1987
NEW RESEARCH
PROGRAM & ABSTRACTS

AMERICAN PSYCHIATRIC ASSOCIATION

140TH ANNUAL MEETING
MAY 9 - 14, 1987
CHICAGO, ILLINOIS

Psychiatry in Medicine • Medicine in Psychiatry

PROGRAM
AND
PAPERS ON NEW RESEARCH

IN SUMMARY FORM

THE ONE HUNDRED AND FORTIETH
ANNUAL MEETING OF THE
AMERICAN PSYCHIATRIC ASSOCIATION

CHICAGO, ILLINOIS
May 9–14, 1987

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

Monday, May 11, 1987, 12 noon–2:00 p.m.
New Research 2—Poster Session—Exhibit Hall, Lower Level, McCormick Place North

SESSION ON AFFECTIVE DISORDERS AND SUBSTANCE ABUSE DISORDERS

Moderator: Gary J. Tucker, M.D.

NR1 Does ECT Exert a Unique Serotonergic Effect?
Matthew V. Rudorfer, M.D., Laura J. Fochtmann, M.D., Emile D. Risby, M.D., John K. Hsiao, M.D., William Z. Potter, M.D.

NR2 Acute ECT Effects on Platelet 5HT Uptake
Jeffrey L. Rausch, M.D., Charles Rich, M.D., S. Craig Risch, M.D.

NR3 Arginine-Aspartate and Electroconvulsive Treatment
Georges D. Cehovic, M.D., Miroslav M. Velek, M.D., Samuel J. Strada, Ph.D.

NR4 Modified Muller's Position for Unilateral ECT
Sidney S. Chang, M.D., Joel Silberberg, M.D., Eileen Enez, R.N., Robert A. deVito, M.D.

NR5 Attitudes Towards ECT: Enduring Effects
Richard D. Weiner, M.D., C. Edward Coffey, M.D., Jonathan M. Farber, Ph.D.

NR6 Topograhic EEG and Event Related Potentials in ECT
Jeffrey A. Coffman, M.D., Daniel J. Martin, M.D., Linda R. Fortin, EEG.T., Catherine H. Lewis, B.S., Michael W. Trello, Ph.D.

NR7 Benzodiazepines Reduce ECT's Therapeutic Effect
Helen M. Pettinati, Ph.D., Kenneth K. Willis, M.D., Stephani M. Nilsen, R.N., Sarah E. Robin, B.A.

NR8 ECT in the Treatment of Epileptic Psychosis
Michael Miller, M.D., Gustav Degreef, M.D., Sukdeb Mukherjee, M.D., Haranath Parepally, M.D.

NR9 Caffeine Augmentation of ECT Seizures
C. Edward Coffey, M.D., Richard D. Weiner, M.D., Gary S. Figiel, M.D., Martha Cress, R.N., W. Vaughn McCall, M.D., E. Frank Shelp, M.D.

NR10 State-Trait Aspects of Noradrenergic Regulation
Larry J. Siever, M.D., Emil F. Coccaro, M.D., Howard Klar, M.D., Richard A. Friedman, Steven Greenwald, M.A., Kenneth L. Davis, M.D.

NR11 CSF Monoamine and Depressive Subtypes
Richard P. Brown, M.D., Marc Stipetic, M.S., Markku Linnoila, M.D., John Keilp, M.A., Michael Stanley, Ph.D., Barbara Stanley, Ph.D., J. John Mann, M.D.

NR12 Photoimmunology and Seasonal Affective Disorder
Robert G. Skwerer, M.D., Lawrence Tamarkin, Ph.D., Thomas A. Wehr, M.D., Frederick M. Jacobsen, M.D., David A. Sack, M.D., Guilio F. Paciotti, M.S., Karen A. Kelly, M.D., Norman E. Rosenthal, M.D.

NR13 Effects of Different Light Wavelength in SAD
Norman E. Rosenthal, M.D., George C. Brainard, Ph.D., Donald Sherry, M.D., Robert G. Skwerer, M.D., Morris Waxler, Karen Kelly, M.D., David A. Sack, M.D., Thomas A. Wehr, M.D., Patricia M. Schulz, M.S.W.

NR14 Morning Light Treatment for Winter Depression
Robert L. Sack, M.D., Alfred J. Lewy, M.D., David M. White, Ph.D., Clifford M. Singer, M.D., Tana M. Hoban, Ph.D.

NR15 The Effects of Bright Light in Normal Subjects
Siegfried F. Kasper, M.D., Susan Rogers, R.N., Patricia M. Schulz, M.S.W., Annette Potter, B.A., Robert G. Skwerer, M.D., Norman E. Rosenthal, M.D.

NR16 Daylight Saving Time Affects Psychiatric Symptoms
Peter A. Bick, M.D., Alison Hannah, A.B.

NR17 Diurnal Variation in Seasonal Affective Disorder
Frederick M. Jacobsen, M.D., Adriana Dreizzen, M.D., Norman E. Rosenthal, M.D., David A. Sack, M.D., Robert G. Skwerer, M.D., Thomas A. Wehr, M.D.

NR18 PET Study of Sleep Deprivation
Joseph Wu, M.D., Monte S. Buchsbaum, M.D., J. Christian Gillin, M.D.

NR19 TSH Response to Sleep Deprivation in Depression
David A. Sack, M.D., Siegfried Kasper, M.D., Thomas A. Wehr, M.D., Robert G. Skwerer, M.D., Hermes Kick, M.D., Gabrielle Voll, M.D.

NR20 Postpartum Depression and Thyroid Autoimmunity
Nelson B. Freimer, M.D., Victor I. Reus, M.D., Luisa Manfredi, B.A.

NR21 HLA, Depression, and Autoimmune Thyroiditis
Victor I. Reus, M.D., Nelson B. Freimer, M.D., Luisa Manfredi, B.A.

NR22 Thyroiditis in Affective and Non-affective Psychiatric Disorders
John J. Haggerty, Jr., M.D., Dwight L. Evans, M.D., Robert N. Golden, M.D., Cort Pederson, M.D.

NR23 Sleep EEG in Mania
James I. Hudson, M.D., Joseph F. Lipinski, M.D., Frances R. Frankenburg, M.D., Victoria J. Grochocinski, Ph.D., David J. Kupfer, M.D.

NR24 Bipolar Illness in Patients with Endometriosis Implications
Dorothy Otnow Lewis, M.D., Florence Comite, M.D., Catherine Mallouh, B.A., Laura Zadunaisky, M.S., Karen Hutchinson, M.D., Bruce Cherksey, Ph.D.

NR25 Receptor Dysregulation in Psychiatric Disorders
Bruce D. Perry, M.D., Steven M. Southwick, M.D., Earl L. Giller, Jr., M.D.

NR26 Depression with/without Panic; Neuroendocrinology
Gregory M. Gillette, M.D., James C. Garbutt, M.D.

NR27 Effect of Dexamethasone Half-Life on DST Response
Peter E. Stokes, M.D., Peter M. Stoll, M.A., Carolyn R. Sikes, M.A., Betty J. Lasley, Ph.D.

NR28 Predictors of HPA Axis Dysfunction in Depression
Joan Kotun, M.D., Roger F. Haskett, M.D., Leon Grunhaus, M.D., John R. Greden, M.D.

NR29 Salivary and Serum Cortisol Levels in the DST
Robert P. Climko, M.D., David Martin, Donald R. Sweeney, M.D.

NR30 Studies of Human CSF Neuropeptides
Wade H. Berrettini, M.D., John I. Nurnberger, Jr., M.D., Joel Gelernter, M.D., Susan Simmons-Alling, M.S.N., Owen Wolkowitz, M.D.

NR31 Insulin Resistance After Oral GTT in Depression
Jay D. Amsterdam, M.D., Andrew Winokur, M.D., Greg Maislin, M.S.

NR32 Vasopressin Test: Effect of Clinical Variables
Juan F. Lopez, M.D., Roger G. Kathol, M.D., William H. Meller, M.D., Richard S. Jaeckle, M.D.

NR33 Blunted Orthostatic Response in Major Depressives
Philip J. Wilner, M.D., Richard P. Brown, M.D., John A. Sweeney, Ph.D., James P. Halper, M.D., Helen Tierney, M.D., J. John Mann, M.D.

NR34 Features of Eye-Tracking in Delusional Depression
Stephen L. Snyder, M.D., John A. Sweeney, Ph.D., Margaret Rea, Ph.D., J. John Mann, M.D., Allen J. Frances, M.D.

NR35 Natural Killer Cell Activity and Age in Depression
Steven J. Schleifer, M.D., Steven E. Keller, Ph.D., Ronald N. Bond, Ph.D., Jacob Cohen, Ph.D., Marvin Stein, M.D.

NR36 Plasma Tranylcypromine and Antidepressant Action
Alan G. Mallinger, M.D., Jonathan M. Himmelhoch, M.D., Michael E. Thase, M.D., David J. Edwards, Ph.D., Steven Knopf, B.S., Carilyn Z. Fuchs, Ph.D.

NR37 Treatment-Induced Changes in Membrane LI Affinity
Alan G. Mallinger, M.D., Jonathan M. Himmelhoch, M.D., Michael E. Thase, M.D., Steven Knopf, B.S., Christine S. Dippold, B.S.

NR38 Olfactory Deficits in Schizophrenia
Lili C. Kopala, M.D., Trevor A. Hurwitz, M.D., Campbell M. Clark, Ph.D., Barry D. Jones

NR39 Fluoxetine Plasma Levels in Treatment of Depression
R. Cameron Dorey, Ph.D., Jorge H. Beber, M.D., Sheldon H. Preskorn, M.D.

NR40 Hydroxymetabolites of Tricyclic Antidepressants
Bruce G. Pollock, M.D., James M. Perel, Ph.D., John P. Foglia, M.S., Lori A. Birder, M.S.

NR41 Variability of Plasma Levels of Antidepressants in the Elderly: A Possible Mechanism
Raymond J. Ancill, M.B., J.S. Kennedy, M.D.

