. The Dissociative Experiences Scales (DES) is a self-report instrument for which effective cut-off scores have not previously been identified. Forty-five subjects were evaluated for presence, type, and degree of symptomatology of a dissociative disorder, using the Structured Clinical Interview for *DSM-III-R* dissociative disorders. DES scores were then compared. Results indicate that a DES cutoff score of 15-20 yields excellent sensitivity and specificity as a screening instrument. The DES can be used to identify cases at high risk, who should be further evaluated using diagnostic instruments such as the SCID-D, or by in-depth clinical follow-up.

NR487 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

ANTISOCIAL DIAGNOSIS: RELATION TO ADULT BEHAVIOR

Robert K. Brooner, Ph.D., Psychiatry, Johns Hopkins, FSKMC D5E 4940 Eastern Avenue, Baltimore MD 21224; George E. Bigelow, Ph.D., Chester W. Schmidt, Jr., M.D.

Summary:

Antisocial behavior is strongly linked to narcotic abuse; however, only a portion of abusers satisfy *DSM-III-R* diagnostic criteria for antisocial personality disorder (ASPD), which require three or more antisocial behaviors prior to age 15. This study assessed the adult antisocial behaviors of narcotic abusers with versus without *DSM-III-R* ASPD (i.e., who differed in their pre-age-15 behavior). Subjects ($N = 238$; 63 percent male; 40 percent white) were assessed diagnostically and behaviorally with a structured interview. All (100 percent) reported recurrent antisocial behavior as adults; only 44 percent met ASPD criteria. The number of adult antisocial behaviors was greater in ASPDs than non-ASPDs (5.5 vs 3.3; $t = 10.843$; $p = 0.0001$), even after controlling for age (ANCOVA; $F = 30.284$; $p = 0.000$). The severity of adult antisocial behaviors was also greater in ASPDs than non-ASPDs, as indexed by use of the weapons in fights($t = -3.432$; $p = 0.0007$), felony arrest ($t = -3.184$; $p = 0.0016$), and the total number of felonies committed ($t = -4.717$; $p = 0.0001$). In summary, having three or more antisocial behaviors before age 15 (i.e., *DSM-III-R*) was associated with more numerous, more aggressive, and more serious illegal activities as adults. Thus, the extent of youthful antisocial behavior (as categorized by *DSM-III-R*) was prognostic of the severity of adult antisocial behavior even within a population in which adult antisocial behavior was commonplace.

NR488 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

COURSE OF ILLNESS AND MULTIAXIAL DIAGNOSIS

Miguel R. Jorge, M.D., Psychiatry, Univ of Pittsburgh, 3811 O'Hara Street, Pittsburgh PA 15213; Juan E. Mezzich, M.D.

Summary:

In response to a growing concern on the course and time-frame of psychiatric illness, we studied key aspects of this area within the scope of a broader investigation supported by NIMH. The relationship between psychopathological syndromes and illness duration and episodicity was empirically assessed on a representative sample (n = 515) of the general psychiatric population presenting for care at the University of Pittsburgh's Western Psychiatric Institute and Clinic. In the total study sample, 17% had up to 6 months of illness duration, 15% from 6 months to 2 years and 68% more than 2 years. Considering the DSM-III Axis I diagnostic groups studied, it was found that the highest proportion of chronicity (more than 2 years of illness duration) appeared among patients with substance use disorders (100%), bipolar disorder (94%), major depression, recurrent (91%), child-onset disorders (87%) and schizophrenic and paranoid disorder (85%). On the other hand, 48% of the patients with major depression, single episode and 53% of adjustment disorders showed no more than 6 months of illness duration. Regarding episodicity, most of the child-onset disorders (87%), major depression, single episode (74%) and adjustment disorders (67%) were found to be continuous or have single episode. An episodic pattern was found for 68% of the patients with bipolar disorder and 64% of major depression, recurrent. The results reveal interesting time-frame patterns which could help for the systematic consideration of course in the upcoming DSM-IV.

NR489 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

SUBTYPING AGGRESSION IN MENTAL RETARDATION

Joyce E. Mauk, M.D., Children's Seashore House, 34 & Civic Center Blvd, Philadelphia PA 19104; David Behar, M.D.

Summary:

Aggressive behavior is a significant problem in management of mentally retarded patients. There are at least 2 subtypes of aggression: affective, in response to an event such as frustration, or non-affective, with no antecedent. Affective aggression seems responsive to lithium, non-affective does not. We modified an interview questionnaire for caretakers of retarded patients (J. of Neuropsychiatry, in press) to identify these subgroups. Data were collected on all 37 of 283 residents of Woodhaven Center, Phila. identified as aggressive by unit managers. Two caretakers of each patient were interviewed. One of each pair was reinterviewed 1 day later to assess test retest reliability. A child psychiatrist blind to the questionnaire results also assigned subtypes. 71% of the aggressive patients were severely to profoundly retarded; 32% were mildly to moderately retarded. 19 were classified as affective and 16 non-affective. 73% of affective were treated with psychotropic medications as compared to 62% of non-affective. The questionnaire showed 80% agreement with the independent psychiatric assessment. Pearson's r correlations for individual items to total score ranged from .36 to .82. Inter-rater reliability was .66 ($p < .001$. Test retest was .88 ($p < .001$). Questionnaire administration to care takers of mentally retarded individuals may be an efficient way to identify aggressive subtypes and predict response to pharmacotherapy.

NR490 **Wednesday, May 16 3:00 p.m. - 5:00 p.m.**

ASSESSING THE ELEMENTS OF PSYCHOSOCIAL FUNCTIONING

Richard E. Gordon, M.D., Psychiatry, University of Florida, 1625 SW 6th Terrace, Gainesville, FL 32601; Katherine Gordon, M.A.

Summary:

Three prospective studies tested the Functional Level (FL) equation, Functional Level (Axis V) = f [Coping skills (C) + SES + Environmental supports(E)] - [Aggravating stresses (Axis IV) + Biomedical impairments (Axes I, II, and III, and severity of illness)], which contains the elements of the DSM-III multiaxial system. First, 22 Florida clinicians rated 24 psychiatric case histories. Then, 16 New York professionals rated 14 patients. Recently, three professionals and 36 Elderhostelers rated 42 histories. The multiple correlations (R^2) between the five predictors and FL in the separate studies and for the combined 74 cases ranged between .91 ($p < .0001$) and .95. Reliabilities of ratings ranged between .82 and .95.

Other studies found smaller correlations when fewer than five predictors were used with FL. Skodol et al (1988a) reported $R^2 = .325$ ($p < .001$) between Axis I diagnoses, symptoms, and education with Axis V rating (FL). When Axes II and IV, but not the C and E elements in the FL equation, were added $R^2 = .69$ ($p < .0001$). These findings suggest that the FL equation may provide a quantifiable, theoretical model for DSM-III. These findings may help in planning patients' treatments.

NR491 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

DEPRESSION MASQUERADING AS PARTIAL COMPLEX SEIZURE

Rajesh Sachdeo, M.D., Neurology, RWJ Medical School, One Robert Wood Johnson Place, New Brunswick NJ 08903; Sudhansu Chokroverty, M.D.

Summary:

Five patients with history of unipolar depression for one to three years were referred by the psychiatrists for evaluation for any organic neurological cause for depression. The patients' ages ranged from 14 to 50 years. There were four women and one man. In addition to depression, patient also complained of many paroxysmal episodes characterized by feelings of epigastric discomfort, palpitation, anxiety, and paranoid delusions lasting for a few seconds to minutes and followed generally by short periods of confusion. Family history was unremarkable. Neurological examination was essentially normal. Depression may sometimes masquerade as partial complex seizure and careful consideration should be given to this diagnosis in patients presenting with atypical depression. Electroencephalograms in all of these patients showed clear evidence of focal epileptiform activities in the temporal regions. Patients seem to have partial complex seizures as well as depression. Patients were treated with antidepressants and anxiolytics for one to three years without significant improvement in depression or the spells. Following neurological evaluation the patients were placed on carbamazepine and after a few weeks the patients remained free of the paroxysmal episodes and depression.

NR492 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

PSYCHATRIC COMORBIDITY IN EATING DISORDERS

Victor Fornari, M.D., North Shore Univ Hospital, 400 Community Drive, Manhassett NY 11030; David E. Sandberg, Ph.D., Michael Matthews, C.S.W., Gerardo Montero, M.D., Myra Kaplan, M.A., Jack L. Katz, M.D.

Summary:

The co-occurrence of eating disorder and affective disorder has been reported extensively; however, the co-morbidity of Anorexia and Bulimia Nervosa with other forms of major psychopathology has not been as extensively studied. In our study, we assessed 91 patients who presented to an Outpatient Eating Disorders Assessment and Treatment Program at a university teaching hospital, using the Schedule for Affective Disorders and Schizophrenia - Lifetime (SADS-L) version for subjects >17 years of age and the Parent and Child Diagnostic Interview for Children and Adolescents (DICA) for patients 17 and younger. The total number of psychiatric diagnoses was compared among patients with Anorexia Nervosa (AN), Bulimia Nervosa (BN), and both AN and BN.

The most frequent co-diagnoses included Major Depressive Disorder, Cyclothymia, Obsessive-Compulsive Disorder, Drug and Alcohol Abuse, Generalized Anxiety Disorder, and Panic Disorder.

In our sample, rarely did patients present with only an eating disorder. In most cases, patients had two to five diagnosable disorders. Treatment strategies must be developed that take into account the clinical characteristics of patients with multiple psychiatric disorders among which is an eating disorder.

NR493 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

SEASONAL MOOD PATTERNS IN BULIMIA AND SAD

Raymond W. Lam, M.D., Psychiatry, Univ of B.C., 2255 Wesbrook Mall, Vancouver BC, Canada V6T 2A1; Leslie Solyom, M.D., Arlene Tompkins, M.S.C.

Summary:

Mood and appetite disturbances are commonly found in bulimia nervosa and seasonal affective disorder (SAD). Seasonal symptom patterns have also been described in bulimia. We examined seasonal mood changes in 26 bulimic patients and 42 SAD patients using the Seasonal Pattern Assessment Questionnaire (SPAQ), a reliable, retrospective, self-rated questionnaire that assesses seasonal changes in mood, sleep, weight, and social activity. Also compared were SPAQ results from previously described randomly sampled populations ($N = 212$, Terman 1988; $N = 416$, Kaspar et al 1989).

A monthly frequency distribution of mood and vegetative symptoms can be derived from the SPAQ. Seasonal variation of depressive symptoms in the bulimic group were more similar to the SAD group than to the random sample. The mean Global Seasonality Score (GSS), an overall assessment of seasonality, was 11.8 (bulimia), 17.4(SAD), and 5.4 (random sample). A tri-modal distribution of GSS scores was found in the bulimic group. 46% of bulimics met case-finding SPAQ criteria for SAD, compared to 90% of the SAD sample, and 4.3% of the random sample ($X^2 = 257.9$, $p < 0.0001$). These data suggest that significant number of unselected bulimic patients have seasonal mood symptoms as severe as that seen in SAD. We propose that a common neurobiologic abnormality, such as serotonergic dysfunction or circadian rhythm disturbance, may underlie the symptoms found in seasonal bulimia and SAD.

NR494 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

CSF BETA-ENDORPHIN DECREASED IN ABSTINENT BULIMICS

Harry E. Gwirtsman, M.D., DIRP/CNE, NIMH Bldg 10/Rm 3S231, 9000 Rockville Pike, Bethesda MD 20892; Walter H. Kaye, M.D., Wade H. Berrettini, M.D., David T. George, M.D., Philip W. Gold, M.D.

Summary:

Patients with bulimia nervosa (BN) have profound disturbances in appetite regulation. Endorphins are implicated in stress-related eating and obesity. Corticotropin releasing factor (CRF) causes decreases in food intake, and also mediates release of proopiomelanocortin (POMC) peptides from the arcuate nucleus. We measured cerebrospinal fluid (CSF) CRF and POMC levels in 14 normal weight BN patients, both on admission (acute), and after 30 days of hospitalization (abstinent state); and in 19 age-matched control women. This study was undertaken both because of appetite regulating effects of these peptides, and their physiologic interrelationships in the CNS.

CSF POMC, beta-lipotropin (B-LPH), beta-endorphin (BE), and ACTH levels were diminished in abstinent BN patients ($p < 0.01$) compared to controls, and showed significant decreased from acute to abstinent state ($p < 0.02$). Plasma BE and ACTH, and CSF MSH were normal in abstinent bulimics. All peptides were normal in acutely ill bulimics. POMC peptides were significantly intercorrelated.

BN patients may have a trait-related deficiency of central POMC peptides, temporarily corrected by binge-purge activity. Alternatively, the stress of abstinence, or decreased caloric intake, may contribute to depletion of the central POMC molecule, and may help to explain why patients with the disorder have such strong proclivity for relapse.

NR495 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

BULIMIA NERVOSA TREATMENT AND BORDERLINE SYMPTOMS

Richard L. Pyle, M.D., Psychiatry, University of Minn, 420 Delaware St. SE Box 393, Minneapolis MN 55455; James E. Mitchell, M.D.

Summary:

In order to determine the extent to which treatment outcome was influenced by Borderline Personality Disorder (BPD) symptomatology, PDQ-R and Hamilton Depression Scales were administered to 46 consecutive female subjects with DSM-III-R diagnosis of bulimia nervosa who were treated with structured group therapy. Subjects in remission at treatment termination ($N = 33$) had a mean pretreatment BPD mean score of 4.5 while subjects not in remission ($N = 13$) had a pretreatment BPD mean score of 4.2. Both outcome groups had a significant decrease in depression scores with minimal change in PDQ-R threshold or impairment for BPD. Post-treatment BPD scores were positively associated with post-treatment purging frequency ($P = > 0.001$). Twenty-six subjects (57%) met DSM-III-R criteria for BPD, either at baseline or post-treatment, but only six (13%) met BPD diagnostic criteria at baseline and post-treatment. These data suggest that high baseline BPD symptoms do not adversely affect treatment outcome for structured group psychotherapy for bulimia nervosa. These data also suggest that high PDQ-R scores may be measuring "state" rather than "trait" variables.

NR496 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

INCREASED 5-HT-1A RECEPTORS IN THE HIPPOCAMPUS OF OBESE ZUCKER RATS: POSSIBLE SIGNIFICANCE TO FEEDING BEHAVIOR

Susan Delanty, A.B.D., Nutrition, Columbia University, 630 West 168th Street RM 307, New York NY 10032; Serge Przedborski, M.D., Robin Marks-Kaufman, Ph.D., Jean L. Cadet, M.D.

Summary:

Generically obese Zucker rats display hyperphagia relative to their lean littermates. Previous studies have suggested a role for serotonin (5-HT) receptors, particularly the 5-HT-1A subtype, in appetite regulation. In the present study, we evaluated 8-OH[^{3}H] DPAT binding in discrete brain regions of genetically obese and lean Zucker rats using quantitative receptor autoradiography. There was significant increases in 8-OH [^{3}H]DPAT-labeled 5-HT-1A receptors in CA2 (+30%), orien layer of CA3 (+17%), CA4 (+14%) and CA1 (+12%) fields of the hippocampus in the obese in comparison to lean rats. In contrast, there were no significant differences in hypothalamic areas. These findings suggest a possible involvement of 5-HT-receptors in the genetic difference between obese and lean Zucker rats. Because of the important role of the hippocampus in behavior and the possible role of the 5-HT systems in appetite regulation, these results may be related to the increased drive to consume food observed in obese Zucker rats.

NR497 **Wednesday, May 16, 3:00 p.m - 5:00 p.m.**

FLUOXETINE IMPROVES OUTCOME IN ANOREXIA NERVOSA

Theodore E. Weltzin, M.D., Psychiatry, Univ of Pitts. WPIC, 3811 O'Hara Street, Pittsburgh PA 15213; Walter H. Kaye, M.D., L.K. George Hsu, M.D., Theresa Sobkiewicz, M.S.W.

Summary:

Anorexia nervosa is a disorder of unknown etiology with a high rate of relapse. It is well known that anorexic patients often desire to pursue weight loss despite treatment. Anorexics usually have obsessions about food and weight as well as the range of obsessions typically seen in OCD. In addition, a substantial amount of anorexics have depressive symptoms. We have treated 21 anorexics during the weight maintenance phase of recovery in an open trial with fluoxetine, a serotonergic reuptake blocker, because this medication has been shown to be effective in the treatment of OCD and depression.

To date 16 of 21 anorexics have remained on fluoxetine (34 ± 13mg/day) for 245 ± 137 days. These 16 anorexics are ages 21 ± 6. They were 68 ± 7% average body weight (ABW) at admission and had been ill for 6 ± 5 years. All 16 anorexics have remained above 85% ABW, and as a group, are 93 ± 4% ABW. Improved scores on standard ratings of obsessional and depressive symptoms were associated with good outcome. The remaining five anorexics dropped out of the study mostly due to side effects.

In this open trial a higher than expected percentage of anorexic patients treated with fluoxetine maintained weight and have not been rehospitalized. This finding is of considerable importance for two reasons. First, fluoxetine may facilitate weight maintenance in anorexia nervosa. Second, fluoxetine may work in anorexia because it reduces obsessive and depressive symptoms.

NR498 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

CALORIC NEEDS AND METABOLISM IN EATING DISORDERS

Theodore E. Weltzin, M.D., Psychiatry, Univ of Pitts. WPIC, 3811 O'Hara Street, Pittsburgh PA 15213; Walter H. Kaye, M.D., Madelyn H. Ferstrom, Ph.D., Donna Hansen, M.A., Claire McConaha, R.N.

Summary:

Recent reports suggest that altered caloric utilization may contribute to relapse in anorexia and bulimia nervosa. Compared to controls, anorexics require more calories to maintain a stable weight (± 1 kg) after a weight restoration program. In contrast, normal weight bulimics require fewer calories than controls to maintain their weight during inhospital treatment.

We measured the caloric needs for weight maintenance (± 1 kg) in 21 anorexics after weight gain (ages 20 ± 7, 94 ± 2 percent ideal body weight (IBW) and 38 normal weight bulimics within one month of stopping bulimic behavior (ages 22 ± 5, 104 ± 13 percent IBW). Restrictor anorexics required significantly ($p < .05$) more caloric intake than bulimic anorexics (49 ± 3 kcal/kg vs 45 ± 3 kcal/kg). Caloric intake in both groups was significantly ($p < .01$) greater than normal weight bulimics (26 ± 3 kcal/kg). In an additional study, we found that 12 normal weight bulimics had a significant ($p < .05$) reduction in resting metabolic rate and a blunting of the thermogenic response to a test meal compared to six matched controls.

These studies replicate and extend previous findings that show that anorexics and bulimics have abnormal caloric utilization. In addition, abnormalities of resting metabolic rate and diet induced thermogenesis may contribute to increased energy efficiency in bulimia. Increased caloric needs and resistance to feeding in anorexia, and reduced caloric needs and pathological overeating in normal weight bulimia, are likely to contribute to relapse and poor outcome in these disorders.

NR499 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

NEW EVIDENCE LINKS ANOREXIA NERVOSA TO OCD

Walter H. Kaye, M.D., Psychiatry, Univ of Pitts. WPIC, 3811 O'Hara Street, Pittsburgh PA 15213; Theodore E. Weltzin, M.D., L.K. George Hsu, M.D., Theresa Sobkiewicz, M.S.W.

Summary:

Several lines of *new* evidence support previous studies that suggest that core psychopathophysiological traits in anorexia nervosa may be similar to those found in patients with obsessive-compulsive disorder (OCD).

The obsessionality of disturbances of body image, pathological feeding, and compulsive exercise in anorexia nervosa are self-evident. When we excluded those behaviors, we found that weight-restored anorexics had almost the entire range of typical obsessions and compulsions found in classic OCD patients except that anorexics had few sexual obsessions and checking compulsions. On the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) 17 anorexics had a mean $\pm$ SD score of 22 ± 5, similar in magnitude to the scores (25 ± 6) reported by Goodman et al (1989) for OCD patients.

Further evidence of a link to OCD is our finding that anorexics, after long-term weight restoration, have increased CSF 5-HIAA, the major brain serotonin metabolite, suggesting a trait-related increase in serotonin activity. A similar disturbance in serotonin activity has been implicated in the pathogenesis of OCD. Finally, we treated 21 anorexics with an open trial of fluoxetine, a serotonin-specific medication effective in the treatment of OCD. Five anorexics dropped out of the study, mostly due to side effects. All 16 anorexics on fluoxetine have remained above 85% ABW for a mean of 8 months and as a group they are 93 ± 4% average body weight (ABW). Compared to their pre-treatment scores, 7 anorexic patients had a 56% reduction in their Y-BOCS score after 6 weeks of fluoxetine and a normalization on EDI scales such as perfectionism. Weight maintenance, in particular, is of considerable importance considering the well known high recidivism rate in anorexia nervosa.

In conclusion cogent arguments suggest that anorexia nervosa is related to OCD and may respond to medications used to treat OCD patients.

NR500 **Wednesday, May 16 - 3:00 p.m.-5:00 p.m.**

PREDICTION OF TREATMENT NONCOMPLETION IN BULIMIA

Allan S. Kaplan, M.D., Psychiatry, Toronto General Hospital, 200 Elizabeth St. CW 1-311, Toronto Ontario 00000, Canada M5G 2C4; Marion P. Olmsted, Ph.D., D. Blake Woodside, M.D., Sarah Maddocks, Ph.D.

Summary:

Identifying characteristics of bulimia nervosa (BN) patients that differentiate between those who complete prescribed treatment programs and those who drop out prematurely has both clinical and theoretical utility. Clinically, the latter group may represent a more treatment resistant sample requiring specialized interventions. Theoretically, the identification of more homogeneous BN populations may help to further elucidate its phenomenology and etiology.

We examined a cohort of female BN patients ($n = 66$) admitted to a day hospital group psychotherapy program for eating disorders. 83% ($n = 55$) completed at least 6 weeks of treatment whereas 17% ($n = 11$) did not. Using discriminant function analysis, these two groups were compared on a variety of demographic, eating, mood and personality variables.

The two groups did not differ on severity of eating symptoms at admission. Dimensions related to psychological functioning significantly ($p < .00001$) differentiated completers from noncompleters and accounted for 40% of the variance in group membership. The latter were characterized by more paranoid and aggressive personality traits, had greater maturity fears and were more body dissatisfied and depressed.

Personality variables rather than eating symptoms may be the important factors in treatment response and possibly long term outcome in BN. Although this may be particularly so for group treatments, further study of treatment noncompletion with other interventions may help elucidate the factors that contribute to treatment resistance in BN.

NR501 **Wednesday, May 16 3:00 p.m.-5:00 p.m.**

PSYCHOPATHOLOGY AND OUTCOME PREDICTION IN ANOREXIA

Edward J. Schork, Ph.D., Psychiatry, Cornell Univ Med Collect, 21 Bloomingdale Road, White Plains NY 10605; Katherine A. Halmi, M.D., Elke D. Eckert, M.D.

Summary:

A follow-up study was conducted on 76 individuals 10 years after they had been hospitalized for treatment of anorexia nervosa. Using *DSM-III-R* criteria, nine (12 percent) still suffered from *anorexia nervosa* at follow-up (two had concurrent *bulimia nervosa*), 17 (22 percent) had *bulimia nervosa* (without anorexia), five, (7 percent) had *died from direct complications* of emaciation, 27 (35 percent) had *eating disorder nos*, and 18 (24 percent) had *no diagnosable eating disorder.* These individuals had taken a standardized objective test of psychopathology, the MMPI, 10 years earlier as they completed a 35-day inpatient treatment protocol (time1). Time1 MMPI responses statistically discriminated patients' eating disorder diagnostic status 10 years later. The *no-diagnosis* group had a mean time1 profile consistently in the normal range. *Those who later died* showed significantly higher elevations on scales indicative of character problems such as impulsivity, poor frustration tolerance, and poor social adjustment); hysterical features, e.g., naivete, self-centeredness, repression, and lack of insight; and suspiciousness and interpersonal distrust. In comparison to the *no-diagnosis* group, those who where still anorectic had time1 MMPI's showing more idiosyncratic thinking and social alienation, somatization, and interpersonal distrust. These findings identify potential negative prognostic features and support the predictive utility of objective psychological testing in anorexia.

NR502 **Wednesday, May 16 3:00 p.m.-5:00 p.m.**

OBESITY: CLINICAL AND SLEEP LAB CORRELATES

Tjiauw-Ling Tan, M.D., Psychiatry, Penn State University, 500 University Drive, Hershey, PA 17033; Joyce D. Kales, M.D., Kelly Slaybaugh, M.D., Thomas P. Kobylski, M.D., Duane D. Shubert, M.D., Donald P. Masey, M.S.

Summary:

Two hundred obese subjects (20% or greater above ideal body weight) were comprehensively evaluated based on clinical, psychological and sleep laboratory assessments designed to provide biopsychobehavioral correlates of this often chronic and potentially life threatening condition. Subjects included 162 women and 38 men with a mean age of $39.1 \pm .07$ years and mean percent above ideal weight of 92.4 ± 3.2. Obese patients were significantly more likely to have experienced emotional stress. Further, those patients with a greater degree of obesity were significantly more likely to have an early age of onset, be divorced, report suicidal ideation, have poor health and significantly less likely to complain of psychosomatic problems. Compared to a control group, obese patients had significantly higher scores on six clinical MMPI scales: scale 4-Pd had the highest elevation suggesting poor impulse control, lack of self-restraint, rebelliousness and social alienation, followed by scales 2-D; 3-Hy; 1-Hs; 8-Sc and 7-Pt. The group also scored significantly higher on the McAndrews Scale, which indicates potential for addiction. This group was found to be at high risk for sleep apnea; there was a very strong positive correlation between weight and degree of sleep apneic activity. The mean number of sleep apneic events per night for the total group of obese patients was 21.6 ± 6.1 compared with 1.2 ± 0.5 for controls. Furthermore, 17 of the patients (14 male and 3 female) had thirty or more apneic events with a mean minimum $Sa0_2$ associated with apneic events of $73.7 \pm 2.0\%$. Although men constituted only 19% of the total obese group, they accounted for 82.4% of those who had sleep apnea.

NR503 **Wednesday, May 16 3:00 p.m.-5:00 p.m.**

SEROTONERGIC RESPONSIVITY IN ANOREXIA NERVOSA

P. Anne McBride, M.D., Psychiatry, Cornell Medical College, 525 East 68th Street, New York NY 10021; George M. Anderson, Jodi Marinacci, B.A., Shelley Berger-Mitnick, B.A., Katherine A. Halmi, M.D.

Summary:

Introduction: Alterations in the function of the neurotransmitter serotonin have been postulated in eating disorders. We report preliminary findings from a study of serotonin-mediated physiological responses and whole blood and plasma serotonin content in young women with anorexia nervosa in the acute phase of the illness, and following restoration of normal weight. *Methods:* The responsivity of CNS serotonergic pathways was assessed by neuroendocrine challenge with a 60 mg oral dose of fenfluramine, and indirect serotonin agonist. The magnitude of serotonin-amplified platelet aggregation, mediated by the platelet 5-HT_2 receptor complex, was measured in conjunction with platelet 5-HT_2 receptor binding indices. *Results:* Acutely ill anorectic women (n = 7) exhibited a wider range of serotonin-amplified platelet aggregation responses (0 = 175% augmentation) than did normal controls (n = 14;54-129% augmentation). Whole blood serotonin content wad elevated (>220 ng/ml) in 3 or 4 of these women. One of 2 anorectic women had a reduced prolactin response to fenfluramine challenge compared with normal controls. However, her prolactin response to thyroid releasing hormone was also low. Prolactin responses to both agents partially normalized following return to normal weight. Additional data will be available at the time of the presentation. *Conclusions:* Preliminary data suggest potential alterations in whole blood serotonin content and platelet 5-HT_2 receptor function in anorexia nervosa. The finding of reduced fenfluramine-induced prolactin release in one acutely ill anorectic subject most likely reflects decreased lactotroph secretory capacity, although an alteration in CNS serotonergic responsivity may also be present.

NR504 **Wednesday, May 16 3:00 p.m.-5:00 p.m.**

LOW CSF IMMUNOREACTIVE-TRH LEVELS IN ANOREXIA

Michael D. Lesem, M.D., Psychiatry, University of Texas, 6431 Fannin, Houston, TX 77030; Walter H, Kaye, M.D., Garth Bissette, M.D., David C. Jimerson, M.D., Charles B. Nemeroff, M.D.

Summary:

In addition to modulating thyroid hormone secretion, thyrotropin releasing hormone (TRH) has behavioral effects in the CNS, including suppression of feeding. This study measured CSF immunoreactive-TRH in patients with anorexia nervosa (AN) to explore whether CNS TRH alternations might contribute to abnormal eating patterns. Medication free women meeting DSM III criteria for AN were hospitalized at NIMH and gave informed consent for studies. Lumbar punctures were performed during the admission low weight phase (LW, N = 19): high calorie refeeding phase following partial weight restoration (RF, N = 18): and stabilized goal weight phase (GW, N = 16). The age-matched control group consisted of 17 healthy women. CSF concentrations of TRH were significantly lower in AN patients at LW (2.69 ± 0.81 pg/ml) than in the controls (3.63 ± 1.20 pg/ml $p < 0.01$). At the RF phase, TRH levels for patients (3.98 ± 2.17) were not different from control values. TRH levels were again low at the GW phase (2.44 ± 1.02, $p < 0.005$). Low CSF TRH levels in AN could possibly reflect reduced activity in the hypothalamic pituitary thyroid axis in response to starvation. CSF TRH levels appear to be influenced by caloric intake, since there is a relative rise during RF at a time of markedly increased food intake and elevated resting metabolic rate. Since TRH decreases feeding in preclinical studies, reduction of CSF TRH levels in AN may reflect adaptive physiological responses to food deprivation.

NR505 **Wednesday, May 16 3:00 p.m.-5:00 p.m.**

CSF QUINOLINIC ACID LEVELS IN ANOREXIA NERVOSA

Mark A. Demitrack, M.D., Psychiatry, University of Michigan, 1500 E Med Ctr Dr Box 0116, Ann Arbor, MI 48109; Melvyn P. Heyes, Ph.D., Margaret Altemus, M.D., Teresa A. Pigott, M.D., Dean D. Krahn, M.D., Blake A. Gosnell, Ph.D., Philip W. Gold, M.D.

Summary:

Thirty to forty percent of tryptophan metabolism involves the production of kynurenines. Among these compounds are quinolinic acid (QA) and kynurenic acid (KA). QA acts as an excitant at central NMDA receptors, and in addition is a kainate-like neurotoxin and convulsant. KA antagonizes QA-mediated neurotoxicity. Many of the key regulatory enzymes in the kynurenine pathway are vitamin B6-, and hence nutrition-dependent. To test the hypothesis that the impaired nutrition in underweight anorexics may affect the stability of this pathway, we measured cerebrospinal fluid (CSF) levels of QA, KA and Ltryptophan (L-TRP) obtained by lumbar puncture in a group of healthy, normal weight females ($n = 8$) and in a group of medication-free female patients meeting DSM IIIR criteria for anorexia nervosa studied while at low weight ($n = 9$), during refeeding ($n = 7$) and after weight recovery ($n = 6$).

All results are reported as nanomolar amounts for normals vs underweight vs refeeding vs weight stable patients. There were no significant differences among groups for levels of QA (13.8 ± 1.5 vs 13.4 ± 1.8 vs 17.3 ± 1.8 vs 14.1 ± 2.0; $df = 3,26$, $F = 0.98$, $p = .4155$) or L-TRP (2.1 ± 0.1 vs 2.0 ± 0.2 vs 2.4 ± 0.3 vs 2.4 ± 0.2; $df = 3, 26$, $F = 1.65$, $p = .2015$). However, there were significant reductions in levels of KA in underweight anorexics compared to controls (2.8 ± 0.4 vs 1.5 ± 0.2* vs 2.1 ± 0.2 vs 2.6 ± 0.5; $df = 3,26$, $F = 3.62$, $p = .0263$, *Bonferroni post-hoc pairwise comparison, $p < .05$)

These results suggest that perturbations in kynurenine metabolism may occur in underweight anorexics, possibly as a consequence of starvation. Such disturbances raise the possibility of QA-medicated neurotoxicity during chronic starvation and may play an important role in the pathophysiology of cognitive impairments in these patients.

NR506 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

PSYCHOTHERAPY OPERATIONS AS PREDICTORS OF OUTCOME

Dan A. Giacomo, M.D., Psychiatry, Cambridge Hospital, 6 Chester, Street, Cambridge, MA 02140; Mona S. Weissmark, Ph.D.

Summary:

It is widely recognized that studies of psychotherapy process and outcome should go hand in hand in order to relate mechanisms of change to therapeutic results. Nevertheless, the variables thus far studied have rendered unanswerable many questions about the nature of the mechanisms of change. The present study was designed to investigate basic therapeutic variables which account for the heterogenous operations of therapists, which are accessible to clinical and experimental manipulation and which are predictive of treatment outcome. Thirty psychotherapy cases (fifteen successful and fifteen unsuccessful) were selected on the basis of patient outcome data. Sixty videotaped transcripts of an early and late session for each case were coded using a newly developed instrument. Specific findings provided tests of hypotheses about distinctive patterns of patient changes from early to late in treatment. For the patients of a successful therapy their evaluations of relational and material parameters shifted toward being significantly more internal, selective and conditional whereas the evaluations of patients of less successful therapy did not significantly change. Findings show that 83% of the variance in treatment outcome could be accounted for by the set of therapist predictor variables (matching, inducers and relational parameters).

NR507 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

SOMATIZATION AND PATTERNING OF FAMILY BEHAVIOR

James L. Griffith, M.D., Psychiatry, Univ of MS School of Med, 2500 North State Street, Jackson, MS 39216; Edward Meydrech, M.D., Melissa E. Griffith, M.S.N.

Summary:

Clinical reports have suggested that family relationships can figure prominently in maintaining symptoms in somatoform and factitious disorders and psychological factors affecting physical condition (PFAPC), and that working therapeutically with families can contribute to symptom remission. We have designed a set of 7 ecosystemic symptom patterns that can be used to describe the patterning of family relationships around somatic symptoms in these disorders.

Utilizing operational criteria for the 7 ecosystemic patterns, we evaluated 149 consecutive psychiatric consultations having a somatoform of factitious disorder or PFAPC diagnosis. 85 patients showed a single ecosystemic symptom pattern, while 64 patients showed multiple coexisting patterns (52 patients with 2 patterns, 9 patients with 3 patterns, and 3 patients with 4 patterns). Two ecosystemic patterns showed a particularly strong association with specific DSM-III-R diagnoses: 1. 85% of patients (17 of 20) diagnosed with Conversion Disorder and 75% of patients (6 of 8) with Somatoform Pain Disorder showed a Captured Symptom Pattern as primary ecosystemic pattern; 2. 100% of patients (14 of 14) diagnosed with Somatization Disorder, 95% of patients (19 of 20) diagnosed with a Factitious Disorder, and 70% of patients (23 of 33) diagnosed with Undifferentiated Somatoform Disorder showed a Mimicry Pattern as primary ecosystemic pattern. Hypochondriasis and PFAPC showed no consistent association with any specific ecosystem pattern.

We discuss the significance of these findings for planning treatments of these disorders that include family and social system interventions, emphasizing the importance of recognizing multiple coexistent patterns when present.

NR508 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

FAMILY SATISFACTION AND ABNORMAL ILLNESS BEHAVIOR

James L. Griffith, M.D., Psychiatry, Univ of MS School of Med, 2500 North State Street, Jackson, MS 39216; Janette Seville, M.A., Edward Meydrech, M.D., Melissa E. Griffith, M.S.N.

Summary:

Clinicians have often observed patients with somatoform or factitious disorders or psychological factors affecting physical condition (PFAPC) to have troubled marital and family relationships exacerbating symptoms. In this study we compared a quantified measure of family dissatisfaction in an "illness behavior" sample with that in a nonpsychiatric sleep disorder sample of patients.

Our "illness behavior" sample consisted of 122 consecutive referrals for psychiatric consultation for a somatoform or factitious disorder of PFAPC. A Family Dissatisfaction Score (FDS) was derived from a self report FACES III Family Inventory. A Beck Depression Scale (BD) and Whitley Index (WI) were also administered and a Global Assessment Scale (GS) was rated by a clinician. As expected, hypochondriasis expressed by WI was significantly correlated with the BD ($r = 0.42$, $p < .0001$), as was the GS with BD (-0.20, $p < .05$). However, FDS calculated by two alternative methods failed in both cases to show any significant correlation with WI, GS, or BD. By contrast, GS and FDS were significantly correlated ($r = -0.47$, $p < .05$) in a comparison sample of 29 patients with nonpsychiatric sleep disorders of excessive daytime sleepiness (27 obstructive sleep apneas & 2 nocturnal myoclonus).

These results suggest that patients with "illness behavior" DSM-III disorders, unlike patients with medical, nonpsychiatric sleep disorder, commonly do not report family dissatisfaction in association with increasing severity of symptoms. Since this finding is contrary to that predicted from clinical reports, we urge caution in interpreting self-report family data in patients with these diagnoses.

NR509 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

NONMEDICAL MANAGEMENT OF PREMENSTRUAL SYNDROME

Teri Pearlstein, M.D., Butler Hospital, 345 Blackstone Blvd, Providence, RI 02906; Ellen Frank, Ph.D., Ana Rivera-Tovar, Ph.D.

Summary:

Despite anecdotal reports that lifestyle changes are helpful to women with premenstrual syndrome, there has been no treatment study examining the efficacy of nonmedical management. We report on the results of an open study of 42 women with prospectively confirmed late luteal phase dysphoric disorder (LLPDD) who underwent a five session group behavioral treatment outlining lifestyle changes in diet, exercise, relaxation and stress reduction. One month following treatment, 25 of 42 subjects (60%) no longer met criteria for LLPDD on the basis of daily symptom charting. Using pairwise comparison t-tests, subjects showed significant decreases in each LLPDD symptom when post-treatment premenstrual means were compared to baseline premenstrual means. Reducing sugar in the diet ($p < .03$) and increasing exercise ($p < .045$) were associated with no longer meeting criteria for LLPDD. There was no association between treatment response and demographic variables, lifetime prevalence of Axis I disorders, or baseline luteal symptom severity. Four months post-treatment, follow-up data was available for 11 of the 25 responders. Eight of these 11 subjects (73%) were still improved. This preliminary open study suggests that group behavioral treatment focusing on specific lifestyle changes may be efficacious in treating women with LLPDD.