NR42 10-Hydroxy-Nortriptyline Inhibits Efficacy in Elderly?
Robert C. Young, M.D., George S. Alexopoulos, M.D., Richard D. Shindledecker, M.A., Amiya K. Dhar, D.Sc., Henn Kutt, M.D., Charles A. Shamoian, M.D.

NR43 Fluvoxamine in Refractory Depression
Pedro L. Delgado, M.D., Lawrence H. Price, M.D., Dennis S. Charney, M.D., George R. Heninger, M.D.

NR44 After Lithium Augmentation: A Retrospective Study
Andrew A. Nierenberg, M.D., Lawrence H. Price, M.D., Dennis S. Charney, M.D., George R. Heninger, M.D.

NR45 Psychopathology in Parasuicide and Failed Suicide
John G. Keilp, M.A., Catherine Raduns, M.A., Susan Evans, B.S., Richard P. Brown, M.D., P. Anne McBride, M.D., J. John Mann, M.D.

NR46 Family Variables Related to Suicidality and Violence
Robert Plutchik, Ph.D., Herman M. Van Pragg, M.D., Hope R. Conte, Ph.D., Susan Picard, M.A.

NR47 Oxford Record-Linkage Study: Diagnosis and Mortality
John C. Simpson, Ph.D., Ming T. Tsuang, M.D.

NR48 Lifetime Course of Illness in Chronic Depression
Robert M. Rohrbaugh, M.D., Diane E. Sholomskas, Ph.D., Earl L. Giller, Jr., M.D.

NR49 Unipolar Depression: Adolescent versus Adult Onset
Thomas H. McGlashan, M.D.

NR50 Social Zeitgebers and Bereavement
Joseph A. Flaherty, Judith A. Richman, Ph.D., Ellen Frank, Ph.D., David J. Kupfer, M.D., K. Hoskinson, M.S.

NR51 The Psychology of Helplessness
Marian L. Fitzgibbon, Ph.D., John A. Sweeney, Ph.D., David F. Cella, Ph.D.

NR52 Problem-Solving in Parasuicides and Outcome
Isaac Sakinofsky, M.D.

NR53 DSM-III Axis II and Medical Utilization
William R. Yates, M.D., James H. Reich, M.D., Mary Nduaguba, Ph.D.

NR54 Psychosocial Sequelae of Marijuana Use
David W. Brook, M.D., Judith S. Brook, Ed.D.

NR55 Epidemiology of Alcohol Dependence Syndrome in U.S.
Alan J. Romanoski, M.D., Gerald Nestadt, M.D., James C. Anthony, Ph.D., Marshal F. Folstein, M.D., Ernest M. Gruenberg, M.D., Paul R. McHugh, M.D.

NR56 Drug Abuse in Alcoholism
Alan C. Whitters, M.D., Remi J. Cadoret

NR57 Li and Alcohol: Clinical and Biological Studies
Jack Hirschowitz, M.D., Robert J. Hitzemann, Ph.D., Beatrice Kovasznay, M.D., Howard LaGrone, M.D., Gail Broggini, R.N., Richard Smith, M.S.W.

NR58 Platelet Serotonin Uptake in Chronic Alcoholics
Jan L. Campbell, M.D., Thomas L. Kent, M.D., Thomas L. Pazdernik, Ph.D., Elizabeth C. Penick, Ph.D., Barbara J. Powell, Ph.D., Donald W. Goodwin, M.D.

NR59 Alcoholism in Homeless People
William R. Breakey, M.B., Pamela J. Fischer, Ph.D.

NR60 Amantadine Treatment of Cocaine Abuse
Leonard Handelsman, M.D., Teresita P. Quesada, M.D., Prakash L. Chordia, M.D., Ira J. Marion, M.A., Joyce H. Lowinson, M.D.

NR61 Persistent Neurochemical Deficit in Cocaine Abuse
Irl Extein, M.D., William Z. Potter, M.D., Mark S. Gold, M.D., Pierre Andre, M.D., William A. Rafuls, M.D., David A. Gross, M.D.

NR62 Neuropsychological Functioning in Cocaine Abusers
Kenneth J. Krajewski, M.D., Heather Doering, B.S.N.

NR63 Morphine Effect on Brain Metabolism in Post-addicts
Edythe London, Ph.D., Emmanuel P. Broussolle, M.D., Jonathan Links, Ph.D., Dean F. Wong, M.D., Robert F. Dannals, Ph.D., Henry N. Wagner, Jr., M.D., Sandy Rippetoe, R.N., Barbara Holicky, R.N., Ron Herning, Ph.D., J.K.T. Toung, M.D., Jerome H. Jaffe, M.D.

NR64 Doxepin in Detoxifying Depressed Opiate Addicts
Steven L. Batki, M.D., Scott M. Wheeler, Ph.D., James L. Sorensen, Ph.D., Reese T. Jones, M.D., Michael Rowbotham, M.D., Kathy Brennan, M.A.

NR65 Cannabis and Higher Functions: Longitudinal Study
Sarabjit S. Mendhiratta, M.B., Vijoy K. Varma, M.B., Ravinder K. Dang, Ph.D., Anil Malhotra, Ph.D., Karobi Kas, M.A., Ritu Nehra, M.A.

Tuesday, May 12, 1987, 9:00 a.m.–10:30 a.m.
New Research 3—Oral/Slide Session—Room L-3, Lower Level, McCormick Place North

NEW RESEARCH ON ORGANIC MENTAL DISORDERS

Chp.: Stuart T. Hauser, M.D.
Co-Chp.: Igor Grant, M.D.

NR66	Biological/Clinical Subtype of Alzheimer's Disease George S. Zubenko, M.D., Bruce M. Cohen, M.D., Charles F. Reynolds III, M.D., Francois Boller, M.D., Ivana Malinakova, M.S., Nanci Keefe, M.A.	9:00 a.m.
NR67	50% Risk in Alzheimer Families at all Proband Ages John C. S. Breitner, M.D., Richard C. Mohs, Ph.D., Marshal F. Folstein, M.D., Jeremy M. Silverman, M.A. Kenneth L. Davis, M.D.	9:15 a.m.
NR68	Functional Deficits in Alzheimer's Disease Jeffrey Borenstein, M.D., Barry Reisberg, M.D.	9:30 a.m.
NR69	Age of Onset in Geriatric Depression With Dementia George S. Alexopoulos, M.D., Robert C. Young, M.D., Barry S. Meyers, M.D., Robert C. Abrams, M.D., Charles A. Shamoian, M.D.	9:45 a.m.
NR70	Late-Onset Psychosis and Structural Brain Injury Ira M. Lesser, M.D., Bruce L. Miller, M.D., Mark Goldberg, M.D., Elizabeth HIII, R.N., Kyle Boone, Ph.D., Milton H. Miller, M.D.	10:00 a.m.
NR71	Neuropsychology and MRI in HIV Infected Groups Igor Grant, M.D., J. Hampton Atkinson, M.D., Caroline J. Kennedy, M.D., Douglas D. Richman, M.D., Stephen A. Spector, M.D., J. Allen McCutchan, M.D.	10:15 a.m.

Tuesday, May 12, 1987, 9:00 a.m.–10:30 a.m.
New Research 4—Oral/Slide Session—Room L-2, Lower Level, McCormick Place North

NEW RESEARCH SESSION ON SCHIZOPHRENIA

Chp.: S. Charles Schulz, M.D.
Co-Chp.: Charles A. Kaufmann, M.D.

NR72	Incidence of Tardive Dyskinesia with Pharmacotherapy William T. Carpenter, Jr., M.D., Douglas W. Heinrichs, M.D., Thomas E. Hanlon, Ph.D., Ann T. Summerfelt, B.A.	9:00 a.m.
NR73	Plasma HVA: Physiologic and Psychiatric Correlates Kenneth L. Davis, M.D., Michael Davidson, M.D., Richard C. Mohs, Ph.D., Anne Girodani, Ph.D., Thomas B. Horvath, M.D.	9:15 a.m.
NR74	Frontal Attention Deficits in Schizophrenia Lewis L. Judd, M.D., Byron Budnick, B.S., Lou Ann McAdams, Ph.D., David L. Braff, M.D.	9:30 a.m.
NR75	Autosomnal Abnormality Linked to Schizophrenia Anne S. Bassett, M.D., Barry D. Jones, M.D., Barbara C. McGillivray, M.D., J. Tapio Pantzar, M.D.	9:45 a.m.
NR76	Late-Onset Schizophrenia: Neuropsychology and MRI Dilip Jeste, M.D., Jackuelyn Harris, M.D., C. Munro Cullum, Ph.D., Mark Zweifach, M.D., Leon J. Thal, M.D., Igor Grant, M.D.	10:00 a.m.
NR77	Stable Remission of Tardive Dyskinesia by L-Dopa Jack I. Ludatscher, M.D.	10:15 a.m.

Tuesday, May 12, 1987, 12 noon–2:00 p.m.
New Research 5—Poster Session—Exhibit Hall, Lower Level, McCormick Place North

NEW RESEARCH ON SCHIZOPHRENIA AND ORGANIC MENTAL DISORDERS

Moderator: Peter S. Jensen, M.D.

NR78 SPECT Brain Imaging in Psychiatry
Ralph A. O'Connell, M.D., Ronald L. Van Heertum, M.D., A. Roland Holt, M.D., David M. Rosenthal, M.D., Stephen B. Billick, M.D., Arnaldo Gonzalez, M.D.

NR79 Prefrontal Cognitive Dysfunction in Schizophrenia?
Terry E. Goldberg, Ph.D., Daniel R. Weinberger, M.D., Karen F. Berman, M.D., N.H. Pliskin, M.A., M. Podd, Ph.D.

NR80 Schizophrenia: CT Data and P300/Clinical Correlates
Robert W. McCarley, M.D., Steven F. Faux, Ph.D., Martha E. Shenton, Ph.D., Marjorie Lemay, M.D., Melanie Cane, A.B., Ruth Ballinger, A.B.

NR81 Limbic System Structural Brain Abnormalities in Schizophrenia by Magnetic Resonance Imaging
Deborah Dauphinais, M.D., Lynn E. DeLisi, M.D., Peter Hauser, M.D., Elliot S. Gershon, M.D.

NR82 Functional Cerebral Blood Volume Imaging with MRI
Thomas A. Kent, M.D., Eugenio Amparo, M.D., Barry Kaplan, M.D., Michael Quast, Ph.D., Ahmad Najafi, Ph.D., Robert Gevedon, B.S.

NR83 Re-evaluation of CT Importance in Schizophrenia
George Serban, M.D., Ajax George, M.D., Mony de Leon, Ph.D., Seymour Siegal, M.D.

NR84 Methods for PET Quantification of Neuroreceptors
Dean F. Wong, M.D., Albert Gjedde, M.D., Larry E. Tune, M.D., Godfrey D. Pearlson, M.D., Chris Ross, M.D., Henry N. Wagner, M.D.

NR85 Frontal System Dementia in Late Schizophrenia
J. Wesson Ashford, M.D., Robert Becker, M.D., Robert Dettling, M.S., Jerry A. Colliver, Ph.D.

NR86 Anteroposterior Callosal Gradient in Schizophrenia
Henry A. Nasrallah, M.D., Nancy C. Andreasen, M.D., Jeffrey A. Coffman, M.D., Stephen C. Olson, M.D., James C. Ehrhardt, Ph.D.

NR87 Emotional Blunting and Cognitive Deficits
V. Chowdary Jampala, M.B., Kathryn R. Juzwyn, M.A., Michael A. Taylor, M.D., Gunnar Larson, M.D.

NR88 EEG Coherence in Untreated Schizophrenics
Edward L. Merrin, M.D., Thomas C. Floyd, M.A., George Fein, Ph.D.

NR89 Schizophrenia: P300 Topography and Positive Symptoms
Martha E. Shenton, Ph.D., Steven F. Faux, Ph.D., Robert W. McCarley, M.D., Ruth Ballinger, A.B., Michael Coleman, M.A., Frank H. Duffy, M.D.

NR90 Schizophrenia: P200 Topography and Negative Symptoms
Steven F. Faux, Ph.D., Martha E. Shenton, Ph.D., Robert W. McCarley, M.D., Ruth Ballinger, A.B., Michael Coleman, M.A., Frank H. Duffy, M.D.

NR91 Eye Tracking in Schizophrenia: State and Trait Components
Margaret M. Rea, Ph.D., John A. Sweeney, Ph.D., Carla M. Solomon, Ph.D., Stephen Snyder, M.D., Allen J. Frances, M.D., J. John Mann, M.D.

NR92 Validity of Thought Disorder Ratings in Schizophrenia
John A. Sweeney, Ph.D., Carla M. Solomon, Ph.D., Margaret M. Rea, Ph.D., Allen J. Frances, M.D., J. John Mann, M.D.

NR93 CSF MHPG, Sleep and Psychosis: State Dependent Changes
Daniel P. van Kammen, M.D., Welmoet B. van Kammen, Ph.D., Jeffrey Peters, M.D., Jules Rosen, M.D., Markku Linnoila, M.D., Nancy Nugent

NR94 Glucose Intolerance in Schizophrenic Subjects
Steven D. Roth, M.D., Giovanni Caracci, M.D., William Barr, Ph.D., Sukdeb Mukherjee, M.D.

NR95 Growth Hormone Response and Neuroleptic Response
Charles M. Beasley, M.D., Mary Magnusson, B.S.N., David L. Garver, M.D.

NR96 CSF 5-Hydroxyindolacetic Acid and Suicide Attempts in Schizophrenia
Jeffery L. Peters, M.D., Daniel P. van Kammen, M.D., Jules Rosen, M.D., Ann V. Nugent, Markku Linnoila, M.D.

NR97 New D1 Dopamine and S2 Serotonin PET Imaging
Dean F. Wong, M.D., John R. Lever, Ph.D., Robert Dannals, Ph.D., James Harris, M.D., Paul Hartig, Ph.D., Henry N. Wagner, M.D.

NR98 Elevated D2 Dopamine Receptors in Schizophrenia
Larry E. Tune, M.D., Dean F. Wong, M.D., Godfrey Pearlson, M.D., Robert F. Dannals, Ph.D., Jonathan M. Links, Ph.D., Henry N. Wagner, M.D.

NR99 Calcium Channels Antagonists and Brain D2 Dopamine Receptor Regulation
Richard C. Shelton, M.D., Aaron J. Janowsky, Ph.D.

NR100 Effects of Caffeine Challenge in Schizophrenics
Peter B. Lucas, M.D., Daniel Hommer, M.D., John Kelsoe, M.D., Mark Rapaport, M.D., Carlos Pato, M.D., David Pickar, M.D.

NR101 Low Dose Depot Neuroleptics for Psychosis in SDAT
Gary L. Gottlieb, M.D., Thomas W. McAllister, M.D.

NR102 Ethnicity and Neuroleptic Drug Dosage
Francis G. Lu, M.D., Ching-Piao Chien, M.D., Gertrude Heming, Ph.D., Ladson Hinton, M.D., Carol Soussain, B.A.

NR103 Benztropine Prophylaxis for Haloperidol Dystonia
George W. Arana, M.D., Donald Goff, M.D., Renee Dupont, M.D., Fred Kanter, M.D., David Greenblatt, M.D., Richard I. Shader, M.D., Marjorie Ornsteen, A.B.

NR104 80% Neuroleptic Reduction in Chronic Psychotics
David Shumway, M.D., Ming Tsuang, M.D., Paul Yin, M.D., Stephen V. Faraone, Ph.D., Walter A. Brown, M.D., Alan I. Green, M.D.

NR105 The Efficacy Clozapine in Refractory Schizophrenia
Jerome Costa, M.D., John M. Herrera, Ph.D., John Sramek, Pharm.D., J. Ananth, M.D.

NR106 Trifluoperazine Plasma Levels and Clinical Response
Philip G. Janicak, M.D., Javaid I. Javaid, Ph.D., Rajiv Sharma, M.D., James Peterson, B.S., David B. Bresnahan, M.D., John M. Davis, M.D.

NR107 Prolactin Shifts Following Neuroleptic Withdrawal
Alan I. Green, M.D., Stephen V. Faraone, Ph.D., Walter A. Brown, M.D.

NR108 An Open Trial of Pimozide for the Negative Syndrome
S. Shalom Feinberg, M.D., Lear Elijovich, M.D., Stanley R. Kay, Ph.D., Abraham Fiszbein, M.D., Lewis A. Opler, M.D.

NR109 Molindone and Haloperidol: Side Effect Differences
Barbara J. Mason, Ph.D., J. John Mann, M.D.

NR110 A New Treatment For Extrapyramidal Disorders
Murray A. Cowen, M.D., William Sacks, Ph.D., Maurice R. Green, M.D., Aristide H. Esser, M.D., Paul Talarico, B.A., Barbara Feitel, Ph.D.

NR111 Propranolol and Benztropine in Akathisia
Lenard Adler, M.D., Stewart Reiter, M.D., June Corwin, Ph.D., Paula Hemdal, M.A., Burt Angrist, M.D., John Rotrosen, M.D.

NR112 Risk Factors for Parkinsonism in TD Patients
Thomas E. Hansen, M.D., Ronald M. Weigel, Ph.D., William L. Brown, B.A., Daniel E. Casey, M.D.

NR113 Objective Evaluation of Respiratory Dyskinesia
Anne S. Bassett, M.D., Barry D. Jones, M.D., Pearce G. Wilcox, M.D., John A. Fleetham, M.D.

NR114 Objective Measurement of Tardive Dyskinesia
C. J. Jos, M.D., David W. Kennard, M.D., Ludwig Heinemann, M.D., Earl Dick, M.D., Anatoly Frishberg, M.D., William True, Ph.D., Srinivas Chilakamarri, M.D.

NR115 Frequency of Life Events in Schizophrenic Patients
Joseph Ventura, M.A., Keith N. Neuchterlein, Ph.D., Jean Hardesty, Ph.D.

NR116 Sex Differences of Neurocognition in Schizophrenia
Gretchen L. Haas, Ph.D., John A. Sweeney, Ph.D., Margaret M. Rea, Ph.D., Allen J. Frances, M.D.

NR117 Impact of Gender on the Course of Schizophrenia
Jill M. Goldstein, Ph.D., Matthias Angermeyer, M.D.

NR118 Five-Year Outcome of Schizophrenia in India: Demographic Correlates
Vijoy K. Varma, M.B., Bankteshwar Tripathi, M.D., Arun K. Misra, M.A.

NR119 Familial and Social Determinants of Outcome
Frederic J. Sautter, Ph.D., Barbara E. McDermott, M.A., David L. Garver, M.D.

NR120 Family Factors Predicting Schizophrenic Relapse
Malca B. Lebell, Ph.D., Stephen R. Marder, M.D., Jim Mintz, Ph.D., Joanne McKenzie, R.N.

NR121 Sex and Prediction of Outcome in Schizophrenia
Karen K. Bardenstein, Ph.D., Thomas H. McGlashan, M.D.

NR122 Schizophreniform Disorder: A Valid Diagnosis?
Robert K. Heinssen, M.A., Thomas H. McGlashan, M.D.

NR123 Inpatient Discharge Status and Long-Term Outcome
Thomas H. McGlashan, M.D., Robert K. Heinssen, M.A.

NR124 Integrating/Sealing Over and Long-Term Outcome
Thomas H. McGlashan, M.D.

NR125 Predicting Diagnostic Stability in Axis I Psychoses
Paul V. Williams, M.D., Thomas H. McGlashan, M.D.

NR126 Training Schizophrenics in Medication Management
Robert P. Liberman, M.D., Thad Eckman, Ph.D., Catherine Phipps, M.S., Karen Blair, M.S.

NR127 Substance Use in Young Adults with Schizophrenia
Mary Ann Test, Ph.D., Lynn Wallisch, M.A., Deborah Allness, M.S.W., William Knoedler, M.D., Katherine Ripp, M.S.W.

NR128 Negative Symptoms and Social Networks
N. Gregory Hamilton, M.D., David L. Cutler, M.D., Catherine Ponzoha, M.A., Ronald M. Weigel, Ph.D.