NR510 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

EXPRESSED EMOTION IN FAMILIES OF DEMENTIA PATIENTS

Daniel J. Luchins, M.D., Psychiatry, University of Chicago, 5841 S. Maryland Avenue, Chicago, IL 60637; Patricia L. Hanrahan, M.A., Mary Mathews, B.A., Sant Signh, M.A.

Summary:

Negative expressed emotion (EE) among families of psychiatric patients has predicted relapse among schizophrenics, and depressed persons. EE includes critical or hostile comments about the patient, and over-involvement. This study analyzed expressed emotion among families of dementia patients ($N = 29$) to determine whether EE is a predictor of institutionalization. Also, audiotaped interviews of families of dementia patients were compared to interviews from a previous study of families with a schizophrenic relative ($N = 24$). Families of dementia victims expressed very little negative emotion. Only 6% were highly critical compared to 67% of the families of schizophrenics, $p < .00001$. However, families of dementia victims had very negative feelings about other aspects of the illness. Additional categories of EE were developed, with interrater agreement of 90%. Most criticism was directed against the burdens of caregiving, followed by negative feelings towards the disease. Self-criticism and criticism of others were minimal. The relationship between these various forms of negative EE and institutionalization will be reported. The frequency of these other forms of negative EE will be assessed in the schizophrenic sample. The relationships between EE measures and the family member's physical and mental health will be reported.

NR511 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

VALIDITY OF THE CATEGORICAL STRUCTURE AND CLUSTERING OF DSM-III-R PERSONALITY DISORDERS

Wim van den Brink, M.D., Groningen Psychiatry, State University, Post Box 30001, Groningen, GR 09700, The Netherlands; Cor J.A. De Jong, M.D.

Summary:

The validity of the categorical structure and the clustering of personality disorders in DSM-III(R) was tested in a consecutive series of 73 psychiatric outpatients and a group of 152 alcoholic inpatients, using a semi-structured interview (SIDP) and a self-report questionnaire (PDQ).

Results regarding the validity of the categorical structure of Axis II (e.g. distribution pattern, diagnostic overlap) were unequivocally negative.

Principal component analysis of the prototypicality scores of the SIDP and the PDQ corroborated the validity of the three DSM-III(R) clusters. The factorstructure was stable over time, instruments and populations. The results are compared with factoranalytic and clusteranalytic findings of others. The three factor solution was very similar to those of Pilkonis & Frank (1988) and Yager et al. (1989). Furthermore, our four factor solution was almost identical with the four factor solutions obtained by Tyrer & Alexander (1979), Kass et al. (1985), and Hyler & Lyons (1988), with a separate factor for pathological compulsive and passive-aggressive traits. Finally, our two factor solution showed great resemblance with the clusteranalytic findings of Morey (1988) who found two superordinate classes of personality disorder: anxious rumination (introversion) and behavioral acting out (extraversion).

The findings strongly support a multi-dimensional approach in the classification of personality pathology with three basic dimensions: introversion-extraversion, psychotism and conscientiousness.

NR512 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

PSYCHOTHERAPY AND BUSPIRONE IN BORDERLINE PATIENTS

Michael Wolf, M.D., Psychiatry, UCI Medical Center, 101 City Drive Rt. 88, Orange, CA 92668; Thomas Grayden, M.D., Danilo Carreon, M.D., Martin Cosgro, M.A., Donald Summers, M.D., Ron Leino, M.D., Jay Goldstein, M.D., Steven G. Potkin, M.D.

Summary:

The purpose of the study is to assess the efficacy of time-limited psychotherapy when augmented with a serotonergic anxiolytic medication. Subjects meeting DSM-III-R criteria for borderline personality disorder were treated with eight sessions of weekly dynamic, supportive psychotherapy and either buspirone or placebo. Of interest is that most of these patients were also diagnosed with hysteroid dysphoria. Eight-three percent of subjects stated that the overall treatment of medication and psychotherapy was at least moderately beneficial. Fifty percent of the subjects rated psychotherapy as the most helpful aspect of the treatment, while the other 50% rated the combination of medication and psychotherapy most helpful. The research protocol included the identification and weekly monitoring of specific target symptoms, and 60% of subjects stated this was beneficial. Ninety percent of subjects expressed their desire to continue with psychotherapy, appreciated that the therapy was free, and enjoyed being in a research study. These preliminary data suggest that an 8-session, dynamic, supportive psychotherapy may be helpful to patients with borderline personality disorder and that close monitoring of target symptoms may be a useful adjunct to therapy. The results of the comparison of adjunctive buspirone to placebo will be presented.

NR513 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

AXIS II PSYCHOPATHOLOGY IN COMBAT PTSD

Rachel Yehuda, Ph.D., Psychiatry, University of Conn., 263 Farmington Avenue, Farmington, CT 06032; Steven M. Southwick, Earl L. Giller, Jr., M.D.

Summary:

Little attention has been paid to the systematic evaluation of Axis II psychopathology in PTSD, particularly as it occurs in combat veterans. Yet, the presence of Axis II psychopathology in PTSD may significantly impact on the course and severity of illness, treatment and prognosis of this disorder. In the present study, DSM-III-R Axis II psychopathology was assessed in 18 hospitalized inpatients and 16 outpatients with Post-traumatic stress disorder (PTSD) using the Personality Disorder Examination (PDE). A high incidence of character pathology was observed in both inpatient and outpatient groups. The most frequently diagnosed disorders were Borderline Personality Disorder, Obsessive-Compulsive Personality Disorder, Avoidant Personality Disorder and Paranoid Personality Disorder. Compared to outpatients, inpatients had a higher incidence of meeting criteria for nearly every personality disorder except Histrionic and Obsessive-Compulsive Disorder. Inpatients were significantly more likely to meet diagnostic criteria for Paranoid Personality Disorder, Schizotypal Personality Disorder, Avoidant Personality Disorder and Self-Defeating Personality Disorder, suggesting that features of these disorders are particularly salient in individuals seeking hospitalization and may be exacerbated prior to an acute episode of PTSD. On the other hand, the lack of an overall difference on raw dimensional personality profiling using subscale raw scores suggests an enduring stability of these personality characteristics which cannot simply be explained as a reaction to acute changes and/or mental state.

NR514 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

BPD/NPD COMORBIDITY: LONGITUDINAL COURSE AND OUTCOME

Eric M. Plakun, M.D., Austen Riggs Center, Main Street, Stockbridge, MA 01262

Summary:

Previous studies from the Austen Riggs Center mean 14-year follow-up study have provided data on longitudinal course and outcome of patients with borderline (BPD) and narcissistic (NPD) personality disorders, demonstrating that more patients with NPD are male and tend to be functioning more poorly than BPD patients with respect to social, intimate and global functioning at baseline and follow-up. The current study examines a group of 11 patients with comorbid BPD and NPD compared to 31 patients with pure BPD and 16 with pure NPD, assessing the implications of comorbidity. Results suggest that the comorbid patients tended to be males, resembled BPD more than NPD on most preadmission measures, but were more symptomatic and had poorer global functioning than either BPD or NPD. Comorbid patients had stormier inpatient treatment courses, with more changes of therapist, crises, transfers and longer hospitalization than BPD or NPD. At follow-up comorbid patients functioned better vocationally, socially and globally than BPD or NPD, despite having more rehospitalizations, outpatient treatment, and suicide attempts than BPD or NPD. Overall the comorbid patients appear to present a significant treatment challenge distinct from NPD or BPD, but do not appear to constitute a poor outcome group of patients with "malignant narcissism" as described by Kernberg.

NR515 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**
WITHDRAWN

NR516 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**
ANTISOCIAL PERSONALITY AND EVENT RELATED POTENTIALS

Sean J. O'Connor, M.D., Psychiatry, Univ of Conn. Hlth. Ctr., 263 Farmington Avenue, Farmington, CT 06032; Victor Hesselbrock, Ph.D., Allan Tasman, M.D.

Summary:

The P3 component of the event related potential (ERP) was examined in the right hemisphere in 17 young men with a DSM-III-R diagnosis of antisocial personality disorder (ASP). The results were compared to a group of 23 controls. Three pairs of ERP paradigms required subjects to perform cognitive tasks of increasing difficulty with analogous tasks performed in both auditory and visual sensory modalities. ASP was associated with larger P3 amplitudes in all tasks reaching significance only with auditory stimuli. P3 latency increased as a function of task difficulty in all subjects, but the ASP group had significantly longer latencies with visual stimuli. Event related potential (ERP) studies indicate that the brains of persons with a diagnosis of ASP may process information differently when compared to controls.

NR517 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**
PLATELET MAO ACTIVITY IN PERSONALITY DISORDERS

Christopher Reist, M.D., Psychiatry, VA Medical Center, 5901 E. 7th Street, Long Beach, CA 90822; Richard J. Haier, Ph.D., Edward DeMet, Ph.D., Aleksandra Chicz-DeMet, Ph.D.

Summary:

Platelet MAO has been related to several psychiatric disorders and personality dimensions and low MAO activity has been suggested as a biological marker of increased vulnerability to psychopathology. The purpose of this study was to measure platelet MAO and traits of sensation-seeking in patients with personality disorders. Twenty-eight male inpatients with a DSM-III-R diagnosis of personality disorder (by SCID-II) were compared to a group of 15 normal controls. Patients with a history of Axis I diagnoses other than adjustment disorder were excluded. All subjects completed the Zuckerman Sensation Seeking (ZSS) Scale, Eysenck Personality Questionnaire, and the Meyers-Briggs Type Indicator. Overall, there was no difference in platelet MAO between patients and controls. When the subgroup of 13 borderline patients, however, was compared to controls, lower MAO activity was found in the borderline group ($p = .049$, 2-tailed). The borderline group also scored much higher on the ZSS subscales. As expected a significant inverse relationship existed between MAO and the ZSS scale, especially in the patient group ($r = -.66$, $p < .01$, 2-tailed). These results are consistent with the view that MAO is a marker of general psychopathology.

NR518 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**
TREATMENT OF PANIC: THE ROLE OF PERSONALITY

Eve D. Richer, Ph.D., Psychiatry, Hillside Div. LIJ, P.O. Box 38, Glen Oaks, NY 11004; Laszlo A. Papp, M.D., Charolette Zitrin, M.D., Evelyn Abeshouse, M.A., Jack M. Gorman, M.D.

Summary:

Research devoted to the comorbidity of personality and anxiety disorders has not provided data to document the impact of the presence of specific personality traits upon the treatment of panic disorder (PD) patients.

We have completed a chart review of 35 PD patients with agoraphobia. We retrospectively made personality assessments. Twenty of these patients presented with DSM III R dependent personality traits including fear of being alone, preoccupation with abandonment, and rejection sensitivity. Fifteen patients presented with passive aggressive personality traits including irritability, fault finding and avoidance of obligation. Patients were randomized into a 26 week double blind treatment utilizing imipramine or placebo with concurrent in vivo exposure and supportive psychotherapy. Annual assessments of the subjects were made over a five year period post treatment protocol, including self report and independent evaluations. Using the original clinicians ratings of clinical improvement, 19 of 20 (95%) of the patients with dependent personality traits, but only 3 of 15 (20%) of the patients with passive aggressive traits showed significant reduction both immediately following treatment protocol and through the 5 year post treatment evaluation ($X^2 = 20.6$; $p < .001$). There was no significant interaction between personality traits and treatment with either imipramine or placebo. These findings suggest that specific personality traits may advance of impede the treatment of panic patients. Theoretical and clinical implications will be presented.

NR519 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

PREMATURE TERMINATION IN WORKING WITH BORDERLINES

Renate Forssmann-Falck, M.D., Psychiatry, VCU-MCV, 1810 Monument Avenue, Richmond, VA 23220

Summary:

The data presented derive from a change-process study which investigates the psychoanalytic psychotherapy of borderlines. The entire therapy is operationalized using the stage process model and videotaped. Stage specific therapist behavior and predicted patient behavior changes are identified. During the beginning of therapy, bonding is the core issue of the therapeutic interventions. At that time, the process is vulnerable to disruptions without subsequent termination. Two therapist-patient interactions are examined at termination. Patient #1 terminated prematurely at the 11th and patient #2 dropped out at the 21st session. Three 5 minute videotaped segments are coded by an independent rater using the Structural Analysis of Social Behavior (SASB). SASB examines therapist-patient interactions at a detailed level on the dimension of focus, affiliation and interdependence. The frequency of SASB codes shows similarities and differences between the terminations. The similarities are 1) a significant number of codes indicating separation, 2) a significant number of codes on Surface I which measures behavior directed towards others, and 3) hostile controlling and hostile submissive therapist codes. Differences are that 1) patient #1 has more complementary codes and 2) patient #2 coded more frequently as taking hostile autonomy. The sequential analyses undergird that the termination with patient #1 was friendlier than with patient #2.

NR520 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

COGNITIVE THERAPY WITH DEPRESSED INPATIENTS

Michael E. Thase, M.D., Psychiatry, WPIC, 3811 O'Hara Street, Pittsburgh, PA 14212

Summary:

It is unclear if the newer "depression-specific" forms of psychotherapy can be adapted for use as primary treatments for depressed inpatients. The severity and suicidality of many depressed inpatients, coupled with powerful economic pressures to shorten length of hospital stay, may even mitigate against their application. Nevertheless, a significant minority of depressed inpatients fail to respond to, do not tolerate, or refuse to take antidepressants; there is a clear need to develop alternative treatments for such patients. We recently have developed an intensive, inpatient version of Beck's cognitive therapy, conducted using an individualized, 28 day/20 session (maximum) therapy protocol (CBT-I). Ten patients (3M:7F; x age = 34 years); x HAM-D = 21.3 (3.7); x Beck - 35.3 (9.6)), admitted to WPIC's inpatient mood disorders units and meeting RDC for probable ($n = 1$) or definite ($n = 9$) endogenous depression, have been treated with CBT-I. Patients were unmedicated and received a mean number 11.3 (1.2) sessions of therapy prior to discharge or termination. Seven patients were discharged with HAM-D *and* Beck scores ≤ 9; pre-post changes on these measures were robust (ΔHAM-D = 59%, t = 8.4, df = 9, $p < 0.0001$; ΔBDI = 77%, t = 7.0, df = 9, $p < 0.0001$). These findings, which match results in our pharmacotherapy protocols, warrant extension and replication under controlled trial conditions. On a cautionary note, two CBT-I responders declined outpatient continuation treatment and relapsed quickly after discharge.

NR521 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

DOPAMINE, HVA AND EARLY NEUROLEPTIC RESPONSE

David L. Garver, M.D., Psychiatry, Univ Ala. at Birmingham, UAB Station, Birmingham, AL 35294; Jeffrey K. Yao, Ph.D., Daniel P. Van Kammen, M.D.

Summary:

Attempts to discriminate several different psychotic diseases within the group of the schizophrenias have been only marginally successful. Various biological "markers" have been used in attempts to discriminate the different psychoses, but generally have not been found to be associated with differences in illness course, in family patterns of illness, or in response to treatment. Differential rates of response to neuroleptic drugs have been suggested to discriminate at least three psychotic illnesses. We have previously shown that rapid (8 < days) neuroleptic responders (RR) have better prognosis both in themselves and in family members than probands and family members of delayed neuroleptic responders (DR) or non-responders. Because D_2 receptor blockade and symptom amelioration occur soon after initiation of neuroleptics in RR, we have suggested that RR psychotics might have a disorder of central dopamine (DA) excess: a "dopamine psychosis." We have also suggested that DR may have a disorder in which DA itself is not as etiologically relevant.

We now report that DA activity, as reflected in drug-free baseline plasma homovanillic acid (pHVA), is significantly elevated in RR psychotics (137.8 + 69.3[SD]pmol/ml; n = 9) as compared to both normal controls (82.0 + 34.4 pmol/ml; n = 7) ($p < 0.04$) and to DR (98.7 + 41.0; n = 14) ($p < 0.02$); DR have pHVA indistinguishable from controls. There was little change in pHVA during the course of treatment response in the RR (137.8 + 69.3 at baseline to 133.6 + 58.8 pmol/ml at day 7 when response was essentially complete). In contrast, comparable antipsychotic response did not occur in the DR until there was a 23 + 15.6 percent decrease from baseline pHVA levels (82.0 + 34.4 to 64.5 + 20.2 pmol/ml). Baseline pHVA correlated poorly with New Haven Schizophrenic Index (NHSI) psychosis scores in the RR psychotics ($r_s = 0.20$), but significantly and positively with psychosis scores in the DR ($r <= 0.48$); $p < 0.05$).

These findings are consistent with two different disease processes underlying psychotic disorders. RR appears to be a disorder of DA regulation, with excess DA being present at drug-free baseline. In RR, interruption of such excess DA neurotransmission by D_2 blockade by neuroleptics results in almost immediate amelioration of psychotic symptoms. In contrast, DA excess is ***not*** found in DR, though even further reduction in DA activity appears to occur concomitantly with antipsychotic response.

NR522 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

GROUP INTERVENTION AND SELF-ESTEEM: WOMEN'S ISSUES

Robert A. Prehn, Ph.D., Administration, The Oaks Hospital, Box 9000, Wilmington, NC 28402; Patricia Thomas, R.N.

Summary:

There have been significant changes in the role of women in society in the last twenty years. Kilpatrick (1989) notes that as women's roles in society change, there is need for healthcare—including psychiatry—to also change in response to the new roles. One recent change in psychiatry has been the advent of clinical tracks designed to expressly address women's unique issues. While well intentioned, there has been little research documenting intervention outcomes. With this in mind, the present research compared the self-esteem scores of two groups of women psychiatric inpatients: those receiving women's issues group intervention and those not receiving this intervention. With the exception of Women's Group, the treatment protocols of the two groups were similar. Both groups completed the Multidimensional Self-Esteem Inventory both pre-test and post-test. Scale scores on the MSEI (e.g., competence, lovability, likability, personal power, self-control, moral self-approval, body appearance, and body functioning) were compared and subjected to an analysis of variance. ANOVA tests indicate significant differences between the two groups, suggesting that Women's Issues Groups do, in fact, contribute to increasing global self-esteem among women psychiatric inpatients.

NR523 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

WITHDRAWN

NR524 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

FACTORS INFLUENCING ADOPTION OF A SKILLS TRAINING PROGRAM FOR THE MENTALLY ILL

Sally J. MacKain, Ph.D., UCLA-NPI, Box 6022, Camarillo, CA 93011; Charles J. Wallace, Ph.D.

Summary:

The Adoption of Innovations in Mental Health (AIMH) project is the study of the dissemination of a set of comprehensive, highly structured treatment "modules" designed to teach social and independent living skills to people with serious mental illness. Field tests were conducted in 17 state psychiatric hospitals, out-patient, day treatment, correctional, and residential care facilities to accomplish a number of objectives: 1) to measure knowledge and skill acquisition among module participants; 2) to assess the fidelity with which the modules were implemented; 3) to gain insights into the process by which innovations are adopted by practitioners.

The results indicated that patients significantly improved their knowledge and performance in terms of the skills taught in the modules. In settings large enough to accommodate an experimental design, the improvement was significantly greater in patients who received a module or modules than in patients assigned to waiting list control groups. Equally as important as the improvements in skills was the accuracy with which staff implemented the modules, irrespective of wide differences in their clinical and educational backgrounds. The variables that influenced a site's decision to implement the modules included its treatment philosophy, administrative mandate, module fidelity, and financial and administrative stability. Size of facility and types of patients treated did not influence the decision to adopt the modules.

NR525 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

INPATIENT TREATMENT OF MENTALLY ILL COLLEGE STUDENTS

Xavior Mastrianni, M.D., Four Winds Saratoga, 30 Crescent Avenue, Saratoga Springs, NY 12866; Frances L. Hoffman, Ph.D.

Summary:

Systematic examination of the treatment needs of college students hospitalized for psychiatric reasons is sparse. Developmental issues, particularly unresolved identity and separation conflicts, complicate psychiatric disorders of this age group. The Four Winds College Service is an inpatient unit specializing in the treatment of college age patients with serious psychiatric disorders. Through the integration of academic opportunities into the therapeutic milieu the program seeks both to treat the mental illness and to foster developmental goals of autonomy, intellectual growth and discovery, and movement toward adult roles. Follow-up interviews with 55 former patients (mean time post-discharge = 14.4 months) reveal high rates of return to college (69%); strong student identity and educational aspirations; and high helpfulness ratings of the academic components of hospitalization. On the other hand, 55% of the respondents report difficulty in the transition back to college. Implications of these and other findings for treatment of this age group will be discussed.

NR526 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

EFFECTS OF BRIEF HOSPITALIZATION ON SEVERAL DIMENSIONS OF PATIENT FUNCTIONING

Paul B. Lieberman, M.D., Psychiatry, Dartmouth Medical, 9 Maynard Street, Hanover, NH 03756; Elise Egerter, M.D., Susan Von Rehn, A.N.C., Ellen Dickie, B.A., Binette Elliott, B.A., Peter Mills, Ph.D., Paul Compton, M.D.

Summary:

Brief psychiatric hospitalization is a widely used treatment for patients at times of crisis, but one whose effects have received very little systematic investigation (1,2). As part of an investigation of the impact of hospitalization we studied 63 subjects admitted to 2 short-term units of a general hospital. The average age was 40.5; 32 were female; 31 had major psychotic, affective or organic mental disorders, the remainder personality, adjustment or anxiety disorders. They were highly symptomatic (average BPRS on admission 23.5) and functionally impaired (average GAS on admission 39.3). The average length of hospitalization was 14.9 days. Patients were assessed on 4 clinically important dimensions at the start and end of hospitalization: symptom level (BPRS), self esteem (Rosenberg Self Esteem Scale), a measure of patients' goals for hospitalization and a measure of how helpful or harmful they perceived other people and treatment. Significant change was noted in all 4 dimensions. Symptomatic improvement was associated with change in other areas. Differential effects of the 2 units were suggested. These data support the hypothesis that brief hospitalization affects clinically important variables in addition to symptoms.

NR527 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

LENGTH OF STAY IN PRIVATE PSYCHIATRIC HOSPITALS

Stephen B. Shanfield, M.D., Psychiatry, Univ of Texas Hlth Sc Ctr, 7703 Floyd Curl Drive, San Antonio, TX 78284

Summary:

Length of stay in the private sector is little investigated. This research draws from 130 cases presented by private psychiatrists to the author in case conferences at three private psychiatric hospitals. Average length of stay for the sample was 50.3 days. The data was analyzed using multiple regression analysis. Length of stay was the outcome variable, and admission variables and data accumulated during the hospital stay were predictor variables.

Admission variables included diagnosis, number of previous hospitalizations, hospitalization within the previous 12 months, transfer from another psychiatric institution, age, sex, marital status, presence of substance abuse or medical problems, level of outside support, loss as a reason for admission, and years out of training for doctor. A HIGH NUMBER OF PREVIOUS HOSPITALIZATIONS and SINGLE STATUS predicted length of stay but only account for 6% of the variance.

Hospitalization variables were lack of clarity of diagnosis, patient outcome, family interference with treatment, administrator/therapist split, PROBLEMS WITH PSYCHOPHARMACOLOGIC INTERVENTION and DIFFICULTY IN ESTABLISHING A RELATIONSHIP WITH THE PATIENT. These latter two variables account for 19% of the variance.

More efficient psychopharmacologic intervention is likely to decrease length of stay. However, psychopharmacologic problems likely reflect individual variations in patient illness patterns which in turn account for a considerable portion of a patient's length of stay.

NR528 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

BRAIN EDEMA AFTER ELECTRICALLY INDUCED SEIZURES

Tom G. Bolwig, M.D., Psychiatry, Rigshospitalet, Blegdamsvej 9, Copenhagen DK 02100, Denmark; Annette Gjerris, M.D., Henning Laursen, M.D., David I. Barry, B.Sc.

Summary:

Cognitive disturbances following electroconvulsive therapy may be caused by a slight brain edema as a consequence of increased cerebrovascular permeability. In an animal model we studied regional brain water content and serum proteins as well as the density of cells in hippocampus and hypothalamus following electroconvulsive seizures (ECS) in the rat. The following groups were studied: Group I and Group II: ECS (50 milliamp.) once daily for 0.3 sec and 0.9 sec respectively. Group III: age matched control animals receiving no ECS. Group IV: ECS (50 milliamp.) 0.3 sec 3 times per week for 4 weeks, group V: age matched controls for group IV. Brain water content was measured by specific gravity, proteins were measured by a peroxidase-antiperoxidase (PAP) method.

RESULTS: group I: no change in water content in any region, Group II: tissue water of the hypothalamus increased by 2.5%, Group IV: similar changes both in hypothalamus and slightly less so in the hippocampus. In all other regions specific gravity was unchanged. PAP-staining in all groups revealed no inter-group difference.

HISTOLOGY: No significant changes of neurons or glia, no myelin break-down, no perivascular cell accumulation. In the regions where edema was demonstrated no histological difference between ECS and controls.

CONCLUSION: In animals treated with electrical current slightly above the seizure threshold in a regimen similar to ECT a slight brain edema develops in regions of interest for memory functions. No signs of cell damage was demonstrated. The findings could help explain unwanted effect of ECT in patients.

NR529 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

ACUTE ABSTINENCE SYNDROME IN MALE COCAINE ADDICTS

William W. Weddington, M.D., Psychiatry, University of IL., 912 S. Wood Street, Chicago, IL 60612; Barry S. Brown, Ph.D., Charles A. Haertzen, Ph.D., Edward J. Cone, Ph.D., Elizabeth M. Dax, M.D., Ronald I. Herning, Ph.D.

Summary:

We examined changes over 28 days in mood states, craving for cocaine, and sleep during acute abstinence reported by 12 male, predominately intravenous-using cocaine addicted subjects residing in a research facility. For comparison, we examined 10 non-addicted control subjects. There were no significant differences between cocaine addicts and controls regarding demographics and selected *DSM-III-R* diagnoses other than psychoactive substance use disorder and antisocial personality disorder. There were significantly higher scores of psychiatric symptoms reported by cocaine addicts one week prior to admission. Mood-distress and depression scores recorded at admission and during acute abstinence were significantly greater than those reported by controls. Addicts' mood-distress scores and craving for cocaine were greatest at admission and decreased gradually and steadily during the 28 day study. There were no significant differences between groups regarding reports of sleep other than difficulty falling asleep and clear-headedness on arising. Although there were significant differences in resting heart rate at admission and over time, there were no significant differences in weight gain or blood pressure.

Given the absence of a classical "withdrawal" pattern, "acute abstinence" may be a more appropriate classification of psychological and physical phenomena experienced by cocaine addicts who initiate abstinence in a controlled environment.

NR530 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

AFFECT DISORDERS IN SUBSTANCE ABUSING ADOLESCENTS

David L. Pogge, Ph.D., Four Winds Hospital, 800 Cross River Road, Katonah, NY 10536; John Stokes, Ph.D., Sheila A. Cooperman, M.D., Philip D. Harvey, Ph.D.

Summary:

Consecutive admissions (N = 119) to the adolescent service of a psychiatric hospital were independently rated for diagnoses of substance abuse or dependence. Discriminant function analysis was applied to psychometric data obtained within the first 14 to 21 days of hospitalization. Separate analyses conducted on cognitive variables, (2) neuropsychological variables, (3) measures of psychiatric disorder (i.e., MMPI), and (4) measures of personality traits and disorders (il.e., the Millon Adolescent Personality Inventory, MAPI) revealed that only the MMPI and MAPI improved upon chance in their separation of the patient groups. Moreover, those variables which entered into these discriminant functions appeared much more closely related to personality traits than to either mood or anxiety disorders. Since the significant variables were able to classify both abusers and non-abusers with greater than 80% accuracy, and since neither indicators of affective symptoms nor anxiety symptoms entered into the equation, this suggests that the variables which determine which adolescent psychiatric patients elect to abuse drugs or alcohol is either unrelated to these syndromes or that the relationship between these disorders and substance abuse behaviors is mediated by the personality traits identified in these analyses.

NR531 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

PRENATAL COCAINE ALTERS U-OPIATE RECEPTOR BINDING

Ronald P. Hammer, Jr., Ph.D., Anatomy, University of Hawaii, 1960 East-West Road, Honolulu, HI 96822; Daniel W. Clow, Ph.D., Linda P. Spear, Ph.D., Cheryl L. Kirstein, Ph.D.

Summary:

Prevalence of cocaine use during pregnancy is increasing. Clinical reports suggest than in utero cocaine exposure affects subsequent behavioral and neurological development of offspring. Cocaine-induced blockade of dopamine reuptake in adults up-regulates opiate receptors in dopaminergic reward regions, suggesting that endogenous opioid systems could be involved in cocaine addiction. We examined brains of juvenile rats exposed to cocaine prenatally to determine whether gestational exposure could produce sustained effects on opioid reward systems. Cocaine (10-40 mg/kg) was administered subcutaneously to pregnant rats from gestation day 6 (first trimester) until birth. On postnatal day 21, offspring were decapitated, brains were frozen and sectioned, sections were incubated in NA^+-containing [^{3}H] naloxone medium, which preferentially labels u-receptors, and analyzed using quantitative *in vitro* autoradiography. Dose-dependent increase of u-receptor labeling was observed in nucleus accumbens and medial prefrontal cortex (mesocorticolimbic dopamine reward regions), striatum, and several limbic regions, including amygdala. Such long-lasting effects on opioid systems may represent a biological substrate for altered reward threshold in affected offspring. Furthermore, these results suggest that cocaine abuse pharmacotherapy should focus on both dopamine and opioid systems, providing additional rationale for treatment with buprenorphine, which has been shown to reduce cocaine self-administration and craving.

NR532 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

FLUOXETINE IN COCAINE ABUSE: DRUG AND PSYCHIATRIC OUTCOME

Steven L. Batki, M.D., Department of Psychiatry, UCSF, SF General Hospital, 1001 Potrero Ave., San Francisco, CA 94110; Luisa B. Manfredi, B.A., James L. Sorensen, Ph.D., Roland Dumontet, Reese T. Jones, M.D.

Summary:

Fifteen methadone maintenance patients who met DSM-III-R criteria for both opioid and cocaine dependence were treated with fluoxetine and weekly group therapy to reduce cocaine use. Twelve (80%) subjects were HIV-infected. Nine subjects (60%) were male and 12 (80%) were Black, and average age was 40 years. Nine subjects (60%) had a lifetime history of Major Depressive Disorder (MDD). Subjects with lifetime MDD reported, on average, more cocaine use than subjects without MDD, although this difference was not significant. Fluoxetine was given each morning for nine weeks on an outpatient basis. Fluoxetine doses ranged from 20 to 60 mg per day with an average of 43 mg per day. There were major reductions in cocaine use, depression, and anxiety during the course of the study. Comparison of intake to week 9 showed a decrease in cocaine use by self-report, from an average of 12.9 times per week to 1.7 times/wk. The proportion of urines positive for cocaine decreased freom 64% at intake to 22% at week 9. Cocaine craving decreased from 13.9 to 6.2, (possible range = 0.24) ($p<0.001$). The mean Beck Depression Inventory score decreased from 13.7 to 5.0 ($p<0.01$) and the mean Hamilton Depression score decreased from 18.5 to 5.5 ($p<0.05$). The mean Hamilton Anxiety score decreased from 11.6 to 4.3 ($p<0.05$). Fluoxetine was well-tolerated in combination with methadone. Few adverse effects were noted, and no subjects had to discontinue fluoxetine. In summary, fluoxetine may have promise as a treatment approach for cocaine abuse in methadone patients with or without Major Depressive Disorder.

NR533 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

PREDICTION OF ALCOHOL DETOXIFICATION OUTCOME

James A. Wilcox, D.O. Psychiatry, Texas Tech University, 424 Executive Center Suite 101, El Paso, TX 79902

Summary:

In this study, 235 patients admitted to an alcohol detoxification unit were evaluated to examine the effect of several variables on the outcome of their detoxification and treatment. The variables included: Blood alcohol level (BAC) on admission, age, gender, SES, race, history of prior treatment, use of multiple drugs, and physical distress as measured by the Clinical Institute Withdrawal Assessment Scale (CIWA). Retrospective statistical analysis was used to determine the relative risk and potential predictive value of these variables on both the need for medical intervention during detoxification and the completion of a 6 week treatment program. Only BAC and CIWA score were found to have predictive value for the need for medical intervention ($p<.01$). Only BAC and history of prior treatment predicted success in completion of current treatment. BAC on admission appears to be an important prognostic variable.

NR534 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

CARBAMAZEPINE FOR BENZODIAZEPINE WITHDRAWAL

Richard K. Ries, M.D., Psychiatry, University of WA, Harborview MC 325 Ninth Ave, Seattle, WA 98104

Summary:

Eighty-five patients in two separate drug treatment centers received carbamazepine (CBZ) for treatment of benzodiazepine (BZP) withdrawal. Two slightly different protocols were used for starting CBZ and discontinuing the BZP in an open, non-blind fashion. Compared to their previous use of BZP or phenobarb taper, medical directors and chief nurses independently rated either CBZ protocol as "much better" in terms of overall effectiveness $p<-01$ rapidity of action $p<.01$ and patient's subjective response $p<-01$. Autonomic symptoms, sedation, and participation in rehab program also favored by the CBZ protocols (p -.05). Only the category rash/allergy was rated equivalent, or by one M.D., "worse" for CBZ. The CBZ protocols, patient profiles, and potential mechanisms will be discussed.

NR535 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

DIAGNOSING ALCOHOLISM IN PSYCHIATRIC PATIENTS

Burns Woodward, M.D., Westwood Lodge Hospital, 45 Clapboardtree Street, Westwood, MA 02090; Jeffrey Fortgang, Ph.D., Maureen Sullivan-Trainor, E.D.M., Helen Stojanov, Steve M. Mirin, M.D.

Summary:

Alcoholism is prevalent among psychiatric patients, and accurately diagnosing alcohol problems is a critical step in treatment planning. We diagnosed alcohol dependence in 35 psychiatric inpatients by blind review of interview protocols and hospital records. We then examined the frequency with which admitting and attending clinicians diagnosed alcohol abuse and dependence in these patients. Alcoholism was underdiagnosed; 24% of the clinicians' diagnoses included no alcoholism diagnosis, 39% were alcohol abuse, and only 37% were alcohol dependence. Underdiagnosis was strongly associated with the presence of comorbid psychosis, as well as with the patient's denial of alcoholism and with less severe alcoholism. This presentation will examine the patient and clinician variables which contribute to underdiagnosing alcoholism and recommend educational and administrative measures to improve clinicians' diagnostic sensitivity.

NR536 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

PERSISTENT COGNITIVE EFFECTS OF PROLONGED COCAINE USE

Michael Sherer, M.D., Amer. Neuroscience Ctr, 1622 O'Frederick Road #510, Gaithersburg, MD 20877; Louis M. French, M.A., Allan F. Mirsky, Ph.D.

Summary:

The behavioral and cognitive symptoms which follow cessation of sustained cocaine use have been increasingly recognized, and the presence of a cocaine withdrawal syndrome is now generally accepted. One method of assessing attentional and cognitive capacities is by examining Event Related Potentials (ERPs), and in particular, the P300 component. Prior work has indicated that acute intoxication with cocaine induces changes in ERPs. In the current study we attempted to extend such observations to the period of time following withdrawal from the drug. We compared retrospectively the ERPs of 5 male cocaine addicts who were inpatients in our hospital with those of a group of 14 male inpatient controls. Addicts were studied a mean of 13 days following last cocaine use. Despite high levels of performance on the choice reaction task (measured in 15 of 19 cases) used to elicit the P300, cocaine addicts had significantly reduced P300 amplitude compared to controls (7.7 $\pm$ 3.1 microvolts vs. 14.0 $\pm$ 3.5 microvolts, $t = 3.49$, $df = 17$, p 0.01). The results support the view that chronic use of cocaine results in cognitive deficits which outlast the period of acute cocaine intoxication.

NR537 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

MANAGEMENT OF PROBLEMATIC BENZODIAZEPINE USE

Joy M. Schmitz, Ph.D., Psychiatry, University of Texas, 1300 Moursund Street, Houston, TX 77030; Eileen McGorry, R.N., Melinda A. Stanley, Ph.D., Daniel L. Creson, M.D., John Grabowski, Ph.D.

Summary:

Six patients with anxiety disorders who had been treated with benzodiazepines for long periods of time were identified from a general adult outpatient population. Although these patients did not consistently meet DSM-III-R criteria for drug dependence, they exhibited problematic drug-seeking behaviors (i.e., "doctor shopping," dose increase requests, treatment noncompliance). Because there are no data-based approaches for managing these behaviors in this population, a behavioral-pharmacological treatment plan was designed to reduce drug-seeking behaviors and daily benzodiazepine intake. Elimination of benzodiazepine administration was not a primary treatment goal.

Initial mean benzodiazepine dosage for this group was 21.66 mg. Diazepam, or equivalent. Continued prescriptions were dependent on compliance with: 1) weekly visits; 2) daily self-monitoring; and 3) 4 weeks stabilization prior to dosage reduction. Outcome data at the end of 90 days revealed a mean dose decrease of 4.5 mg. Diazepam, or equivalent. Therefore, the goal of systematic dose reduction was achieved. Clinically significant behavior changes included compliance with prescribed regimen, regular attendance, and cessation of "doctor shopping." These preliminary findings suggest the efficacy of a behavioral-pharmacological treatment plan aimed at modification of drug-seeking behavior associated with benzodiazepine use. We currently are using more structured assessment techniques to evaluate the use of this intervention further.

NR538 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

AXIS II AND SUBSTANCE ABUSE IN EATING DISORDERS

Michael Newman, M.D., Fair Oaks Hospital, 19 Prospect Street, Summit, NJ 07901; Michele Lemaire, M.D., Mark S. Gold, M.D.

Summary:

To determine if clinical characteristics could distinguish substance abusing (SA+) from non-substance abusing (SA-) eating disorder patients, the Eating Attitude Test (EAT-40), Eating Disorder Inventory (EDI), Beck Depression Inventory, and Personality Disorder Questionnaire (PDQ-R) were administered to 40 consecutive hospitalized patients. Eighteen were SA+ and 22 were SA-. No significant differences in age, age of onset of the eating disorder or distribution of eating disorders diagnoses (anorexia; bulimia and anorexia; bulimia) existed between the two groups. The SA+ had a significantly longer duration of illness (7.2 $\pm$ 5.3 vs 4.2 $\pm$ 3.8; t 2.0, $p < .05$) compared with the SA- group. No differences existed on measures of depression and eating disorder symptomatology and the SA+ had strong tendency to have higher scores on the body dissatisfaction subscale of the EDI (19.8 $\pm$ 7.7 vs 15.3 $\pm$ 7.0; t 1.9, $p < .06$). The SA+ group had a total of 87 personality disorder diagnoses compared with 55 in the SA- group and were significantly more likely to have a diagnosis of antisocial (6 vs 0; $p < .004$), paranoid (15 vs 12; $p < .05$), and borderline (9 vs 4; $p < .04$) personality disorders. These findings suggest that differences in previous studies of personality disorders in eating disorder patients may have been accounted for by differences in comorbidity of substance abuse and eating disorders in the populations studied.