NR129 The Nature of Social Skill in Schizophrenia
Alan S. Bellack, Ph.D., Randall L. Morrison, Ph.D.

NR130 Rehabilitating Schizophrenics in a Rural Region
Hugues J. Cormier, M.D., Gaston Guimond, M.D., Luc Allard, MP.s.

NR131 What Difference Does Case Management Make?
Paula N. Goering, Ph.D., Donald Wasylenki, M.D., Marianne Farkas, Sc.D., William J. Lancee, MS.c., Ron Ballantyne, M.S.W.

NR132 Perceptual Abnormalities of Alzheimer Patients
Richard C. Mohs, Ph.D., Bruno Giordani, Ph.D., John C.S. Breitner, M.D., Michael Davidson, M.D., Thomas B. Horvath, M.D., Kenneth L. Davis, M.D.

NR133 CSF Biological Measures in Alzheimer's Disease
Nunzio Pomara, M.D., Peter A. Lewitt, M.D., Michael Stanley, Ph.D., Matthew Galloway, Ph.D., Garth Bissette, Ph.D., Carol Tamminga, M.D.

NR134 Treatment Outcome in Organic Mania
Sashi Shukla, M.D., Anne Hoff, Ph.D., Thomas Aronson, M.D., Brian L. Cook, M.D., Lina Jandorf, M.A.

NR135 Atypical Mental Disorder or Temporal Lobe Syndrome?
Dietrich Blumer, M.D., Mary Heilbronn, Ph.D., Mark W. Shatz, Ph.D., Robert T. Simkins, D.O.

NR136 White Matter Brain Injury and Delusions
Bruce L. Miller, M.D., Ira M. Lesser, M.D., Mark Goldberg, M.D., Elizabeth Hill, R.N., Kyle Boone, Ph.D., Milton H. Miller, M.D.

NR137 Symptoms of Depression in Senile Dementia of the Alzheimer Type
William J. Burke, M.D., Eugene H. Rubin, M.D., Martha Storandt, Ph.D., John C. Morris, M.D., Leonard Berg, M.D.

NR138 Diagnosis of Alzheimer Subtypes with PET Scan
Gary W. Small, M.D., David E. Kuhl, M.D., Walter H. Riege, Ph.D., J. Wesson Ashford, Ph.D., Denson G. Fujikawa, M.D., E. Jeffrey Metter, M.D.

NR139 IV Nicotine Treatment of Alzheimer's Disease
Paul A. Newhouse, M.D., Trey Sunderland, M.D., Pierre N. Tariot, M.D., Allan Mellow, M.D., Brian Lawlor, M.D., Dennis L. Murphy, M.D.

NR140 Affective Family History in SDAT and Depression
Godfrey D. Pearlson, M.D., Christopher Ross, M.D., Barry W. Rovner, M.D., Larry E. Tune, M.D., Marshal F. Folstein, M.D.

NR141 Psychiatric Symptoms in Clinical Alzheimer Disease
Christopher A. Ross, M.D., Godfrey D. Pearlson, M.D., Barry W. Rovner, M.D., Larry E. Tune, M.D., Marshal F. Folstein, M.D.

NR142 Lymphopenia in Probable Alzheimer's Disease
Gary Tollefson, M.D., Michael Garvey, M.D., Erhard Haus, M.D., J. Bryan Warren, M.D., Michel C. Godes, R.N., Michael Luxenberg, Ph.D.

NR143 A New Scale Assessing Depressed Mood in Dementia
Trey Sunderland, M.D., Ina S. Alterman, M.S.W., Donna Yount, R.N., James L. Hill, Ph.D., Pierre N. Tariot, M.D., Paul A. Newhouse, M.D., Dennis L. Murphy, M.D., Robert M. Cohen, M.D.

NR144 Caregiver Stress in Dementia: Predictors of Coping
William Borden, M.A., Rhoda Frankel, M.A., Benedict L. Gierl, M.D.

NR145 The Cerebellar-Vestibular Basis of Disabilities or Dyslexia
Harold N. Levinson, M.D.

NR146 Psychiatric Illness in HIV-Infected Men and Controls
J. Hampton Atkinson, M.D., Igor Grant, M.D., Caroline J. Kennedy, M.D., Douglas D. Richman, M.D., Stephen A. Spector, M.D., J. Allen McCutchan, M.D.

NR147 Misdiagnosis and Undertreatment of AIDs Referrals
James J. Strain, M.D., George Fulop, M.D., Jay Strain, B.S.

NR148 Neuropsychiatric Findings and Developmental Problems
George U. Balis, M.D., Spyros J. Monopolis, M.D.

NR149 Cognitive State EEG and Drug Toxicity in the Aged
Ira R. Katz, M.D.

NR150 Laterality, Symptoms and Diagnosis
Bruce E. Wexler, M.D.

NR151 Psychopathology and Sydenham's Chorea
James A. Wilcox, D.O., Henry A. Nasrallah, M.D.

NR152 Two-Year Outcome of Caregivers for Chronically Ill
Peter V. Rabins, M.D., Melinda Fitting, Ph.D., James Eastham, Sc.D., James Zabora, M.S.W., Maria Poggi, M.S.

Wednesday, May 13, 1987, 9:00 a.m.–10:30 a.m.
New Research 6—Oral/Slide Session—Room L-3, Lower Level, McCormick Place North

NEW RESEARCH ON AFFECTIVE DISORDERS

Chp.: Robert M.A. Hirschfeld, M.D.
Co-Chp.: P. Anne McBride, M.D.

NR153	Seasonal Variation in Clinical and Laboratory Characteristics of Depression Roger F. Haskett, M.D., Kevin Murphy, Ph.D., Joan Kotun, M.D., James E. Shipley, M.D., Leon Grunhaus, M.D.	9:00 a.m.
NR154	Cognitive Therapy versus TCAS in Older Depressives Gary L. Gottlieb, M.D., Aaron T. Beck, M.D.	9:15 a.m.
NR155	A Family Study of Rapid-Cycling Bipolar Illness John I. Nurnburger, Jr., M.D., Juliet J. Guroff, M.S., Joel Hamovit, M.S.W., Wade Berrettini, M.D., Elliot S. Gershon, M.D.	9:30 a.m.
NR156	Increased Adrenal Weight in Suicide Victims Athanasios P. Zis, M.D., Katerina Dorovini-Zis, M.D.	9:45 a.m.
NR157	Platelet 5-HT2 Receptors: Depression and Suicide P. Anne McBride, M.D., Richard P. Brown, M.D., Michael Demeo, M.D., John Keilp, M.A., Michael Stanley, Ph.D., J. John Mann, M.D., Barbara Stanley, Ph.D., Margaret Polley, Ph.D.	10:00 a.m.
NR158	5-HT Function and History of Suicidal Behavior Emil F. Coccaro, M.D., Larry J. Siever, M.D., Howard Klar, M.D., Lee Harter, R.N., Kim Owen, M.D., Kenneth L. Davis, M.D.	10:15 a.m.

Wednesday, May 13, 1987, 9:00 a.m.–10:30 a.m.
New Research 7—Oral/Slide Session—Room L-2, Lower Level, McCormick Place North

NEW RESEARCH ON PERSONALITY DISORDERS

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

NR159	Psychosis in Borderline Patients with Depression Kenneth R. Silk, M.D., Naomi E. Lohr, Ph.D., Drew Westen, Ph.D.	9:00 a.m.
NR160	A Family History Study in Borderline Personality Jeremy J. Silverman, Ph.D., Larry J. Siever, M.D., Howard Klar, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.	9:15 a.m.
NR161	Confirmation of Psychosis in Borderlines Paul S. Links, M.D., Meir Steiner, M.D., Jan Mitton, R.N.	9:30 a.m.
NR162	Personality Disorder and Depression: A Family Study Mark Zimmerman, B.A., William H. Coryell, M.D.	9:45 a.m.
NR163	Do Personality Traits Affect Antidepressant Response? Eric D. Peselow, M.D., Faouzia Barouche, M.D., Paul J. Goodnick, M.D., Ronald R. Fieve, M.D.	10:00 a.m.
NR164	Validity of Structured DSM-III-R Axis II Diagnosis Andrew E. Skodol, M.D., David Kellman, M.D., John M. Oldham, M.D., Steven E. Hyler, M.D., Lyle Rosnick, M.D.	10:15 a.m.

Wednesday, May 13, 1987, 12 noon–2:00 p.m.
New Research 8—Poster Session—Exhibit Hall, Lower Level, McCormick Place North

NEW RESEARCH ON ANXIETY, PRE-MENSTRUAL, EATING, PERSONALITY DISORDERS, AND OTHER ISSUES

Moderator: Geraldine Farias-Daniels, M.D.

NR165 The Efficacy of Lorazepam in Panic Disorders
Dennis S. Charney, M.D., Scott W. Woods, M.D., Wayne K. Goodman, M.D., John H. Krystal, M.D., Linda M. Nagy, M.D., George R. Heninger, M.D.

NR166 Lorazepam Treatment of Panic Disorder
Elizabeth F. Howell, M.D., Michele Laraia, M.S.N., James C. Ballenger, M.D., R. Bruce Lydiard, M.D.

NR167 Alprazolam versus Clonazepam in Panic Disorders
Mark Pollack, M.D., Jerrold F. Rosenbaum, M.D., George Tesar, M.D., John B. Herman, M.D., Gary S. Sachs, M.D., Lee S. Cohen, M.D.

NR168 Failures in Exposure and Treatment of Agoraphobia
Iver Hand, M.D., Martina Fischer, Jorg Angenendt

NR169 Longterm Effects of Behavior Therapy for Gamblers
Iver Hand, M.D., Rudiger Klepsch, Aygmunt Walzlo

NR170 Five-Year Relapse Rate After Phobia Treatment
Charlotte M. Zitrin, M.D., Maryann Juliano, Ph.D., Michael Kahan, M.D.

NR171 Course of Panic Disorder
Diana P. Sandberg, M.D., Mark Gallops, M.Phil., Jack M. Gorman, M.D., Michael R. Liebowitz, M.D., Donald F. Klein, M.D., Abby J. Fyer, M.D.

NR172 Regional Cerebral Blood Flow in Panic Disorder
Harold H. Harsch, M.D., Michael Goldstein, Ph.D., Robert S. Hellman, M.D., Laurens D. Young, M.D., Ronald S. Tikofsky, Ph.D., B. David Collier, M.D.

NR173 Cerebral Ventricular Site in Panic Disorder
Charles H. Kellner, M.D., Thomas W. Uhde, M.D.

NR174 Chronic Benzodiazepine Use: Abrupt Discontinuation
Edward E. Schweizer, M.D., Karl Rickels, M.D., W. George Case, M.D.

NR175 Panic Disorder, Vertigo, and the Protirelin Test
Cary L. Hamlin, M.D.

NR176 Coronary-Prone Behavior and Adrenergic Receptors
Jeffrey P. Kahn, M.D., Arthur Perumal, Ph.D., Robert Gully, T. Smith, Thomas B. Cooper, M.A., Donald F. Klein, M.D.

NR177 Idiopathic Cardiomyopathy and Panic Disorder
Jeffrey P. Kahn, M.D., Ronald E. Drusin, M.D., Donald F. Klein, M.D.

NR178 Psychiatric Morbidity in Chest Pain Patients
Peter J. Geier, M.D., James R. Hillard, M.D., Lawson R. Wulsin, M.D.

NR179 Neuroendocrine Responses to Clonidine in Mental Illness
Patrick J. Rogue, M.D., Fabrice Duval, M.D., Jean-Luc Deliry, M.D., Marc-Antoine Crocq, M.D., Christian Beaubernard, Ph.D., Jean-Paul Macher, M.D.

NR180 Catecholamine Levels and Symptoms of Anxiety
Monica N. Starkman, M.D., Oliver G. Cameron, M.D., Randolph M. Nesse, M.D., Thomas Zelnik, M.D.

NR181 Serotonin and Norepinephrine Behavioral Response in Obsessive-Compulsives
Eric Hollander, M.D., Michael Fay, R.N., Michael R. Liebowitz, M.D.

NR182 Neurologic Soft-Signs in Obsessive-Compulsive Disorders
Eric Hollander, M.D., Erica Schiffman, M.D., Michael R. Liebowitz, M.D.

NR183 Fluvoxamine in Obsessive Compulsive Disorders
Wayne K. Goodman, M.D., Dennis S. Charney, M.D., Lawrence H. Price, M.D., Steven A. Rasmussen, M.D., George R. Heninger, M.D., Pedro L. Delgado, M.D., John H. Krystal, M.D.

NR184 Obsessive Compulsive and Tourette's Disorders
Roger K. Pitman, M.D., Robert C. Green, M.D., Michael A. Jenike, M.D., M. Marsel Mesulam, M.D.

NR185 Antidepressants for Post-traumatic Stress Disorders
Julia Bess Frank, M.D., Thomas R. Kosten, M.D., Earl L. Giller, M.D., Ellie Dan, B.A.

NR186 Lactate Infusion in Post-traumatic Stress Disorder
Asaf Aleem, M.D., John M. Rainey, M.D., Aurelio Ortiz, M.D., Vikram Yeragani, M.D., Robert Pohl, M.D., Richard Berchou, Pharm.D.

NR187 Menstrual Cycle Effect on Evoked Potential Measures
Allan Tasman, M.D., Nancy DePalma, M.S., Victor Hesselbrock, Ph.D., Sean J. O'Connor, M.D.

NR188 Event Related Potentials and the Pharmacodynamics of Analgesia
Allan Tasman, M.D., Sean J. O'Connor, M.D., Steven R. Cox, Ph.D., Nancy DePalma, M.S.

NR189 Premenstrual Changes: Patterns of Daily Ratings
Stephen W. Hurt, Ph.D., Richard D. Shindledecker, M.A., Sally A. Severino, M.D.

NR190 State Related Changes in Life Events and Perceptions in MRMD
Peter J. Schmidt, M.D., Christine Hoban, M.S.W., David R. Rubinow, M.D.

NR191 Hypertension and Impotence
Ismet Karacan, M.D., Max Hirshkowitz, Ph.D., Nelda Wray, M.D., Richard E. Borreson, M.D., Patricia J. Salis, M.A.

NR192 Sleep APNEA Found in 38% of Elderly Inpatients
Daniel F. Kripke, M.D., Sonia Ancoli-Israel, Ph.D., William J. Mason, M.A., Jennifer Bloomquist, R.N.

NR193 Delayed Sleep Phase Syndrome Revisited
Beth Buckwald, B.S., Norman E. Rosenthal, M.D., Shawana Murray, M.D., David A. Sack, M.D.

NR194 Parental Psychopathology in Anorexia Nervosa
Edward J. Schork, Ph.D., Katherine A. Halmi, M.D., Elke D. Eckert, M.D., Nancy Williams, Ph.D., Louis Chavez, M.A., Tina Trudel, M.A.

NR195 Evidence for Serotonin Dysregulation in Anorexia
Timothy D. Brewerton, M.D., Edward A. Mueller, M.D., Harry A. Brandt, M.D., Michael D. Lesem, M.D., Dennis L. Murphy, M.D., David C. Jimerson, M.D.

NR196 Risk Factors for Bulimia Among High School Females
Donna E. Andrews, Ph.D., Marjorie H. Klein, Ph.D., John H. Greist, M.D., Mary Gulbrandson, R.N.

NR197 2-Deoxy-D-Glucose Effects on Appetite in Bulimia
Harry H. Brandt, M.D., Alan Breier, M.D., Owen Wolkowitz, M.D., David Pikar, M.D., Steven M. Paul, M.D., David C. Jimerson, M.D.

NR198 Is Anorexia Nervosa Occurring More Frequently?
Alexander R. Lucas, M.D., C. Mary Beard, M.P.H, William O'Fallon, Ph.D., Leonard T. Kurland, M.D.

NR199 Bulimia on Campus: Incidence and Recovery Rates
Adam Drewnowski, Ph.D., Doris Yee, Dean D. Krahn, M.D.

NR200 Amylase Levels in Bulimia
David C. Lindy, M.D., B. Timothy Walsh, M.D., Steven P. Roose, M.D., Madeline Gladis, M.A., Linda M. Wong, B.A.

NR201 Pattern of Onset of Bulimic Symptoms in Anorexia
Joy A. Kassett, M.S.W., Elliot S. Gershon, M.D., Harry Gwirtsman, M.D., Walter H. Kaye, M.D., Harry A. Brandt, M.D., David C. Jimerson, M.D.

NR202 Zinc Deficiency and Bulimia
Laurie Humphries, M.D., Craig McClain, M.D.

NR203 Bulimia Treated with Carbamazepine and Imipramine
Allan S. Kaplan, M.D., Paul E. Garfinkel, M.D., David M. Garner, Ph.D.

NR204 Reduced Resting Metabolic Rate in Bulimic Patients
Eva Obarzanek, Ph.D., Michael D. Lesem, M.D., David C. Jimerson, M.D.

NR205 Altered CSF Neuropeptide Relationships in Eating Disorders
Walter H. Kaye, M.D., Wade H. Berrettini, M.D., Harry H. Gwirtsman, M.D., David C. Jimerson, M.D., D.T. George, M.D.

NR206 DSM-III Personality Disorder Among Bulimics
William R. Yates, M.D., Bruce Sieleni, M.D., James H. Reich, M.D.

NR207 DSM-III Personality Disorders in the Elderly
Robert C. Abrams, M.D., Robert C. Young, M.D., George S. Alexopoulos, M.D., Jonathan H. Holt, M.D.

NR208 Gender Differences in Narcissistic Styles
Judith A. Richman, Ph.D., Joseph A. Flaherty, M.D.

NR209 DSM-III Personality Disorders in the Community
James H. Reich, M.D., William Yates, M.D., Mary Nduaguba, Ph.D.

NR210 Correlates of Personality Disorders in the Community
Mark Zimmerman, B.A., William H. Coryell, M.D.

NR211 Psychiatric Mortality in the Community
Jane M. Murphy, Ph.D., Richard R. Monson, M.D., Donald C. Olivier, Ph.D., Arthur M. Sobol, M.A., Alexander H. Leighton, M.D.

NR212 Personality Dimensions in Candidates for Phototherapy: A Pilot Study
Patricia M. Schulz, M.S.W., David A. Sack, M.D., Robert G. Skwerer, M.D., Beth Buckwald, B.S., Sigfried Kasper, M.D., Norman E. Rosenthal, M.D., Susan Rogers, R.N.

NR213 5-HT Function in Borderline Personality Disorders
Emil F. Coccaro, M.D., Larry J. Siever, M.D., Howard M. Klar, M.D., Richard A. Friedman, M.D., Andrea Moskowitz, R.N., Kenneth L. Davis, M.D.

NR214 MDD and Panic Disorder: Effects of Comorbidity on Treatment Outcome
Leon J. Grunhaus, M.D., Yoseph Harel, Ph.D., Tina A. Krugler, B.A., Roger F. Haskett, M.D., John F. Greden, M.D.

NR215 Schizotypal Personality/Biologic Correlates
Zvi Zemishlany, M.D., Larry J. Siever, M.D., Howard M. Klar, M.D., Miklos F. Losonczy, M.D., Stephen Greenwald, M.A., Kenneth L. Davis, M.D.

NR216 Hormonal Responses to Fentanyl: Diurnal Variation
Ede Frecska, M.D., Mihaly Arato, M.D., Csaba M. Banki, M.D., Gyorgy Bagdy, Ph.D., Andras Perenyi, M.D., Marton I.K. Fekete, M.D.

NR217 Rating the Expression of Facial Affect in Children
Kytja K.S. Voeller, M.D., Robert J. Bartucci, M.D., Christiana M. Leonard, Ph.D.

NR218 Right Hemisphere Dysfunction and ADD
Kytja K.S. Voeller, M.D., Kenneth M. Heilman, M.D.