NR539 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

THE 1990 CRACK USER: CONSEQUENCES OF DAILY CRACK

Mark S. Gold, M.D., Research, Fair Oaks Hospital, 19 Prospect Street, Summit, NJ 07901

Summary:

There has been considerable debate concerning the typical user of crack, the patterns of use, the effects which cause users to seek help, and the effect of crack on criminal activity. We have recently completed (January 1990) a structured interview study of 200 consecutive 800-COCAINE callers who were using crack. The callers came from 42 states and the composite caller was a 24 year-old (range 12-42), single, unemployed, high school graduate spending $200-300 per week on crack while having a total family income of less than $15,000 per year. They had tried cocaine HCl by insulfation for the first time 3 years before calling the hotline. Currently they are using cocaine weekly or many times a week (51%) but not daily or many times a day (45%). They have not had an Emergency room visit or felony due to crack. The relationship between frequency, dose and consequences of crack use was analyzed. Daily users ($n = 89$; DU) spent 200-300% more on crack per week ($p < 0.01$) than non-daily users (ND). Thirty-one percent of DU were employed while 53% of ND were employed ($p < 0.01$). DU were poorer (total family income $\leq$9,000 per year) and at least two times as likely: (1) a high school dropout; (2) crack-related emergency room visit(s); (3) felony; (4) drug dealing. There were no significant differences between the two groups in age of first use, route of first use or other demographic features. Felony and cocaine selling correlates with total dollars spent on crack per week and not with age, education, employment, total family income, and other demographic variables. While only 5% of the 200 callers had an income $\geq$$50,000 per year the affluent high dose users were equally likely to commit a felony or sell crack as a high dose person who was poor.

NR540 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

DRUG TESTING FALSE NEGATIVE RATE BY NIDA CRITERIA

Magnus Lakovics, M.D., The Horsham Clinic, 722 East Butler Pike, Ambler, PA 19002; David Martin, Ph.D.

Summary:

Mandatory drug testing of certain Federal employees, contractors and workers in regulated, industries recently went into effect using technical criteria established by the Department of Health and Human Services and administered by the National Institute of Drug Abuse (NIDA). The NIDA criteria screens only for five (5) drugs of abuse: marijuana, amphetamines, cocaine, opiates and PCP. NIDA criteria for positive marijuana concentration is 100 ng/ml and for amphetamines 1000 ng/ml which are five (5) and three (3) times less sensitive respectively than positive criteria routinely used in clinical settings. Also, clinical criteria require screens with a wider range of drugs to include propoxyphene, methadone, barbiturates, benzodiazepines, methaqualone and alcohol which would be missed using NIDA criteria. This less sensitive and limited screen may encourage continued or alternate drug abuse behavior as the rates of false negative findings will be higher than those using a clinical criteria. To demonstrate this rate one hundred (100) consecutive inpatient clinical drug screens were retrospectively analyzed using NIDA criteria. A significant rate of false positives approximating 50% were found when using only the NIDA criteria. These data will be presented noting the rates of false positives by specific drug and positive cutoff criteria in order to present an effective approach that will compliment the NIDA drug screen especially when applied to federal workers in sensitive positions who are in follow-up testing programs.

NR541 **Wednesday, May 16, 3:00 p.m.**

A 5-HT1A TREATMENT OF COMORBID ANXIETY AND ALCOHOLISM

Gary D. Tollefson, M.D., Psychiatry, St. Paul Ramsey, 640 Jackson Street, St. Paul MN 55101; Jon Montague-Clouse, M.S., Sherrie L. Lancaster, R.N.

Summary:

The use of alcohol to self medicate anxiety dates back over 100 years ("tension-reduction hypothesis)." Several studies underscore the association between alcoholism and other psychiatric disorders. Both have been interdigitated with serotonin (5-HT). In this study we hypothesized that (1) comorbid anxiety is treatment responsive; (2) anxiolysis would impact alcohol seeking and recidivism; and (3) anxiolysis could be safely and effectively achieved with a novel 5-HT_{1A} agent. We evaluated 51 individuals abstinent from 30-90 days with comorbid generalized anxiety and alcoholism (SCID). After a one-week placebo run-in, subjects were randomized under a double-blind to either buspirone or placebo for 24 weeks. The population included 20 Cloninger Type I and 30 Type II alcoholics. Of the original 51 subjects, 42 completed at least four weeks in the protocol. Outcome measure, e.g. the HAM-A and SCL-90, significantly favored buspirone versus placebo ($P = 0.013$). 16/22 buspirone patients versus only 6/20 placebo patients achieved a full response. A similar trend was observed with the HAM-D. While the Addiction Severity Index failed to demonstrate a strong interrelationship between level of anxiety and alcohol behaviors, individual items and subjective global assessment favored active drug. The pharmacotherapy of anxiety and alcoholism has not been extensively studied. Benzodiazepine profiles limit their utility in this population. We demonstrated a novel 5-HT anxiolytic was effective in reducing anxiety in associated alcoholism consonant with theories of 5 = HT involvement. A non-dependency producing anxiolytic may also impact craving, use, and relapse rates.

NR542 **Wednesday, May 16, 3:00 - 5:00 p.m.**

SEROTONERGIC ABNORMALITY IN ALCOHOLISM

Myung A. Lee, M.D., Psychiatry, Cleveland and VA Hospital, 10000 Brecksville Road, Brecksville, OH 44141; Herbert Y. Meltzer, M.D.

Summary:

There is extensive research for a serotonergic (5-HT) abnormality in alcoholism. Clinical and pre-clinical studies suggest that decreased 5-HT function may be involved in alcoholism. Therefore, we examined 5-HT receptor responsivity in alcoholics by using 5-HT agonists, L-5-hydroxytryptophan (L-5-HTP), a precursor of 5-HT, and MK-212 (6-chloro-2-[1-piperazinyl] pyrazine), a direct-acting 5-HT_2 and 5-HT_{1C} receptor agonist. Non-depressed male inpatients meeting DSM-III-R criteria for alcohol dependence (alcohol free ≥ 2 wks) were orally administered L-5-HTP 200 mg ($N = 12$, age = 42 yrs), MK-212 20 mg ($N = 14$, age = 42 yrs), or placebo. The plasma cortisol and prolactin (PRL) responses to these challenges were compared with those of 12 (age = 33 yrs) and 9 (age = 39 yrs) male normal controls, respectively. The data were analysed using ANCOVA and differences in age and placebo responses were adjusted. The increase in plasma cortisol following L-5-HTP was significantly lower in alcoholics compared to the normal controls ($p < 0.03$). The plasma PRL increase, but not the plasma cortisol increase, following MK-212 was also significantly lower in the alcoholics compared to normal controls ($p < 0.02$); six out of 14 alcoholics had decreased plasma PRL levels after MK-212, but none of the normal controls did. L-5-HTP had no significant effect on plasma PRL levels in either group. These data are consistent with previous reports of a serotonergic abnormality in alcoholism. This serotonergic abnormality in alcoholism appears to be different than those with depression.

NR543 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

THE CASE STUDY: 2. WHEN IS AN ALCOHOLIC AND ALCOHOLIC?

Thomas P. Beresford, M.D., Psychiatry, Univ of Michigan, 400 E. Eisenhower Pkwy. Ste A, Ann Arbor, MI 48104, Frederic C. Blow, Ph.D., Elizabeth Hill, Ph.D., Kathleen M. Singer, R.N.

Summary:

Previous scholars have noted the wide variations that investigators, trained in various disciplines with their respective research methods, have used to define terms such as "alcoholic," "problem drinker," or "alcohol abuser." The *DSM-III-R* criteria for alcohol dependence offered a synthesis of many of the previous definitions, and their implied methods of recognizing alcoholism, as a way of offering a clinically useful diagnostic method. In a study of general hospital patients, we interviewed 1,146 subjects with a semi-structured interview. We matched interview data against the *DSM-III-R* criteria for alcohol dependence and arrived at a prevalence rate of 34 percent among our study subjects. In reviewing this result, we noted that not all positive respondents offered symptoms or signs in all three of the general domains (impaired control, social decline, tolerance/withdrawal) contained in the *DSM-III-R* criteria. When these were required, prevalence dropped to 27 percent. Further tightening of symptom criteria yielded prevalences of 21 percent and 16 percent. Experience with this large sample suggests that the *DSM-III-R* criteria can be applied with greater and lesser degrees of rigor resulting in prevalence variations that may differ by as much as two-fold. Use of the *DSM-III-R* criteria as a standard measure of alcohol dependence may not be justified without careful attention to the method of application.

NR544 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

BENZODIAZEPINE SELECTION BY SUBSTANCE ABUSERS

Robert J. Malcolm, M.D., Psychiatry, Med Univ of S. Carolina, 171 Ashely Avenue, Charleston, SC 29425; Amanda Johnston, Ph.D., Kathleen T. Brady, M.D., Malcolm Cunningham, M.D.

Summary:

Patients hospitalized at an addiction treatment center with primary or secondary benzodiazepine (BZ) abuse or dependency (n = 136) were grouped by type of BZ abused. Diazepam (DZ) was abused by 79 (58%) patients and was BZ of choice for 59 (43%). Alprazolam (ALP) had been abused by 39 (29%) patients and was BZ of choice for 19 (14%) patients. Chlordiazepoxide, lorazepam and clorazepate were each the BZ of choice for 4% of the patients. Patients taking either ALP or DZ were stratified by their primary abuse diagnoses: BZ abuse with secondary cocaine, opiate or alcohol abuse; primary alcohol and secondary BZ; primary cocaine and secondary BZ; opiate and secondary BZ. For primary BZ and primary alcohol groups, DZ and ALP were equally likely to be named as BZ of choice. For all other groups, abusers were six times more likely to abuse DZ than ALP. This was significantly different (chi-square = 7.9, $p = 0.004$). There was also a significant difference between ALP abusers (13 of 19) and DZ abusers (19 of 59) for evidence of anxiety disorders based on clinical grounds or psychometric testing (chi-square = 9.4, $p = 0.002$). BZ withdrawal treatment time for ALP abusers (14.1 ± 6.4 days) was significantly longer ($t = 3.019$, $p < 0.02$) than that of the DZ abusers (10.3 ± 5.8 days) ANOVA comparisons performed on the McAndrews Addiction Proneness Scale of the MMPI across the groups stratified by primary drug of abuse indicated significant differences ($f = 4.7$; df 5,96; $p < 0.001$), with the primary BZ groups having the lower scores (post hoc test $p < 0.05$) than the primary opiate, cocaine, or alcohol groups. Ninety-four percent of the BZ users were polysubstance abusers, and the remaining 6% (n = 8) abused BZs alone. In this latter group, two admissions occurred because of withdrawal symptoms from lorazepam of ALP rather than from any evidence of abuse. In the present sample DZ was the most frequently abused BZ and was strongly favored by cocaine and opiate abusers. BZ abuse alone rarely led to hospitalization. MMPI characteristics of BZ abusers indicated less addictive behaviors than patients who primarily abused cocaine and opiates.

NR545 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

SMOKING CESSATION ON AN IN PATIENT UNIT

Jeffrey M. Jonas, M.D., Cape Psych Centers, Cape Cod Hospital P.O. Box 640, Hyannis, MA 02601; Jeff Eagle, Ph.D., Allyson McClave, B.S., Nancy Smith, M.S., Alice Zimmerman, M.Ed.

Summary:

A number of strategies have been proposed for the treatment of nicotine addiction. We studied the effect of mandatory nicotine cessation on an inpatient psychiatric unit, coupled with an educational program and administration of nicotine gum. We obtained follow-up data on 39 smokers admitted to the Cape Psychiatric Center in Hyannis, Massachusetts, obtained by raters blind to the purpose of the study. The smoking assessment was conducted by a structured telephone interview. All patients were psychiatric inpatients and admitted for reasons other than nicotine addiction. Each patient was instructed in the proper use of nicotine gum, was forbidden to smoke at any time during the hospitalization, and was given self-help materials regarding smoking cessation. At the time of discharge, patients were given prescriptions for nicotine gum and again reminded how to chew the gum properly. At the time of admission, the 39 subjects smoked a mean of 21.6 cigarettes per day (S.D. = 13.6). On follow-up, 35 of the subjects had resumed smoking, a mean of 21.3 cigarettes per day (S.D. = 15.4). Five individuals stopped smoking and, of these, 4 stated that they had stopped because of the inpatient program. Of note, however, is the fact that none of these individuals were smoking more than 5 cigarettes a day at the time of admission. Relapse occurred immediately in 28 cases, within 1 week in 3 cases, within 1-4 weeks in 2 cases, and after 1 month in 2 other cases. We conclude that mandatory cessation of smoking on a inpatient unit, coupled with the administration of nicotine gum and educational materials is not an adequate method for treating nicotine addiction. Our data suggests that other, more structured, programs will be necessary to treat this disorder.

NR546 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

NICOTINE DEPENDENCE, NICOTINE GUM AND BRIEF TREATMENT

Michael G. Goldstein, M.D., The Miriam Hospital, 164 Summit Avenue, Providence, RI 02906; Raymond S. Niaura, Ph.D., David B. Abrams, Ph.D., Cheryl A. Eaton, B.A.

Summary:

This study evaluated the effectiveness of matching cigarette smokers, based on the severity of nicotine dependence, to brief treatment with or without nicotine gum. 173 Subjects, recruited from medical outpatient settings, were classified as high or low dependent on the basis of Fagerstrom Tolerance Questionnaire (FTQ) scores. Subjects were randomly assigned within the high and low dependent subgroups to either brief treatment alone, or brief treatment plus nicotine gum. Subjects were offered 4, 15 minute, individual treatment sessions and a self-help manual. Short-term outcomes were analyzed according to carbon monoxide verified ($\leq$8ppm) self-reported quit status. Loglinear analyses of quit rates 3 weeks after beginning treatment showed a significant interaction (chi sq (1) = 4.37, $p < .05$) between treatment condition (no gum;gum) and dependence category (high FTA; low FTQ). As expected, high dependence subjects who received gum had the best quit rates (32%) while high dependence subjects who received no gum were least likely to quit (12%). Patterns of quit rates at the end of treatment were similar though they did not achieve statistical significance. Six and 12-month outcomes will also be reported. The importance of patient-treatment matching will be discussed in light of these findings.

NR547 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

SMOKING CESSATION, NICOTINE DEPENDENCE AND CLONIDINE

Lirio S. Covey, Ph.D., Clinical Psychiatry, NYS Psychiatric Inst., 722 West 168th Street, New York, NY 10032; Alexander H. Glassman, M.D., Fay Stetner, M.S., Gregory W. Dalack, M.D.

Summary:

Multiple trials have shown that the nicotine chewing gum is more effective with high-dependent than low-dependent smokers. This relationship between a pharmacological agent and level of nicotine dependence was examined in data from 148 women seen in two placebo-controlled clinical trials of clonidine for smoking cessation. In the pilot study, a four-week trial involving 44 women, a positive effect of clonidine compared to placebo was twice greater among high-dependent smokers compared to low-dependent smokers. In the second study, a 10-week trial with 104 women, this interaction between clonidine and level of nicotine dependence was also seen. For low-dependent smokers, there was a trend for clonidine to be more effective than placebo (odds ratio = 1.2 confidence limits = .4, 4.1). In high-dependent smokers, clonidine was found to be significantly more effective than placebo (odds ratio = 5.9; confidence limits = 1.4, 24.0). Both clonidine and the nicotine gum have been shown to alleviate tobacco withdrawal symptoms. This effect appears to be more pronounced in highly dependent smokers.

NR548 **Wednesday, May 16, 3:00 p.m. - 5:00 p.m.**

INTERACTION OF ALCOHOL WITH IMMUNE CELLS

Martha Sarasua, M.D., Psychiatry, Metro Health Med. Ctr., 3395 Scranton Road #R416, Cleveland, OH 44109; Suio-Ling Chen, Ph.D.

Summary:

Alcohol has been shown to suppress immune responses both *in vivo* and *in vitro*. The effect of ethanol on the interaction between immune cells and a common antigen was investigated. Peripheral blood mononuclear cells (PBMC) were isolated from normal human male controls. The isolated PBMC were exposed *in vitro* to a common antigen, tetanus toxoid, in the presence of varying concentrations of ethanol and their proliferation was monitored by ^{3}H-thymidine uptake. Monocytes exposed to the antigen (tetanus toxoid) in the presence of varying concentrations of ethanol were incubated with isolated lymphocytes from the same controls and lymphocyte proliferation was monitored by ^{3}H-thymidine uptake to test the effects of ethanol on the ability of monocytes to present antigen to lymphocytes. Alcohol significantly reduced the proliferation of PBMC following exposure to tetanus toxoid in a dose dependent manner. In addition, alcohol significantly inhibited antigen presentation by monocytes. Alcohol also increased lymphocyte membrane fluidity and reduced lymphocyte viability in a concentration dependent manner. The data show direct effects of alcohol on immune cells membranes and suggest that alcohol-related immuno-suppression could result from alterations occurring at the level of the cell membrane.

NR549 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

PROFILES OF HOSPITALIZED BENZODIAZEPINE ABUSERS

Kathleen T. Brady, M.D., Psychiatry, VA Medical Center, 109 Bee Street, Charleston SC 29403; Amanda Johnston, Ph.D., Robert J. Malcolm, M.D., Malcolm Cunningham, M.D.,

Summary:

Patients seeking treatment at an inpatient facility for substance abuse over a 5 year period were stratified according to presence or absence of benzodiazepine (BZ) abuse. One hundred and thirty six patients hospitalized with a primary or secondary diagnosis of BZ abuse were compared to non-benzodiazepine (NOBZ) substance abusers (N = 1,347) on multiple demographic variables. A significantly ($P < 0.05$) greater percentage of patients in the BZ group were over 30 (76% vs 56%), female (54% vs 32%), caucasian (99% vs 88%), married (54% vs 43%), professional (11% vs 5%) and had 16 more years of education (33% vs 19%). Only 6% (N = 8) of BZ abusers used BZ's alone. At discharge, 49% (67 of 136) of the entire BZ group had an Axis I diagnosis other than substance abuse disorder. The most common Axis I diagnosis was depressive disorder (18%), followed by adjustment disorder (14%), somatoform disorder (5%), bipolar disorder (4%), and anxiety disorder (4%). Of the patients who abused BZ's alone, 6 of the 8 had another Axis I diagnosis. Three patients were diagnosed with adjustment disorder, 1 with panic disorder, 1 with a major depression and 1 with somatoform disorder. Thirty two % of the sample obtained BZ from illicit sources, 63% from prescribed sources and 5% from unknown sources. Of the 63% that obtained BZ from prescribed sources, 10% of the physicians were psychiatrists and 30% were primary care physicians. In conclusion, BZ abuse was rarely found in the absence of other substance abuse. A hospitalized BZ abuser in this population was likely to be a well-educated caucasian female, over 30 with high probability of having an additional psychiatric illness, particularly when the BZ abuse occurs in the absence of other substance abuse.

NR550 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

DISCRIMINANT FUNCTION EEG ANALYSES OF THE ABUSERS

John J. Straumanis, M.D., Psychiatry, LSU Med. Center, P.O. Box 33932, Shreveport, LA 71130; Frederick A. Struve, Ph.D., Yoram Raz, M.A., Gloria Patrick, M.S.

Summary:

Our previous studies have shown significant quantitative EEG differences between chronic THC users and non-users. Present study reports on use of discriminant function analyses of the EEG data to separate THC users from non-users.

Subjects from the above studies were used. The dependent variable was non-use or daily use of THC. Candidate predictors were Absolute and Relative Power, Asymmetry and Coherence for four EEG bands at 21 electrode sites and transformations of these scores. The discriminant function analysis and the Jack-knifed replication were robust. Only two predictors–Absolute Power of alpha at F_3 (AF_3a) and P_3 (AP_3a) yielded a successful discriminant formula: D = (1.7416)(AF_3a) + (-1.0048)(AP_3a).

		PREDICTED		*JACK-KNIFE*	
ACTUAL GROUP	*N*	THC	NO THC	THC	NO THC
THC USER	27	27	0	26	1
NON-USER	53	4	49	4	49
CLASSIFICATION		95% Correct		93.8% Correct	

In analyses using additional Ss, discriminant scores were also related to duration and amount of THC use and abstinence duration in Ss who stopped.

NR551 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

CLINICAL NEUROBIOLOGY OF COCAINE WITHDRAWAL

Christopher J. McDougle, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Lawrence H. Price, M.D., Joseph Palumbo, M.D., Herbert D. Kleber, M.D., George R. Heninger, M.D.

Summary:

Three phases of withdrawal have been described in chronic cocaine abusers (Phase 1: Crash,Phase 2: Withdrawal,Phase 3: Extinction). Pharmacological challenge with L-DOPA 250 mg/carbidopa 25 mg was used to investigate DA function during phases 1 and 2 of cocaine withdrawal in humans. *METHOD:* Six male inpatients with *DSM-III* cocaine dependence received 1.5 mg/kg of cocaine p.o. 3X/day for three consecutive days (maintenance treatment period 1 (MTP1)). Subjects then received placebo cocaine 3X/day for nine consecutive days (maintenance treatment period 2 (MTP2). Subjects and ward staff were blind to the content of the cocaine capsules. Each subject received randomized challenge tests of active or placebo carbidopa on the two days following MTP1 (Phase 1 withdrawal), and one week following MTP2 (Phase 2 withdrawal). Plasma prolactin (PRL), growth hormone (GH), MHPG, and HVA (all reported as ng/ml), were obtained following each challenge. *RESULTS:* PRL (N = 6) decreased following carbidopa during challenge set 1 (mean $\pm$ SD,-3.6 $\pm$ 1.4vs -1.1 $\pm$ 1.4, $p<0.001$) and 2(-4.2 $\pm$ 1.7 vs -1.0 $\pm$ 1.1,$p<0.001$) compared to placebo. Change in PRL was not different between challenge sets 1 and 2. GH (N = 5) increased following carbidopa during challenge set 1 (22.1 $\pm$ 13.1 vs 3.1 $\pm$ 4.9,$p<0.03$) but not during set 2, compared to placebo. There was a trend toward increased GH response to carbidopa compared to placebo between challenge sets (19.0 $\pm$ 13.3 vs 9.2 $\pm$ 9.9, $p<0.07$). MHPG (N = 4) increased following carbidopa during challenge sets 1 (2.4 $\pm$ 1.1 vs 0.9 $\pm$ 1.0, $p<0.006$) and 2 (2.8 $\pm$ 1.6 vs 1.1 $\pm$ 1.3, $p<0.008$) compared to placebo. Change in MHPG was not different between challenge sets 1 and 2. During challenge set 1, HVA (N = 2) decreased (0.2) following placebo and increased (277.1) following active carbidopa. During challenge set 2, HVA (N = 2) decreased (1.2) following placebo carbidopa and increased (221.8) following active carbidopa. During challenge set 2, HVA (N = 2) decreased (1.2) following placebo carbidopa and increased (221.8) following carbidopa. *CONCLUSION:* These data suggest that Phase 1 (Crash) of cocaine withdrawal may be associated with altered DA metabolism compared to Phase 2 (Withdrawal). Behavioral, physiological, and neurobiological data will be compared to data from normal controls.

NR552 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

NALOXONE-PRECIPITATED OPIOID WITHDRAWAL

Philip D. Kanof, M.D., Psychiatry, Bronx VA Hospital, 130 West Kingsbridge Road, Bronx, NY 10468; Leonard Handelsman, M.D., Marvin J. Aronson, Ph.D., Robert C. Ness, Ph.D., Karen J. Rubinstein, M.A., Kenneth J. Cochrane, Ph.D.

Summary:

The clinical characteristics of naloxone-induced opioid withdrawal were studied in 20 male patients with opioid dependence stabilized on 12 mg methadone bid. Using an intrasubject design, each patient received two intravenous pharmacological challenges: one with naloxone (0.05, 0.10, 0.15, 0.20 mg; 5 patients each dose), and one with saline placebo. Measures of opioid withdrawal (SOWS, WOWS and OOWS scales), mood states (POMS), cognitive performance (Stroop test, digit span), and changes in autonomic parameters were assessed following each pharmacological challenge. Naloxone produced dose-dependent increases in opiate withdrawal scale scores and in symptoms of dysphoria as measured by the POMS. Differences within subjects between naloxone and placebo infusions in POMS scores were highly correlated with differences in opioid withdrawal assessed by both subjective (SOWS: $r = 0.89$, $p < 0.001$; WOWS: $r = 0.62$, $p < 0.01$) and objective (OOWS: $r = 0.86$, $p < 0.001$) scales. Opiate withdrawal scale scores and POMS scores following naloxone administration returned to levels seen after the placebo infusion within one hour after the pharmacological challenge. The results indicate that marked dysphoria can be induced in opioid dependent subjects by pharmacological precipitation of a withdrawal syndrome. Spontaneous withdrawal may account for some of the symptoms of dysphoria commonly seen in opioid-dependent patients.

NR553 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

SEASONAL CHANGE OF MELATONIN RHYTHM IN ALCOHOLICS

Anil K. Jain, M.D., Psychiatry, VA Medical Center, 4801 East Linwood, Kansas City, MO 64128; Surendra Kelwala, M.D., Jan Campbell, M.D., Barbara Powell, Ph.D., Sailaja Yerasi, M.D., Sleman Khoury, M.D.

Summary:

Pineal hormone melatonin has a well documented circadian rhythm. Altered melatonin secretion and rhythm has been documented in several psychiatric disorders. In this project we studied the nocturnal melatonin rhythm of 14 chronic alcoholic inpatients and 18 controls. To control for seasonal changes (circannual rhythm), 8 patients and 7 controls were enrolled in winter (Feb-March) and 6 patients and 11 controls were enrolled in summer (June-Jul-Aug-Sept). The patients were abstinent and drug free for at least 2 weeks. The blood samples were drawn from 10 p.m. to 7 a.m. at the hour. Melatonin was measured by radioimmunoassay. There were no differences in the amplitudes of melatonin secretion between alcoholics and controls in winter. But there was a markedly lowered level of melatonin secretion in alcoholics during summer when compared to controls reaching $p < .05$ level of significance at 1,3,4,& 7 a.m. (ANOVA followed by post hoc Scheffe). A comparison of the 2 alcohol groups - summer and winter - also showed a strong trend for lowered melatonin secretion in summer, but the difference failed to reach statistical significance due to small sample size. The table gives the hourly amplitudes of the melatonin secretion of the three groups.

Time	10	11	12	1	2	3	4	5	6	7
Summ.Alcoh.	45.0 ± 20	53.5 ± 29	63.2 ± 31	54.2 ± 30	55.3 ± 35	57.8 ± 27	48.3 ± 20	55.7 ± 44	43.3 ± 23	31.7 ± 14
Summ.Controls	55.4 ± 19	75.1 ± 32	91.4 ± 50	101.4 ± 47	90.7 ± 41	94.2 ± 34	99.4 ± 42	84.3 ± 35	63.9 ± 27	58.7 ± 30
Wint.Alcoh.	45.9 ± 22	63.1 ± 28	77.3 ± 37	87.7 ± 38	89.1 ± 30	90.7 ± 49	83.7 ± 48	78.9 ± 54	70.0 ± 32	59.4 ± 18

Low melatonin secretion and circannual melatonin rhythm in alcoholics is a finding that needs further study.

NR554 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

EFFECT OF COMBINED SUBSTANCE USE ON LABORATORY MARKERS OF ALCOHOLISM

Michael Chang, M.D., Psychiatry, Honolulu VA OPC, P.O. Box 50188, Honolulu, HI 96850; Jungwha Kwon, M.D., Roger S. Hamada, Ph.D., Paul Yahiku, Ph.D.

Summary:

This paper examines the commonly used laboratory indicators of heavy alcohol use (elevated MCV, GGTP, and AST values) in subgroups of drug-using and non-drug using alcoholic males admitted to an inpatient alcoholism treatment program. Three hundred and twenty-eight consecutive admissions meeting DSM-III diagnostic criteria for alcohol abuse or dependence were studied. Seventy-five percent of the subjects used both alcohol and drugs. The most frequently used drugs were marijuana, cocaine, amphetamines and tranquilizers. Overall, subjects who used drugs with alcohol had significantly lower MCV and GGTP values than subjects who used alcohol alone. More specifically, cocaine use was associated with lower MCV values, marijuana use with lower AST values, and heroin use with higher AST and GGTP values. These differences between drug-using and non-drug-using alcoholics were significant even after controlling for variables that affect the laboratory values such as age, quantity, frequency, and duration of alcohol consumption. Our findings indicate that any study of laboratory markers of alcoholism needs to consider concomitant illicit drug use patterns.

NR555 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

AUTOMATED GROUP THERAPY SCORES AS A PREDICTOR OF ALCOHOLISM TREATMENT ATTENDANCE

Michael Chang, M.D., Psychiatry, Honolulu VA OPC, P.O. Box 50188, Honolulu, HI 96850

Summary:

This paper examines the relationship between performance in group therapy and length of stay in a chemical dependency program. Each patient's performance in every group was evaluated on seven items such as mood, attention, self-disclosure, comments made, attribution of responsibility, commitment to sobriety and overall participation. The data was gathered with the use of a simple automated group progress note module that replaced the handwritten group progress notes. The major findings of this paper were: 1) Group performance scores improve with each group session attended; 2) Low group performance scores within the first few sessions are highly predictive of dropout but high performance scores are not as predictive of high attendance; 3) Among the group performance score attributes examined, the highest score obtained during treatment correlated best (correlation coefficient = .4971, $p < .001$) with group attendance. The three conclusions of this paper, combined with the observation that 40% of our patients attended two groups or less, has had a profound effect on our clinical treatment strategies. Our clinicians now consciously make every effort to help each patient participate actively during their first and second group sessions.

NR556 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

AMANTADINE TREATMENT OF COCAINE WITHDRAWAL

Marian P. Droba, M.D., Psychiatry, University of Penna, Phila. VAMC 39th and Woodland, Philadelphia, PA 19104; Arthur I. Alterman, Ph.D., Charles P. O'Brien, M.D., Karen A. Sweeney, PA.C

Summary:

We treated 30 new cocaine dependent outpatients under random double-blind conditions with amantadine (A) 100 mg. twice daily or placebo (P) for 8-14 days as initial treatment with a day program or prior to inpatient rehabilitation. The patients were seen each weekday to fill out questionnaires, have pill counts, vital signs, breathalyzer, and urine toxicology and briefly see an M.D. or physician's assistant. Patients received two transit tokens and a meal pass after visits. We used chi square and ANOVA comparing A and P groups and week 1 of treatment with week 2. There were no group demographic differences except group A was older than group P (means 37.6 and 32.2 respectively). There was significant improvement of both groups with time (week 1 vs 2) for craving and withdrawal scale scores and no differences with time on self-reported craving, days cocaine used, scale of well-being scores, study completion, or urine positive for drugs. Follow-up at one-month will be presented. The retention rate of the study subjects (93 percent) was better than day treatment program retention without medication intervention (60 percent) at two weeks. We conclude short-term initial amantadine when accompanied by extra attention is not superior to placebo accompanied by extra attention.

NR557 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

NEUROBIOLOGICAL RESPONSE TO ALCOHOL AND ALCOHOL CONSUMPTION IN SOCIALLY SEPARATED RHESUS MONKEYS

Gary W. Kraemer, Ph.D., Psychiatry, Univ. of Wisconsin, 22 N. Charter Street, Madison, WI 53715; Michael H. Ebert, M.D., Dennis E. Schmidt, Ph.D.

Summary:

The objective of this study was to determine whether individual differences in the response of brain biogenic amine systems to alcohol were associated with individual differences in the magnitude of social separation induced alcohol consumption in rhesus monkeys. In Phase 1 of the experiment, adult rhesus monkeys were separated from their social group and given tap water or 0.5-2.0 g/kg alcohol via nasogastric intubation. In Phase 2, the monkeys were separated from their social group, intubated with water as in Phase 1, and then allowed to drink alcohol in a sweetened 6% solution. In each phase, motor activity and fluid consumption were measured, and cerebrospinal fluid (CSF) and blood were collected 90 minutes after intubation.

Differences in water consumption, motor activity, and levels of CSF norepinephrine and 5-hydroxyindoleacetic acid after alcohol intubation in Phase 1 were correlated with the rate of voluntary alcohol consumption in Phase 2. However, the relationships observed were not those that were anticipated on the basis of previous studies. The results indicate that variation in CSF norepinephrine and 5HIAA following alcohol treatment is significantly correlated with later alcohol consumption rate. Multiple correlations between water consumption, activity, CSF norepinephrine, CSF 5HIAA, or blood alcohol concentration (BAC) 90 minutes after placebo or alcohol in Phase 1, and mean measured alcohol intake and BAC in Phase 2 were from $r = 0.78$ to 0.94 ($p < .03$ to $p < .001$). In general, monkeys that voluntarily consumed the most alcohol were relatively insensitive to the neurochemical effects of alcohol as reflected in these dependent measures.

NR558 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

WHO COMPLETES RESIDENTIAL ADDICTIONS PROGRAMS?

Lionel P. Solursh, M.D., Psychiatry, DVA Medical Center, 2460 Wrightsboro Road, Augusta, GA 30910; Robert C. Ness, Ph.D., William Nolan, Ph.D., Lois Cecil, M.A., Mary A. Forney, Ed.D.

Summary:

Voluntary inpatient treatment programs for the addictions rarely report rates of program completion, but rates varying between 50-90% are assumed or cited when the question is addressed. Social-psychological factors discriminating "completers" from "drop-outs" are even less frequently reported or analyzed as predictors of program completion or subsequent outcomes. During the first year of our longitudinal study of intratreatment change and the course of recovery among 256 addicted male veterans, we observed an 81 percent completion rate. Significant differences were identified between "completers" and "drop-outs": 1. Black males are overrepresented among completers. 2. Completers tend to give a history of stable employment and do not live alone. 3. Completers are likely to have been in one or no prior treatment program. 4. Completers are likely to have used alcohol once a month or less during the past year. 5. Completers are more likely to report one drug-related arrest in their lifetime, rather than none or several such arrests. The "course of recovery", quantified at periods of one and six months, will be analyzed with respect to prior completion and to the predictor variables enumerated above. Implications for program development, treatment planning, and evaluation research design are discussed.

NR559 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

COCAINE AND HOSPITAL COURSE IN SCHIZOPHRENIA

John P. Seibyl, M.D., Psychiatry, West Haven VAMC, 950 Campbell Avenue, West Haven, CT 06516; Sally Satel, M.D., Dominic Anthony, M.S.W, Steven M. Southwick, M.D., Rajani Nadkarni, M.D., William Giakas, M.D., Robert Malison, M.D., Dennis S. Charney, M.D., John H. Krystal, M.D.

Summary:

Cocaine's effects on brain monoamine systems may be clinically important in schizophrenia including the expression of positive symptoms, negative symptoms, and acute and chronic extrapyramidal side effects. While prevalence of cocaine abuse in schizophrenics is reported to be high, the impact of cocaine abuse in schizophrenia is poorly understood. *Methods:* Hospital charts were obtained from the roster of schizophrenics treated in the Schizophrenia Clinic of the West Haven VA Medical Center. Individual hospitalizations were analyzed for substances used and psychosocial functioning prior to hospitalization, presenting symptoms on admission, inpatient clinical management, course of pharmacotherapy, and duration of hospitalization. *Results:* Cocaine-abusing schizophrenics (N = 10) had greater frequency of hospitalizations compared with non-cocaine using substance abusing (N = 11) and non-substance abusing patients (N = 8). Within cocaine group analyses revealed significantly less aggressivity, homicidal ideation, and use of restraints in patients presenting after cocaine use. This same group showed increased suicidality. Symptoms of paranoia and psychomotor agitation were not different in patients presenting after cocaine use compared to their non-cocaine admissions. Cocaine hospitalizations required markedly higher antipsychotic doses. Overall, the cocaine cohort exhibited higher rates of unemployment and legal problems. *Comment:* Cocaine use has significant effects on the course of hospitalization in schizophrenics, including neuroleptic dose.

NR560 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

EXCITATORY AMINO ACID ANTAGONIST FOR OPIATE WITHDRAWAL

John H. Krystal, M.D., Psychiatry, Yale Univ Sch of Medicine, West Haven VA Medical Center, West Haven, CT 06516; Kurt R. Rasmussen, Ph.D., George K. Aghajanian, M.D.

Summary:

Better non-opiate treatments are needed for opiate dependency. This report describes one such novel strategy, the suppression of opiate abstinence symptoms using the excitatory amino acid antagonist, kynurenic acid. *Method:* Two studies were conducted. The first study examined the capacity of intracerebroventricularly (i.c.v.) kynurenate in doses of 0.1 ug/ml and 1.0 g/ml (N = 2 rats per dose). The second study evaluated intraperitoneal (i.p.) kynurenate's effects in doses of 10 mg/kg, 100 mg/kg, and 500 mg/kg (N = 4 rats per dose). Both studies followed a similar method for inducing dependence and withdrawal. Rats were implanted with a 75 mg. morphine pellet daily for two days beginning three days prior to withdrawal testing. On the third day, animals were adapted to a test cage for 30 min. prior to kynurenate administration. Thirty minutes later, naltrexone 10 mg/kg, s.c. was administered to elicit withdrawal. Withdrawal behaviors were rated using methods previously described. *Results:* Kynurenate produced a dose-dependent reduction in the overall severity of opiate abstinence when administered through both the i.c.v. and i.p. route. In the first study, kynurenate appeared to reduce writhing, wet dog shakes, salivation, and chewing. In the second study, kynurenate significantly reduced writhing, ptosis, lacrimation, and salivation. Kynurenate (i.p.) also showed a trend to reduce wet dog shakes and jumping. *Implications:* This is the first study to directly link excitatory amino acid systems in the brain to symptoms of opiate withdrawal. These findings suggest that excitatory amino acid antagonist treatments might be developed to reduce abstinence symptoms in humans.

NR561 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

COCAINE ABUSE: CHANGES IN AXIS II WITH TREATMENT

Helen M. Pettinati, Ph.D., Research, Carrier Foundation, Route 601, Belle Mead, NJ 08502; Bradley D. Evans, M.D., Jacqueline Jensen, M.A., Kathleen Meyers, M.S., Veronique Valliere, B.A., Ayshe B. Ergin, M.S.

Summary:

Axis II diagnoses are important in treatment planning and in determining the prognoses of substance dependent patients. Recent studies report differences in the prevalence of personality disorders based on the kind of chemical addiction (Mirin & Weiss, 1988), and gender (Griffin, 1989). Also, instability of Axis II diagnoses over time has been identified in this patient population (Blume, 1989). It is unclear as to whether certain distinctive personality traits observed in substance abusers, such as impulsivity, are preexisting, or rather, characteristic of substance abuse and will dissipate with treatment. There were 104 patients (81 inpatients, 23 outpatients) in short-term, intensive rehabilitative treatment (4 wks, inpatient, 6 wks, outpatient) for cocaine and/or alcohol use disorders who were assessed in their fourth week post-admission using the *Structured Clinical Interview for DSM-III-R Personality Disorders* (SCID-II), and using several self-report personality questionnaires. All patients were again evaluated at 1-month post-discharge. During treatment, significantly more cocaine dependent females (90%) met DSM-III-R criteria for a personality disorder compared to either alcohol dependent females (27%) ($p = .005$) or cocaine dependent males (44%) ($p = .04$). In addition, 36.5% of the patients were determined to be highly impulsive and borderline personality disorder was significantly related to high impulsivity ($p = .01$). There was a significant decrease in the number of patients who were impulsive at 1 month post-treatment ($p = .01$), compared to when they were evaluated during treatment. However, a significant proportion of the patients assessed as highly impulsive during treatment had elected to drop from the aftercare program by the 1-month post-discharge evaluation. Both aftercare treatment dropouts and completers are being followed for demographic comparison. Results will also be reported for these patients at 3 and 12 months post-discharge.

NR562 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

TROUBLED DOCTORS: A NEW SURVEY OF MEDICAL BOARD ACTIONS

Norma Josef, M.D., Psychiatry, Wayne State Univ, Lafayette Clin 951 W Lafayette, Detroit, MI 48202; R. John Kinkel, Ph.D.

Summary:

Studies of physician impairment, negligence, and misconduct have steadily increased in the last decade. Very few of these investigations, however, have generated large samples of data with sufficient controls to suggest what the determinants of antisocial behavior among physicians might be. This study examines 642 cases of physician misconduct sanctioned by medical boards in a five state area (Michigan, Ohio, Indiana, Illinois, Wisconsin). During the period of 1978 to 1983 the sanctioning rate for physician misconduct increased dramatically for the most part. We found that 48.3 percent of all violations dealt with substance abuse in one form or another: personal alcohol or substance abuse and/or improper drug prescribing. These data suggest that recent ethnographic work purporting to show that there are a significant number of doctors who sell controlled substances for street consumption is not far from the mark. The most important determinants of physician misconduct prove to be age and specialty. Older, male doctors (50 years+) and general practitioners are more likely to come in contact with medical boards for sanctioning than others. Our findings with regard to age are similar to those of Schwartz and Mendelson (1989): older physicians have more behavioral and occupational performance problems than we would predict given their distribution in the general population. Theories (Levinson, 1978) that offer plausible explanations of these trends and possible public policy implications of this research are discussed.

NR563 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

EFFECTS OF WITHDRAWAL STRESS ON TRICYCLIC THERAPY

Joseph A. Kwentus, M.D., Psychiatry, Modesto Psych Center, 1501 Claus Road, Modesto, CA 95355; William A Kehoe, Pharm.D, Arthur F. Harralson, Pharm.D.

Summary:

Acute changes in tricyclic antidepressant protein binding may alter therapeutic response and have been inadequately studied during treatment for withdrawal from substance abuse. We compared imipramine binding in chemically dependent (CD), depressed (D) and healthy persons.

Eighteen patients (12 CD, 6 D) receiving imipramine and 10 healthy controls were evaluated. Total and free serum concentrations were determined on treatment days 1, 3, and 7 by HPLC assay. Alpha-l-acid glycoprotein (AAG) concentrations were determined at these times by RID assay. The SCL-90-R was used to asses general psychological stress (GSI subscale).

ANOVA revealed no significant differences between any of the groups for AAG ($p > 0.9$). Linear regression showed a trend ($p = 0.065$) for declining AAG in CD patients over the 7 days. Free drug fractions did not differ between groups (2.9-6.6%) and were inversely related to AAG. GSI scores were not different between patient groups ($p > 0.1$). As GSI increased, there was a trend ($p = 0.087$) for AAG to increase and free drug fraction to decrease.

In summary: 1) imipramine protein binding and free fraction are similar in CD and D patients, 2) AAG tends to decrease with time in CD patients, and 3) psychological stress may increase AAG and decrease imipramine free fraction. Future studies of tricyclic actions during withdrawal should consider protein binding effects.

NR564 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

TREATMENT NEEDS OF PSYCHIATRICALLY ILL ALCOHOLICS

Barbara J. Mason, Ph.D., Psychiatry, Cornell Univ Med. Col., 525 East 68th Street, New York, NY 10021; James H. Kocsis, M.D.

Summary:

INTRODUCTION: Recent studies have demonstrated that alcoholics with severe co-morbid psychopathology are significantly less likely to benefit from the traditional alcoholism or psychiatric treatment programs to which they are commonly referred. The aim of the current study is to systematically identify how treatment needs of alcoholics with high psychiatric severity (HPSA) differ from those alcoholics with low psychiatric severity (LPSA) and non-substance abusing inpatient depressives (NSAD). METHOD: Admissions to the general medical and psychiatric services of the Cornell University Medical Center were screened for alcoholism with the MAST and CAGE. Need for treatment was assessed with the Addiction Severity Index (ASI) structured interview in seven potential problem areas: medical, employment, alcohol use, drug use, legal, psychiatric, and family/social. Patients were assigned to HPSA and LPSA groups on the basis of ASI global ratings of psychopathology and DSM-III diagnoses were made with the computerized Diagnostic Interview Schedule (DIS). SUBJECTS: 29 percent of psychiatry and 21 percent of general medical service patients met study criteria for alcoholism. Subjects were 47 HPSA, 15 LPSA, and 29 NSAD. Subjects were generally equivalent on demographic variables across groups and treatment services, except that there were significantly more female depressives and male alcoholics. RESULTS: HPSA's were significantly more impaired than either comparison group on ratings of family and social relationships. They also displayed the medical, alcohol, and drug related problems of the LPSA's, and the psychiatric severity of the NSAD's. DISCUSSION: These data lend support to the hypothesis that HPSA have complex treatment needs that are not identical with those of IPSA's or NSAD's.

NR565 **Wednesday, May 16, 3:00 p.m.-5:00 p.m.**

NEUROLECTRIC CHANGES IN ACUTE COCAINE INTOXICATION

Allan Tasman, M.D., Psychiatry, Univ Conn. School, 263 Farmington Avenue, Farmington, CT 06032; Sean J. O'Connor, M.D., Nancy Kluck, M.S.

Summary:

Five female Dutch Belted rabbits were prepared with an indwelling jugular catheter and permanent stainless steel electrodes resting on the dura. EEG recordings were made one week apart from each rabbit following the intravenous injection of saline solution containing 0, 1 and 2 mgKg doses of cocaine, hydrochloride. Auditory and visual stimuli were used to elicit brain responses before and after each injection. Two baseline recordings in each stimulus modality were made. Subsequent recordings were made immediately following injection, then every five minutes for three, then every 15 minutes for five more sessions. Dose related, significant cocaine effects appeared immediately in the EPs and persisted for approximately 30 minutes following injection. EEG records were averaged to obtain evoked potential to responses to each stimulus. In the auditory modality, there was a significant decrease from baseline in the amplitude of the component of the evoked potential component occurring approximately 150 milliseconds after the stimulus. In the visual modality, there was a significant increase in the amplitude of the component appearing approximately 250 milliseconds following the stimulus. The finding that changes attributable to cocaine vary across stimulus modality indicates that cocaine may exert its effect in different ways on various sensory systems.

NR566 **Thursday May 17, 9:00 a.m. - 10:30 a.m.**

HIV SEROPREVALENCE AND RISK IN PSYCHIATRIC PATIENTS

Michael H. Sacks, M.D., Psychiatry, Cornell University, 525 East 68 Street, New York 10021; Helen Dermatis, Ph.D., Salome Looser-Ott, M.A., Samuel W. Perry III, M.D.

Educational Objectives:

To determine the seroprevalence of HIV infection and describe HIV risk behaviors in acute psychiatric inpatients

Summary:

AIM. To assess HIV seroprevalence and risk behaviors in acute psychiatric inpatients. *METHODS.* Four hundred consecutive acute psychiatric patients admitted to a hospital in NYC between the ages of 18-55 are being tested for HIV in an unlinked design using waste bloods remaining from admission screening tests. Prior to the "unlinking" basic demographic and risk behaviors included in the admission note are recorded. *RESULTS.* To date, four (6 percent) out of 66 subjects were found to be seropositive. Out of the four seropositive patients, three engaged in homosexual activities and one patient had a history of intravenous (IV) drug use. Three of the patients are physically asymptomatic and one patient has AIDS. Only two of the seropositive patients were aware of their HIV status at admission. Of the patients who did not know their status, one had a diagnosis of bipolar disorder and the other alcohol abuse. Of those patients who knew their status, one had a diagnosis of Xanax abuse, and the other major depression. AIDS risk behavior documented in 21 percent of the sample included IV drug use (10 percent), homosexual/bisexual behaviors (5 percent), combined IV drug use and multiple sexual contacts (3 percent), and combined homosexual behaviors and multiple sexual contacts (3 percent). *CONCLUSION.* These findings indicate that a substantial proportion of acute psychiatric inpatients engage in HIV risk behaviors, and of those patients who are seropositive, 50 percent may not be aware of their being positive. AIDS related services needed by psychiatric patients may vary as a function of psychiatric diagnosis.

References:

Sacks, MH; Perry, S; Graver, R; Shindeldecker, MA; Hall, S; HIV-Related Risk Behaviors in Acute Psychiatric Inpatients. *Hosp Comm Psychiatry* (in press).

Binder, RL: AIDS antibody tests on an inpatient psychiatry unit. *Am J Psychiatry* 144:176-180, 1987.

NR567 **Thursday May 17, 9:00 a.m. - 10:30 a.m.**

COGNITIVE IMPAIRMENT IN HIV INFECTED HEMOPHILIACS

Netta Horesh, Ph.D., Psychiatry, Tel Hashomer, 4 Rahavat Ilan, Givat Shemuel 51905, Israel; Elie Lepkifker, M.D., Sigmond Sancovici, M.D., David Varon, M.D., Suzy Floru, M.D., Uri Martinowitz, M.D.

Educational Objectives:

The findings suggest that cognitive changes may appear even in the early stages of HIV infection in asymptomatic hemophiliacs and support the hypothesis of an early CNS involvement by HIV. Therefore AZT treatment might be indicated already in the asymptomatic stage of the disease.

Summary:

The aim of the study was to determine whether cognitive impairment may be evidence in HIV positive asymptomatic hemophiliacs prior to the development of the full blown syndrome of AIDS. We compared the performance on Wechsler Intelligence Scale and the Bender Gastalt test among three groups of hemophilic patients: 6 AIDS patients, 30 asymptomatic HIV seropositive and 20 HIV seronegative patients. One-way ANOVA and Duncan test revealed that both AIDS and asymptomatic seropositive hemophiliacs exhibited in comparison to seronegatives psychomotor slowing and decreased performance on subtests of visual memory, fine motor control, visual-motor coordination, accuracy, integrative ability, concentration, and learning ability ($p<0.05$ - $p<0.01$). AIDS patients were more impaired than asymptomatic serpositives only for learning ability and concentration. In contrast to the low prevalence of cognitive impairment frequently reported in asymptomatic seropositive homosexuals and drug addicted, these results indicate that cognitive disturbances already appear in asymptomatic HIV seropositive hemophiliacs, suggesting an earlier CNS involvement by HIV in hemophiliacs. Therefore patients who are still clinically asymptomatic might benefit from Zidovudine (AZT) treatment during these early stages. Moreover, neuropsychological investigation is shown as a sensitive method in documenting early brain involvement in HIV infection.

References:

1. Faulstich ME: Psychiatric aspects of AIDS. *Am J Psychiatry* 144:551-556, 1987.
2. Harter DH: Neuropsychological status of asymptomatic individuals seropositive to HIV-1. *Ann Neurol* 26:589-591, 1989.

NR568 **Thursday May 17, 9:00 a.m. - 10:30 a.m.**

ANALYSIS OF P3 LATENCIES IN AIDS DEMENTIA

Leonard Handelsman, M.D., Psychiatry, Bronx VA Medical Center, 130 Kingsbridge Road, Bronx, NY 10468; Marvin J. Aronson, Ph.D., Thomas B. Horvath, M.D., Ann Peterson, M.S., Jeffrey Jacobson, M.D., Robert Ness, Ph.D.

Educational Objectives:

1. Analyze potentially useful information encoded in the P3 auditory event-related potential paradigm. 2. Apply this information to the stratification of HIV-related cognitive disorder.

Summary:

Information encoded in the P3 auditory event-related potential (AERP) has been used to analyze cognitive deficits in a wide range of neuropsychiatric disorders (1,2). Twenty HIV-, 10 HIV + asymptomatic, and 7 AIDS patients (without active medical debility) were administered the P3 paradigm using the following parameters: random presentation of oddball stimulation (beep) 15 percent; common tone 1000 HZ; oddball tone, 2000 HZ presented by standard program (Nicolet Pathfinder II). Results of three runs of 200 sweeps each were averaged from CZ-mastoid record. Subjects were well known to investigators and studied under conditions to eliminate the acute effects of intoxicating drugs. The latency of the first peak of the P3 complex (P3A) differed between HIV- and HIV + groups (ANOVA, $F=5.9$, df 2,34, $p<.006$, Neuman-Keuls $p<.05$). The P3A latency may be an early functional marker for CNS involvement in HIV infection. A principal components analysis of P3 paradigm middle and late latencies yielded two significant factors reflecting middle (P1,N1) and later (P2,N2) latencies; P3 latency was loaded similarly on both factors. The middle latency factor different between patients with AIDS and all asymptomatics (ANOVA, $F=6.0$, df 2,34 $p<.006$; Neuman-Keuls, $p<.05$). This suggests that AIDS patients were relatively deficient during the initial phases of cortical information processing (probably localizable to temporal cortex). Results could not be ascribed to age, drug use, or general medical condition.

References:

1. Pfefferbaum A, Wenegrat BG, Ford JM et al Clinical applications of the P3 component of event related potentials II. Dementia, depression and schizophrenia *Electroencephalog Clin Neuroophysiol* 59:104-124, 1984.
2. Goodin DS, Starr A, Chippendale T et al Sequential change in the P3 component of the auditory evoked potential in confusional states and dementing illnesses *Neurology* 33:1215-1218, 1982.

NR569 **Thursday May 17, 9:00 a.m. - 10:30 a.m.**

SPECT BRAIN IMAGING OF HIV PATIENTS WITH HMPAO

Scott W. Woods, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Stephanie O'Malley, Ph.D., Lawrence H. Price, M.D., Christopher J. McDougle, M.D., Paul B. Hoffer, M.D., Thomas R. Kosten, M.D.

Educational Objectives:

To understand the value of SPECT brain imaging with HMPAO in asymptomatic HIV+ patients.

Summary:

An abnormal pattern of relative subcortical hypermetabolism has been reported early in the course of HIV dementia due to infection using positron emission tomography (Rottenberg et al. Ann Neurol 1987;22:700). The present pilot study aimed to extend this report to HIV+PTS not yet manifesting clinical dementia using a more generally available SPECT rCBF technique.

After giving informed consent, eleven HIV+ (6M, 5F, 31 $\pm$ 8 yrs) and ten HIV- (5M,5F,36 $\pm$ 5 yrs) methadone-maintained PTS without clinical dementia participated. Although initially it appeared that the HIV-PTS would be an ideal control group, subsequent experience suggested a considerable risk of seroconversion in these PTS. Therefore, eleven healthy subjects (HS,8M,3F,29 $\pm$ 7 yrs) were also recruited. Subjects underwent SPECT scanning using the Strichman 810X Brain Imager after injection of 20 mCi Tc-99m HMPAO. Regions of interest corresponding to the striatum (STR) and the whole slices containing the STR (WS) were delineated by an operator blind to diagnosis.

The STR/WS ratio was increased in HIV+PTS compared to HS on the left (1.26 $\pm$ .08 vs. 1.19 $\pm$ .05,$p < .05$) but not on the right. HIV-PTS showed intermediate STR/WS ratios, which were not significantly different from either of the other groups. While there was considerable overlap between HIV+ and HS groups, two HIV+PTS had left STR/WS ratios 3 or more standard deviations above the HS mean.

The STR/WS ratio is in the normal range in most HIV+PTS on HMPAO scanning prior to the onset of clinically evident dementia. However, it appears possible to identify a sub-group of these PTS who have evidence of elevated relative left STR blood flow. These patients could be considered for prophylactic anti HIV pharmacotherapy.

References:

1. Neirinckx RD, Canning LR, Piper IM et al. Technetium-99m d, 1-HM-PAO: A new radiopharmaceutical for SPECT imaging of regional cerebral blood perfusion. J Nucl Med 1987; 28:191-202.

2. Rottenberg DA, Moeller JR, Strother SC, et al.: The metabolic pathology of the AIDS dementia complex. Ann Neurol 1987; 22:700-706.

NR570 **Thursday May 17, 9:00 a.m. - 10:30 a.m.**

NEUROANATOMICAL ABNORMALITIES IN LATE ONSET DEPRESSION

Anand Kumar, M.D., Psychiatry, Univ of Pennsylvania, 3615 Chestnut St Ralst, Pen., Philadelphia, PA 19014; David Yousem, M.D., Gary Gottlieb, M.D.

Educational Objectives:

To characterize Late Onset Depression as a distinct clinical entity with certain specific neuroanatomical abnormalities.

Summary:

We examined the relationship of Late Onset Depression, (LOD)-(unipolar depression with the first depressive episode occurring after age 60), to global cortical atrophy (GCA) and Deep White Matter (DWMH) and periventricular (PVH) hyperintensities on magnetic resonance imaging (MRI). Nine subjects with LOD who met DSM-III-R criteria for major depressive disorder (mean age $\pm$ SD = 74 $\pm$ 6, Hamilton rating scale score for depression 21 $\pm$ 5) and 9 healthy controls (mean age $\pm$ SD = 67 $\pm$ 6) were scanned using a 1.5 Telsa GE Signa scanner with head coil (TR = 3000, TE = 30 and 80 msec). All subjects were free of significant medical and neurologic illness including hypertension. MRI sections were 5mm thick and inteleaved, with no gaps, and only T2 weighted axial images were used in the analysis. Images were examined by a neuroradiologist (DY) blind to the clinical status of all subjects. Both DWMH and PVH were graded on a 0-3 scale (0 = absent, 3 = severe; Frazekas et al. AJNR, 1987), while GCA was rated on a 0-4 scale (0 = absent, 4 = severe; Largen et al., Biol Psy 1984). Eighty-eight percent of subjects with LOD were rated as having GCA grade 2 or greater as opposed to thirty-two percent of controls ($p < 0.05$, robust rank order test). Fifty-five percent of subjects with LOD and only eleven percent of controls were rated as displaying DWMH grade 2 or greater ($p < 0.05$). There were no differences in the rating of PVH between the two groups. These preliminary data demonstrate that LOD may be associated with certain specific neuroanatomical abnormalities that may be significant in the pathophysiology of depression.

References:

1) F. Fazekas, J.B. Chawluk, A. Alavi et al. MR Signal abnormalities at 1.5 T in Alzheimer's dementia and normal aging. AM J Neuro Radiol (1987) May/June 8:421-426

2) C.C. Coffey, G.S. Figiel, W.T. Djang et al. Leucoencephalopathy in elderly depressed patients referred for ECT. Biol Psy (1988) 24:143-161.

NR571 **Thursday May 17, 9:00 a.m. - 10:30 a.m.**

POSTURAL HYPOTENSION AND CHOLINERGIC THERAPY IN ALZHEIMER'S DISEASE

Nunzio Pomara, M.D., Geriatric Psychiatry, Nathan Kline Inst., Orangeburg, NY 10962; Dennis Deptula, Ph.D., Rajkumar R. Singh, Philip A. De Simone, Ph.D.

Educational Objectives:

To present data suggesting that a readily obtainable physiological measurement, e.g., postural change in blood pressure, may identify AD patients unlikely to respond to cholinomimetic therapy alone.

Summary:

No more than half of Alzheimer's disease (AD) patients who completed the dose-finding phase of double-blind multicenter trials of two cholinesterase inhibitors (THA and HP 029) demonstrated a therapeutic response, due, perhaps, to heterogeneity in underlying neurotransmitter abnormalities. Peripheral markers for a subgroup of cholinomimetic responders have not been established.

Several lines of evidence suggest central noradrenergic alterations as well as decreased reactivity of peripheral B-adrenergic receptors and impaired sympathetic nervous system response in AD. Since a blood pressure (BP) drop at the baroreceptors after postural changes elicits an immediate reflex and produces a strong sympathetic discharge which increases cardiac output and total peripheral vascular resistance through the release of norepinephrine and the activation of cardiovascular adrenergic receptors, we investigated whether responders to HP 029 differed from nonresponders in pretreatment postural BP and pulse changes.

All 23 subjects were medication-free and met NINCDS-ADRDA criteria for probable AD. Responders and nonresponders did not differ significantly in pretreatment supine BP or pulse. Moving from a supine to sitting position, nonresponders demonstrated a significantly greater pretreatment systolic BP decrease than responders ($p < .002$) and, in fact, only nonresponders exhibited a significant systolic BP drop. Neither group differed significantly in alterations in diastolic BP or pulse after postural changes.

References:

1) Murphy MF. HP 029: A New Anticholinesterase for Alzheimer's Disease. American College of Neuropsychopharmacology Abstracts of Panels and Posters. 28th Annual Meeting, Dec 10-15, 1989, Maui, Hawaii

2) Franceschi M, Ferini-Strambi L, Minicucci F, Sferrazza-Papa A, Smirna S. Signs of cardiac autonomic dysfunction during sleep in patients with Alzheimers disease. *Gerontology,* 32:327-334, 1986.

NR572 **Thursday May 17, 9:00 a.m. - 10:30 a.m.**

INCREASING RATE OF DEPRESSION IN YOUTH

Neal D. Ryan, M.D., CADS, WPIC, 3811 O'Hara Street, Pittsburgh, PA 15068; Douglas Williamson, B.S., Joaquim Puig-Antich, M.D., Satish Iyengar, Ph.D.

Educational Objectives:

Understand the evidence for an increasing rate of depression in youth and why this cannot be mediated solely through genetic mechanisms. Be able to discuss the limitations of cross sectional studies such as this compared to prospective longitudinal studies.

Summary:

Studies of major depression (MDD) in adults have demonstrated a secular (temporal) increase in lifetime rates of depression. This study is the first examining whether or not this increase is also seen in childhood forms of depressive disorder. Depressed and normal child probands were ascertained as part of a larger study of the familial transmission of depression. The probands were not further examined for this analysis, rather the patterns of age of onset of depression in their siblings as ascertained by direct interview of sibling and parent (86 siblings of normal probands and 77 siblings of MDD probands) were separately examined using life table statistical techniques (Cox proportional hazards model). Examining the pattern of first onset of major depression or bipolar disorder in the siblings of both normal probands and MDD probands there was a significant year of birth effect in both groups ($X^2 = 6.69$, $P < 0.01$, $X^2 = 7.46$, $P < 0.006$)-those born in more recent years had a higher cumulative risk of depression. The current data do not reveal whether this increase is a birth cohort effect (youth born more recently are at greater risk) or a period of effect (youth in the '80s experiencing more depression than same age youth in the '70s). The magnitude of these findings cannot be explained by genetic factors, suggesting that an environmental effect or an interaction of environment with genetics is responsible.

References:

Klerman GL, Lavori PW, Rice J, Reich T, Endicott J, Andreasen NC, Keller MB, Hirschfield RMA: Birth-Cohort Trends in Rates of Major Depressive Disorder Among Relatives of Patients with Affective Disorder. *Arch Gen Psychiatry,* July, 1985.

Gershon ES, Hamovit JH, Guroff JJ, Nurnberger JI: Birth-Cohort Changes in Manic and Depressive Disorders in Relatives of Bipolar and Schizoaffective Patients. *Arch Gen Psychiatry,* April 1987.

NR573 **Thursday May 17, 9:00 a.m. - 10:30 a.m.**

CHILDREN'S GRIEF DURING FIRST YEAR POST-PARENTAL DEATH

Elizabeth B. Weller, M.D., Psychiatry, The Ohio State University, 473 W. 12th Avenue, Columbus, OH 43210; Beth Groshans, M.A., Mary A. Fristad, Ph.D., Ronald A. Weller, M.D.

Educational Objectives:

To reach the audience about the course of bereavement during the first year post-parental death in prepubertal children.

Summary:

This study assessed longitudinal functioning of 38 bereaved prepubertal children. Psychiatric symptomatology was assessed at 1,6, and 13 months post-parental death. Subjects were compared with two age matched control groups: 38 hospitalized depressed children and 19 healthy community sample children. Children and parents were interviewed individually using standard instruments. Bereaved children experienced fewer symptoms than inpatient depressed children but more than healthy control children. Of 24 psychiatric symptoms assessed, nine were experienced by over 40% of bereaved children at one month. These include: sad affect (57%); irritability (57%); impaired concentration (46%); fatigue (43%); low self-esteem (41%); social withdrawal (41%); suicidal ideation (41%); separation anxiety (41%); loss of pleasure (40%). By six months, only two symptoms were endorsed by over 40% of children: sad affect (47%) and irritability (44%). By 13 months, no symptom was endorsed by over 40% of the bereaved children. Symptom endorsement peaked at one month for 53% of children, 35% peaked at six months; and 12%, at 13 months. Results indicate for a majority of bereaved children, symptoms subside during the first year post-parental death, however, one-third of children experience their most severe reactions six months post-loss.

References:

Elizur E & Kaffman M (1982) Children's bereavement reactions following death of the father: II Journal of the Amer Acad Child Psychiat, 21, 474-480

Van Eerdewegh MD, Bieri MD, Parilla RH, & Clayton PJ (1985) The bereaved child: variables influencing early pathology. British Journal of Psychiatry, 147, 1180-194.

NR574 **Thursday May 17, 9:00 a.m. - 10:30 a.m.**

CHILDREN'S RESPONSES TO THE CHALLENGER DISASTER

Lenore C. Terr, M.D., Psychiatry, Univ of California, 450 Sutter Suite 2534, San Francisco, CA 94108; Daniel Bloch, Ph.D., Michael Beat, M.D., John Reinhart, Ph.D., Suzanne Matayer

Educational Objectives:

1) To show what emotional effects are held in common between post-traumatic stress disorders and non-pathological reactions to distant disasters in children.

2) To show how children's and adolescent's responses after seeing a distant event are different from responses to hearing about the same event.

Summary:

Five to six weeks after the Challenger spacecraft exploded, 30 third graders and 30 tenth graders who had seen the spacecraft explode "live" on TV were randomly selected from schools in Concord, New Hampshire and given structured interviews lasting 45 minutes each. A control group of 30 randomly selected third graders and 30 randomly selected tenth graders from Porterville, California, who had first heard about the spacecraft explosion rather than seeing it, were given the same structured interview seven weeks after the disaster. The interviews were repeated 13 months after the disaster. A group of 10 children who had been at Cape Canavaral watching the disaster were also interviewed.

Striking findings in both East Coast and West Coast groups at 5-7 weeks included: 1) visualizations of the disaster, 2) related fears, and 3) fantasies. At 13 months post-disaster, visualization remained prominent, but fears and fantasies diminished. An important finding at 13-14 months were clear memories especially in groups that had watched the shuttle explode "live." Seeing the self in certain space appears to be an important kind of long term memory related to disaster.

NR575 **Thursday May 17, 9:00 a.m. - 10:30 a.m.**

PSYCHOSIS AND SUICIDAL BEHAVIOR IN CHILDREN

Richard Livingston, M.D., Psychiatry, Univ of AR. Med Sciences, 800 Marshal, Little Rock, AR 72202

Educational Objectives:

After this presentation, the learner will be able to list psychotic symptoms associated with depression and suicidal behavior in children.

Summary:

Major depression, bipolar disorder, schizophrenia and substance abuse, all conditions in which psychotic symptoms may occur, are known to be associated with suicide in adults and adolescents. The purpose of this study is to investigate associations of psychotic symptoms with suicidal behavior in prepubertal children. Ninety children ages 6-12 admitted consecutively to a psychiatric unit were interviewed using the Diagnostic Interview for Children and Adolescents, scored by a child psychiatrist blind to suicide status. The 90 included 17 who had attempted suicide and another 22 who had threatened suicide. All the attempters were dysphoric (i.e., had major depression or dysthymia), compared to half the threateners ($X^2 = 11.84$, $df = 1$, $p < .001$). Three attempters and 4 threateners reported auditory hallucinations, 1 attempter and 6 threateners ($X^2 = 17.4$, $df = 1$, $P < .0001$); all these were male. The frequency of these and other psychotic symptoms and their diagnostic correlates will also be presented.

Psychotic symptoms are associated with depressive disorders in this sample, and reported visual hallucinations are associated with a history of suicide attempts. Further study of psychosis as a risk factor is warranted.

References:

Pfeffer CR: The Suicidal Child, New York, Guilford Press, 1986

Pfeffer CR: Suicide Among Youth: Perspectives on Risk and Prevention. Washington, DC American Psychiatric Press, Inc. 1989

NR576 **Thursday May 17, 9:00 a.m. - 10:30 a.m.**

SPECIFICITY OF A BIOLOGICAL MARKER FOR TEMPERAMENT

Michel Maziade, M.D., Univ Laval Robert-Giffard, Centre De Recherche, 2601 de la Canardiere, Beauport, Quebec, Canada G1J 2G3; Louise Theriault, Ph.D., Robert Cote, Ph.D., Chantal Merette, Ph.D., Hughues Bernier, M.Ss., Georges LeBlond, Ph.D.

Educational Objectives:

To obtain a summary of present knowledge on child temperament as a risk factor for psychiatric disorders.

Summary:

Extreme temperament on Factor 1 (TF1) (a cluster of low adaptability, withdrawal from novelty, high emotional intensity, general negative mood) predisposes children to developing behavior disorders in the general population (Maziade et al, 1989). Children with such a temperament are also overrepresented in the child psychiatric population (Maziade et al, in press). However, all previous risk studies used a definition of temperament that was only phenomenological. The identification of a biological marker for specific temperament traits is imperative. In a sample of five- to nine-year-old children consecutively referred to the psychiatric clinic ($N = 70$), we found preliminary evidence of an association between difficult temperament on Factor 1 (TF1) and a decreased heart rate variability (taken as an index of physiological arousal) assessed in the laboratory. Blind measurements of the temperamental phenomenology, dimensions of family functioning, maternal mood, *DSM-III* diagnosis were made. Heart rate was recorded (30 min) during two separate visits to the laboratory, in rest conditions and during cognitive tasks. A multiple regression analysis, in which TF1, family behavior control and the "TF1 X family" interaction were entered as independent variables, showed a statistically significant effect of the "TF1 X family" interaction on cardiac variability (CV) ($R^2 = .25$, $F = 5.24$, $p < .005$). As hypothesized, low adaptability and withdrawal were correlated ($r = .47$, $p < .03$) to a decreased CV, depending on the type of family functioning. Other temperamental features and the clinical symptoms were not found associated with CV. The association with CV appears specific to TF1 and suggests that children with a difficult temperament on Factor 1 display a lower threshold of physiological arousal.

References:

(1) Maziade M et al. Significance of extreme temperament in infancy for clinical status in pre-school years: I. Value of extreme temperament at 4-8 months for predicting diagnosis at 4.7 years. *British Journal of Psychiatry,* 154, 535-543, 1989.

(2) Maziade M et al. Extreme temperament and diagnosis: Study in a consecutive child psychiatric sample. *Archives of General Psychiatry,* in press.

NR577 **Thursday May 17, 9:00 a.m. - 10:30 a.m.**

SUB-CORTICAL ABNORMALITIES IN AUTISM

Jacques Thivierge, M.D., CRULRG, 2106 De La Canardiere, Beauport, PQ, Canada G1J 2G3; Robert Cote, Ph.D., Michel Maziade, M.D

Educational Objectives:

To learn about the possible contribution of sub-cortical structures in autism. To learn about the possible usefulness of an additional way of recording BAER

Summary:

Previous studies of the neurobiology of autism using the brain stem auditory evoked response have given contradictory results. The present study considers two supplementary methods: (i) an ipsilateral masking procedure was added and (ii) the records of every child were compared to normative values (corrected for age and sex) and a large number of normal children. Twenty autistic (*DSM-III-R*) and 13 mentally retarded children (NV IQ<75) were assessed. The results show: (1) eighty percent of the autistic children have abnormal interpeak latencies (IPL) as compared to 15 percent of the mentally retarded, (2) the I-V and III-V IPL increased values are only seen in our autistic, (3) the ipsilateral masking procedure doubles the rate of detection of the higher brain stem abnormalities in the autistic children.

References:

Thievierge J et al: Brainstem auditory evoked potentials (BAER): Normative study in children and adults. Electroencephalogr Clin Neurophysiol, 68:479-484, 1987.

Gilbert C et al: Auditory brainstem responses in childhood psychosis. *J Autism Dev Disord,* 13(2):181-195, 1983.

NR578 **Thursday, May 17, 12 noon - 2:00 p.m.**

NONCOMPLIANCE OF PATIENTS HOSPITALIZED WITH AIDS

Michael Blumenfield, M.D., Psychiatry, NY Medical College, Room B-006 Psych. Institute, Valhalla, NY 10595; Jane Milazzo, R.N., Gary Wormser, M.D.

Summary:

Compliance with medical treatment is an important concern in the management of patients with a wide array of medical disorders. A chart review of 20 hospitalized AIDS patients was done to determine the degree of non-compliance and was compared to a control population of 20 male leukemics. The AIDS and leukemic patients had hospital stays averaging 45.8 and 41.0 days respectively.

Forty per cent of the AIDS patients refused blood tests compared with none of the leukemic patients. (P 0.002) Forty percent of the AIDS patients refused some medication, compared to 35 percent of the leukemics (P = NS). Twenty percent or more of the AIDS patients refused bone marrow, lumbar puncture, bronchoscopy, blood gasses, i.v. infusion or heparin lock placement, while only 0-5 percent of patients with leukemia had similar refusals.

Ninety percent of AIDS patients declined some procedure or treatment leading to mean refusal rate of 19.7 refusals per hundred hospital days. Compared to the controlled population of male leukemics, the mean rate of refusal per hospital day for AIDS patients was over four times greater than the leukemic patients. (P 0.05).

Reasons for non-compliance among hospitalized AIDS patients needs to be studied further especially the possibility that the attitudes of the treatment staff may influence the non-compliance.

NR579 **Thursday, May 17, 12 noon - 2:00 p.m.**

REACTIONS BY COCAINE ADDICTS TO HIV-SEROSTATUS

William W. Weddington, M.D., Psychiatry, University of IL, 912 S. Wood Street, Chicago, IL 60612; Charles A. Haertzen, Ph.D., Judith M. Hess, M.A., Barry S. Brown, Ph.D.

Summary:

We compared retention in treatment and psychological reactions during drug abuse treatment by 22 HIV-antibody positive, physically asymptomatic cocaine addicts to 22 matched HIV-seronegative cocaine addicts. All subjects participated in an outpatient clinical research project. There were no significant differences between groups in sociodemographics and psychiatric symptom scores on entrance or cocaine use except for route of administration ($X^2 = 11.59$, $df = 2$, $p < .005$). There were no significant differences among groups regarding being informed of serostatus and beginning treatment. There was a trend ($p = .079$) for more seropositives to complete treatment. Using end-point analysis to compare 11 seropositive subjects who completed a minimum of 2 weeks of treatment to a matched seronegative comparison group, there were no significant differences in mood states except for "anger/hostility" (interaction of group x time; $F = 2.24$, $df = 13/260$, $p < .05$). Informing drug abusers in treatment regarding positive HIV-serostatus was not associated with a lower treatment-retention rate or adverse psychological reactions when counseling regarding HIV issues was integrated with drug abuse treatment.

NR580 **Thursday, May 17, 12 noon - 2:00 p.m.**

BUSPIRONE TREATMENT FOR ANXIETY IN HIV INFECTION

Dan Alan Hirsch, Ph.D., Psychiatry, 767, Memorial Hospital, 1275 York Avenue, New York, NY 10021; Joanne Fishman, Ph.D., William Breitbart, M.D., Maurice Emery, D.Pharm, Jeffrey Schwimmer, M.D.

Summary:

Reactive anxiety is a profound problem for those individuals diagnosed as HIV seropositive. Both self-report and clinician-rated instruments confirm elevated levels of anxiety in this population. Traditional anti-anxiety therapies often produce adverse side effects (sedation) and the need for alternative treatment is crucial. This research examines the efficacy of a new anxiolytic treatment (buspirone) in HIV positive asymptomatic gay men. Ten of a planned sample of 50 HIV positive individuals have been entered into an eight-week double-blind, placebo-controlled clinical trial of buspirone. Weekly assessments evaluate a spectrum of both generalized and AIDS-specific psychological symptoms. The average study subject is a white, thirty-six-year-old gay male. On baseline assessment, two-thirds of the sample qualified for a psychiatric diagnosis of generalized anxiety disorder and 1/3 received a diagnosis of an adjustment disorder with anxious features. After eight weeks of trial participation, all placebo subjects (5/10) retained their *DSM-III-R* psychiatric diagnoses while the subjects (5/10) receiving buspirone could no longer be given a clinical diagnosis. Further, patient self-report data (anxiety scale on the Brief Symptom Inventory) confirm this reduction in distress ($r = .89$). The data suggest that a short trial with buspirone is effective for anxiety management in HIV positive men and the unique anxiolytic activity and low side effect profile of this medication make it an ideal agent for this population.

NR581 **Thursday, May 17, 12 noon - 2:00 p.m.**

FLUOXETINE TREATMENT FOR AIDS RELATED DEPRESSION

Daniel L. Creson, M.D., HIV + Clinic, UT Mental Sci Inst., 1300 Moursund, Houston, TX 77030; Eileen McGorry, R.N., John D. Roache, Ph.D., Melinda A. Stanley, Ph.D., Germaine B. Welch, M.A.