NR219 Parental versus Child Report of Childhood Depression
Mary A. Fristad, Ph.D., Elizabeth B. Weller, M.D., Ronald A. Weller, M.D., Marijo Teare, B.S.

NR220 Lyme Disease: Great Imitator of the 1980's?
Anita M. Lopker, M.D.

NR221 The Role of Interpersonal Functioning in Type-A Behavior
Janelle M. Bessette, M.A., James Halper, M.D.

NR222 Psychosocial Sequelae of Bariatric Surgery
Pauline S. Powers, M.D., Dale Lee Coovert, B.A., Alexander Rosemurgy, M.D., Felecia R. Boyd, ARNP

NR223 Psychological Distress in Elderly HMO Members
Bentson H. McFarland, M.D., Donald K. Freeborn, Ph.D., Clyde R. Pope, Ph.D., John P. Mullooly, Ph.D.

NR224 Ego Mechanisms of Defense and Compliance in Diabetes
Alan M. Jacobson, M.D., Elizabeth Glefand, Ed.D., Stuart T. Hauser, M.D., Joseph I. Wolfsdorf, M.D., Donald Wertlieb, Ph.D., William Beardslee, M.D.

NR225 Screening for Depressions of Bereavement
Selby Jacobs, M.D., Fay Hanson

NR226 Mortality Following the Loss of an Adult Son
Itzhak Levav, Erik Peritz, Ph.D., Jeremi Kark, M.D., Yehiel Friedlander, Ph.D.

NR227 Visits to Office-based Psychiatrists: U.S., 1985
Gloria J. Gardocki, Ph.D.

NR228 Beyond DRG's: Variables that Predict Length of Stay
Cynthia L. Cohen, M.P.H., John A. Sweeney, Ph.D., Gretchen Haas, Ph.D., Allen J. Frances, M.D.

NR229 Reliability of Telephone Interviews
Annamarie Paulson, M.D., Raymond Crowe, M.D., Russell Noyes, M.D., Bruce Pfohl, M.D.

NR230 Scaling of Stressful Life Events Among a Group of Students in Iran
Morteza Mohajer, M.D., Yasaman Mottaghi-Poor, Ph.D.

NR231 The Validity of the Standardized Psychiatric Exam
Alan J. Romanoski, M.D., Gerald Nestadt, M.D., Peter Rabins, M.D., Marshal F. Folstein, M.D., Paul R. McHugh, M.D., Ernest M. Gruenberg, M.D.

NR232 Artificial Intelligence Based Therapeutic Dialogue
David Servan-Schreiber, M.D., Irving I. Binik, Ph.D.

NR233 Reduced Nocturnal Penile Tumescence in Depression
Michael E. Thase, M.D., Charles F. Reynolds, M.D., J. Richard Jenning, M.D., Joseph Howell, M.S., Ellen Frank, Ph.D., David J. Kupfer, M.D.

Thursday, May 14, 1987, 9:00 a.m.–10:30 a.m.
New Research 9—Oral/Slide Session—Room L-3, Lower Level, McCormick Place North

NEW RESEARCH ON CHILDHOOD DISORDERS

Chp.: Jon A. Shaw, M.D.
Co-Chp.: Alan F. Breier, M.D.

NR234	Plasma Levels of Imipramine in Hospitalized Children Steven J. Bupp, M.D., Sheldon H. Preskorn, M.D., Elizabeth B. Weller, M.D., Ronald A. Weller, M.D.	9:00 a.m.
NR235	Somatic Symptoms in Bereaved Children Bela Sood, M.D., Elizabeth B. Weller, M.D., Ronald A. Weller, M.D., Mary A. Fristad, Ph.D., Jennifer Moye, B.A.	9:15 a.m.
NR236	Mothers' Reports of Depression in Their Children Naomi Breslau, Ph.D., Glenn Davis, M.D., Kenneth Prabucki, B.A.	9:30 a.m.
NR237	Mother/Child Reports of Child Psychopathology Alan M. Jacobson, M.D., Janet E. Milley, M.A., Stuart T. Hauser, M.D., Donald Wertlieb, Ph.D., Joseph I. Wolfsdorf, M.D., Raymonde D. Herskowitz, M.D.	9:45 a.m.
NR238	Does Early Parental Loss Cause Adult Depression? Alan F. Breier, M.D., John Kelsoe, M.D., Stacy Beller, B.S., Paul Kirwin, B.S., Owen M. Wolkowitz, M.D.	10:00 a.m.
NR239	Perinatal Complications and Psychiatric Illness Stephen L. Buka, M.S., Ming T. Tsuang, M.D., Lewis P. Lipsitt, Ph.D.	10:15 a.m.

Thursday, May 14, 1987, 9:00 a.m.–10:30 a.m.
New Research 10—Oral/Slide Session—Room L-2, Lower Level, McCormick Place North

NEW RESEARCH ON ANXIETY DISORDERS

Chp.: Susan J. Fiester, M.D.
Co-Chp.: Minna R. Fyer, M.D.

NR240	Provocation of Panic with 35% Carbon Dioxide Minna R. Fyer, M.D., Judy Uy, M.D., Jose Martinez, B.S., Raymond Goetz, Ph.D., Donald F. Klein, M.D., Jack M. Gorman, M.D.	9:00 a.m.
NR241	Cognitive Therapy of Panic Disorder Leslie Sokol-Kessler, M.S., Aaron T. Beck, M.D.	9:15 a.m.
NR242	Simple Phobia: Evidence for Heterogeneity Joseph A. Himle, M.S.W., Kathleen M. McPhee, M.D., Oliver G. Cameron, M.D., George C. Curtis, M.D.	9:30 a.m.
NR243	Long Term Efficacy of Alprazolam in Panic Disorder Linda M. Nagy, M.D., John H. Krystal, M.D., Scott W. Woods, M.D., Dennis S. Charney, M.D.	9:45 a.m.
NR244	Antidepressants in Generalized Anxiety Disorders Karl Rickels, M.D., Edward E. Schweizer, M.D., Robert W. Downing, Ph.D.	10:00 a.m.
NR245	High Rates of Behavioral Inhibition in Children of Agoraphobics Jerrold F. Rosenbaum, M.D., Joseph Biederman, M.D., Michelle Gersten, Ed.D., Nancy Snidman, Ph.D., Steven J. Reznick, Ph.D., Jerome Kagan, Ph.D.	10:15 a.m.

NEW RESEARCH PAPERS

in Summary Form

NR1 **Monday, May 11, 12:00 noon–2:00 p.m.**

DOES ECT EXERT A UNIQUE SEROTONERGIC EFFECT?

Matthew V. Rudorfer M.D. Lab Clinic Science Nat Inst Ment Hlth 9000 RKV PK BL10 RM 2D46 Bethesda, MD 20892, Laura J. Fochtmann, M.D., Emile D. Risby, M.D., John K. Hsiao, M.D., William Z. Potter, M.D.

Summary:

All effective antidepressant (AD) treatments demonstrate common actions on the norepinephrine (NE) system but a disparity in serotonin (5HT) effects in preclinical studies. In patients we confirm a distinct action of electroconvulsive therapy (ECT) on the principal 5HT metabolite, 5HIAA in the cerebrospinal fluid (CSF) measured at baseline (>3 wk medication-free) and again 1 wk after completion of ECT. Whereas ADs are associated with falls in CSF MHPG (the major NE metabolite) and 5HIAA, ECT in 7 patients did not consistently alter mean CSF MHPG (47.6 pmol/ml pre to 49.1 pmol/ml post); on the other hand, mean CSF 5HIAA in the patients rose 23.5% from a baseline 99.9 pmol/ml to 123.4 pmol/ml ($p<.05$) a week after completion of the ECT course. Data from the 5HT-mediated serum prolactin response to a low-dose clomipramine (CMI) infusion paradigm before and after ECT, to be presented, will address the issue of the functional significance of the finding of increased 5HIAA with this treatment. Preliminary findings in a rat model are negative. Not only are we not finding the expected increase in cortical 5HT receptors, but we are not seeing any meaningful alteration of prolactin responsivity to CMI infusion following completion of a course of 8 ECS administrations given on alternate days. Our most robust finding in humans is actually of a highly significant ($p<.02$) 34.5% elevation of CSF concentrations of the primary dopamine (DA) metabolite, homovanillic acid (HVA) with ECT; 1 wk post-ECT mean CSF HVA was 231.0 pmol/ml, compared with a baseline of 171.8 pmol/ml in our 7 patients. Further studies are under way to clarify the role of DA, as well as 5HT, in producing the therapeutic action and the potential toxicity of ECT.

NR2 **Monday, May 11, 12:00 noon–2:00 p.m.**

ACUTE ECT EFFECTS ON PLATELET 5HT UPTAKE

Jeffrey L. Rausch M.D. Psychiatry UCSD M003 UCSD Dept. of Psychiatry, La Jolla, CA 92093, Charles Rich, M.D., S. Craig Risch, M.D.

Summary:

Recently low baseline levels of platelet imipramine (IMI) binding sites have been reported to increase significantly after ECT treatment in six depressed patients although data have not been available for platelet 5HT uptake. We have now examined 5HT uptake in six depressed patients during the week before and the week after ECT in order to test for changes in 5HT transport associated with ECT.

We found that the depressed patients had significantly ($p<0.05$) lower Vmax of platelet 5HT uptake prior to ECT (22.9 ± 7.6 pm/2 x 10^{-7} platelets) than the six matched control subjects (37.5 ± 9.1). After a single ECT treatment, the Vmax significantly ($p<0.05$) increased to levels (34.6 ± 10.1) no longer significantly different from control. Since Hamilton depression scores significantly increased after the single treatment in our subjects, it possible that the Vmax of platelet 5HT uptake reflects state-dependent changes in depression in response to ECT therapy. Although it remains to be determined how the two changes covary, our data would indicate a rapid change in uptake, compared to the previously reported increased density of imipramine binding sites. Changes in platelet 5HT uptake are of interest, since the regulation of serotonin turnover is regulated, in part, by mechanisms that control serotonin uptake, and ECT is known to significantly reduce serotonin turnover.