Summary:

HIV + infection and AIDS/ARC illnesses are associated with decreased energy, functional impairment, and major depression. Sedating side effects of tricyclic antidepressants limit their effectiveness for these patients. Nine male, HIV + patients with symptoms of depression were treated with fluoxetine (Prozac) 20mg, qd. Chart reviews showed the following results. Six of nine subjects completed four or more weeks of treatment. All six subjects showed global clinical improvement: three reported improved sleep, five increased energy, five mood improvement, and four decreased impairment of daily functioning. These improvements were noted despite declining physical health. Of three non-completing patients, one reported increased energy, improved mood and sleep patterns at the second week of treatment. Only two patients reported adverse effects of feeling jittery. Based on these data, a double-blind parallel-group placebo-controlled six week treatment outcome study was designed to verify whether fluoxetine (20, qd) decreases depressive symptoms without unwanted sedation in patients diagnosed with AIDS or ARC. Results for the first patient showed that fluoxetine decreased POMS anxiety and confusion ratings and increased vigor; scores for clinician-rated Hamilton Anxiety and Depression Scales were decreased. Study will show whether fluoxetine can improve functioning for AIDS/ARC patients.

NR582 **Thursday, May 17, 12 noon - 2:00 p.m.**

EFFECT OF PSYCHOEDUCATION AFTER HIV TESTING

Baruch Fishman, Ph.D., Psychiatry, Cornell Medical Center, c/o Sam Perry 525 E. 68th St., New York, NY 10012

Summary:

Objective: Assess the differential effectiveness of three psychoeducational interventions in reducing emotional distress among at-risk individuals seeking HIV testing.

Methods: Following notification of HIV antibody test results, 214 seronegative (HIV-) and 94 seropositive (HIV+) physically asymptomatic males and females (CDC II/III) were randomly assigned to 1) standard counseling (SC), or 2) a psychoeducational interactive video program or 3) six sessions of brief cognitive-behavioral stress prevention training (SC+SPT). Standardized measures of anxiety, depression, and psychiatric symptoms were assessed before and three months after notification and analyzed with multiple analyses of variance (MANOVA).

Results: Subjects were sociodemographically heterogeneous and represented all risk behaviors (gay/bisexual men, heterosexuals, former intravenous drug users). Mean distress measures of *all* subjects were significantly reduced at follow-up without an overall serology effect. MANOVA revealed that change scores of HIV+ and more emotionally distressed HIV- were significantly greater among those receiving SPT.

Conclusions: These findings support the value of psychoeducational interventions for individuals who seek HIV testing. SPT is essentially effective for HIV+ and for those HIV-with greater distress.

NR583 **Thursday, May 17, 12 noon - 2:00 p.m.**

EFFECT OF HIV TESTING ON HOMOSEXUAL RISK BEHAVIORS

Lawrence B. Jacobsberg, M.D., Psychiatry, Cornell Medical Center, 525 E. 68th Street, New York, NY 10012

Summary:

Objective: To determine the effects of HIV antibody testing with counseling on HIV-related risk behaviors among gay and bisexual men.

Methods: A self-report risk behavior questionnaire was given to 347 physically asymptomatic gay/bisexual men (CDC II/III) when they voluntarily sought confidential HIV testing in a private office setting (T1) and when they returned for follow-up three (T2) and six (T3) months after notification.

Results: Among 122 HIV+ and 225 HIV- subjects, number of sexual partners during the past month did not significantly change after serological notification (T1: none = 18 percent; 1 = 37 percent, 2 = 17 percent; >2 = 28 percent; T2: none = 20 percent; 1 = 40 percent; 2 = 19 percent; >2 = 22 percent; T3: none = 15 percent, 1 = 39 percent; 2 = 20 percent; 2 = 26 percent). Similarly, rates of any anal intercourse during past month did not significantly change (T1: 37 percent; T2: 31 percent; T3: 34 percent). Notification of serological status did not affect rates of high-risk behaviors (e.g. anal intercourse without condom), which remained generally low.

Conclusions: Effects of HIV testing on risk behaviors can be studied in a completely confidential setting without notification of others. Most gay/bisexual males have reduced high-risk behaviors prior to voluntary HIV testing, but remain sexually active. Knowledge of being HIV+ or HIV- does not further reduce or increase risk behaviors.

NR584 **Thursday, May 17, 12 noon - 2:00 p.m.**

PSYCHOSOCIAL VARIABLES AND CD 4 CELLS IN HIV + ADULTS

Samuel W. Perry III, M.D., Psychiatry, Cornell Medical Center, 525 E. 68th Street, New York, NY 10012

Summary:

Objective: Determine if psychosocial factors correlate with total CD4, currently the best predictor of disease progression among HIV-infected individuals (HIV+).

Methods. Among 108 males and eight females (CDC II/III), Pearson correlations were obtained between entry measures of total CD4 and standardized measures of psychiatric symptoms, anxiety, depression, bereavement, hopelessness, social support, hardiness, health attributional style, and stressful life events. Psychiatric diagnoses were obtained by standardized clinical ratings. Total CD4 and emotional distress were assessed three months later. HIV+ on zidovudine were excluded.

Results: Significant correlations were found at entry between total CD4 and both state anxiety and death(s) during the past two years of a spouse or close sexual partner; however, none of the 22 psychosocial factors at entry revealed a significant effect on total CD4 three months later after controlling for the initial immune measures by hierarchal regression.

Conclusion: Among HIV+, psychosocial factors do not directly affect total CD4. Caution is necessary before attributing disease progression to the direct effects of emotional distress on the immune system.

NR585 **Thursday, May 17, 12 noon - 2:00 p.m.**

DEPRESSIVE SYMPTOMS AFTER HIV ANTIBODY TESTING

Allen J. Frances, M.D., Psychiatry, Cornell Medical Center, 525 E. 68th Street, New York, NY 10012

Summary:

Objective: To determine the rate, course, and predictors of depressive symptoms after notification of HIV serological status.

Methods: Standardized clinical ratings of current and lifetime depressive illness (SCID) were obtained at entry (T1) on 312 adults voluntarily seeking HIV antibody testing with psychoeducational counseling. The physically asymptomatic (CDC II/III) subjects were assessed two (T2) and six (T3) months later with the Beck Depression Inventory (BDI).

Results: Mean BDI scores decreased from entry (T1: 9.49 +/−8.00; T2: 5.44 +/− 6.82; T3: 6.51 +/− 7.37), without significant relation to serological status. Even among the 40 subjects with a current depressive illness diagnosis at entry, the same pattern was observed (T1: 18.18 +/− 10.29; T2: 9.90 +/− 11.02; T3: 13.85 +/− 10.27). The subjects with a lifetime history but no current episode of depressive illness at T1 were more likely to have a BDI>12 at T3 than subjects without either a current or lifetime depressive illness at T1 (chi square = 5.7, df = 1, p = .02).

Conclusions: Depressive symptoms generally decrease during the first six months after HIV testing with adequate counseling even among the subpopulation with depressive symptoms prior to serological notification. Depressive symptoms occur more frequently at six months among subjects with a prior history of depression. These findings help identify notified HIV testing subjects at risk for psychiatric morbidity.

NR586 **Thursday, May 17, 12 noon - 2:00 p.m.**

NEUROLEPTIC-INDUCED EPS IN PATIENTS WITH AIDS ENCEPHALOPATHY

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Summary:

A retrospective chart review was undertaken to study the acute occurrence and severity of EPS in patients with AIDS encephalopathy compared to controls in response to treatment with neuroleptics. Cases and controls with neuroleptic exposure of less than one month were included. Cases with focal brain lesions, history of parkinsonian features, meningitis, and street drug use immediately prior to admission were excluded. Controls were patients admitted for acute psychosis who were age- and sex-matched and had no known risk factors for HIV. Patients were stratified by neuroleptic dose on mg/kg basis. Neuroleptic dose was adjusted for by conversion to chlorpromazine equivalents. Results were assessed by rating the presence or absence of EPS in response to neuroleptics and by grading EPS severity using the Hoehn and Yahr scale. Of 804 charts reviewed, 31 patients with AIDS encephalopathy and 32 controls met the study criteria. In our sample, AIDS patients were found to have a 2.4 fold greater likelihood of having EPS in response to neuroleptic therapy than controls (Mantel Haenszel odds ratio = 2.41, 95 percent confidence interval = 0.68 - 8.61).

The most common type of EPS noted in AIDS patients was rigidity (43 percent of cases), followed by akathisia (35 percent) and dystonia (22 percent). When present, EPS tended to be more severe in AIDS patients (Hoehn and Yahr scores of 3 and 4).

These preliminary results indicate a need for caution in using neuroleptics in AIDS patients and a heightened awareness as to the occurrence of EPS in this group.

NR587 **Thursday, May 17, 12 noon - 2:00 p.m.**

INCIDENCE OF PSYCHIATRIC DISORDER IN HIV INFECTION

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Summary:

Objective. To examine the one year incidence and clinical correlates of psychiatric disorder in human immunodeficiency virus (HIV) infection. We have observed elevated lifetime prevalences of selected psychiatric disorders in HIV illness, which often preceded the AIDS epidemic, suggesting a vulnerability that might be reflected in a high annual incidence of psychiatric conditions. *Method*. Subjects were ambulatory HIV+ and HIV- homosexual men (N = 61) participating in a longitudinal cohort study, who were examined at baseline and annually with the Diagnostic Interview Schedule (DIS-III-A), neuropsychologic (NP) testing, and magnetic resonance imaging (MRI). *Results*. The *annual incidence* of psychiatric diagnoses were:

Diagnosis	CDC IV (N = 11) %	CDC II/III (N = 32) %	HIV- (N = 18) %
Major Depression	0.0	12.5	5.6
Gen. Anxiety Disorder	18.2	15.0	27.8
Alcohol Use Disorder	0.0	6.3	5.6

Overall, 2 of 5 incident major depressive episodes and 6 of 12 cases of generalized anxiety were recurrent disorders, whereas all of alcohol use disorder was recurrent rather than new onset. NP impairment and MRI abnormality at baseline did not predict incident cases of psychiatric disorder. *Conclusions*. Recurrent *and* new onset psychiatric disorder may characterize men at high risk for AIDS. These rates do not vary among AIDS, asymptomatically infected, and uninfected men, and all groups warrant careful assessment.

NR588 **Thursday, May 17, 12 noon - 2:00 p.m.**

QUANTITATIVE SPECT IN AIDS DEMENTIA

Gordon H. Harris, M.S., Psychiatry, Johns Hopkins, 600 N. Wolfe St. Meyer 3-166, Baltimore, M.D. 21205; Godfrey D. Pearlson, M.D., Frederick Schaerf, M.D., Justin C. McArthur, M.D., Edwaldo E. Camargo, M.D., Jonathan M. Links, Ph.D., Norman D. LaFrance, M.D.

Summary:

Nine mildly demented HIV-1 seropositive men without evidence of CNS opportunistic infection, eight cognitively normal HIV-1 seropositive men, six at risk gay men who were sero-negative, and eight uninfected neurologically normal controls were studied using I-123-IMP single photon emission computed tomography (SPECT). Quantitative data were generated from transverse SPECT slices at the basal ganglia level, using a recently developed analysis method. This required outlining the transverse brain image with a cursor. The program then defined a cortical ring 2cm inside this brain boundary.

Cortical samples ($1cm^2$) in the mid portion of these boundaries at 6° were created. An index of right/left cortical asymmetry showed that most patients with HIV-1-related dementia and a proportion of HIV-1-positive nondemented individuals had values two or more standard deviations from the normal control mean. The percentages of abnormal scans in both patient groups were significantly higher than both comparison groups ($p<.05$), by chi-square.

These data may reflect heterogeneous perfusion irregularities resulting from CNS infection by HIV. The power of these asymmetries to predict the later occurrence of dementia in currently cognitively normal HIV-1 carriers remains to be determined.

NR589 **Thursday, May 17, 12 noon - 2:00 p.m.**

P3 AS A MARKER OF COGNITIVE CHANGE IN HIV DEMENTIA

Leonard Handelsman, M.D., Psychiatry, Bronx VA Medical Center, 130 Kingsbridge Road, Bronx, NY 10468; Marvin J. Aronson, Ph.D., Thomas B. Horvath, M.D., Ann Peterson, M.S., Karen Holloway, M.D., Jill Wiener, M.D.

Summary:

P3 latency has been used to analyze cognitive deficits in neuropsychiatric disorders(1,2). As part of a broader cross-sectional study of HIV dementia in drug users, 15 subjects had repeat P3 studies from 3-15 months after the initial assessment. The P3 paradigm was a standard auditory oddball sequence: 15% oddball: common tone, 1000 Hz, oddball tone, 2000 Hz. Five subjects with AIDS were judged by clinical consensus of a psychiatrist and neurologist to have experienced noticeable cognitive changes (4 worse, 1 improved). Ten other subjects (6 HIV+, 4 HIV-) were judged to be clinically stable. The difference between tests within subjects in P3 latency in "stable" subjects was small: mean = 6 msec; range -28 to +9. In contrast, the patients judged to have changed manifested substantial changes in P3 latency: (-79) msec for the improved subject and from +35 to +193 msec for the worsening subjects. These results suggest that P3 latency is stable across measurements even in the context of confounding factors associated with drug use when clinical status is judged to be stable. The power to detect (or cross-validate) small changes in cognitive status is high. In contrast, the robust changes in P3 in clinically changing subjects suggest the usefulness of the P3 latency as a *longitudinal* marker of cognitive function in advanced HIV disease.

NR590 **Thursday, May 17, 12 noon - 2:00 p.m.**

MALE PROSTITUTES AS A VECTOR FOR HIV TO HETEROSEXUALS

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Summary:

A representative sample of 211 New Orleans male street prostitutes were interviewed and tested for antibodies to the Human Immunodeficiency Virus (HIV). The personal sexual orientation and lifestyle characteristics of the sample as well as their specific sex and drug use practices were evaluated to determine the prostitute's potential as a vector for transmission of HIV into populations with currently low infection rates. Additionally, information about the customers of the prostitutes was obtained from the sample. The period of prevalence of HIV in the sample was high (175 per 1,000). Many of the male prostitutes had wives or girlfriends, some of whom were prostitutes themselves. The subjects reported that a majority of their customers were bisexual or heterosexual and many were thought to be married. Results from the study support the argument that male prostitutes serve as a bridge for HIV infection into the heterosexual and bisexual male population and to women.

NR591 **Thursday, May 17, 12 noon - 2:00 p.m.**

WHICH ROLE DOES DRUG USE PLAY ON THE MENTAL STATE OF HIV PATIENTS?

Georg Pakesch, M.D., Psychiatry, University of Vienna, Wahringer Gurtel 18-20, 1090 Vienna, Austria; Norbert Loimer, M.D., Dorothea Pfersmann, M.D., Josef Grunberger, M.D., Klaus Guggenberger, M.D.

Summary:

Controversial reports exist about the extent and the incidence of the AIDS dementia complex. The aim of this study was to investigate the extent and the frequency of cognitive impairment and thymopsychic changes in drug addicted HIV-patients.

In the study 42 patients age between 22 and 50 have been included. 16 patients showed AIDS group II/III, 26 group IV (CDC). Noopsychic performance has been measured by PMT-Raven and MWT, visual retention by Benton-Test and specifical memory by the Numerical Memory Test. Attention and concentration was objectivated by Alphabetic Reaction Test. Personality was assessed by MMPI, state and trait anxiety by STAI, 1 and 2. By means of a clinical psychiatric exploration psychopathological features were documented using AMDP and BPRS, depressed mood was rated by HAMD. The results were compared to a group of normal probands (n = 100) and a group of HIV-negative i.v. drug users (n = 31).

The results showed impairment of visual retention, specifical memory and concentration, which reached statistical significance only compared to the norm population, but not to the control group of HIV-negative i.v. drug users. Depressive symptoms were found to be higher in HIV-patients than in the control groups. These results suggest that as reason for changes of the mental state of HIV-patients not only the HIV-infection but also drug use and depression has to be taken into consideration.

NR592 **Thursday, May 17, 12 noon - 2:00 p.m.**

HIV RISK AND COCAINE USE IN ALCOHOLIC INPATIENTS

John C. Mahler, M.D., Psychiatry, NY Hosp. Cornell Med Ctr, 21 Bloomingdale Road, White Plains, NY 10605; Donna Yi, M.D., Helen Dermatis, Ph.D., Michael H. Sacks, M.D.

Summary:

Introduction- In a recent study of HIV seroprevalence in opiate addicts, Chaisson et al reported an association between IV cocaine use and risk for HIV seropositivity. Schleifer et al recently found that HIV seropositivity in inner city alcoholic men was associated with intravenous drug use. To our knowledge no study has examined alcohol dependent patients to determine whether coexistent cocaine dependence is associated with HIV risk behaviors and seroprevalence. *Methods-* A standardized questionnaire for assessment of HIV risk behaviors was administered to 25 consecutive admission to a 28 day inpatient alcohol treatment program (14 males, 11 females). All patients met DSM-III-R criteria for alcohol dependence on admission and sixty percent were also diagnosed with cocaine dependence. HIV risk behaviors in alcoholic patients with and without cocaine dependence were compared using Chi-square analyses. *Results* Eighty percent of alcoholic patients with cocaine dependence engaged in HIV risk behaviors compared to 30% of patients without cocaine dependence ($df = 1$, $X^2 = 4.64$, $p < 0.05$). HIV risk behaviors in alcohol and cocaine dependent patients included: i) heterosexual intercourse without condoms with prostitutes, multiple partners, and known or suspected intravenous drug users (53%); and ii) intravenous drug use (33%). Patients with cocaine dependence had significantly more sexual partners in the past two years with 80% of cocaine dependent patients having 3 or more partners ($df = 1$, $X^2 = 4.64$, $p < 0.05$). *Conclusion-* These preliminary data suggest that cocaine dependence is associated with significantly higher rates of HIV risk behaviors in patients with alcohol dependence. Additional findings on HIV seroprevalence and risk behaviors will be presented from this ongoing study of 100 subjects.

NR593 **Thursday, May 17, 12 noon - 2:00 p.m.**

DEMENTIA AND MOOD DISORDER IN HIV+ GAY MEN

Robert A. Bornstein, Ph.D., Psychiatry, Ohio State University, 473 W. 12th Avenue, Columbus, OH 43210; Henry A. Nasrallah, M.D., Patricia Rosenberger, Ph.D., Michael Para, M.D., Robert Fass, M.D.

Summary:

The incidence of neuropsychological deficit and mood disorders was examined in 25 asymptomatic HIV+ patients and 17 subjects with more advanced disease. The neuropsychological test battery included measures of concept formation, memory, vigilance, and reaction time. Patients were classified as impaired if they obtained scores that were 1 SD or more below normative levels on 3 or more tests. The current and lifetime incidence of mood disorders and alcohol/drug abuse was based on the SCID-R. It was found that 25% of the asymptomatic patients and 56% of the ARC/AIDS patients were rated as impaired ($X^2 = p < .05$). The most frequent abnormalities were observed on the Paced Auditory Serial Addition Test. The groups did not differ in terms of current or lifetime alcohol/drug abuse, nor current mood disorder. Forty-four percent of the asymptomatic patients and 76% of the ARC/AIDS had lifetime histories of mood disorders (X^2 $p < .025$). Episodes of mood disorder often were associated with HIV diagnosis or disease progression. These data suggest that a significant proportion (25%) of asymptomatic HIV+ patients demonstrate mild but consistent neuropsychological abnormalities. The greater incidence of these deficits in the ARC/AIDS patients cannot be attributed to alcohol or drug use. Further, the higher incidence of lifetime mood disorders in the ARC/AIDS patients suggests that previous history of mood disorder may have a role in disease progression.

NR594 **Thursday, May 17, 12 noon - 2:00 p.m.**

SELF-DEFEATING PATTERN ANALYSIS IN FOCUSED THERAPY

Jody Lanard, M.D., Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139; J. Christopher Perry, M.D.

Summary:

Many patients at high risk for acquiring Human Immunodeficiency Virus report unprotected sexual relations despite knowledge of HIV transmission factors. Identifiable self-defeating patterns may underlie refractory high risk sexual behavior. To begin assessing this premise, Perry developed the Self-Defeating Pattern Scales representing six patterns from the literature. They include self-defeating behavior in the service of: 1) harm avoidance, 2) guilt alleviation, 3) blaming/punishing others, 4) resisting others, 5) sabotaging success, and 6) attaining love/sex/attachment. Twenty-four random transcribed Relationship Anecdote Paradigm interviews (developed by Luborsky) were rated for the patterns. Inter-rater reliability ranged from kappas of .65 to .81 for patterns 1-4. Prevalence was too low to calculate kappas for patterns five and six. Pattern identification was used to focus treatment of a woman having unprotected sexual relations with her AIDS-afflicted lover, despite previous psychotherapy and adequate AIDS knowledge. This patient's patterns associated with sexual risk-taking alleviating guilt and blaming/punishing others - were identified by rating two audiotaped early sessions, and targeted thereafter. She stopped having unprotected sex within six sessions, and is HIV-antibody negative fourteen months later. Scored sessions during the next year revealed a decrease in self-defeating behavior for the two patterns (slope = -.04 and -.096 behaviors/session, respectively). Cognitive reflection and affective awareness increased measurably for pattern two. The significance and effectiveness of this approach should be evaluated by: 1) assessing prevalence and stability of the patterns in high-risk persons, and 2) performing a pilot study of the focused intervention.

NR595 **Thursday, May 17, 12 noon - 2:00 p.m.**

PSYCHIATRIC MORBIDITY IN AIDS MEDICAL INPATIENTS

Stephen Snyder, M.D., Psychiatry, Mount Sinai Med Center, 317 East 17 St. 508 Fierman, New York, NY 10003; Andrew Reyner, M.D., Eileen Bogursky, Henry Gomez, James J. Strain, M.D.

Summary:

INTRODUCTION: Although psychiatric morbidity in medical inpatients with AIDS is known to be widespread, no study has prospectively determined its nature or frequency. *METHOD*: Forty-two acute medical admissions with AIDS were interviewed using DSM-III-R criteria; objective ratings of morbidity (Mini-Mental State, CES-D, Speilberger State Anxiety Scale) were obtained. *RESULTS*: Twenty-seven patients (64.3%) had current Axis I disorders. Most common were Organic Mental Disorders (OMD's — N = 21). DSM-III-R Major Depression was uncommon (N = 1); most full depressive syndromes occurred in patients with OMD's such as Organic Mood Disorder (N = 5); partial depressive syndromes were most often diagnosed as Adjustment Disorder (N = 5). Mean Mini-Mental State score was 24.2 + 7.03, mean CES-D was 20.9 + 17.0. Recent functional status (Karnofsky Rating Scale) was positively correlated with cognitive capacity (Mini-Mental state: $r = .374$, $p < .05$) and negatively with anxiety (Speilberger: $r = -.533$, $p < .01$), but not with depression (CES-D). *DISCUSSION*: This study is the first to prospectively demonstrate serious mental disorders in the majority of a sample of AIDS medical inpatients. High levels of both cognitive impairment and depression were found. The results suggest that the concepts of Organic Mood Disorder and Adjustment Disorder may be more useful than Major Depression in understanding mood disturbance in this population. Poor recent functional status may be an important predictor of both anxiety and cognitive impairment.

NR596 **Thursday, May 17, 12 noon - 2:00 p.m.**

SCID DIAGNOSIS IN PSYCHOGENIC SEIZURE PATIENTS

Stephen Snyder, M.D., Psychiatry, Beth Israel Med. Center, 317 East 17 St. 508 Fierman, New York, NY 10003; James Rowan, M.D., David Rosenbaum, M.D., Daniel Luciano, M.D., Robin Fein, M.S.W.

Summary:

INTRODUCTION: Although major psychopathology is known to underlie psychogenic seizures, previous studies have not used structured diagnostic instruments sensitive to a broad enough range of mental disorders. *METHOD*: Ten patients with psychogenic seizures confirmed by intensive video-EEG monitoring were evaluated using the Structured Clinical Interview for DSM-III-R (SCID). *RESULTS*: Three patients were diagnosed as undifferentiated somatoform disorder. Seven met criteria for at least one mental disorder other than a somatoform disorder. All seven had agoraphobic symptoms and qualified for either panic disorder with agoraphobia or agoraphobia without history of panic disorder. Mood disorders (N = 5) were also prominent, as was alcohol abuse in remission (N = 3) and somatization disorder (N = 3). In seven of the ten patients, multiple other conversion symptoms in addition to psychogenic seizures were present. Phobic symptoms were elicited in eight patients. *DISCUSSION*: In this pilot sample, psychogenic seizures commonly appeared to be embedded in a complex illness which characteristically included phobic behavior and multiple other somatic and conversion symptoms, as well as anxiety, mood or substance use disorders or somatization disorder. To our knowledge, the presence of phobic behaviors and multiple conversion symptoms have not previously been reported in any study of this kind. Theoretical and treatment implications of the findings are explored.

NR598 **Thursday, May 17, 12 noon - 2:00 p.m.**

TREATMENT VARIABLES IN ADOLESCENT SUBSTANCE ABUSE

Yifrah Kaminer, M.D., Western Psychiatric Adapt, 3811 O'Hara Street, Pittsburgh, PA 15213; Oscar G. Bukstein, M.D., Ralph Tarter, Ph.D., Mostefa A. Kabene, Ph.D.

Summary:

A comparison between completers versus noncompleters in an inpatient treatment program for adolescent substance abusers wtih comorbid psychiatric disorders will be reported.

The dropout rate of patients from substance abuse programs is consensually recognized to be very high and needs to be dramatically reduced in order to decrease relapse. This paper reports on a nine month prospective study of consecutive discharges in an inpatient treatment program for adolescent substance abusers with comorbid psychiatric disorders. A discharge-dropout interview was administered on two groups of patients upon discharge: a) those leaving on term and b) those leaving against medical advice. The interview, designed to evaluate patient's assessment of their treatment program, probed the following domains: treatment variables and benefits; program regulations and structure; interpersonal variables and milieu. Also, environmental variables and patient variables were evaluated. The differences between completers and noncompleters and suggestions for prevention-intervention in this age group among dually diagnosed adolescents are discussed.

NR599 **Thursday, May 17, 12 noon - 2:00 p.m.**

METHYLPHENIDATE THERAPY OF AGGRESSIVE ADOLESCENTS

Stuart L. Kaplan, M.D., Psych Center, Rockland Children's, Convent Road, Orangeburg, NY 10962; Joan Busner, Ph.D., Samuel Kupietz, Ph.D., Evelyn Wasserman, M.D., Boris Segal, M.D.

Summary:

To study the effects of methylphenidate on aggression in aggressive adolescents, 30 mgs methylphenidate BID was administered to 6 inpatient and 3 outpatient male adolescents who met DSM-III criteria, based on structured psychiatric interview, for both aggressive conduct disorder and ADDH. Subjects' mean age = 14.4 years (SD = .88); mean Tanner Stage = 3.4 (SD = 1.7); mean IQ = 86.0 (SD = 6.0); mean weight = 65 kgs (SD = 10.3). The first three subjects were studied in open design; the next six subjects were studied in a placebo controlled double blind crossover design. Dependent variables were the Adolescent Antisocial Behavior Checklist (AABC) and the Connors 39 item TRS. RESULTS. The open subjects improved. Repeated measures oneway analyses of variance of the 6 double blind subjects indicated significant aggression reduction of AABC total and 4 (of 6) subscales under methylphenidate compared to baseline or placebo conditions ($p's < .05$); Connors Hyperactivity and Aggression factor scores analyses were in the same direction, but were not significant. The results suggest that methylphenidate may be efficacious in the treatment of aggression in aggressive conduct disordered adolescents who also meet criteria for ADDH.

NR600 **Thursday, May 17, 12 noon - 2:00 p.m.**

THE EMPIRICAL STUDY OF DEFENSE AND COPING IN PRESCHOOLERS

Michael P. Bond, M.D., Psychiatry, Jewish General Hospital, 4333 Cote Ste Catherine Road, Montreal, Quebec, Canada H3T 1E4; Margaret Schibuk, M.D., Rachelle Bouffard, M.D.

Summary:

The authors developed a semi-structured play interview to study the regulatory processes, or defense and coping mechanisms, of preschool children. Specific stories and situations were used to serve as standardized stimuli in a video-taped semi-structured interview. The tapes were then evaluated for description of regulatory processes specific to this age group, as well as classic defense mechanisms well described in adulthood. A glossary of operational definitions with exemplars was then created. The regulatory processes are hypothesized to cluster into functionally defined categories, and a manual was constructed defining the adult and child processes in each of these clusters. The interview, manual, and scoring sheet comprise an instrument which allows for the assessment of defense and coping mechanisms of childhood, and the testing of interrater reliability. Further research with this instrument will permit longitudinal study of the development of defense and coping mechanisms in childhood.

NR601 **Thursday, May 17, 12 noon - 2:00 p.m.**

EFFECTIVENESS OF DAY TREATMENT FOR CHILDREN

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Summary:

Twenty-three consecutive admission to a psychodynamically-oriented day treatment program were assessed. A paired t-test was used to compare pretest-posttest scores. Children were 6 to 12 years old and had a diagnosis of: oppositional defiant disorder, attention deficit disorder, conduct disorder or depression. Discharge scores revealed a significant improvement on all standardized scales for behavior ($p<.0001$), academics ($p<.05$), personality measures ($p<.0001$) and family measures ($p<.05$). A one way analysis of variance showed that parents reported a significantly greater improvement than both teachers and primary therapists ($p<.000$). Although all children showed improvement, parents reported significantly lower ($p<0.05$) improvement rates for children with conduct disorder as compared to others. Teachers found that younger boys (aged 6-9) improved significantly more ($p<.05$) than older boys (aged 10-12) in total behavior score and externalizing subscores of the Revised Child Behavior Profile. Multiple regression analyses were carried out to determine which variables contribute most to behavioral improvement. At discharge, 87% of children were reintegrated back into regular school as compared to only 17% who were attending regular school at admission. Results of the study will be discussed in light of whether day treatment program development should be encouraged and which children are best suited for these programs.

NR602 **Thursday, May 17, 12 noon - 2:00 p.m.**

INTERPERSONAL PROBLEMS IN ADULT CHILDREN OF DIVORCE

Robert A. Bolgar, M.D., Psychiatry, Bradley Hospital, 1011 Veterans Memorial Parkway, East Providence, RI 02915; Hallie Frank, Ph.D., Joel Paris, M.D.

Summary:

Long-term outcome of children of divorce has been widely addressed in the clinical literature but empirical studies have been few. This research examines whether young adult children of divorce are troubled by more interpersonal problems and whether particular divorce experiences are associated with these problems. Sex differences are also considered. One hundred fifty-five university students from divorced families and 253 students from intact families were administered the Inventory of Interpersonal Problems, which contains six subscales representing common interpersonal difficulties. Parent divorce significantly differentiated the sample on one subscale: Hard to be Submissive. Hypothesized differences on interpersonal intimacy and excessive responsibility were not found. The results were the same for male and female children of divorce. Pre- and post-divorce variables, such as custody, age of the child, and parental hostility, contact, and remarriage, all separated out subgroups of children of divorce reporting more interpersonal problems: subgroups of daughters of divorce tended to report difficulties with intimacy and overcontrol, sons of divorce tended to reported difficulties with submission, and both sexes reported difficulties with sociability. Since divorce is so common, understanding its long-term effects is important for clinical work.

NR603 **Thursday, May 17, 12 noon - 2:00 p.m.**

BORDERLINE PERSONALITY DISORDER IN ADOLESCENCE

William L. Grapentine, M.D., Bradley Hospital, 1011 Veterans Memorial Parkway, Riverside, RI 02915; C. Picariello

Summary:

A study has been undertaken to examine whether the diagnosis of borderline personality disorder (BPD) can be validated in an adolescent population. Using two separate instruments (Diagnostic Interview for Borderlines (DIB) and DSM) consecutively - admitted hospitalized female adolescents (ages 13.0 - 17.11) were diagnosed as borderline or non-borderline. Each group was then evaluated for evidence of depression, substance use disorder, and PTSD using the DICA and for a history of physical/sexual abuse, delinquent behavior, and self-injury using structured questionnaires. Forty-one patients were admitted to the study; 17 were diagnosed as borderline, 24 as non-borderline. The two groups did not differ significantly regarding race, age, SES, IQ, or severity of illness. Depression was prevalent in both groups (30/41). The borderline population was significantly more likely ($p<.05$) to carry diagnoses of substance use disorder and PTSD and histories of physical/sexual abuse, delinquent acts, and self-injurious behaviors of all types. Results suggest that the diagnosis of BPD is valid in the adolescent age period and that comorbid diagnoses, historical events, and significant behaviors are similar to those found in adults.

NR604 **Thursday, May 17, 12 noon - 2:00 p.m.**

CROSS-CULTURAL ADJUSTMENT OF JAPANESE CHILDREN

Hisako M. Koizumi, M.D., Psychiatry, Harding Hospital, 445 E. Granville Road, Worthington, OH 43085; Jennifer Farkas, Ph.D., Tetsunori Koizumi, Ph.D.

Summary:

This is part of an ongoing 5 year prospective study to investigate the process of adjustment of 30 Japanese children and their mothers in American society. We test the hypothesis that the adjustment process follows a certain tile-profile known as the U-curve hypothesis. The study employs combinations of semi-structured interviews, questionnaires and scales such as Child Depression Inventory and UCLA Loneliness Scale. Assessments are done separately with the child and the mother at their arrival, 6 month point, one year point and 2 year point as of this study. The U-curve is found to be one of the four adjustment patterns at one year point. Adjustment is defined here in terms of three components of functioning: behavioral, cognitive and emotional. The same four patterns recur with stability at 2 year point, suggesting that a phase of acute adjustment is completed within one year. How children adjust over a longer run is associated with their functioning prior to cross-cultural experience.

NR605 **Thursday, May 17, 12 noon - 2:00 p.m.**

QUALITY OF CARE PROBLEMS IN AN OCHAMPUS PROJECT

William Sonis, M.D., Philadelphia Child Guid., 34th St. & Civic Center Blvd., Philadelphia PA 19104; Jeffrey Berlant, M.D., Cynthia Tudor, Ph.D., Margaret Keyes, M.A.

Summary:

Systemetrics/McGraw-Hill was awarded a contract to monitor the quality of mental health care in a fixed-price, case managed Ochampus mental health care demonstration. A representative sample of 3,318 charts over a two-year period were sampled by provider and level of care (LOC) and were revised for quality of care problems by a board-certified specialist. Problems were rated on a severity scale of one (least serious) to five (most serious).

Approximately 59% of the cases reviewed were children and adolescents under the age of 18 years. The predominant diagnostic group for these sampled cases differed by age cohort (0-12, 13-17, 18-54, 55+ years). Disruptive disorders predominated in children, mood disorders predominated in the adolescent and adult groups, and psychoactive substance use disorders predominated with the older adults. There was a shift in the ratio between disruptive and emotional disorders between childhood (2.2:1) and adolescents and adults (1:1.8).

At least one quality problem was identified in between 46-48% of cases having completed the review process regardless of age. At least one serious problem (severity level three, four or five). Between 20-22% of the completed cases. Children (0-12 years) treated at a residential LOC had the highest percentage (25%) of severity level three, four or five quality problems, while older adults (55+ years) treated at a partial LOC had the lowest percentage (11%) of quality problems. A majority (67-73%) of quality problems were clinical care, rather than documentation or case management problems. Clinical care problem rates by LOC in children (0-12 years) were about the same, while clinical care problems in adolescents and adults occurred predominantly at the acute LOC.

In order to assess the significance of these problem rates, comparative data from other geographic areas are needed and hopefully will be available in a follow on project.

NR606 **Thursday, May 17, 12 noon - 2:00 p.m.**

ADOLESCENT AIDS RISK: A HOSPITAL SURVEY

Dewleen G. Baker, M.D., Psychiatry, Univ of Connecticut, 231 Bethesda Avenue ML#559, Cincinnati, OH 45267; Douglas Mossman, M.D.

Summary:

Adolescents account for just 1% of reported cases of AIDS, but the risk-related behavior of adolescents suggests that sub-groups of teenagers may have a high likelihood of becoming HIV-infected. To our knowledge, few studies have examined HIV status in psychiatric populations, and no studies have assessed risk-related behavior in adolescent psychiatric patients.

As part of the gynecologic care offered our female in-patients at a state-funded, acute-to-long term children's psychiatric facility, we obtained thorough sexual and substance-use histories on 26 girls (ages 10-17). Hospital policy precluded universal HIV testing, but consenting girls were examined for other sexually-transmitted diseases (STDs) as their symptoms or history warranted.

Twelve girls (46%) reported one or more high-risk sexual activities (multiple partners and/or unprotected intercourse with partners whose sexual history was unknown or who used intravenous drugs). Cocaine use and daily drug or alcohol use were associated ($p < 0.005$) with high-risk sexual behavior; STDs and diagnosis of conduct disorder were associated with higher levels of sexual activity ($p < 0.10$) and with substance abuse ($p < 0.05$). We conclude that conduct-disordered and substance-abusing adolescents comprise a psychiatric population at especially high risk for HIV infection.

NR607 **Thursday, May 17, 12 noon - 2:00 p.m.**

CHILDHOOD PSYCHIATRIC STATUS AND CRIMINALITY

Michael S. Lundy, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City IA 52242; Bruce M. Pfohl, M.D., Samuel Kuberman, M.D.

Summary:

Psychiatric disturbance in childhood is a risk factor for adult mental illness, but the relationship between the two is complex. Severity of childhood disturbance correlates with adult outcome, but specific predictors of long-term functioning are few. Psychiatrically-hospitalized children comprise a highly dysfunctional subgroup and appear to be at high risk for poor outcome. We present findings from an ongoing historical prospective study of children hospitalized at the University of Iowa, and focus on a single measure of poor outcome: adult imprisonment. Our sample of 170 persons (138 males, 32 females) was derived from all children 4 to 12 years of age admitted to the psychiatric hospital between 1970 and 1983. Persons below 18 at follow-up, or with mental retardation were excluded. Twenty-three males (17 percent of 138) had adult prison records. Assaultive behavior in childhood correlated with adult imprisonment ($X^2 = 8.5$, $p = 0.004$), and any combination of assault, stealing, lying, or runaway behavior showed a stronger association ($X^2 = 11.2$, $p = 0.001$). Other predictors were criminality in a biological parent ($X^2 = 4.8$, $p = 0.03$) and treatment with psychoactive medication ($X^2 = 5.8$, $p = 0.02$). Diagnosis, I.Q. and parental psychiatric illness were not correlated with poor outcome. Male gender, deviant behavior in early childhood (severe enough to require hospitalization and medication), and parental criminality, predicted adult imprisonment.

NR608 **Thursday, May 17, 12 noon - 2:00 p.m.**

PANIC ATTACKS IN SIXTH AND SEVENTH GRADE GIRLS

Chris R. Hayward, M.D., Psychiatry, Stanford University, Behavioral Medicine Program, Stanford CA 94305; Joel D. Killen, Ph.D., C. Barr Taylor, M.D., Larry Hammer, M.D., Iris Litt, M.D., Darrell Wilson, M.D.

Summary:

In a school-based study of 818 sixth and seventh grade girls the lifetime prevalence of interview-determined, four symptom panic attacks was 5.6 percent. There was no significant age difference between those with and those without panic attacks. However, the panic group scored significantly higher on Tanner staging (a classification of sexual maturity, $t = 3.2$, $df = 749$, $p < 0.01$). Using analysis of covariance to control for the effect of Tanner stage and age, the panic group scored significantly higher on self-report measures of depression ($F = 19.74$, $df = 1,605$, $p < 0.0005$) and agoraphobic avoidance ($F = 25.8$, $df = 1,740$, $p < 0.0005$). We also compared self-reported cigarette smoking and alcohol use between the panic group and the nonpanic group. There were no significant differences in alcohol use; however the panic group was significantly more likely to have tried cigarette smoking (chi-square = 4.5, df = 1, p 0.05). In a previous study, we also found an increase in depression and cigarette smoking in adolescents with panic attacks. An unanticipated observation was that Tanner stage was a better predictor of panic in this age group than chronologic age, suggesting that sexual maturation and the associated hormonal changes may be important in the development of panic attacks in young girls.

NR609 **Thursday, May 17, 12 noon - 2:00 p.m.**

CONSULTATION/LIAISON PSYCHIATRY: CONCORDANCE WITH RECOMMENDATIONS

Graeme C. Smith, M.D., Psych Med, Monash University, Prince Henry's Hosp St Kilda, Melbourne, VIC 03004, Australia; Louise N. Seward, M.D., Geoffrey W. Stuart, Ph.D.

Summary:

Consultees' concordance with psychiatric consultants' recommendations for psychotropic medication and diagnostic action and their representation of psychiatric consultation in discharge summaries were studied retrospectively in a series of 270 consultations on the consultation-liaison psychiatry service of a 400 bed general hospital with a referral rate of 6.7%. Using quantitative concordance criteria, consultee response was examined as a function of 35 variables characterising the patient, the consultee, the consultant, the consultation and the recommendations. 62% of files had a psychotropic drug recommendation and only 60% of these had a single recommendation. The concordance rate for psychotropic drug recommendations was 86%. No factors were significant for concordance overall, but the type of referring unit, number of recommendations and specification of the type of drug and dosage were found to be significant for concordance in some cases. The concordance rate for the representation of psychiatric diagnosis was 53%; type of medical diagnosis, total days hospitalised, days hospitalised at the time of consultation and consultant's status were found to be significantly related variables. Only 5.2% of files contained a diagnostic action recommendation; the concordance rate was 48%. It is concluded that such data are essential for valid outcome studies.

NR610 **Thursday, May 17, 12 noon - 2:00 p.m.**

DUAL DIAGNOSIS IN SOMATOFORM PAIN DISORDER

Peter B. Polatin, M.D., Psychiatry, UTSW Med Ctr Dallas, 5323 Harry Hines Blvd. F5-400, Dallas, TX 75235; Regina K. Kinney, B.A., Robert J. Gatchel, Ph.D.

Summary:

Chronic pain is commonly associated with depression and an increased incidence of other psychopathology. The present study evaluates comorbidity in various DSM-III-R diagnoses with somatoform pain disorder. One hundred patients with low back pain in excess of six months, beginning an outpatient physical rehabilitation program, were administered the SCID I and II under psychiatric supervision. The sample, homogeneous as to pain site, therapeutic setting, chronicity, and demographics, consisted of 61 males and 39 females. 98% received the diagnosis of somatoform pain disorder. When this category was excluded from analysis, 84% met lifetime diagnostic criteria for other Axis I disorders. 62% fulfilled lifetime criteria for major depression, 35% for substance abuse, and 30% for anxiety disorders. 60% met criteria for current Axis I disorders. Additionally, 58% fulfilled diagnostic criteria for at least one Axis II disorder, the most frequent being paranoid (32%), avoidant (16%), and passive aggressive (14%). These findings indicate that while chronic pain patients may develop psychiatric symptoms secondary to pain, pre-existing psychopathology may also express itself in a chronic pain syndrome. Correlation of pain duration with specificity and multiplicity of Axis I and II disorders is of additional interest for future research.

NR611 **Thursday, May 17, 12 noon - 2:00 p.m.**

DEPRESSION AND RECENT DIAGNOSIS OF LEPROSY

Mitchell G. Weiss, M.D., Social Medicine, Harvard Medical School, 25 Shattuck Street, Boston, MA 02115; Dinsha R. Doongaji, M.D., Ashit Sheth, M.D., Ruis Fernandes, M.D., Sanjay Siddharth, M.B., My Acharekar, M.D.

Summary:

Leprosy remains a major health problem in many developing countries and a significant problem among Southeast Asian refugees in the United States. As the ultimate metaphor for stigma and despair with deep-seated cultural meanings, it exemplifies medical conditions with a serious emotional burden, and studies of the co-occurrence of leprosy and psychiatric morbidity emphasize depression, which may be severe. Ongoing research at the KEM Hospital, Bombay employs the Explanatory Model Interview for Classification (EMIC), the SCID and the Combined Hamilton Depression and Anxiety Rating Scale to study recently diagnosed patients with leprosy as they begin medical treatment and in follow-up two months later, comparing culturally based beliefs and practices, depression and anxiety among study patients with leprosy ($n = 56$) and controls with vitiligo ($n = 19$) and tinea versicolor ($n = 12$). Eleven of the 56 study patients (20%) fulfilled DSM-III-R criteria for major depression, and 14 others (25%) were diagnosed with adjustment disorder. This preliminary report discusses the emotional burden of leprosy with reference to cultural beliefs and practices. It indicates how mental health professionals can help other clinicians identify and respond to psychiatrically significant sequelae of stigmatizing medical illness in general, thereby reducing their emotional burden and improving compliance with medical treatment.

NR612 **Thursday, May 17, 12 noon - 2:00 p.m.**

PSYCHOLOGICAL COMORBIDITY AND INCREASED LENGTH OF STAY

Stephen M. Saravay, M.D., L&C Psychiatry, Long Island Jewish, 270-05 76th Avenue, New Hyde Park, NY 11042; Barbara Weinschel, Ph.D., Simcha Pollack, Ph.D., Nancy Alovis, Ph.D., Robert A. Stern, M.D., Robin Horwitz, M.D.

Summary:

A Nurses Psychiatric Admission Screening Questionnaire (NPASQ) given to 449 patients found that 87 (19%) were "high risk" for at least one of nine psychiatric factors predicted to correlate with increased length of stay. In a subgroup made up of 53% high risk patients (41 high risk and 36 low risk) who had completed Beck Depression Inventories, Mini Mental State Exams and Karnofsky Performance Status Scales, depression and organicity scores were found to account for 22% of the variance of increased length of stay. A prior study not using the admission screening showed a variance of only 11%.

Depression, organicity and physical impairment showed correlations with length of stay of .41 ($P = .001$), .28 ($P = .025$) and .36 ($P = .003$) (all P values are 2-tailed), supporting the results of an earlier study. Moreover, psychological comorbidity accounted for more of the variance in length of stay than did physical impairment. The NPASQ had moderate overall internal reliability of .65 and correlations with psychological scores demonstrating reliability and construct validity.

The findings suggest that simple admission screening instruments used in conjunction with brief psychological tests may have practical use in selecting a group of general medication inpatients for psychiatric intervention who are at higher risk for increased length of stay due to psychological comorbidity.

NR613 **Thursday, May 17, 12 noon - 2:00 p.m.**

STRESS, HEART RATE VARIABILITY AND HEART TRANSPLANTATION

Richard P. Sloan, Ph.D., Psychiatry, Columbia University, 622 W. 168th Street, Box 427, New York, NY 10032; Peter A. Shapiro, M.D., Jack M. Gorman, M.D., Jerome B. Korten, M.S., Michael M. Myers, Ph.D.

Summary:

We evaluated the mechanisms of cardiovascular response to mental stress by studying the heart rate (HR) and heart rate variability (HRV) responses to a mental arithmetic (MA) task in 11 cardiac transplant recipients, whose hearts are denervated, and 10 normal controls. Time- and frequency-domain analyses were used to characterize low frequency HRV (0.06-0.15 Hz) and respiratory sinus arrhythmia (RSA) (0.15-0.75 Hz). RSA is an index of parasympathetic tone. HR increased in response to the stressor in both the transplant and control groups (1.94 bpm, $p = .05$, and 8.21 bpm, $p = .01$, respectively); the control group HR response was greater ($P = .05$). As expected, baseline HRV was decreased in transplant patients compared to controls. However, both groups showed significant HRV responses to the stressor. As the figure shows, the magnitude of percent change in RSA was similar. However, RSA decreased in controls but increased in transplant recipients during the task. Thus, the expected inverse association between HR and RSA changes was seen only in the controls. Moreover, RSA changes were rapid, even in the transplant group, which cannot be accounted for by stress-induced gradual changes in plasma catecholamine levels. These data support the hypothesis that cardiovascular effects of mental stress depend largely, but not entirely, on reduction of parasympathetic cardiac stimulation. The seemingly paradoxical increase in "parasympathetic" tone in response to mental stress seen in the denervated-heart subjects suggest that intra-cardiac factors also modulate the stress response.

NR614 **Thursday, May 17, 12 noon - 2:00 p.m.**

SUBSTANCE USE DISORDERS IN CHRONIC FATIGUE PATIENTS

Henry R. Kranzler, M.D., Psychiatry, Univ of Conn. Hlth. Ctr., 263 Farmington Avenue, Farmington, CT 06032; Victor Hesselbrock, Ph.D., Peter Manu, M.D., Thomas J. Lane, M.D., Dale A. Matthews, M.D.

Summary:

Chronic fatigue (CF) and substance abuse (SU) disorders are both prevalent among medical outpatients. To examine the co-morbidity of these disorders in relation to other psychiatric disorders, 100 outpatients (65 females) with CF were evaluated. The mean age of these patients was 41 years and the median duration of their CF was 9 years. Twenty-eight percent met DSM III-R criteria for a lifetime diagnosis of substance abuse/dependence, including alcohol (17%), cannabis (10%), opioids (4%), cocaine (3%), amphetamines (3%), and anxiolytics (3%). No differences were found in terms of gender, age, duration or severity of CF, or prevalence of medical illnesses. Anxiety and mood disorders were each found in 52% of the entire sample. CF patients with co-morbid psychiatric disorders reported a higher frequency of lifetime depressive symptoms and a higher score on the Beck Depression Inventory (BDI) than patients with CF alone. These groups did not differ in lifetime prevalence of other psychiatric symptoms. Depressed SU patients ($N = 15$), compared with other patients ($N = 32$), reported more lifetime depressive symptoms (including both suicidal ideation and intent), but were similar on the BDI and the prevalence of other lifetime psychiatric symptoms. A history of SU is prevalent among CF patients and is associated with a history of more depressive symptoms. These findings will be discussed in terms of the diagnosis and treatment of psychiatric co-morbidity in medical patients.

NR615 **Thursday, May 17, 12 noon - 2:00 p.m.**

THE EFFECTS OF DEFERRAL LEGISLATION UPON TREATMENT ACCEPTANCE

Dale A. D'Mello, M.D., Psychiatry, Michigan State University, St. Lawrence 1210 W. Saginaw, Lansing, MI 48915; Michael Bowden, A.C.S.W., Beverly Anderson, Msibi Bhekumusa, B.A., Kevin R. Bowman, B.S.

Summary:

Public Act 118 of 1986 in the State of Michigan provides a person who has been petitioned for commitment with the opportunity to defer the court hearing and voluntarily accept treatment. The consequences of this legislation have not been previously reported.

A preliminary review of the outcome of 706 consecutive involuntary admissions within a tri-county region of mid-Michigan revealed that 319 (45%) patients agreed to accept inpatient psychiatric treatment. Two hundred and fifty-one (35%) of these deferred commitment. Sixty-eight (10%) accepted formal voluntary admission.

The establishment of the deferral process has significantly reduced the frequency of commitment hearings without violation of due process. It has increased patients' acceptance of psychiatric treatment. The influence of various demographic, diagnostic and treatment variables upon treatment choice will be presented.

NR616 **Thursday, May 17, 12 noon - 2:00 p.m.**

DELIRIUM DURING INTRAAORTIC BALLOON PUMP THERAPY: INCIDENCE AND MANAGEMENT

Kathy M. Sanders, M.D., Psychiatry, Mass General Hospital, Warren 608 Fruit Street, Boston, MA 02114; Theodore A. Stern, M.D., Patrick T. O'Gara, M.D., Terry S. Field, M.P.H., Scott L. Rauch, M.D., Rachel E. Lipson, M.D., Kim A. Eagle, M.D.

Summary:

The records of 200 consecutive patients treated with an intraaortic balloon pump (IABP) at the Massachusetts General Hospital during 1988 were retrospectively reviewed to determine the frequency of behavioral complications associated with IABP placement and how they were managed. Use of neuroleptics, anxiolytics, and narcotics were recorded, as were prior medical and psychiatric disorders, complications of IABP placement, and clinical outcome. Preliminary analysis of 176 cases showed that 41 (23%) were women (mean age = 68 years). They had a mortality rate (41%) twice that of the males (21%). The mean age for men was 60 years. Sixty-three cases (36%) received high doses of either narcotics ($\geq$30 mg morphine or its equivalent/d), anxiolytics ($\geq$45 mg diazepam or its equivalent/d), or neuroleptics ($\geq$30 mg haloperidol or its equivalent/d). Forty of the 63 cases (63%) had delirium. Twenty-seven (68%) of those with delirium survived their hospital admission; four individuals developed persistent organic brain syndromes. When delirium was diagnosed and treated with high-dose neuroleptics there was a significantly higher survival rate when compared to those cases managed with high-dose narcotics.

Further analysis will be directed towards a characterization of the demographics of this patient population and a search for positive correlations between histories of alcohol and/or psychotropic medication use, psychiatric illness, prior neurologic or multisystem disease, and the occurrence of delirium requiring high-dose treatment.

NR617 **Thursday, May 17, 12 noon - 2:00 p.m.**

NEURAL NETWORKS IN PSYCHIATRIC DECISIONMAKING

Eugene C. Somoza, M.D., Psychiatry, Cincinnati VAMC, 3200 Vine Street, Cincinnati, OH 45220; John Somoza, B.S.

Summary:

Neural networks (NN) differ from conventional computers in that they are trained to learn from experience rather than programmed from predetermined algorithms. In many clinical situations one must recognize patterns in order to make decisions. Quite often, it is very difficult to translate this knack for good decisionmaking (often called "clinical judgment") into formal rules; thus, the use of NN for recognizing psychiatric patterns holds great promise. In this study, a 50-element, back-propagation NN was trained to distinguish patients admitted from those not admitted. The information about each patient given to the NN included: GAF score, severity of the primary stressor, degree of suicidality, and total BPRS score. The NN was trained on 127 emergency room patients seen in August and October 1989 (43 admitted and 84 not) and then tested on 214 patients who presented in September and November. The accuracy of the network varied with the number of elements in the hidden layer, the number of training sessions, and other parameters to be discussed. Values of sensitivity and specificity of 75 to 80 were obtained for this NN that was not fully optimized. A comparison of the pattern used by residents to admit patients compared with that of full time staff members, as well as optimization techniques will be discussed.

NR618 **Thursday, May 17, 12 noon - 2:00 p.m.**

THE VIOLENT PSYCHIATRIC EMERGENCY

Kimberly A. White, M.D., Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139; James C. Beck, M.D., Bruce C. Gage, M.D.

Summary:

This study identifies variables that contribute to the decision to hospitalize potentially violent patients. 1500 consecutive psychiatric emergency patients at a city hospital were screened. Patients were included if potential violence was a salient clinical issue at the time of assessment (N = 99). Evaluating clinicians completed a questionnaire on the subject's demographics, clinical variables, index violent episode, and emergency treatment and disposition. Patients were interviewed again 3 days later to evaluate for subsequent violence. The sample was predominantly adult (mean age 34 years), male (61%), white (80%), single (62%), and unemployed (79%). 47% had major affective disorders of schizophrenia, 23% had alcohol or drug abuse. The index violent act was assault and battery for 58%; verbal threat or general concern for violence in 42%. Psychosis and restraint in the emergency room were associated with hospitalization. With these factors held constant, no other variable was significant. Neither a past history of violence nor any characteristic of the index violent episode correlated with hospitalization. There were nine episodes of subsequent violence, all by hospitalized patients. Mania predicted future violence. The results illustrate that clinicians accurately assessed future violence, but not on the basis of variables identified in studies of violence in community samples.

NR619 **Thursday, May 17, 12 noon - 2:00 p.m.**

MORE ON ECT AND PARKINSON'S DISEASE: CLINICAL EFFECTS

Richard Douyon, M.D., New York University, Manhattan Psych Center, Research Dept. D-14A, Wards' Island, NY 10035; Michael Serby, M.D., Bruce Klutchko, M.D., John P. Rotrosen, M.D.

Summary:

Forty to 60 percent of patients with Parkinson's disease (PD) have depression, dementia, or both. Most of them are treatment resistant or cannot tolerate levodopa therapy. For many years, these patients have been treated successfully with electroconvulsive therapy (ECT). To examine the effects of ECT in patients with PD who are depressed, we conducted two open pilot studies.

In the first experiment, seven patients received an average of seven bilateral ECT sessions. Five of seven patients showed improvement in motor function as well as mood after two ECTs. All aspects of PD improved and the oldest patients had the greatest improvement. Four patients remained well for up to six months.

For the second trial, we hypothesized that ECT will specifically decrease parkinsonism after two sessions, and that this therapeutic effect is independent of its effect on depression. We also predicted that ECT will worsen the cognitive function in patients with PD. A total of nine patients participated in this study and they received an average of eight bilateral ECTs. The clinical changes were measured with the New York University PD scale (NYUPD), the Hamilton Depression scale (HAM-D), and the Mini-Mental State Exam (MMSE). A one way ANOVA showed that motor and affective symptoms improved significantly ($F = 13.6$, $df = 3,6$, p .004 and $F = 7.8$, $df = 3,6$, p .01 respectively), but the cognition did not change ($F = .28$, $df = 3,6$, p .83) after ECT. We carry out an arc sine transformation which indicate no difference between the mean percent change of NYUPD scores and the mean percent change of HAM-D scores after two ECTs (Paired $t = .6$, $df = 1$, p .5).

We will discuss the use of ECT and maintenance ECT in depressed and nondepressed patients with PD.

NR620 **Thursday, May 17, 12 noon - 2:00 p.m.**

HOMOCYSTEINE, B12 AND FOLATE IN GERIATRIC DEPRESSION

Iris R. Bell, M.D., Geriatrics, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Joel S. Edman, M.S., Jacob Selhub, Ph.D., Frank D. Morrow, Ph.D., David W. Marby, B.S., Douglas C. Shepard, M.S.

Summary:

Geriatric major depression is often preceded and/or accompanied by subcortical arteriosclerotic damage and other cerebrovascular insults. Elevated total serum homocysteine (THC), an amino acid intermediate in the folate and B12 dependent methionine cycle pathway, is one factor in arteriolar damage and stroke; THC also serves as precursor of S-adenosylmethionine, a compound with antidepressant properties. Lindenbaum et al (1988) reported high THC in some vitamin B12 responsive neuropsychiatric syndromes despite low normal serum B12 levels. The present study examined homocysteine by high-pressure liquid chromatography and B complex vitamin status in 29 geriatric (age 74 $\pm$ 7) and 15 young adult (age 31 $\pm$ 5) acute, nonalcoholic inpatients with major depression. 17% of the elderly and none of the young adults had high THC (all geriatric THC: 12.9 $\pm$ 6.8; all young adult THC: 8.4 $\pm$ 2.3 nmols/ml, $P = .003$). Within the elderly group, patients with high THC (25 $\pm$ 7 nmols/ml) had significantly lower vitamin B12 (203 $\pm$ 73 vs. 423 $\pm$ 234 pg/ml) and folate (6 $\pm$ 2 v. 10 $\pm$ 4 ng/ml, $P = .001$), but not vitamin B2 or B6, than those with normal THC (10 $\pm$ 3 nmols/ml). Only one high THC patient was B12 deficient. Montgomery-Asberg Depression Rating Scale (26 $\pm$ 6 v. 26 $\pm$ 5) and Mini Mental State (25 $\pm$ 4 v. 26 $\pm$ 6) scores did not differ between high and normal THC geriatric depressives. Nonetheless, the data support and possibility of a subset of geriatric depressives with underlying vitamin B12 and/or folate-related metabolic factors (i.e. high THC) in their neuropsychiatric presentation.

NR621 **Thursday, May 17, 12 noon - 2:00 p.m.**

MRI ABNORMALITIES IN ELDERLY DEPRESSIVES

Peter V. Rabins, M.D., Psychiatry, Johns Hopkins, Meyer 279 600 N. Wolfe Street, Baltimore, MD 21205; Godfrey D. Pearlson, M.D., Elizabeth H. Aylward, Ph.D., Ashok J. Kuman, M.D.

Summary:

MRI scans of 21 patients 60 years old or older with major depression, 16 patients with Alzheimer's disease (AD) and 14 age-matched controls were compared. The three groups were similar in age ($F = .22, p = .80$). Scans were rated using the CERAD protocol. Compared to controls, depressives had larger superficial cerebral sulci ($p = .05$), temporal sulci ($p < .01$), sylvian fissures ($p < .01$), larger lateral ventricles ($p < .05$), third ventricles ($p < .01$), temporal horns ($p < .05$) and severity of subcortical white matter lesions ($p < .05$) than normals. Depressives had more basal ganglia lesions than normals ($p < .05$) but similar severity of periventricular white matter lesions. There were no statistically significant differences on any MRI measure between depressives with delusions ($n = 7$) and those without ($n = 14$). Depressives who received ECT ($n = 12$) were similar to patients not undergoing ECT ($n = 9$) on all MRI ratings except for more temporal horn atrophy ($p = .05$). Age of onset of depression correlated positively with degree of cortical sulci rating ($p < .01$) but with no other MRI measure. There was no relationship between a history of hypertension or current blood pressure and the severity of white matter lesions.

NR622 **Thursday, May 17, 12 noon - 2:00 p.m.**

INPATIENT PSYCHIATRIC TREATMENT OF DEMENTIA

Peter V. Rabins, M.D., Psychiatry, Johns Hopkins, Meyer 279 600 N. Wolfe Street, Baltimore, MD 21205; Chris Nicholson, R.N.C.

Summary:

Non-cognitive symptoms are now recognized as an important source of morbidity in patients with dementia. To determine the inpatient treatment needs of dementia patients we reviewed the charts of 121 patients hospitalized on the psychiatric services of the Johns Hopkins Hospital over a 24 month period. 68 (56%) patients had AD, 26 (22%) patients had a vascular dementia and 25 (21%) patients had other dementing illnesses. The most common reasons for admission were agitation (55%), depressive symptoms (42%), hallucinations or delusions (41%), sleep disorder (32%), assessment of cognitive change (32%), and weight loss or food refusal (22%). Patients were hospitalized for an average of 18.6 days. 64 (53%) patients were discharged home, 33 (27%) patients were discharged to a nursing home and 14 (12%) patients were transferred to other hospital units. Patients with agitation were more likely to be discharged to nursing homes ($p = .0001$) as were patients with more dependency in activities of daily living ($0 = .02$). Greater need for nursing care existed in patients with agitation ($p = .003$), delirium ($p = .0008$) and Alzheimer's disease (p .0001). We conclude that inpatient psychiatric hospitalization provides important assessment and treatment services for a minority of individuals with dementia and is a necessary component in any system that provides care to dementia patients.

NR623 **Thursday, May 17, 12 noon - 2:00 p.m.**

EEG CORRELATES OF COGNITIVE DECLINE IN NORMAL ELDERLY

Peter C. Williamson, M.D., London Psych Hospital, 850 Highbury Avenue, London ON, Canada N6A4H1; Harold Merskey, D.M., Sandra L. Morrison, M.A., Kiran Rabheru, M.D., Kim Wands, B.SC., Vladimir Hachinski, M.D.

Summary:

The objective of this investigation was to examine the quantitative EEG of 49 healthy elderly subjects with particular attention to those who may show evidence of very early cognitive decline. The subjects were participating as a control group in a longitudinal study of dementia. EEG power and coherence at eight locations were correlated with scores on the Extended Scale for Dementia (ESD). This scale has been shown to have a high level of internal consistency and correlates highly with duration of illness and electroencephalographic changes in Alzheimer's disease. In keeping with other recent quantitiatve EEG studies, slow activity was not found to increase with normal aging. Significant correlations between the ESD and EEG power were seen in the beta band even when age, education, occupation, and medication effects were controlled (up to $p < 0.006$). The correlation was seen mostly in frontal and central locations but was also found in the left posterior regions. No significant correlations were found between the ESD and EEG coherence. Five subjects were found to show very early signs of cognitive decline but still scored in the normal rage for the ESD. These subjects had much less beta (up to $p < 0.001$) and alpha (up to $p < 0.002$) activity compared to subjects not showing cognitive decline. The five subjects also tended to have decreased levels of delta ($p < 0.020$) and theta ($p < 0.08$) coherence compared to the rest of the group. These findings suggest that beta activity is associated with cognitive performance in the elderly and that reduction in this activity may be associated with cognitive decline.

NR624 **Thursday, May 17, 12 noon - 2:00 p.m.**

RISK OF INSTITUTIONALIZATION IN ALZHEIMER'S DISEASE

Cynthia D. Steele, M.P.H., Psychiatry, Johns Hopkins University, J.H. Hosler 320 600 N. Wolfe, Baltimore, MD 21205; Barry W. Rovner, M.D., Marshal F. Folstein, M.D., Gary A. Chase, Ph.D.

Summary:

210 community dwelling patients with Alzheimer's Disease by NINCDS criteria were examined by psychiatrists prospectively as part of a longitudinal study. At each visit, the Modified Present State Examination was conducted, the Hamilton Depression Scale and the Brief Psychiatric Rating Scales were completed. Frequency of behavioral problems was assessed with the Psychogeriatric Dependency Rating Scale. Neuropsychological tests of cognition were also conducted. 25 patients who were institutionalized in the first 3 years of the study were compared to 25 who were not. Patients who were institutionalized had higher scores on the standardized psychiatric rating scales but not on formal tests of cognition. These results suggest that potentially treatable (non-cognitive) behavioral and psychiatric symptoms are risk factors for institutionalization and that their treatment might delay or prevent institutionalization in some cases. This work advances previous observations that psychiatric and behavioral problems are associated with nursing home placement by using standardized methods of known reliability and validity to assess and quantify them.

NR625 **Thursday, May 17, 12 noon - 2:00 p.m.**

DISTURBED BEHAVIOR IN DEMENTIA: N-OF-1 TREATMENT TRIALS

Lawrence R. Herz, M.D., Psychiatry, Bedford (MA) VAH, 200 Springs Road, Bedford, MA 01730; Ladislav Volicer, M.D., Virginia Ross, M.A.P., Yvette Rheaume, R.N.

Summary:

There is a dearth of information about, and no accepted protocol for, treatment of behavioral disturbances in dementia. Often environmental manipulation is insufficient, but reported pharmacotherapeutic results may not fit the needs or tolerance of the individual patient. Response to and side effects of common therapy are more variable in elderly populations. To examine alternatives to the usual therapeutic approach, we offered a service of individualized therapy.

We began 11 patients selected as behavior-disordered by the unit staff in randomized, double-blind, repeated-crossover treatments of an antipsychotic, a benzodiazepine, and an anticholinergic sedative. Each trial period was of a single psychoactive agent in a patient who had already failed to improve with the staff's initial pharmacotherapy. We hypothesized that examination of shift-by-shift ratings of behavior would allow us to decide on a single best therapy, which would improve behavior over the referral baseline. We further predicted that the course of trials would be short relative to the progression of the disease, so the results would have prolonged usefulness. We planned also to asses functional measures in those enrolled. The initial data analysis supports the hypotheses. Further, patients were less behavior-disordered at the end of the study on the most successful medication than on the referral medication. An unexpected medication effect emerged: the antipsychotic proved far more efficacious than we had expected compared to the others.

The data will be presented and their statistical and visual analysis described. Advantages of N-of-1 studies will be detailed, as well as limitations to their use.

NR626 **Thursday, May 17, 12 noon - 2:00 p.m.**

META-ANALYSIS OF NEUROLEPTIC EFFICACY IN DEMENTIA

Lon S. Schneider, M.D., Psychiatry, Univ of Southern Calif., 1934 Hospital Place, Los Angeles, CA 90033; Vicki E. Pollock, Ph.D., Scott A. Lyness, M.A.

Summary:

The clinical management of the agitation, combativeness and psychosis that occurs in many dementia patients frequently involves the use of neuroleptic medication. Prior qualitative reviews of the literature suggest that neuroleptics are "modestly effective" and that no single neuroleptic is better than another (e.g., Salzman, 1987). Yet, results of individual studies are not sufficiently powerful to assess this. To more precisely evaluate the clinical efficacy of neuroleptics in agitated dementia, a meta-analysis of the seven published trials that used random-assignment, double-blind, placebo-controlled methods was performed. Effect size estimates for each study were calculated and then analyzed by Stouffer's method. Although neuroleptics were significantly more effective than placebo (one-tailed $p = .004$), the mean effect size was small ($r = 0.18$). Clinically, the improvement rate changed from 0.41 to 0.59 (binomial effect size display), indicating that 18% of 100 dementia patients benefitted from neuroleptics beyond that of placebo. The opinion that no one neuroleptic is significantly better than another also was supported quantitatively by meta-analyses of the nine double-blind, controlled studies comparing thioridazine or haloperidol to other neuroleptics. These analyses quantify previous conclusions of a small but consistent and reliable, effect of neuroleptics in dementia. Clinical implications of the use of neuroleptics in this population are discussed.

NR627 **Thursday, May 17, 12 noon - 2:00 p.m.**

HYDROXYNORTRIPTYLINE KINETICS IN THE ELDERLY

Lon S. Schneider, M.D., Psychiatry, Univ of Southern California, 1934 Hospital Place, Los Angeles, CA 90033; Julie Dopheide, PharmD, Ray Suckow, Ph.D., Thomas B. Cooper, M.A., Ruby Palmer, R.N., R. Bruce Sloane, M.D.

Summary:

Pharmacokinetic factors may contribute to altered tricyclic antidepressant drug effects in the elderly. Although age does not seem to influence nortriptyline (NT) plasma levels, its principal metabolite, E-10-hydroxynortriptyline (E-10-OHNT), does appear to increase with age. E-10-OHNT is biologically active, inhibits noradrenergic uptake, impairs cardiac condition, and may be inversely correlated with clinical improvement. NT is extensively metabolized in the liver; E-10-OHNT is conjugated and excreted renally. Steady state levels of E-10-OHNT have been correlated with creatinine clearance. We performed a single dose pharmacokinetic pilot study of NT in 14 younger (26.5 yrs $\pm$ 3.0 sd) and 12 older (67.7 $\pm$ 5.9) normal volunteers in order to assess relative determinants of E-10-OHNT formation and elimination in the older group. NT itself showed no significant age-group effect with respect to area-under-the-curve (AUC) or elimination rate constant (K_{el}). However, the availability of total E-10-OHNT was 1.45 greater in the elderly as evidenced by AUC comparisons ($t_{(24)} = 3.16$, $p = .004$) and the apparent K_{el} for E-10-OHNT was slower ($t_{(24)} = 2.51$, $p = .02$). AUC for E-10-OHNT and creatinine clearance were significantly correlated in the older group only ($r = -.79$, $p = .002$). Multiple regression analyses suggested that diminished renal clearance, not increased hyroxylation, was responsible for the larger AUC of E-10-OHNT in the older group but not the younger. Older subjects will have steady state levels and longer half lives than younger subjects.

NR628 **Thursday, May 17, 12 noon - 2:00 p.m.**

CHALLENGE STUDIES IN ALZHEIMER'S DISEASE

Linda M. Bierer, M.D., Psychiatry, Bronx VA Med Ctr, 130 West Kingsbridge RD 116A, Bronx, NY 10468; Michael Davidson, M.D., Rami Kaminsky, M.D., Peter J. Knott, Ph.D., James Schmeidler, Ph.D., Kenneth L. Kavis, M.D.

Summary:

Preclinical data suggests that the addition of noradrenergic agents may augment the therapeutic response of patients with Alzheimer's disease to cholinomimetic treatments. As combined pharmacotherapies may be associated with untoward side effects in elderly patients, a series of challenge studies was initiated to provide an indication of clinical tolerance to cholinergic/noradrenergic treatments. We have studied the hemodynamic, behavioral, and cognitive responses of AD patients to the administration of physostigmine (2mg q2h) plus single, oral doses of clonidine (0mg, 0.05mg, 0.1mg, 0.2mg, 0.3mg), and to yohimbine (0mg, 10mg, 20mg) in the absence and presence of physostigmine. The physostigmine/clonidine combination was well tolerated ($N = 10$) and associated with dose dependent decrements in mean arterial pressure (MAP), plasma MHPG, word recall ($F = 4.0$, $df = 2,24$, $p < .05$), and ability to concentrate ($F = 3.6$, $df = 4,24$, $p < .05$). The physostigmine/yohimbine combination was less well tolerated. Yohimbine administration ($N = 10$) was associated with increments in MAP and with improvement in recall of test instructions ($F = 5.6$, $df = 2,10$, p.05) and multiple step commands ($F = 5.9$, $df = 2,10$, $p < .05$). These studies represent initial demonstrations of the feasibility of proceeding with combined cholinergic/noradrenergic pharmacotherapeutic strategies in AD patients.

NR629 **Thursday, May 17, 12 noon - 2:00 p.m.**

CLINICAL CORRELATES OF HPA AXIS FUNCTION IN ALZHEIMER'S DISEASE

Brian A. Lawlor, M.D., Psychiatry, Mt. Sinai Hospital, Box 1230 One Gustave Levy Pl, New York, NY 10029; Richard C. Mohs, M.D., Gabriel K. Tsuboyama, M.D., Moshen Aryan, M.D., Bonnie M. Davis, M.D., Michael Davidson, M.D., Kenneth L. Davis, M.D.

Summary:

Although nonsuppression of plasma cortisol after dexamethasone administration and elevation of baseline cortisol occurs frequently in Alzheimer's disease, the clinical correlates of this apparent HPA axis "overactivity" are poorly understood. Animal studies indicate that hypercortisolemia can induce cognitive impairment, while in clinical populations elevated cortisol has been associated with depression and with increased motor and psychic agitation. Since AD patients can have all of these symptoms, possible correlates of hypercortisolemia include both cognitive (memory, praxis, and language) and non-cognitive complications (depression, agitation, and psychosis) of AD. We examined the relationship between baseline cortisol and the cognitive and noncognitive subscales of the Alzheimer's Disease Assessment Scale (ADAS) in 28 carefully characterized patients with probable Alzheimer's disease (AD). The data were analyzed using Pearson Correlation coefficients (2-tailed level of significance). There were significant correlations between baseline cortisol and the level of cognitive, but not non-cognitive impairment on the ADAS (total cognitive score: $r = 0.36$, $p < 0.05$, $n = 28$); memory subscore: $r = 0.41$, $p < 0.02$; $n = 28$). Interestingly, there were no significant relationships between basal cortisol and measures of depression, agitation, or psychosis on the non-cognitive portion of the ADAS. These data would suggest that elevated basal cortisol levels in AD are not a reflection of depressive symptoms or behavioral complications but are more closely related to the degree of cognitive impairment seen in this illness. This is consistent with the view that the hypercortisolemia is related to the extent of hippocampal cell loss in AD, since neuronal loss in the hippocampus can produce both memory loss and elevated cortisol.

NR630 **Thursday, May 17, 12 noon - 2:00 p.m.**

ACUTE EFFECT OF BUSPIRONE AND LORAZEPAM ON MEMORY

Brian A. Lawlor, M.D., Psychiatry, Mt. Sinai Hospital, Box 1230 One Gustave Levy Pl, New York, NY 10029; Jeanne L. Radcliffe, M.P.H., Trey Sunderland, M.D., Susan E. Molchan, M.D., Rick A. Martinez, M.D., Dennis L. Murphy, M.D.

Summary:

The sedative and amnestic effects of the benzodiazepines are often problematic in the management of anxiety and agitation in frail elderly populations. Although the non-benzodiazepine anxiolytic, buspirone does not adversely affect cognitive functioning in younger subjects, its effects on memory processes in older populations has not been studied. We administered single oral doses of buspirone (20 mg), lorazepam (1 mg), and placebo to 10 older volunteers (mean age 62.5 $\pm$ 2.3 years, 7 males 3 females), in a double-blind, placebo-controlled study, randomized for order to determine whether buspirone has less cognitive impairing effects than a standard benzodiazepine in this older population. Cognitive measures included tests of vigilance, attention, episodic and semantic memory, and a continuous performance task (CPT) performed 90 min following drug administration. In comparison to placebo, lorazepam produced predictable decrements in memory function, with significant increases in intrusion errors in the vigilance task, and more frequent commission errors on the CPT. In contrast, buspirone produced no significant changes on any of the cognitive measures compared to placebo, demonstrating it's "memory sparing" effect in this older subject group. Buspirone's lack of cognitive toxicity in older subjects may be an important consideration in the choice for the treatment of anxiety in frail elderly population with and without underlying cognitive impairment.

NR631 **Thursday, May 17, 12 noon - 2:00 p.m.**

AGING AND THE RELATIONSHIP BETWEEN MOOD AND ANXIETY

Dennis Deptula, Ph.D., Geriatric Psychiatry, Nathan Kline Inst., Orangeburg, NY 10962; Rajkumar R. Singh, M.D., Nunzio Pomara, M.D.

Summary:

There is accumulating evidence that the elderly show increased sensitivity to the adverse effects of many psychotropic medications on cognitive performance. The current study examined whether the elderly are also more sensitive to the adverse effects of "negative" emotional states (i.e., anxiety and depression) on memory.