NR3 **Monday, May 11, 12:00 noon–2:00 p.m.**

ARGININE-ASPARTATE AND ELECTROCONVULSIVE TREATMENT

Georges D. Cehovic M.D. Pharmacology, University South Ala Medical Science Bld Mobile, AL 36688, Miroslav M. Velek, M.D., Samuel J. Strada, Ph.D.

Summary:

L-ARGININE-L-ASPARTATE (AA) AND ELECTROCONVULSIVE TREATMENT (ECT). G. Cehovic*, M. Velek*, S. J. Strada*, Departments of Pharmacology* and Psychiatry**, University of South Alabama, Mobile, Alabama 36688, USA.

Previous work has shown that administration of AA increases markedly ^{32}P incorporation into specific brain proteins, whereas ECT consistently decreased these same proteins in rats.

In these studies, the convulsive electrical stimulus (100 V, 0.4 sec. of duration) was delivered to both groups of rats from a Medcraft B 24 ECT device using ear clip electrodes. For administration of AA an oesophageal tube was inserted. Treated rats received 6 daily doses of AA at 9 A.M.; the control group received 1 ml of tap water (T.W.) instead. ECT was administered for six consecutive days at 3 P.M. and the rats continued to receive AA thereafter. In ECT treated rats, SDS-PAGE slabs showed a decrease in ^{32}P incorporation in all protein bands except for those of lower molecular weight in AA pretreated rats (0.5g/kg/day). We observed also a faster recovery (3-6 x shorter) after ECT in rats receiving AA than in ECT-control rats. The recovery time was assessed from some general behavioral characteristics including the degree of consciousness, improvement of sensory functions, searching and tail reflexes, spontaneous movements and resistance to passive movements. These behavioral features will be documented in a videotape. The enhanced recovery time after ECT rats treated with AA may have clinical implication for the use of ECT in human subjects. Post ECT amnesia may be shortened by AA treatment. Further testing of memory functions in rats and humans following the administration of AA appears warranted. AA and research support provided by lab. Sarget, France.

NR4 **Monday, May 11, 12:00 noon–2:00 p.m.**

MODIFIED MULLER'S POSITION FOR UNILATERAL ECT

Sidney S. Chang M.D. Psychiatry VA Medical Center 940 Belmont Street Brockton, MA 02401, Joel Silberberg, M.D., Eileen Enez, R.N., Robert A. deVito, M.D.

Summary:

One of the advantages with MECTA machine is the capability to check the impedance between electrodes and scalp before ECT. With Muller's method of electrode placement (fronto-frontotemporal) for unilateral ECT, both the stimulating and monitoring (EEG) electrodes can be held securely by a head-band, and the impedance can easily be tested before ECT. However, Muller's placement may require higher energy to induce seizures. The d'Elia's position (temporo-parietal) has less abortive seizures due to a wider distance between the electrodes, but the parietal electrode has to be held by hand, and therefore, the safety test for impedance can not be done properly. We modified the Muller's placement and moved the second (temporal) electrode along the head-band posteriorly to about half an inch behind the ear to widen the interelectrode distance. We have administered unilateral ECT for 20 inpatients with this modified method. Using a MECTA machine, with frequency of 50–70 Hz, pulse width of 0.5–1.5 msec. and duration of 1.0–2.0 sec., 18 (in 11 patients) of the 144 total treatments failed on the first trials, but subsequently with increased energy all had adequate seizures. The rate of clinical response was 70% and no unusual or serious side effect was noticed. This modified method appears to have a higher success rate of inducing seizures than the Muller's method, and the pretreatment safety test for impedance can still be done with a MECTA machine.

NR5 **Monday, May 11, 12:00 noon–2:00 p.m.**

ATTITUDES TOWARDS ECT: ENDURING EFFECTS

Richard D. Weiner M.D. Psychiatry Duke University Psych SVC, Durham, VA Med Ctr Durham NC 27705, C. Edward Coffey, M.D., Jonathan M. Farber, Ph.D.

Summary:

Thirty-three subjects who took part in an ECT research study approximately 5 years previously were administered an ECT attitudes questionnaire. Parts of this instrument were also administered to 11 individuals who had served as clinical matched control subjects in the original study and who had never received ECT. Subjects who received ECT reported their ECT experience as very therapeutic, with perceived duration of this effect lasting greater than a year in two-thirds of the population. Compared to non-ECT controls, subjects receiving ECT were much more likely to rate ECT as more effective than medication ($p<0.01$). Subjects who received ECT also belived that ECT was no more dangerous than antidepressant medication, although they reported a more frequent occurrence of memory problems and confusion with ECT. Overall, 94% of ECT patients responded that they would agree to receive ECT again if severely depressed, other treatments had not worked, and their physician recommended its use. Relationships between present self-ratings and both type of ECT received and objective measures of therapeutic outcome and memory function done at the time of the index episode will also be presented.

NR6 **Monday, May 11, 12:00 noon–2:00 p.m.**

TOPOGRAPHIC EEG AND EVENT RELATED POTENTIALS IN ECT

Jeffrey A. Coffman M.D. Psychiatry Ohio State University 473 West 12th Avenue Columbus, OH 43210, Daniel J. Martin, M.D., Linda R. Fortin, EEG.T., Catherine H. Lewis, B.S., Michael W. Torello Ph.D.

Summary:

Several studies have found increased slow wave amplitude and predominance in patients following treatment with ECT, but few investigations have included evaluations of event related potentials. We investigated amplitude latency and spatial distribution of the auditory evoked response (N_{100} and P300 components) taking advantage of a full 10–20 montage and newly available topographic processing of the data.

To date we have studied 9 depressed patients (DSM-III major depression) prior to and following completion of ECT. The group included 5 males and 4 females with a mean age of 51 $\pm$ 14 yrs. We compared the pre-treatment results of the depressed patients to a similar group of 12 normal volunteers (Age = 49 $\pm$ 13 yrs.) as well as to their own post-treatment results. The experimental paradigm included tone pip presentation and odd pips serving as event related potential stimuli. Level of attention and artifact were controlled.

RESULTS: We found significant differences in spatial localization of the N_{100} component between depressed patients and controls with more controls showing central or leftward localization while depressed patients showed a rightward displacement of the component (Fisher's exact test, $p<.05$). In addition, the depressed patients following completion of the ECT showed a trend toward developing a "normal" pattern of localization. We also found significant differences between controls and depressed patients (pre ECT) as well a pre ECT and post ECT patients in N_{100} amplitude (lower among depressed patients and prior to ECT) and N_{100} latency (delayed among depressed patients and prior to ECT). Further shifts toward "normalized" N_{100} spatial distribution were profound among improved patients. Results of these measures at later points in treatment and correlations of response to the measures will be reported.

We feel that our results support the impression that changes in spatial, temporal, and amplitude parameters of the N_{100} component of the auditory evoked response may reflect alterations in neurophysiology secondary to depression and effective treatment.

This research was supported in part by a seed grant from the Bremer Foundation to M. W. Torello, Ph.D.

NR7 **Monday, May 11, 12:00 noon–2:00 p.m.**

BENZODIAZEPINES REDUCE ECT'S THERAPEUTIC EFFECT

Helen M. Pettinati Ph.D. Research Carrier Foundation P.O. Box 147 Belle Meade, NJ 08502, Kenneth W. Willis, M.D., Stephina M. Nilsen, R.N., Sarah E. Robin, B.A.

Summary:

Although d'Elia (1982) and Ottosson (1982) have made pleas for discontinuing the use of benzodiazepines during electroconvulsive therapy (ECT), in current clinical practice some patients are continued on a daily regimen of a benzodiazepine during ECT. Few would dispute the logic that these drugs raise the patient's seizure threshold, making it inefficient for inducing a seizure. However, little empirical work exists on the extent, if any, to which benzodiazepines may compromise the therapeutic effectiveness of ECT when a seizure of adequate duration has occurred. A single study (Stromgren et al., 1980) has reported that more ECT treatments were required by patients concurrently taking benzodiazepines, but in Johnstone et al.'s (1980) Northwick Park ECT study: "improvement scores were similar in patients with and without diazepam." The present study assessed the response to ECT in patients who were taking a benzodiazepine during their ECT course, using Hamilton depression ratings done blind to medication profile for 30 ECT patients. Of the 30, 10 were nonresponders; all (100%) nonresponders had been taking a benzodiazepine during their ECT course. This was a significantly higher frequency compared to the number of responders taking a benzodiazepine ($p = .06$). In the 20 patients who did show a therapeutic response to ECT, the change in the Hamilton depression scores from pre- to post-6th ECT was significantly smaller in ECT responders ($p<.01$, 2-tailed) who had been taking a benzodiazepine during ECT, leaving this group with significantly more depression after 6 ECTs than responders not taking a benzodiazepine ($p < .05$, 2-tailed).

NR8 **Monday, May 11, 12:00 noon–2:00 p.m.**

ECT IN THE TREATMENT OF EPILEPTIC PSYCHOSIS

Michael Miller M.D. Neuropsychiatric NYS Psych Institute 722 West 168th St. Box 72 New York, NY 10032, Gustav Degreef, M.D., Sukdeb Mukherjee, M.D., Haranath Parepally, M.D.

Summary:

The treatment of chronic psychoses associated with epilepsy presents a therapeutic dilemma. Although evidence suggests that ECT may have both antipsychotic and anticonvulsant effects, its efficacy and safety in the treatment of chronic epileptic psychoses has not been systematically evaluated. We will present our findings from an ongoing study addressing the effects of ECT on psychosis and seizure manifestations in patients with chronic refractory psychoses associated with epilepsy.

ECT was administered thrice weekly using brief square wave pulse stimulation. Of the first 8 patients in the series, 4 had a chronic schizophrenia-like psychosis, 2 a bipolar-type affective disorder, and 2 a paranoid psychosis. One patient had primary generalized seizures and 7 had complex partial seizures of whom 3 had secondary generalized seizures. Five patients exhibited frequent episodic aggressive dyscontrol, often in the context of post-ictal confusion. ECT was associated with a marked decrease in the frequency, duration, and severity of episodic dyscontrol in all 5 cases. ECT was associated with marked improvement of psychosis in 5 of the 8 patients. None of the patients showed increased seizure frequency of worsening of psychosis during ECT. ECT was associated with modification of spontaneous seizure patterns and abolition of post-ictal confusion. These effects will be described in detail. Our preliminary findings suggest that ECT may be a safe therapeutic alternative in cases of chronic epileptic psychoses with significant acute therapeutic effects in some cases.