The subjects were forty-five normal young (ages 18-35) and forty-five normal elderly (ages 60-79) medication-free volunteers. Psychiatric and medical evaluations excluded subjects with substance abuse and psychiatric or neurological disorders. Subjects were administered a self-rated visual analogue mood rating scale and Buschke Selective Reminding Test, a widely used recall memory test.

Within the elderly group, performance on the Buschke was negatively correlated with self ratings of anxiety ($r = -.29$, $p < .05$), depression ($r = -.35$, $p < .025$), and withdrawal ($r = .55$, $p < .001$), suggesting that higher ratings of these negative emotions are associated with poorer recall memory. In contrast, in the young group, mood ratings did not significantly correlate with the total recall score. Moreover, within young, higher ratings of anxiety were actually associated with better recall of "high imagery" words ($r = .33$, $p < .05$); words which are easier to learn.

These data suggest that the elderly may be more sensitive to the disruptive effects of anxiety and other negative mood states on memory than young. Possible treatment implications will be discussed.

NR632 **Thursday, May 17, 12 noon - 2:00 p.m.**

COGNITION IN EARLY VERSUS LATE-ONSET ALZHEIMER'S DISEASE

Steven Sevush, M.D., Psychiatry, University of Miami, 1500 NW 12 Avenue Ste. 1103, Miami, FL 33136; Nancy Leve, M.A., Andrew Brickman, Ph.D., Robert Morgan, Ph.D.

Summary:

It has been suggested that patients with early-onset (EO) probable Alzheimer's disease (PAD) show greater language impairment than those with late-onset (LO) disease. Studies supporting this view may, however, have lacked adequate control for duration and severity of disease in the two groups.

We addressed this issue by administering a broad cognitive battery to 150 PAD patients and 40 age-, sex- and education-matched normal controls. Performance by EO and LO patients was compared by means of an analysis that controlled for estimated duration of illness. Significant differences were found for frequency and mean severity of impairment in verbal recall, naming, and abstract thinking, with LO patients showing greater deficits than EO patients in each case. No significant differences were observed for other cognitive measures or for global cognitive score.

These results support the notion that differences in age at disease onset correlate with differences in pattern of cognitive impairment in PAD patients but do not corroborate the finding of greater language impairment in EO patients. Rather, they indicate that LO patients suffer greater impairment in functions that show decline in normal elderly individuals, possibly reflecting a combined effect of PAD and normal aging in older PAD patients.

NR633 **Thursday, May 17, 12 noon - 2:00 p.m.**

PSYCHIATRIC DISORDERS AND MEDICAL DRGS: TYPE AND LENGTH OF HOSPITAL STAY

George Fulop, M.D., Psychiatry, Mount Sinai Hospital, 1 Gustave Levy Place Box 1228, New York NY 10029; James J. Strain, M.D.

Summary:

Introduction: In view of the potential therapeutic and cost-offset benefits of a psychiatric intervention in the medical inpatient, it is important to identify those patients at risk for psychiatric comorbidity (PC). Elderly medical inpatients have increased rates of PC, and have been shown to have prolonged hospital stays (1). *METHOD*: The medical discharge abstracts of 27,213 geriatric (age >65) admitted to the medical/surgical wards at the Mount Sinai Hospital (1985-1987) were reviewed for the presence of a PC and the length of hospital stay (LOS logarithmic transformation). Within the most prevalent diagnosis-related groups (DRGs), the nature and distribution of PC were described. *RESULTS*: I. Examples of the medical DRGs with frequent PC patients included:

DRG 11 MAJOR BOWEL PROCEDURES N = 657

		LOS (log) (DAYS)	T-test
PC	N = 51	3.1 ± .7	p < .008
No PC	N = 606	2.8 ± .6	

DRG 138 CARDIAC ARRHYTHMIA N = 256

		LOS (log) (DAYS)	T-test
PC	N = 40	1.8 ± .9	p < .05
No PC	N = 216	1.5 ± .9	

II. The portion of DSM-III Disorders among PC patients:

	DEMENTIAS	DELIRIUM	DEPRESSION	SUBSTANCE ABUSE	OTHER
Major Bowel Procedures	10%	59%	24%	5%	2%
Cardiac Arrhythmia	5%	50%	12%	13%	20%

CONCLUSION: This study highlights those elderly inpatients with frequent comorbidity (by DRG group) and the associated prolonged hospital stay. The varying proportions of DSM-III disorders provide interesting hypotheses of disease co-association.

NR634 **Thursday, May 17, 12 noon - 2:00 p.m.**

A FOLLOW-UP STUDY OF DEMENTIA IN BEIJING

Ge Li, Ph.D., Psychiatry, Beijing Medical Univ, Bronx VA Psych116A KingsBridge, Bronx NY 10468; Yu-Cun Shen, M.D., Cuang-Hui Chen, M.D., Yo-Wen Zou, M.D., Su-Ran Li, M.D., Mian Lu

Summary:

A three-year follow-up study of 1,090 elderly aged, 60+ years, was conducted to determine incidence of dementias in the west district of Beijing. This population had been studied first in a cross-sectional survey of dementia in 1986. The follow-up examination employed the same interviewers, psychiatrists, instruments (MMSE, CRBRS and DDDS), and diagnostic criteria for dementia (*DSM-III*). Out of the 1,090 elderly, 739 were re-interviewed, 86 had died, and 256 were lost to follow-up. The average annual incidence of moderate and severe dementia in individuals 60+ years was 0.30 percent (95 percent confidence interval, [CI] 0.08-0.52 percent). When mild and potential demented cases were included, the incidence was 0.56 percent (95 percent, CI 0.26-0.86 percent). As expected, the rate increased sharply with aging. No sex difference was found. The prevalence rate of moderate and severe dementia was 1.10 percent among those aged 65+ years, similar to that (1.82 percent) in the first investigation in 1986. Our results showed that multi-infarct dementia was somewhat more common than Alzheimer dementia (ratio 3:2) for both the incident cases as well as the prevalent ones. This ratio is different from that reported in western countries. In addition, our study showed that those elderly with less education, less income, and limited physical activity had higher risk for the development of dementia. The age-adjusted risk for death in dementia patients was three times higher than that in entire sample of elderly (SMR = 2.95). No specific cause of death was observed.

NR635 **Thursday, May 17, 12 noon - 2:00 p.m.**

QUANTITATIVE MRI AND SPECT IN ALZHEIMER'S DISEASE

Godfrey D. Pearlson, M.D., Psychiatry, Johns Hopkins, 600 N. Wolfe St. Meyer 3-166, Baltimore MD 21205; Gordon J. Harris, M.S., Richard E. Powers, M.D., Patrick E. Barta, M.D., Edwaldo E. Camargo, M.D., John A.O. Besson, M.D., Jonathan A. Links, Ph.D., Larry E. Tune, M.D.

Summary:

We studied 27 Alzheimer's disease (AD) patients, 15 with MRI, 15 with single photon emission computer tomography (SPECT), and 10 patients with both techniques. These patients were blindly compared to 16 elderly matched normal controls who had both SPECT and MRI. AD patients met *DSM-III-R* criteria for PDD and NINCDS/ADRDA criteria for probable AD. All subjects were tested with Mini Mental State Examination, Recognition Span Test, Boston Naming Test, and Category Naming Test. T1-weighted 3 mm coronal MRI sections were taken through the temporal lobes and assessed by a neuropathologist, using locally developed computer-graphic volumetric techniques. Local ratios of regional cerebral blood flow were determined by injection of six mCi of I-123 IMP. Quantitative data were generated from transverse SPECT slices at the basal ganglia level, using a recently developed computer analysis method, which defined a cortical ring 2cm inside the brain boundary, and calculated count rates in five equal regions, per hemisphere (36° each) normalized by calculating their ratio to the cerebellar mean value. Discriminant function analysis showed the greatest separation for SPECT, using parietal values, which correctly identified 88 percent of patients and controls. MRI Hippocampal and amygdala MRI volumes correctly identified 90 percent of both patients and controls. Parietal cortical SPECT values (but not those from sensory-motor-control areas), were highly correlated with severity of cognitive symptoms.

NR636 **Thursday, May 17, 12 noon - 2:00 p.m.**

SOMATIZATION IN OLDER PANIC DISORDER PATIENTS

Javaid I. Sheikh, M.D., Psychiatry, Stanford University, School of Medicine TD-114, Stanford CA 94305; Gregory R. Bail, B.A.

Summary:

Previous research by our group has documented that older panic disorder patients (ages 55 and above) with a history of early onset (before age 55) of panic attacks are phenomenologically different from patients with a history of late onset (at or after age 55) of panic attacks. Specifically, the former manifest a significantly greater number of symptoms during panic attacks, express more fearful cognitions, and are considerably more avoidant. Based on these findings, we hypothesized that the early-onset panic disorder (EOPD) patients may also manifest more somatization and visceral sensitivity compared to late-onset panic disorder (LOPD) patients. A sample of 20 older subjects (14 EOPD, 6 LOPD) diagnosed as having panic disorder based on the DSM-III-R were evaluated using the Self-Report Inventory for Somatic Symptoms (SISS). As hypothesized, EOPD subjects showed significantly higher scores on the total somatization disorder score (TSDS) compared to LOPD subjects (1 = 13.35, sd = 8.06 vs. 1 = 7.50, sd = 3.93; p 0.05) The two groups were quite simiilar, however, on visceral awareness and non-specific neurotic symptoms. Implications of the present findings for future phenomenological research as well as possible treatment methods will be discussed.

NR637 **Thursday, May 17, 12 noon - 2:00 p.m.**

A COMPARISON OF LATE-ONSET PARANOIA AND PARAPHRENIA

Alastair J. Flint, M.D., Psychiatry, Toronto Hospital, 399 Bathurst Street, Toronto Ontario, Canada M5T 2S8; Sandra L. Rifat, M.S.C., M. Robin Eastwood, M.D.

Summary:

Kraepelin distinguished paranoia (a chronic illness characterised by well-organized delusions without hallucinations, thought disorder or personality deterioration) from paraphrenia (delusions plus hallucinations). Kendler and Winokur subsequently confirmed the validity of paranoia in patients younger than 60 years. Controversy surrounds the nosology of paranoid disorders in older individuals. The purpose of this study was to examine the concept of paranoia beginning in old age and compare it with late paraphrenia. Twenty-one patients with late paraphrenia were compared on 18 demographic, clinical, investigational, and treatment variables with 12 patients with late onset paranoia. All subjects had first onset of symptoms at 60 years or over. Exclusion criteria included personality deterioration, affective disorder, dementia and delirium, previous psychosis, and history/examination findings of any neurological disorder. Despite the negative neurological history, the paranoia group had significantly more clinically unsuspected (silent) cerebral infarction on CT brain scan ($p = 0.003$) and was less responsive to antipsychotic medication ($p = 0.024$) even though both groups were comparable for dose and duration of medication, side effects, and noncompliance. The results suggest that paranoia and paraphrenia in old age differ, and that stroke is an important risk factor for late paranoia and may contribute to a relatively poor prognosis.

NR638 **Thursday, May 17, 12 noon - 2:00 p.m.**

CIRCADIAN TEMPERATURE AND ACTIVITY RHYTHMS IN ALZHEIMER'S DISEASE

Andrew Satlin, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont MA 02178; Martin H. Teicher, M.D., Harris Lieberman, Ph.D., Ladislav Volicer, M.D., Yvette Rheaume, R.N.

Summary:

Sleep-wake cycle disturbances suggest that circadian rhythms may be disrupted in patients with Alzheimer's disease (AD). We previously reported changes in the circadian rhythm of locomotor activity in AD patients. In this study, we examined the circadian rhythms of core-body temperature and activity measured concurrently. Thirteen patients with probable AD and 5 normal elderly controls were studied. Eight of the AD patients were in end-stage disease (Mini-Mental State Exam = 0) and 5 had mild disease (mean MMSE = 17). All subjects were activity-monitored for three days. The eight end-stage AD patients and the controls had concurrent continuous temperature monitoring.

A cosinor analysis found that the amplitude of the locomotor cycle in AD patients was only 58% that of controls ($p = .0058$), and the acrophase of this cycle in AD patients was more than 4 hours later than in controls ($p = .021$). The end-stage patients exhibited more robust differences. However, the AD patients and controls had similarly well-entrained core-body temperature circadian rhythms, with no differences in amplitude, phase, or the range of temperature variability. These findings suggest that the endogenous oscillator may not be affected by AD, and that AD patients may have disturbances in the synchrony of locomotor rhythms with this oscillator. This may provide a basis for treating sleep-wake disorders in AD with potent entraining stimuli, such as bright light pulses.

NR639 **Thursday, May 17, 12 noon - 2:00 p.m.**

LIFE REVIEW IN OLDER ADULTHOOD: A COMPARATIVE STUDY

Rhoda Frankel, M.A., Geriatrics, Illinois State Psych Ctr, 1601 W. Taylor, Chicago IL 60612; William Borden, Ph.D., Benedict Gierl, M.D., Alice Ras, B.A.

Summary:

This study examined the effects of a structured life review group process on psychological well-being and self-esteem in two groups of community-dwelling elderly: 1) persons with chronic mental illness in an out-patient psychiatric clinic, and 2) persons with no history of mental illness in a community center. Participants completed standardized instruments assessing levels of functioning before, during, and after the seven-week group process. They also completed a semi-structured interview at the end of the group. All sessions were audio-taped and videotaped. Results of data analysis show a marked increase in psychological well-being and self-esteem among persons in each group. While the outcomes were similar, the process of each group was different in the ways that members used reminiscence. Persons in the psychiatric group used reminiscence in a therapeutic manner characterized by ventilation, validation and peer support, while members of the community group tended to use the life review process for entertainment, story-telling, and creation of a life narrative. Findings indicate that the adaptive value of life review processes must be considered in the context of individual differences and situational factors. Developmental, research, and clinical implications are reviewed.

NR640 **Thursday, May 17, 12 noon - 2:00 p.m.**

AGGRESSIVE/DISRUPTIVE BEHAVIORS IN NURSING HOMES

Blaine S. Greenwald, M.D., Psychiatry, Hillside Hospital, P.O. Box 38, Glen Oaks NY 11004; Elisse Kramer, Ph.D., Jacob Reingold, M.S., Elaine B. Jacks, R.N., Steven Staum, C.S.W. Conn Voley, M.D.

Summary:

Behavioral disturbances in long-term-care facilities cause consternation amongst other residents, visitors, and staff; contribute to staff burnout/turnover; and provoke use of psychotropics and restraints. To ascertain prevalence of physical aggression (PA) and verbal disruption (VRD), data were collected via Patient Review Instruments (PRI) (a NY-State Department of Health assessment device completed quarterly by trained nurse-raters) in 3,156 residents of eleven diversified NY-Metropolitan area nursing homes.

Recurrent PA and VRD were manifest in 8.5% and 15.2% of residents, respectively. 42.8% of aggressive behaviors and 63.4% of verbal disruption were unpredictable/unprovoked. Compared to nonaggressive, nondisruptive counterparts, both PA and VRD patients were significantly more demented; lived primarily in skilled nursing rather than health-related facilities; were slightly older; and were more represented in not-for-profit institutions. PA and VRD were intercorrelated ($p < .0001$). A significantly higher proportion of PA residents were men. This proportion increased for *unprovoked* aggression. In contrast, a similar sex distribution characterized verbal disruption.

Disturbing and potentially dangerous behaviors were identified in approximately 10-15% of nursing home residents and associated with a dementia diagnosis. Improved psychiatric service delivery is needed. Findings suggest that demented men in skilled nursing settings may merit special attention.

NR641 **Thursday, May 17, 12 noon - 2:00 p.m.**

INCESSANT SCREAMING IN ADVANCED DEMENTIA

Blaine S. Greenwald, M.D., Psychiatry, Hillside Hospital, P.O. Box 38, Glen Oaks, NY 11004; Elisse Kramer, Ph.D.

Summary:

Incessant screaming, a perplexing and troublesome phenomena encountered in skilled nursing facilities, has been little studied.

This study evaluated prevalence and clinical/demographic correlations of screaming. Three facilities surveyed revealed a 5.9% prevalence rate (55/937 residents) of persistent screaming (Cohen-Mansfield Agitation Inventory (CMAI)). Twenty screamers assessed with standard geropsychiatric rating scales (GDS, BehaveAD, MOSES) were compared with twenty sex-matched nonscreamers on their same unit. Amongst screamers, mean CMAI screaming frequency approached several times/hour; mean duration of screaming was approximately 1.5 years; and mean GDS indicated advanced dementia (5.60 +/− .75). 65% (13/20) screamed intelligibly; 45% screamed abusively. Abusive and nonabusive screamers were indistinguishable.

Compared to nonscreamers, screamers provoked greater negative staff attitudes ($p < .001$); were physically restrained more often ($p < .001$); had greater irritability ($p < .005$), self-care deficits ($p < .04$), depression-anxiety ($p < .07$), aggression ($p < .0001$), global behavior disturbances ($p < .002$); and were more sedated ($p < .05$). Screamers and nonscreamers had similar ages; dementia onset, severity, and duration; distribution of dementia diagnoses (AD, MID, mixed); number of medications and medical diagnoses; BehaveAD psychosis factors; MOSES withdrawal factor; visual/hearing problems; and family involvement.

Clinical, phenomenological, biological and treatment implications will be discussed.

NR642 **Thursday, May 17, 12 noon - 2:00 p.m.**

COST OFFSET: PSYCHIATRIC INTERVENTION IN SURGERY

James J. Strain, M.D., Psychiatry, Mt. Sinai School of Med., 1 Gustave Levy Place Box 1128, New York, NY 10029; John Lyons, M.D., Marianne Fahs, Ph.D., Jeffrey S. Hammer, M.D., A. Lebovits, Ph.D.

Summary:

Aims: To examine the cost offset effects from a similar psychiatric liaison intervention for elderly surgery patients in two study sites. Mechanisms underlying the effectiveness of the intervention will be reported.

Method: At the Mount Sinai Hospital (MSH) (NYC) and the Northwestern Memorial Hospital (NMH) (Chicago), all consenting patients 65 years and older admitted for the acute surgical repair of a fractured hip were observed for psychiatric morbidity and length of hospital stay (LOS) during a control and an experimental liaison psychiatry intervention year. The study instruments included: Geriatric Depression Scale, Arthritis Impact Measurement Scale, Spielberger State-Trait Anxiety Inventory, Mini-Mental State; disease staging - Horn scale; functional scale; and direct and indirect costs. *Results*: 56 percent of the MSH and 52 percent of the NMH patients evaluated evidenced major *DSM-III* pathology, e.g., organic mental disorder, affective disorder. At MSH, LOS for the control and intervention years was 21.7 ($N = 85$) and 19.6 days ($N = 114$) ($P = .05$) and for a $191,000 savings; NMH was 15.5 ($N = 63$) versus 14.1 ($N = 94$) ($p = .05$) for a $56,400 cost reduction. Controls did not differ from intervention subjects with regard to post-discharge placement. Hip fracture patients on Halcion in contrast to Dalmane ambulated further at discharge: meters 44.6, S.D. 32.3 versus 31.1, S.D. 19.9 [$t(223) = 2.67$, $p < .01$]. *Conclusion*: Referral consultation in contrast to the psychiatric liaison screen method resulted in 10 percent and 79 percent of the population, evaluated, respectively: The majority had *DSM-III* pathology. Patients placed on short acting hypnotics ambulated significantly further at discharge. A psychiatric intervention was associated with enhanced functional capacity, and decreased hospital costs. Comorbidity and policy will be presented.

NR643 **Thursday, May 17, 12 noon - 2:00 p.m.**

RDC EVALUATION OF CANCER PATIENTS DURING TREATMENT

James J. Strain, M.D., Psychiatry, Mt. Sinai School of Medicine, 1 Gustave Levy Place Box 1128, New York, NY 10029; A. Lebovits, Ph.D., Steven J. Schleifer, M.D., Jeff Tanaka, Ph.D.

Summary:

Introduction: The nature and frequency of psychiatric disorders in ambulatory cancer patients undergoing treatment is unknown. This paper reports psychiatric morbidity longitudinally in women treated surgically and chemotherapeutically for breast cancer. *Method*: 107 women with a recent mastectomy for breast cancer undergoing their first course of chemotherapy were evaluated at the onset of treatment, at 13 and 26 weeks using: RDC, SCL-90 analogue (Somatic, Depression, Anxious, Hostile, Global), criteria. Research assistants achieved inter-rater reliability of r = .7. *Results*:

RDC-Categories	*Initial*	*13 (weeks)*	*26 (weeks)*
Major/Minor Depression	7 (6.5%)	12 (11.2%)	16 (15%)
General Anxiety	7 (6.5%)	2 (1.9%)	3 (2.8%)
Past Depression	34 (32%)		
Past Anxiety	21 (19.6%)		

There was a significant increase in depression as treatment proceeded, whereas anxiety diminished. Half of the sample experienced past depression (32%) and anxiety (19.6%). Regression analysis demonstrated previous hospitalizations and past depression predicted depression at 13 and 26 weeks ($p = .0039$). Younger patients ($p = .043$) and clinic patients ($p = .05$) were more anxious (SCL-90 analogue). *Conclusion*: The sample demonstrated significant past depression, a tendency for initial anxiety, and increasing depression with treatment that indicates the need for ongoing evaluation and psychiatric intervention.

NR644 **Thursday, May 17, 12 noon - 2:00 p.m.**

QUANTITATIVE EVOKED POTENTIAL CORRELATES OF COGNITIVE IMPAIRMENT IN AGING

E. Roy John, Ph.D., Psychiatry, NYU Medical Center, 550 1st Avenue, New York, NY 10016; Leslie S. Prichep, Ph.D.

Summary:

Visual and auditory EP's were recorded from the 19 electrodes of the 10/20 System in 279 persons, divided into young and elderly normal groups and 5 groups with Global Deterioration Scores (GDS) ranging from 2 to 6.

Two types of quantitative analysis were performed. In the first method, the mean amplitude of N1P2 was calculated. In the second method, principal component analysis (PCA) with Varimax rotation was carried out on the normal data. This permitted the EP, recorded from any electrode, to be reconstructed as a linear combination of 6 factors each weighted by a factor score. Using normative data, factor Z-scores were constructed to quantify the statistical probability of the contribution of each factor to any EP wave-shape. Topographic maps of average factor z-scores were constructed for each GDS group.

The data from both analyses reveal a progressive abnormality of visual and auditory EP's with increasing impairment, for all except the primary component and for all but the primary cortical receiving area for the stimulus modality. The results do not indicate selective dysfunction of any cortical region in cognitive deterioration of aging.

NR645 **Thursday, May 17, 12 noon - 2:00 p.m.**

A PROSPECTIVE EEG STUDY OF DELIRIUM IN THE ELDERLY

Ira R. Katz, M.D., Psychiatry, Medical College of PA, 3200 Henry Avenue, Philadelphia, PA 19129; Jana Mossey, Ph.D., Sharon M. Curlik, D.O., Richard N. Harner, M.D., Neal M. Sussman, M.D., Kathryn A. Knott, R.N.

Summary:

In research designed to develop methods for monitoring the elderly to detect reversible states of cognitive impairment, we have been conducting repeated measures of the EEG background in elderly patients living in a residential care setting. Data are available on 28 subjects assessed before and during medical/surgical hospitalization. EEG changes (baseline to worst hospital EEG) was categorized by reference to prediction intervals derived from repeated measures in medically stable subjects. We find significant associations between EEG change and independent clinical diagnosis of delirium (Fisher's exact $p = .036$, .027, .019, and .011 for delta, theta, alpha, and any change, respectively). Patients with any EEG change had greater decrements on the Minimental State Examination ($F = 6.33$; $p < 0.02$). Sensitivity of the EEG for the detection of delirium was 80%; specificity was 72%. Further research is needed to determine whether apparent false positives represent subclinical cases of delirium.

NR646 **Thursday, May 17, 12 noon - 2:00 p.m.**

MENTAL COMPETENCY TESTING OF DEMENTED ELDERLY

Benedict Gierl, M.D., Dept. of Geriatrics, Ill State Psych. Inst., 1601 W. Taylor St., Chicago, IL 60612; Alice Ras, B.A.

Summary:

This paper presents the results of analysis of data collected over several years by a geropsychiatrist on 82 patients above age 60 who were referred for a competency assessment or who in the course of treatment needed this in order to manage their care. Of sixty-six found to have some form of cognitive impairment, 56 were seen as partially or totally incompetent for personal and/or financial decisions. An organic diagnosis was highly coordinated with advanced age ($P < .001$ on 2 tailed t-test), errors on the Mental Status Questionnaire (MSQ) ($p < .000$ on 2 tailed t-test) and a higher stage on the Global Deterioration Scale (GDS) ($P < .000$ on 2 tailed t-test). The GDS score correlated strongly with MSQ ($r = .78$). A discriminate function analysis was completed to determine the extent to which competency could be predicted by other variables. In order of importance these variables are: GDS score, number of behavioral problems, age, occupation, race and availability of retirement funds. Hence, competent elderly performed better on the GDS, had fewer behavioral problems, tended to be younger, to have higher status occupations, tended to be white, and to have retirement funds available.

NR647 **Thursday, May 17, 12 noon - 2:00 p.m.**

QUANTITATIVE I-123 LABELED IOFETAMINE SPECT ANALYSIS IN DEPRESSION

P. David Mozley, M.D., Depression Res. Unit, University of Penna, 3400 Spruce Street, Philadelphia, PA 19104; Abass Alavi, M.D., Jay D. Amsterdam, M.D.

Summary:

SPECT brain imaging studies with I-123 labeled iofetamine (IMP) have been used to investigate several neuropsychiatric disorders, but this technique has not been used much to evaluate patients with major depression. In this pilot study, 15 patients meeting *DSM-III-R* criteria for major depression have been examined so far. Six patients met criteria for a unipolar disorder and nine patients met criteria for a bipolar disorder.

Methods: After standard reconstruction of the images, a recently developed technique was used to draw and analyze regions of interest (ROI) on every tomographic slice. The coronal sections were used to analyze the right and left temporal lobes separately. Measurements were made of the total IMP activity, the mean IMP activity per pixel, the maximum activity per pixel, and the ratio of the mean activity per pixel in the ROI to the mean activity per pixel in the cerebellum.

Results: Asymmetries in temporal lobe IMP activity were found by visual inspection of the images in 11 of 15 patients. The total IMP activity in the right temporal lobes of these 11 patients appears to exceed that in the left by 10 to 40 percent. Temporal lobe differences in the maximum IMP activity per pixel have ranged from 5 to 17 percent. Differences in the mean activity per pixel have ranged from less than 3 to 12 percent.

While the pathophysiological significance of these preliminary results is uncertain, IMP SPECT imaging may represent a useful clinical and research tool for studying some patients with disorders of mood.

NR648 **Thursday, May 17, 12 noon - 2:00 p.m.**

INCREASED BLINK RATES IN DRUG-NAIVE SCHIZOPHRENICS

Dr. Arthur Mackert, Psychiatry, FU Berlin, Eschenallee 3, Berlin (West) 19 D 01000, FRG Germany; Klaus-Malte Flechtner, M.D., Johannes Kasper, M.D., Dr. Hans-Peter Volz, Charles Woyth, M.D.

Summary:

Blink rates are increased in schizophrenics and decreased in patients with Parkinson's disease (KARSON 1983). STEVENS (1978) hypothesized therefore that the spontaneous blink rate is elevated by increased central dopamine activity in schizophrenics. Neuroleptics should decrease blinking by blockade of central dopamine receptors. This hypothesized neuroleptic effect has never been studied in drug-naive schizophrenics.

Eye blinks were investigated during a standardized visuomotor task in 15 drug-naive inpatients (RDC, 8 males and 7 females, mean age 30 ± 11 years) and 15 age- and sex-matched healthy volunteers. 8 remitted patients were followed up after a mean duration of 62 ± 50 days of neuroleptic therapy. Whereas the schizophrenics demonstrated the same precision in executing the visuomotor task as did normal controls, their mean blink rate was highly increased (16.2 ± 10.8 vs. 9.3 ± 6.4, $p < 0.05$). Following neuroleptic treatment, the blink rates decreased and were no longer statistically distinct from controls (16.0 ± 6.8 to 8.3 ± 5.3). The changes in blink rate correlated with changes in several BPRS-items: 'anxiety' ($r = 0.75, p < 0.02$), 'hostility' ($r = 0.78, p < 0.02$),and 'unusual thought contents' ($r = 0.59$, $p < 0.05$), but not with the cumulative neuroleptic dose given between the first and second testing.

In conclusion, blink rates in schizophrenics are increased in drug-naive state and decreased by neuroleptics. The results also suggest an influence of psychopathology on blink rates.

NR649 **Thursday, May 17, 12 noon - 2:00 p.m.**

CLINICAL NEUROIMAGING IN TRAUMATIC BRAIN INJURY

Jeffrey L. Clothier, M.D., Neurobehavior, Laurelwood Hospital, 4000 S. Wellman, Conroe TX 77384; Thomas W. Freeman, M.D., John Cassidy, M.D., Kenneth Bonnet, Ph.D.

Summary:

Six patients with combined neurological and psychiatric disabilities in the subacute and chronic phase of traumatic brain injury were studied with SPECT and MRI imaging, routine EEG, brain electrical activity mapping, and neuropsychological testing. The clinical phenomenology of the behavioral disorder and clinical neurological examination are compared with the results of the assessment techniques. The SPECT imaging was superior to MRI and route EEG in validating results of the neuropsychological studies. SPECT abnormalities corresponded to abnormalities present on the MRI, however, in a few cases SPECT and cEEG revealed defects in functioning distant to MRI localized lesions. Preliminary examination of the results suggest patients with diffuse injuries can be accurately distinguished from patients with focal injuries by SPECT. The implications for the clinical care of the patient with TBI will be discussed.

NR650 **Thursday, May 17, 12 noon-2:00 p.m.**

FRAGILE X ADULTS: NEUROPSYCHOLOGY, BRAIN METABOLISM AND ANATOMY

Declan Murphy, M.D., Natl. Inst. on Aging, Building 10 Room 6C103, 9000 Rockville Pike, Bethesda MD 20892; Mark B. Shapiro, M.D., James Haxby, Ph.D., Randi J. Hagerman, M.D., Stanley I. Rappaport, M.D.

Summary;

Fragile X syndrome (fra X) is characterised by mental retardation, minor physical anomalies and the presence of a fragile site near the tip of the long arm of the X chromosome at Xq27-28. Reports have recently suggested a link between fra(X) and autism. The patients received a battery of neuropsychological testing. Cranial and ventricular volumes were measured with quantitative computed tomography (CT) and regional cerebral metabolic rates for glucose (rCMRglc) were measured with [18-F] 2-fluro-2-Deoxy-D-glucose (18FDG) in six male patients with fra(X) (mean age 25.5, range 19-31). Controls for the CT study were twenty males (mean age 27.5, range 21-37) and controls for the PET study were eight males (mean age 27.5, range 22-31). Controls for the neuropsychological tests were 20 Down syndrome (DS) subjects. The mean mental age of the fra(X) group was 6.6 yrs $\pm$ 2.3 (SD) whilst that of the DS group was 6.8 $\pm$ 3.0(SD); Peabody Picture Vocabulary test. As measured with quantitative CT 5 male patients had a significantly ($p < 0.05$) increased intracerebral volume (1439 $\pm$ 79 cm^3) as compared to controls (1243 $\pm$ 124 cm^3). Volumes of the right and left lateral ventricles and the third ventricle did not differ between groups. However all five patients had greater right lateral ventricle volumes than left—as opposed to nine out of twenty controls. Global grey matter CMRglc in six fra(X) patients was 8.85 $\pm$ 0.76 mg/100g/min in controls. Fra(X) patients scored significantly lower on block and object span than the DS controls ($p < 0.05$). In addition the fra(X) subjects had relatively stronger linguistic than manual expressive skills. The reverse was true of the DS controls. The results of this study show that the larger brains in fra(X) syndrome are not accompanied by cerebral cortical atrophy. Alterations in resting regional or global glucose metabolism, as measured with 18 FDG and PET do not occur in fra(X) syndrome.

NR651 **Thursday, May 17, 12 noon - 2:00 p.m.**

MRI ABNORMALITIES IN LATE-ONSET SCHIZOPHRENIA

Terry L. Jernigan, Ph.D., Psychiatry, VA Medical Center, 3350 La Jolla Vill. Dr. V116A, San Diego, CA 92161; Dilip V. Jeste, M.D., Jackuelyn M. Harris, M.D., David Salmon, M.D.

Summary:

Relatively little work has been done on brain imaging in late-onset schizophrenic patients. *METHODS*: We compared MRI scans of 13 *DSM-III-R*-diagnosed late-onset psychotic (LOP) patients (10 with schizophrenia, three with delusional disorder; 6F, 7M; mean age 61 $\pm$ 4 years), with those of 24 normal controls, and 30 patients with probable Alzheimer disease (AD). The groups were comparable in age and gender. A standard imaging protocol was used for all patients, and morphometrics were performed "blind" to patient identification, using standardized procedures. Estimates were obtained of total supratentorial cranial volume, ventricular and cortical sulcal CSF volumes, grey matter volumes of cortical and subcortical structures, and abnormality in the cerebral white matter. *RESULTS*: LOP patients had significantly more white matter abnormality (lengthened T_2) than normal controls ($p < .05$). A decrease in supratentorial cranial volume and an increase in ventricular CSF fell just short of significance ($p < .10$). No decrease was observed in any grey matter structure. In striking contrast, AD patients showed highly significant volume reduction in all cortical and subcortical structures, significant increase in white matter abnormality, but normal cranial volume. *COMMENT*: LOP patients had some structural abnormalities, but were distinctly different from AD patients. We will present further data at the meeting, and discuss neurobiologic implications of our findings.

NR652 **Thursday, May 17, 12 noon - 2:00 p.m.**

MRI IN SCHIZOPHRENIA: COMPUTER AIDED MEASURES OF BRAIN AND CSF

Martha E. Shenton, Ph.D., Psychiatry, Harvard Medical School, VAMC-116A 940 Belmont Street, Brockton, MA 02401; Ron Kikinis, M.D., Robert W. McCarley, M.D., Tamas Sandor, D.P., David Metcalf, B.S., Ferenc Jolesz, M.D.

Summary:

Most MRI studies in schizophrenia (SZ) rely upon manually-performed linear measurements, routine use single slices (cm), and do not fully exploit volumetric information. We report the first MRI study of SZ to use automated computerized image processing to make volume measurements of brain and CSF spaces in a sample of 10 chronic, male, right-handed, neuroleptic-medicated SZs (DSM-III-R) and 12 normal control subjects (NCLs). NCLs were matched for sex, handedness, and age (SZs = 40.9 ± 6.15 years; NCLs = 40.3 ± 9.27 years). Data from conventional spin echo sequences obtained with a Signa GE 1.5T MR Scanner were processed for multiple axial slices using: 1) a semi-automated algorithm to identify the intracranial cavity (ICC) for a 120mm slab beginning 15mm below the internal acoustic canal (including all of lateral and 3rd ventricles and most of the IVth), 2) a fully automated segmentation of this slab into brain, CSF, and vessels/connective tissue, and 3) a semi-automated separation of CSF into subarachnoidal and ventricular spaces. Measures were corrected for head size. Results showed no differences between NCLs and SZs in CSF volume, ventricular volumes, brain volume, brain/CSF ratio, vessels/connective tissue, or VBR. Of note, 11 out of 12 NCLs showed a LEFT > RIGHT lateral ventricular volume (dependent $t = -4.40$, $df = 11$, $p < 0.001$), while three out of 10 SZs showed the reverse—RIGHT > LEFT. In conclusion, we were able to derive accurate volumetric measurements from MRI. These initial findings warrant further analyses in a larger sample and within smaller regions, such as temporal horns.

		ICC	CSF	Brain Slab Volume	Lateral Ventricles	3&4 Vent.	Right Vent.	Left Vent.	Vessel/ Conn Tissue
SZ	Mean	1545.35cm³	229.98cm³	1267.95cm³	17.06cm³	5.20cm³	8.03cm³	9.03cm³	25.16cm³
	s.d.	±84.88	±31.69	±78.53	±6.42	±1.05	±3.17	±3.64	±4.40
NCL	Mean	1505.03cm³	237.02cm³	1212.23cm³	24.21cm³	5.76cm³	11.19cm³	13.02cm³	25.72cm³
	s.d.	±119.82	±41.38	±92.49	±12.72	±2.29	±5.92	±6.85	±6.42

NR653 **Thursday, May 17, 12 noon - 2:00 p.m.**

MORPHOMETRY OF BRAIN STRUCTURES IN SCHIZOPHRENIA

Manuel F. Casanova, M.D., CBDB, NIMH, 2700 Martin L. King Jr. Ave SE, Washington, DC 20032; Dennis Atkinson, M.D., Terry Goldberg, Ph.D., Mark Zito, M.S., E. Fuller Torrey, M.D., Daniel R. Weinberger, M.D.

Summary:

Enlargement of the ventricles during gestation often results in conformational abnormalities of the interhemispheric gyri. The present study addresses the time of onset of the ventriculomegaly observed in some schizophrenic (SC) patients by analyzing shape descriptors of the cingulate cortex and corpus callosum (CC). The patient population consisted of 15 monozygotic twins discordant for schizophrenia, five pairs concordant for the illness and five normal monozygotic twin pairs. Magnetic resonance images were analyzed with a computerized image analysis system (Loats) for various morphometric parameters. Analysis of the cingulate cortex at two coronal levels did not reveal any differences between the twin pairs. The results failed to elucidate the time of onset of the ventricular enlargement in schizophrenia. Significant shape abnormalities of the CC were evident in all the groups studied; however, only in the SC patients was the distortion consistent with an upwards bowing. Previous studies suggest that upwards bowing of the CC is secondary to ventriculomegaly. Since all of our twin pairs shared the same genetic constitution, the authors suggest that the conformational abnormality of the CC in SC patients, and hence ventriculomegaly, is the result of an environmental lesion.

NR654 **Thursday, May 17, 12 noon - 2:00 p.m.**

MRI OF SUPERIOR TEMPORAL GYRUS AND HALLUCINATIONS

Patrick E. Barta, M.D., Psychiatry, Johns Hopkins, 600 N. Wolfe Meyer 3-166, Baltimore, MD 21205; Godfrey D. Pearlson, M.D., Richard E. Powers, M.D., Stephanie Richards, B.S., Larry E. Tune, M.D.

Summary:

Using image processing techniques applied to brain MRI, 12 of 15 male schizophrenics (mean age 31), compared to individually matched controls, showed reduced volume of the superior temporal gyrus. (Matching was pairwise on age, race, parental SES, and years of education). Three-millimeter T1-weighted coronal cuts perpendicular to the AC-PC line were acquired from the genu to the splenium of the corpus callosum on a 1.5 T MRI scanner. These were rated blindly by a neuropathologist, using a standard anatomic MRI atlas. Images were displayed directly from 9-track tape on a DEC graphics workstation, and outlined using custom graphics software developed in our lab in ULTRIX (UNIX) using X-windows.

A reduction in superior temporal gyrus (STG) volume was found, which was more marked ($p < .01$) on the left side. Its magnitude was not accounted for either by overall brain shrinkage or by diffuse reduction in temporal lobe size. The region of the superior temporal gyrus assessed corresponds primarily to Brodmann's area 22, an auditory association area. Previous studies by Penfield & Perot have demonstrated that electrical stimulation of this region elicits complex hallucinations.

In the current investigation, the degree of left superior temporal lobe gyral shrinkage correlated significantly ($r = 0.70$, $p < .001$) with severity of hallucinations on the SAPS, but not with global SAPS or SANS score.

NR655 **Thursday, May 17, 12 noon - 2:00 p.m.**

QUANTITATIVE EEG CORRELATES OF COGNITIVE DETERIORATION IN THE ELDERLY

Leslie S. Prichep, Ph.D., Psychiatry, NYU Medical Center, 550 First Avenue, New York, NY 10016; E. Roy John, Ph.D., Barry Reisberg, M.D., Steven Ferris, Ph.D., Kenneth Alper, M.D., Robert Cancro, M.D.

Summary:

This poster will present data from the quantitative analysis of the EEG, using the neurometric method, in large samples of normal elderly ($n = 41$), patients with mild cognitive impairment ($n = 70$) and patients presenting with a continuum of primary cognitive deterioration from mild to severe ($n = 133$), compatible with dementia of the Alzheimer's type (DAT). Findings will be shown as topographic maps of neurometric EEG features. These measures were found to be a sensitive index of degree of cognitive impairment, especially reflected in increased absolute and relative power in the theta band, with delta increasing in later stages of deterioration. These abnormalities were not localized or lateralized, nor were any particular structures differentially implicated. Results suggest that Neurometric EEG features are sensitive to the earliest presence of subjective cognitive dysfunction and might be useful in the initial evaluation of patients with suspected dementia, as well as in estimating the degree of cognitive deterioration in DAT patients.

NR656 **Thursday, May 17, 12 noon - 2:00 p.m.**

THE BRAIN: ASYMMETRIES, NON-LINEAR DYNAMICS AND BEHAVIOR

Peter F. Andrus, M.D., 1734 Western Avenue, Albany, NY 12203

Summary:

The central nervous system is defined as the organ of perception, synthesis and complex motor reaction. Input to this system undergoes filtering, modulation and synthesis before translation into output events. The organization of these output events, i.e., behaviors, presupposes the integrity of neural structures. The resultant electrical activity can be quantified by quantitative electroencephalographic techniques. Coherence, the measure of opposing or cooperative neural events, can be employed to measure relative degrees of structural symmetry or asymmetry. These, in turn, reflect neural functioning in "normal" to "abnormal" degrees. "Mental illness" is a developmental event occasioned by oscillations resulting from asymmetrical structural dynamics.

Such dynamical systems can be understood by the non-linear mathematical techniques of "chaos theory". This study uses ten quantitative EEG records to represent mathematically defined states of abnormal function. Transition phase states or eigenfunctions, such as "borderline", are now clarified. A continuum between internal events, e.g., spontaneous bursting, and external events, e.g. periodic input, and phenomenon such as entrainment and kindling, lead to complex motor reactions, i.e., behavior. The hypothesis that "behavior is prolonged, modified seizure activity" is advanced. The concept of "forced normalization" is examined in this light.

NR657 **Thursday, May 17, 12 noon - 2:00 p.m.**

TEMPORAL LOBE STRUCTURE BY MAGNETIC RESONANCE IN BIPOLAR AFFECTIVE DISORDERS AND SCHIZOPHRENIA

Alessandro Rossi, M.D., Psychiatry, University of Laquila, L'Aquila, 67100, Italy; Paolo Stratta, M.D., Vittorio Dimichele, M.D., Massimo Gallucci, M.D., Alessandra Splendiani, M.D., Massimo Casacchia, M.D.

Summary:

Functional psychosis is conventionally subdivided into schizophrenia and manic depressive psychosis. Possible brain abnormalities specifically related to each disorder may be regarded as validating criterion for these diagnoses. The present MR study was designed to further investigate this issue.

15 patients with a DSM III bipolar disorder and 15 patients with a DSM III schizophrenic disorder agreed to participate in the study. Patients had recovered from an index episode and matched for age and sex. MR images were acquired through an Ansaldo Esatom 5000 0.5 Tesla scanner using a SE sequence (TR 2400, TE 120 msec) to obtain 15 coronal slices (5 mm thick) after a midsagittal pilot scan (TR 220, TE 20 msec) was obtained. The coronal plane was oriented perpendicularly to the etmoidal plane. Left and right temporal lobe areas were measured where visualized, usually slice 4-10, and then totalled to produce estimates of the volume of these structures. Left and right lateral ventricles were also measured. Measurements were done from film onto a digitizing tablet (Digitizer KD 3300) interfaced to an IBM AT equipped with Autocad.

No between group differences were observed but a statistically significant hemisphere factor emerged (two-way mixed ANOVA $p<0.05$), the left temporal lobe being smaller than the right in the schizophrenic group. This finding is consistent with the view that schizophrenia is a disorder related to an abnormal development of cerebral asymmetry.

Results from an expanded sample will be discussed in the light of the search for structural abnormalities specifically related to schizophrenia or bipolar disorder.

NR658 **Thursday, May 17, 12 noon - 2:00 p.m.**

BRAIN DOPAMINE IMAGING BY SINGLE PHOTON TOMOGRAPHY

Robert M. Kessler, M.D., Radiology & Psychiatry, Vanderbilt Med Center, Nashville, TN 37232; John R. Votaw, Ph.D., Tomas de Paulis, Ph.D., Dennis E. Schmidt, Ph.D., Jeffrey A. Clanton, M.S., Mohammed S. Ansari, B.S., K.P. Holdeman, M.D., Rhonda Pfeffer, B.S., Ronald G. Manning, Ph.D., Michael H. Ebert, M.D.

Summary:

[125I] epidepride is a potent dopamine receptor (D2) ligand with extremely high striatal: cerebellar ratios (234:1) *in vivo* rats. This suggests its utility in imaging brain dopamine symptoms by single photon emission computerized tomography (SPECT). *In vivo* studies of the regional brain uptake and kinetics of epidepride were performed in rhesus monkeys. Following IV injection of 2.5-10 mCi epidepride there was rapid cerebral uptake of epidepride with a peak striatal uptake of 0.6% injected dose being observed at 83 minutes following injection. Ratios of striatum to surrounding brain increased from 2:1 at 25 minutes to 15:1 at 4 hours and 58:1 at 6.4 hours after injection. Haloperidol (0.2mg/kg IV) displaced virtually all striatal uptake down to the level of surrounding brain with a T1/2 of striatal washout of 67 minutes. Amphetamine (1 mg/kg IV) was administered six hours after epidepride injection. No significant loss of striatal epidepride uptake was seen indicating that endogenous dopamine does not displace epidepride *in vivo*. Two normal volunteer male subjects received 5mCi (specific activity 6000Ci/mmol) of [123I] epidepride and serial tomographic images were obtained with a rotating gamma camera at times up to 16 hours post injection. Peak striatal uptake of 2.5-3% of injected dose was attained at 45 minutes post injection. Striatal uptake declined in both subjects with a T1/2 of 13 hours. There was rapid washout of [123I] epidepride from surrounding brain resulting in striatal:surrounding brain ratios of 2:1 at 20 minutes post injection, 10:1 at 4 hours, 16-25:1 at 7.5 hours, and 40-50:1 at 16 hours post injection. Epidepride is a superior ligand for SPECT, and can be used to image dopamine rich structures in human brain.

NR659 **Thursday, May 17, 12 noon - 2:00 p.m.**

CONTRAST ENHANCED MRI STUDY OF ECT

Raymond A. Faber, M.D., Nursing, University of Texas, 1700 Red River, Austin, TX 78701; Dolores Sands, Ph.D., J. Neal Rutledge, M.D., Roger McCary, M.D., Jean Swinney, MA., Heather Becker, Ph.D.

Summary:

In an effort to define any anatomical changes associated with electroconvulsive therapy (ECT), we obtained contrast enhanced magnetic resonance imaging (MRI) scans before and after courses of ECT in 14 patients aged 29 to 77 with major depression. Following methohexital, succinylcholine and oxygenation, 7 patients received right unilateral d'Elia electrode placement, 6 received bilateral electrode placement and one received left unilateral placement brief-pulse induced convulsions. At 1.5 Tesla mixed and T2 weighted axial images, T1 weighted sagittal images and T1 weighted axial images with and without the gadolinium salt, gadopentetate dimeglumine (Magnevist), for contrast enhancement were performed prior to the initiation of ECT, after the fifth ECT, and finally two months thereafter.

Prior to ECT several older patients were found to have mild generalized atrophy and leukoencephalopathic changes. No significant changes were found on any of the post-ECT MRI scans. To date our findings are in agreement with prior reports using unenhanced MRI scans before and after ECT revealing no effects on brain structure.

NR660 **Thursday, May 17, 12 noon - 2:00 p.m.**

REDUCED CEREBRAL VOLUME IN SCHIZOPHRENIA

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

Summary:

The principal aim of the present study was to explore the nature and extent of global cerebral volume reduction in schizophrenics measured by MRI. This study examined cerebral volumes in schizophrenics compared to volunteer controls matched for age and sex.

Volumes of cerebral structures were calculated by direct post-processing of digital IR MRI data using a PIXAR workstation and volumetric accumulation with the method achieving high interrater reliability (intraclass correlations $\pm$ 0.96). Scans selected were a random subsample of a larger dataset (20 schizophrenics, 20 controls)

Two-way ANCOVA (controlling for height) revealed a significant sex by group interaction in total cerebral volume (F-4.48, $p < .01$), and a significant main effect for sex ($F = 8.70$, $p < .001$). Mean cerebral volumes (in cc); 1238 ± 65, 1133 ± 111 for male and female controls; 1205 ± 105, 981 ± 43 for male and female schizophrenics respectively.

For comparability with previous results of area-related studies of relative brain size we found that single slice area data predicted volume well ($R^2 = 0.783$). Further, extracranial measurement of nasion-inion diameter predicted total volume reasonably well ($R^2 = 0.616$)

These results suggest that global reduction in brain volume may accompany schizophrenia, especially among females. Clinical, functional, and anatomic correlates remain to be determined.

NR661 **Thursday, May 17, 12 noon - 2:00 p.m.**

CORRELATES OF HIPPOCAMPUS HYPOPLASIA SCHIZOPHRENIA

Henry A. Nasrallah, M.D., Psychiatry, Ohio State University, 473 West 12th Avenue, Columbus OH 4321p; Bernhard Bogerts, M.D., Stephen C. Olson, M.D., Steven B. Schwarzkopf, M.D., Jeffrey A. Coffman, M.D.

Summary:

Postportem studies in schizophrenia have provided evidence of gross hypoplasia of the hippocampus in a proportion of patients. Histopathology point to disruption of neurodevelopmental processes (such as neuronal migration). We conducted a brain magnetic resonance imaging (MRI) study to compare schizophrenic patients with and without hypoplasia of the hippocampus. Our hypothesis was that there would be biopsychosocial differences between the two groups.

Patients fulfilling DSM-III-R criteria for schizophrenia (N = 54) consented to participate in the study. MRI scans were obtained on a GE 1.5 Tesla scanner. T1-weighted 5mm coronal sections were visually rated for gross reduction of the medial temporal lobe (hippocampus/amygdala complex) by a neuropathologist (BB) unaware of the diagnosis (scans of 90 normal and psychiatric controls were mixed with the 54 schizophrenia scans).

37% (N = 20) of the schizophrenic patients were found to have definite (+2) or equivocal (+1) hippocampal hypoplasia. When compared to the group of 34 schizophrenic patients with normal hippocampus size, no differences were found in age of onset, negative symptom score, obstetric complications, family history of psychosis, premorbid adjustment score or deteriorating course. However, the hippocampus abnormality patients were found to have significantly smaller mean global positive symptom score ($p = .024$), larger lateral ventricals ($p = .001$), larger third ventricles ($p = .0019$), and were older (34.9 vs 30.9 years, $p = .042$), with a trend for paranoid subtype ($p = .1$). The implications of these biopsychosocial differences between schizophrenic patients with and without hippocampal hypoplasia will be discussed in light of the neurodevelopmental model of schizophrenia.

NR662 **Thursday, May 17, 12 noon - 2:00 p.m.**

FUNCTIONAL AND PHYSIOLOGICAL MARKERS IN PATIENTS AT RISK FOR DEMENTIA OF THE ALZHEIMER'S TYPE

Richard J. White, Psychiatry, Ohio State Univ, 473 W. 12th Avenue, Columbus, OH 43210; Michael W. Torello, Ph.D., Robert A. Bornstein, Ph.D., Jeffrey A. Coffman, M.D., Henry A. Nasrallah, M.D., Elizabeth Burns, Ph.D.

Summary:

Dementia of the Alzheimer's type menaces the elderly. Previously, we reported a possible early detection paradigm involving neuropsychological (NP) and auditory evoked potential (AEP) variables. In addition to increasing the N, we have replicated findings reported earlier. We recruited a group of 28 at-risk patients 50-60 years who have a first degree relative with probable AD; 13 controls were recruited. A full complement of NP variables and AEP data were collected. In the AEP data set, an at-risk increase in N100 amplitude ($p < .018$) was found at the patient's maximal electrode; topographic mapping detected a greater difference over the frontal lobe ($p < .007$, F3 amplitude). P300 amplitude variations were not found, but topographic mapping revealed a non-significant at-risk deficit fronto-temporally (F4 & F8). Relating the NP and AEP data sets, we discovered a positive relation between P3 amplitude and the Wechsler visual immediate recall score. The regression equation predicted visual recall based upon group and P3 amplitude ($r\text{-}sq = .21$, $p < .016$). 13 NP variables were examined based upon their theoretical relationship to cognitive processing and vigilance (new Wechsler). Formulating a deficit criterion for each subject, we counted the number of variables in which he displayed a *deficit* of greater than 1.5z. In the at-risk group, this criterion could be predicted by the P3 amplitude over the fronto-temporal lobe (F4 electrode, $p < .032$, $r\text{-}sq = .19$). As P3 increased, the deficit decreased. No such relationship existed for the control group. Longitudinal followup will determine the relevance of these intriguing data which build upon our earlier findings.

NR663 **Thursday, May 17, 12 noon - 2:00 p.m.**

DRUG CONDITIONING OF DOPAMINE METABOLISM

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Summary:

Drugs such as methadone, morphine, bulbocapnine, droperidol and bromocriptine are known to produce changes in behavior and dopamine metabolism (DAM). A buzzer as a conditioned stimuli (CS) paired with these drugs as unconditioned stimuli (US) produce changes by CS alone as those produced by the drug as US. Conditioned changes in DAM induced by these drugs were measured in whole brain and in regional areas of the brain including the basal ganglia, septal area, hypothalamus, midbrain and cortex. The results showed conditioning of DAM in the basal ganglia to these drugs. Clear cut conditioning of DAM was observed in the septal area for droperidol and bromocriptine. Partial regional conditioning to droperidol was observed in the hypothalamus; none in the midbrain or cortex. The brain, like many other visceral organs, can be conditioned in terms of neurotransmitter metabolism. Conditioned behavioral changes produced by these drugs were also observed. Guidelines for doing controlled experiments in this area are presented. The conditioning of DAM could have significant relevance in the mechanism of action of psychotropic drugs, as well as, in the understanding of mental illness that involve altered dopaminergic functioning.

NR664 **Thursday, May 17, 12 noon - 2:00 p.m.**

NEUROFIBRILLARY DEGENERATION IN ALZHEIMER'S DISEASE

William Bondareff, M.D., Psychiatry, Univ So. California, 1520 Roscomare Road, Los Angeles, CA 90077; Claude M. Wischik, M.D., Martin Roth, M.D.

Summary:

Alzheimer (1907) described the transformation of intracellular tangles to extracellular tangled bundles of fibrils. We have used antibodies directed against proteins known to be involved in the cellular pathology of Alzheimer's disease (AD) to probe this process of neurofibrillary degeneration further.

Antibodies raised against antigens in the fuzzy coat of paired helical filaments (PHF) were found to immunolabel intracellular tangles exclusively. Selective immunolabelling of extracellular tangles was accomplished with a monoclonal antibody raised against an antigen in the PHF core. It was shown that labelling of extracellular tangles was associated with the removal of fuzzy coat antigens, exposure of epitopes in the PHF core, and the appearance of amyloid immunoreactivity. Antibodies raised against ubiquitin labelled both intracellular and extracellular tangles.

These findings suggest that changes undergone by intracellular tangles as they are transformed into extracellular tangles *in vivo* are similar to changes in the structure of PHFs accompanying protease digestion *in vitro*. They suggest that the degradation of neurofibrillary tangles in AD occurs in a series of distinct stages, including: ubiquitination of some as yet unidentified molecule, a change in tau immunoreactivity, the partial proteolysis of tau protein in extracellular tangles, and the appearance of amyloid immunoreactivity in certain degenerating extracellular tangles. It can be anticipated that further immunocytochemical analysis of tangle degradation *in situ* will help explain processes underlying the death of neurons in AD.

NR665 **Thursday, May 17, 12 noon - 2:00 p.m.**

WITHDRAWN

NR666 **Thursday, May 17, 12 noon - 2:00 p.m.**

BRAIN DYSFUNCTION AS A PREDICTOR OF OUTCOME

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Summary:

The present report examines the prognostic relationship between neurobehavioral functions and three discrete components of outcome (social skills, work function, rehospitalization) after discharge.

Method. A sample of 51 schizophrenic and affective disorder inpatients was administered the Luria-Nebraska Battery. The outcome measures of Harrow, Grinker, et al. (1978) evaluated course 2.3 years post-discharge. The principal analyses examined whether specific areas of cerebral deficit (premorbid early-acquired abilities, sensorimotor functions, and complex integrative skills) were independently associated in a predictive sense with major components of clinical outcome (social functioning, work or vocational status, and rehospitalization).

Results. Canonical correlation analysis indicated one significant canonical variate relating the neurobehavioral and outcome variables ($p < .025$). Examination of the correlations indicates that it is predominantly the premorbid neurobehavioral component which influences this relationship. The largest association with the outcome variables is for work role functioning.

Implications. These findings underscore the role of cerebral dysfunction in limiting clinical outcome, particularly chronic cognitive—perceptual disturbance of early onset. This form of compromised ability is consistent with structural brain abnormalities found in young psychiatric patients with no evidence for gross abnormality. Determination of early premorbid deficits may be important to assess in treatment planning, notably when imaging findings are unavailable or equivocal.

NR667 **Thursday, May 17, 12 noon - 2:00 p.m.**

MAJOR DEPRESSION AND PERSONALITY DISORDER

Mark Zimmerman, B.A., Psychiatry, Chicago Medical School, 13000 W. Heiden Circle #3103, Lake Bluff, IL 60044; Bruce M. Pfohl, M.D., William Coryell, M.D., Caryn Corenthal, M.A., Dalene Stangl, M.A.

Summary:

The authors examined an interview and paper-and-pencil assessment of the *DSM-III* personality disorders (PDs) in depressed inpatients, and depressed relatives of psychiatric patients and never-ill controls who had a lifetime history of major depression. The rates of PDs according to the Structured Interview for *DSM-III* Personality Disorders (SIDP) were similar in the two groups, except for borderline PD which was more frequent in the inpatients. Of the individuals with a PD, the patients were more likely to have two or more PDs, and the borderline and histrionic patients were more prototypic of these disorders than were the borderline and histrionic relatives. In contrast to the SIDP results, the rates of PDs according to the Personality Disorders Questionnaire (PDQ) were higher in the patient sample. These results thus extend the previously described high rates of PDs in depressed patients to a sample of individuals with a lifetime history of treated or untreated depression, and they suggest that interview assessments of personality are less sensitive to the state effects of depression than are questionnaires.

NR668 **Thursday, May 17, 12 noon - 2:00 p.m.**

PSYCHIATRIC ASPECTS OF CNS MYELINOLYSIS

Barbara P.I. Karp, M.D., OCD, NINDS NIH Bldg 10 RM 5N-226, Bethesda, MD 20892; Robert Laureno, M.D.

Summary:

Central and extra-pontine myelinolysis, a neurologic illness associated with the rapid correction of hyponatremia, can cause symptoms of pseudobulbar palsy, quadriplegia, and may lead to death. Behavioral changes including labile affect, pathological crying and mutism may develop prior to the onset of radiologic abnormalities and other symptoms more easily recognized as "organic" in nature, and may lead to psychiatric consultation. We reviewed the records of eight patients with neurologic deterioration following treatment of hyponatremia for psychiatric symptoms prior to and after correction. Prior to correction all patients had lethargy and variable symptoms of a generalized encephalopathy (including nausea, vomiting, and confusion) which cleared with treatment in seven. Symptoms of myelinolysis appeared a variable time after correction. In seven patients the first signs of myelinolysis, occurring 0.5-7 days after correction, were mutism and change in behavior. Psychiatric consultation was obtained in three patients who received tentative diagnoses of conversion reaction, depression, and/or acute psychosis and treatment with antidepressants, anxiolytics, and/or neuroleptics. With the development and recognition of corticobulbar and corticospinal tract signs, underlying neurologic illness was recognized and therapy adjusted. Behavioral changes in the remaining patients, including mutism, change in affect, agitation, confusion and emotional lability, were not treated as primary psychiatric illness. Five patients went on to have long-term psychiatric symptoms including personality change, inappropriate affect and/or delusions which had not been present prior to the development of myelinolysis. Psychiatrists, therefore, need to be aware of not only the symptomatology of hyponatremia, but also of myelinolysis, a possible complication of its treatment.

NR669 **Thursday, May 17, 12 noon - 2:00 p.m.**

VIOLENCE AND TEMPORAL LESION, CT SCAN, MRI DATA

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Summary:

Head CT and MRI scanning was done in 13 patients with violent behavior and organic mental syndromes developed after head injury or CVA. Positive findings were recorded in 10 out of 13 patients. In four cases, CT scan revealed extended low density lesion in the anterior part of the right temporal lobe involving hippocampalamygdaloid region in two out of four cases. In one case with negative CT, the MRI scan showed a limited area of cortical destruction in the anterior T2 and T3. In another case, a gliotic scar was seen in the left orbitofrontal region. Generalized cerebral atrophy was observed in the four remaining cases. Seizure disorder was reported in three out of five cases with localized temporal lobe lesion. These findings may be compared with the results of animal and human studies showing the important role of the amygdaloid complex in the regulation of violent behavior (Egger and Flynn, 1981, Heath, 1980). It is suggested that the release of programs for violent behavior may result from the unilateral destruction of amygdaloid nuclei coupled with the stimulation of preserved limbic structures by the mechanisms of kindling.

NR670 **Thursday, May 17, 12 noon - 2:00 p.m.**

PHYSIOLOGICAL EVIDENCE OF EXAGGERATED STARTLE RESPONSE IN PTSD

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Summary:

One of the diagnostic criteria for Posttraumatic Stress Disorder (PTSD) is an exaggerated startle response. This behavioral abnormality has been thought to be particularly prevalent in combat-related PTSD. To date, however, exaggerated startle in combat-related PTSD has not been empirically verified. The current study compared a group of Vietnam combat veterans with PTSD (N = 20) to a control group of combat veterans without PTSD (N = 18) on a physiological measure of startle reactivity: Eyeblink electromyographic (EMG) amplitude to acoustic and tactile stimuli. The two groups were further subdivided into responders and non-responders, based on whether or not subjects showed evidence of stimulus-elicited eyeblink activity. The PTSD responder group had significantly greater eyeblink amplitude than the control responders at intermediate intensities of acoustic stimuli. When the PTSD responders were compared to the PTSD non-responders, statistically nonsignificant but potentially interesting trends emerged in the manifestation of both negative (eg. emotional numbing, withdrawal) and positive (eg. perceptual aberration, atypical thought) symptoms.

NR671 **Thursday, May 17, 12 noon - 2:00 p.m.**

CHRONIC MK801 TREATMENTS IN A NEUROPSYCHIATRIC MODEL

Andrew B. Norman, Ph.D., Psychiatry, Univ College of Medicine, 231 Bethesda Avenue, Cincinnati, OH 45267; Lisa M. Ford, M.D., Magda Giordano, M.S., P.R. Sanberg, Ph.D.

Summary:

The excitotoxin quinolinic acid (QA) when injected into the rat striatum mimics the neurodegenerative abnormalities observed in Huntington's disease (HD). Furthermore, following QA lesions of the rat striatum, the behavioral effects of haloperidol and the D_1 dopamine receptor antagonist SCH23390 were abolished. The non-competitive glutamate N-methyl-D-aspartate receptor antagonist MK801 (4 mg/kg i.p.) prevented this loss of neuroleptic-induced catalepsy and the neurodegeneration elicited by QA. It might be expected that treatments with MK801 or similar drugs may prevent the neurodegeneration characteristic of HD. However, chronic treatment with receptor antagonists such as MK801 may lead to a supersensitivity to the effects of agonists. We therefore investigated the functional consequences of chronic treatments of MK801. Male Sprague-Dawley rats were treated with MK801 (1 mg/kg i.p.) or vehicle and the locomotor responses were measured in Digisian Activity Monitors. MK801 produced increases in locomotor activity concomitant with ataxia. Rats were then administered MK801 (1mg/kg/day) or vehicle for 21 days. Following the final injection the locomotor responses were monitored again. There were significant changes in the topography of locomotion and increased rearing behavior compared with the initial responses to MK801. There were no significant changes in the number or affinity of D_1 or D_2 dopamine receptors in the striatum following chronic MK801 treatments. Following a two day withdrawal from chronic MK801 or vehicle treatment rats were given intrastriatal injections of QA (100 nmoles). In vehicle treated rats this dose of QA produce a 60 percent loss of D_1 dopamine receptors. In rats withdrawn from chronic MK801 treatment a significantly greater loss of D_1 dopamine receptors was observed. Thus, chronic treatment with MK801 may cause a supersensitivity of striatal neurons to the excitotoxic actions of NMDA receptor agonists.

NR672 **Thursday, May 17, 12 noon - 2:00 p.m.**

MORE ABOUT SPECT SCANS IN NEUROPSYCHIATRY

Ben Zimmer, M.D., ANI, 7777 Steubenville Pike, Oakdale, PA 15071; Robert Fields, Ph.D., Christopher Starratt, Ph.D., Mustafa Adatepe, M.D., Trevor R.P. Price, M.D.

Summary:

The role of single photon emission computed tomography (SPECT) in psychiatry remains controversial. Elsewhere, Trzepacz, et al reports on the greater clinical utility of single photon emission computerized tomography (SPECT) (a "physiologic" measure) than other imaging techniques in the evaluation and treatment of behavioral disorders. This report attempts to develop correlates between SPECT and a battery of neuropsychological tests first retrospectively and then followed prospectively.

Twenty-six patients ($M^5$12, $F^5$14) (x 46.4; white; r. handed) with co-existing neurological and psychiatric disorders received comprehensive neuropsychological (NP) evaluations (n26), SPECT scans (n25) and CT or MRI scans (n17). Three received repeat NP and SPECT evaluations. Results revealed that among these dually diagnosed patients, CT/MRI scans represent the most conservative diagnostic tool detecting dysfunction in 50% (10/17) of cases, whereas abnormalities detected by SPECT and by NP testing were 84% (21/25), 92% (24/26) of cases respectively.

Overall agreement between diagnostic tools was greatest among SPECT and CT/MRI 75% (12/16) and SPECT and NP tests 76% (19/25) with less agreement between CT/MRI and NP 59% (10/17). Agreement on localization of deficits (i.e. anterior versus posterior) was greatest between SPECT and CT/MRI 75% (24/32) with less agreement between the other measures 59% (20/34) for NP versus MRI and 64% (32/50) for NP versus SPECT. In general, agreement was greater for anterior than posterior dysfunction. Thus, SPECT appears to have considerable convergent validity with other diagnostic tools, however, its role in answering specific questions warrants further study. We found for example, that significant changes in NP testing correlated with serial SPECT scans in patients with resolving traumatic brain injury and resolving anoxic encephalopathy, but not in a patient with a developing hydrocephalus.

NR673 **Thursday, May 17, 12 noon - 2:00 p.m.**

COMPARISON OF COMPUTER AND MANUAL WISCONSIN CARD SORT TEST

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Summary:

Reliability is an important aspect of measurement for neuropsychological research, especially for tests which depend upon interaction between the subject and examiner. The Wisconsin Card Sorting Test (WCST) is a widely used test of this kind, and has been standardized for manual administration by Heaton. In order to further reduce or eliminate some sources of variability, we have automated both the administration and the scoring of the WCST. There are potential problems in automation of neuropsychological tests, for example, important factors which influence performance may be overlooked. Other obvious factors also may affect performance but cannot at this time be duplicated by a computer. This study compared performance between the standard manual Heaton version of the WCST and the computerized version we have developed. In a group of 21 normal and psychiatric subjects, no significant differences in performance were found. In particular, the standardized differences between group computer and manual scores for Perseverative Responses and Perseverative Errors were -0.01 and -0.04, respectively. This data suggests that the computerized form of the WCST may offer the advantages of more consistent administration and improved accuracy in data acquisition and scoring.

NR674 **Thursday, May 17, 12 noon - 2:00 p.m.**

HEMISPHERIC ASYMMETRY IN EMOTIONAL AWARENESS

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Summary:

While the right hemisphere is known to predominate in the perception of facial emotion, individual differences in this characteristic are prominent and are not well understood. We tested whether performance on the Levels of Emotional Awareness Scale (LEAS), a cognitive-developmental measure of emotion, correlated with the degree of right hemisphere dominance on the Levy Chimeric Faces Test (a 36-slide test of whether chimeric faces with a half-smile and half-neutral expression look happier if the half-smile is in the right or left visual field (LVF)). Forty-six right-handed medical students were tested. The mean Laterality score, or proportion of LVF responses, was 47%. Controlling for the effect of verbal ability (using the Vocabulary Subtest of the Schipley Institute of Living Scale), the partial correlation between LEAS and Laterality was .456 ($p < .001$), indicating that greater emotional awareness is associated with a greater degree of right hemisphere dominance in the perception of facial emotion. THese findings in normal individuals are consistent with the association that has been made between an impairment in right hemisphere function and a syndrome beginning early in life characterized by emotional and interpersonal difficulties, shyness, visuospatial disturbances and aprosodia.

NR675 **Thursday, May 17, 12 noon - 2:00 p.m.**

THE SCID-EPILEPSY

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Summary:

The Structured Clinical Interview for DSM-III-R - Epilepsy Version (SCID—Epilepsy) is a revision of the SCID - Patient Version for evaluating life-to-date ictal, post-ictal, and interictal behavioral disturbances among epileptics. The SCID-Epilepsy (1) clarifies diagnostic algorithms to allow Axis I and II diagnoses in patients for whom the etiological contribution of organicity is unknown; (2) documents atypical syndromes; and, (3) probes the relationship between epilepsy course and behavior for each DSM-III-R diagnosis. The SCID-Epilepsy was administered to 45 consecutively admitted patients with medically intractable complex partial seizures and video-sphenoidal EEG demonstration of ictal epileptiform discharges. The most commonly diagnosed interictal syndromes were depressive: 26 patients (58%) had a history of a depressive spectrum disorder after seizure onset. 16 (36%) had a history meeting criteria for diagnosis of one or more Major Depressive Episodes. Personality Disorders were diagnosed in 10 cases (22%). Psychotic Disorders (3 cases, 7%), Psychoactive Substance Use Disorders (3 cases, 7%), and Somatoform Disorders (2 cases, 4%) were less common. The SCID-Epilepsy is the first structured interview for psychiatric diagnosis in seizure disorders, and may prove a valuable instrument for future research.

NR676 **Thursday, May 17, 12 noon - 2:00 p.m.**

TREATMENT OF EMOTIONAL INCONTINENCE WITH FLUOXETINE

Andrew Hornstein, M.D., Psychiatry, Helen Hayes Hospital, Route 9W, West Haverstraw, NY 10993; James Flax, M.D., Glenn Seliger, M.D., Joseph Herbert, M.D., Karl Schroeder, M.D.

Summary:

Emotional incontinence is a behavioral syndrome characterized by involuntary weeping, grimacing, and/or laughter. It is frequently associated with neurologic disease and has been described in stroke, multiple sclerosis, head injury, ALS, central pontine myelinolysis and anoxia. The neuroanatomy and neurochemistry of emotional incontinence is poorly understood. Based on reports of successful treatment with tricyclic antidepressants, we investigated the efficacy of fluoxetine, a specific serotonin re-uptake blocker, in twelve patients (7 with cerebrovascular disease, 3 with multiple sclerosis, 1 with anoxia and 1 with dementia) with emotional incontinence. All twelve patients demonstrated dramatic improvement in emotional lability within 3 to 14 days. Whereas prior reports have implicated noradrenergic and dopaminergic pathways in the pathophysiology of emotional incontinence, our data also suggest a role for the serotonergic system. Emotional incontinence appears to be a pure motor release phenomena associated with organic neuropathology with little or no primary affective content. These patients require neurologic investigation as well as symptomatic treatment.

NR677 **Thursday, May 17, 12 noon - 2:00 p.m.**

PLATELET MARKERS IN ANXIETY, DEPRESSION AND STRESS

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Summary:

Investigation of the neurobiological relationship between anxiety and depression follows from observations of symptom overlap. Altered brain serotonin (5-HT) systems have been associated with the pathophysiology of both disorders, and may serve as a common biochemical pathway. We measured 3H-imipramine and 3H-paroxetine binding sites in blood platelets of drug-free psychiatric patients and controls; these ligands bind to sites associated with the 5-HT transporter in brain and platelets. Compared to controls, the maximal binding capacity (Bmax) of 3H-imipramine was significantly lower in platelets of patients with DSM-III-R diagnoses of Major Depression, Dysthymia, Generalized Anxiety, and Panic disorders; the affinity constant (Kd) was higher for depressive patients than controls. 3H-Paroxetine binding was significantly reduced only in patients with anxiety disorders; no differences in Kd were observed.

The effects of stress on platelet binding were also examined in first-year medical students during exams, since stress has associated with the onset of anxiety and depression. We found that, compared to after vacation, the Bmax of both 3H-imipramine and 3H-paroxetine binding were significantly decreased during exams, with no change in Kd. Taken together, these results suggest that alterations within the 5-HT uptake system may be common to anxiety, depression, and stress.

NR678 **Thursday, May 17, 12 noon - 2:00 p.m.**

SEROTONERGIC FUNCTION IN BORDERLINE PERSONALITY

Eric Hollander, M.D., Psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; David Kellman, M.D., Concetta DeCaria, M.A., Daniel Stein, M.D., Michael R. Liebowitz, M.D., Lyle E. Rosnick, M.D.

Summary:

Six adult inpatients (2 male/4 female; mean age = 27.8 years) with borderline personality disorder diagnosed by structured interview and 10 normal controls received challenges with the serotonergic agonist m-CPP and placebo in a double-blind, randomized design. Subjects also had neuropsychiatric assessment for soft-signs and neuropsychological function. Neuroendocrine and behavioral findings from these patients, who are novelty-seeking and impulsive were contrasted with similar findings from a previous study of 20 obsessive-compulsive (OCD) patients, who are risk aversive. Impulsive -borderline personality patients had blunted prolactin and cortisol responsivity to m-CPP compared to controls, although less blunted than the OCD patients. Behavioral response to m-CPP seems heterogeneous in the borderline patients, with either a calm, high, relaxed, detached response or an irritable, anxious response. This contrasts to the dysphoric/obsessive response in 55% of the OCD patients. There was less neuropsychiatric impairment in the borderline patients than in the OCD patients. Implications of these findings will be discussed.

NR679 **Thursday, May 17, 12 noon - 2:00 p.m.**

DOPAMINE SENSITIVITY AND COCAINE ABUSE

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Summary:

Ten male cocaine abusers received a single dose of the dopamine agonist apomorphine (0.75 mg SQ). Self ratings of cocaine craving, anxiety and depression decreased following apomorphine, particularly for patients in the craving phase. Decrease in cocaine craving following apomorphine correlated with decrease in pHVA ($r = .54$, $p = .05$), suggesting decreased dopamine turnover. Prolactin decreased by 28% and growth hormone increased by 580% following apomorphine. Lifetime cocaine use correlated negatively with baseline pHVA ($r = .67$, $p = .03$) and positively with peak delta pHVA ($r = .63$, $p = .04$) following apomorphine, consistent with upregulated dopamine receptors. However, patients had blunted endocrine response to apomorphine compared to controls, suggesting a less efficient, dysregulated dopamine system. Implications for a dopamine hypothesis of cocaine abuse are discussed.

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FOUR-FACTOR MODEL OF SCHIZOPHRENIA

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Summary:

Schizophrenia is now generally regarded as a heterogeneous condition, but the nature of its diversity remains poorly understood. The prevailing concepts include Kraepelin's subtypes, which after 80 years still dominate the American diagnostic system, and the newer positive-negative distinction. The Kraepelinian model, however, has not sufficed for treatment or prognostic decisions, and the positive-negative model may be valid but insufficient to accommodate the phenomenology of schizophrenia. We therefore undertook to study the factorial validity of this two-factor model, its sufficiency, and its relatedness to the Kraepelinian typology for schizophrenia. We administered the strictly operationalized 30-symptom Positive and Negative Syndrome Scale (PANSS) to 240 schizophrenic inpatients. Principal component analysis indicated four orthogonal factors that encompassed the spectrum of psychopathology: negative, positive, depressive, and excited. Symptoms of the Kraepelinian subtypes were associated with combined syndromes: positive-depressed (paranoid), negative-depressed (catatonic), and positive-negative (disorganized). The findings suggest that: (a) the positive-negative model is valid but incomplete; (b) schizophrenic subtypes derive from a hybrid of unrelated but co-occurring dimensions that may define the fundamental elements of psychopathology; (c) a four-factor model that includes affective dimensions better encompasses the heterogeneity of schizophrenia and has implications for evolving syndrome-specific treatments.

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