NR9 **Monday, May 11, 12:00 noon–2:00 p.m.**

CAFFEINE AUGMENTATION OF ECT SEIZURES

C. Edward Coffey M.D. Psychiatry Duke Medical Center Box 3920 Durham, NC 27710, Richard D. Weiner, M.D., Gary S. Figiel, M.D., Martha Cress, R.N., W. Vaughn McCall, M.D., E. Frank Shelp, M.D.

Summary:

A decline in seizure duration occurs frequently during a course of ECT and may result in brief or missed seizures and limited clinical benefit. Previously we reported that pretreatment with caffeine i.v. lengthened ECT seizures in 8 drug-free inpatients with major depression (MD) and declining seizure times. We now describe 2 studies which conform and extend our original findings.

In an open, single-blind study of 20 inpatients with DSM-III MD, caffeine pretreatment (250–750 mg) resulted in a statistically significant ($p<.01$) increase in seizure duration (mean 127%). The extent of the increase in seizure duration was greater at higher dosages of caffeine. A clinical remission was achieved in all 19 patients who completed the course of ECT. In general, caffeine was well tolerated; the major side effect was anxiety ($N=3$). There were no associated adverse cardiovascular effects or prolonged post-ECT disorientation.

The results of an ongoing prospective, double-blind randomized study will also be reviewed, comparing the effects of caffeine vs. placebo on clinical outcome and encephalopathic side effects of ECT.

These studies suggest that caffeine may be a potentially safe and highly effective technique to augment ECT.

NR10 **Monday, May 11, 12:00 noon–2:00 p.m.**

STATE-TRAIT ASPECTS OF NORADRENERGIC REGULATION

Larry J. Siever M.D. Psychiatry VA Medical Center 130 W. Kingsbridge Rd Bronx, NY 10468, Emil F. Coccaro, M.D., Howard Klar, M.D., Richard A. Friedman, Steven Greenwald, M.A., Kenneth L. Davis, M.D.

Summary:

In order to determine which abnormalities of the noradrenergic system are state-dependent and which are state-independent (trait), indices of noradrenergic release/metabolism (sequential samples of plasma norepinephrine [NE] and MHPG over an 8-hour period) and/or responses to clonidine were evaluated in 28 acute depressed, 16 remitted depressed, and 11 normal controls. Seven (7) patients have been studied in both the acute and remitted states. Blunted GH responses (< 5 ng/ml) to clonidine did not differ between the acute depressed patients (71%, $^{15}/_{21}$) and the remitted depressed patients (69%, $^{11}/_{16}$) but the depressed patients significantly differed from the normal controls (36%, $^{4}/_{11}$) ($p<0.05$, Fisher's Exact). Of the 5 patients studied with clonidine in two studies, those four patients who had blunted GH responses to clonidine in the acute state remained blunted in the remitted state. The clonidine-induced fall in plasma MHPG tended to be reduced in the acute depressed patients (-0.08 ± 0.42 ng/nl, $n=20$) compared to the controls (-0.32 ± 0.45, $n=7$) ($p=0.07$, ANOVA). Preliminary results suggest an erratic variable rhythm of plasma MHPG and NE in acute depression that tends to normalize in remission. These results raise the possibility that diminished adrenergic receptor responsiveness may represent a trait or vulnerability marker for depression, while overt dysregulation of NE release/metabolism may be partially state-dependent.

NR11 **Monday, May 11, 12:00 noon–2:00 p.m.**

CSF MONOAMINE AND DEPRESSIVE SUBTYPES

Richard P. Brown M.D. Psychiatry Payne Whitney Clinic 525 3 68th St New York, NY 10021, Marc Stipetic, M.S., Markku Linnoila, M.D., John Keilp, M.A., Michael Stanley, Ph.D., Barbara Stanley, Ph.D., J. John Mann, M.D.

Summary:

In order to distinguish subtypes of major depressions by CSF monoamines, 21 nonendogenous major depressives, 13 endogenous major depressives, and 11 major depressives with endogenous and psychotic features (all unipolar, drug-free, in hospital were studied. HVA was much lower in the endogenous group vs. nonendogenous vs. psychotic groups (125 pmol/ml vs. 212 vs. 190, p=008). HVA and 5-HIAA correlated (r=.8, p=.0001) but 5-HIAA was not lower in any grup (88 vs. 109 vs. 109, p=.2). MHPG was also similar (43 vs. 42 vs. 49). HVA correlated inversely with Hamilton Anxiety total and Ham-D anxiety items but positively with SIB total and paranoia items (p=.50). Mixture analysis of distributions of CSF values showed that 16 patients had distinctly low combined 5-HIAA/HVA and were older, more endogenously and psychotically depressed, anxious, agitated, treatment-resistant less borderline, and tended to have made more violent suicide attempts. 5 psychotic depressives had low 5-HIAA/HVA, were more anergic and tended to have made more recent suicide attempts compared to the other 6 psychotics with normal HVA/HIAA. These results confirm prior findings of: 1) lower HVA in endogenous depression and its relation to specific symptoms; 2) a low HVA/5-HIAA subtype; 3) higher mean HVA in psychotic endogenous depression vs. endogenous depression. CSF monoamines may permit characterization of depressive subgroups.

NR12 **Monday, May 11, 12:00 noon–2:00 p.m.**

PHOTOIMMUNOLOGY AND SEASONAL AFFECTIVE DISORDER

Robert G. Skwerer, M.D. Psychobiology NIMH 9000 Rockville Pike Bethesda, MD 20892, Lawrence Tamarkin, Ph.D., Thomas W. Wehr, M.D., Frederick M. Jacobsen, M.D., David A. Sack, M.D., Guilio F. Paciotti, M.S., Karen A. Kelly, M.D., Norman E. Rosenthal, M.D.

Summary:

Patients with major, non-seasonal depression have been reported to have impaired cell-mediated immunity as measured by mitogen testing. To characterize the cellular immune response in patients with SAD, peripheral blood lymphocytes from 9 drug-free, depressed seasonals were evaluated with mitogen testing prior to and during bright, white light treatment during the fall and winter. Lymphoproliferative responses to mitogen (PHA) were decreased by 80% ($p<0.01$) after 7 to 10 days of treatment (2500 lux, 4–5 hrs/day). Twenty-four hour plasma cortisol profiles were not significantly different during light treatment compared to baseline. All the patients responded ($p<0.05$) to the light treatments as assessed by weekly Hamilton Rating Scales. Possibly, this lymphocyte response could result from cumulative u.v. light exposure. To further explore this and also investigate whether the decreased response to mitogens during light therapy was state or treatment dependent, we studied 5 euthymic, drug-free seasonals and 12 healthy controls in the spring and summer. In contrast to the winter study, lymphocyte responses in controls and patients significantly increased ($p<0.01$, $p<0.05$; respectively) after 1 week of light treatment. Additionally, 1 day of light exposure caused a significant increase ($p<0.01$) in lymphocyte activity, suggesting that the effect of bright light is probably not a result of u.v. light (250–400nM, 0.01 J/cm^2) exposure. Serum cortisol, sampled once on each morning of mitogen testing, did not vary significantly throughout the paradigm. In a second approach to investigate the effects of bright light on T cell function, we performed analogous experiments using unshaven Sprague-Dawley rats. Results are supportive of our human findings and will be discussed at the conference.

NR13 **Monday, May 11, 12:00 noon–2:00 p.m.**

EFFECTS OF DIFFERENT LIGHT WAVELENGTH IN SAD

Norman E. Rosenthal M.D. NIMH 9000 Rockville Pike BL10 4S239 Bethesda, MD 20892, George C. Brainard, Ph.D., Donald Sherry, M.D., Robert G. Skwerer, M.D., Morris Waxler, Karen Kelly, M.D., David A. Sack, M.D., Thomas A. Wehr, M.D., Patricia M. Schulz, M.S.W.

Summary:

Phototherapy with bright, full-spectrum light has been shown to have marked antidepressant effects in patients with seasonal affective disorder (SAD). It is not currently known which part of the spectrum is important for achieving these antidepressant effects. In order to investigate this question we are currently studying a group of patients with SAD in a crossover design in which patients are randomly assigned to two of three lighting conditions for one week each. During treatment conditions patients are exposed to light for two hours twice a day. Patients are withdrawn from light for one week between treatments. Lighting conditions consist of equal quanta exposures (2.3×10^{15} photons/sec/cm^2) of red, blue or white light, achieved by using different light sources and adjusting the number of lamps and lamp distance from the patient. Light sources used are Vitalites (Durotest Corp.), which have been used previously for SAD phototherapy at NIMH; red F40R (half-peak bandwidth, 615-655 nm) and blue F40BB (half-peak bandwidth 430-465 nm) lamps, donated by the Westinghouse division of Phillips Inc. At this time 17 SAD patients have been treated with a total of 24 conditions. Mean decreases (±S.D.) in Hamilton Depression Rating Scale scores for red, blue and white lights are 1.8±6.3, 5.4±5.6, and 10.8±4.7 respectively. It appears as though red light has efficacy equivalent to that of placebo treatments used previously; white is as effective as the active treatments in earlier studies, and blue has intermediate efficacy. The study is ongoing and final results and their implications will be discussed at the time of presentation.

NR14 **Monday, May 11, 12:00 noon–2:00 p.m.**

MORNING LIGHT TREATMENT FOR WINTER DEPRESSION

Robert L. Sack M.D. Psychiatry Oregon Health Sci. Univ Mail Code L460 OHSU Portland, OR 97201, Alfred J. Lewy, M.D., David M. White, Ph.D., Clifford M. Singer, M.D., Tana M. Hoban, Ph.D.

Summary:

Winter depression (WD) is a syndrome characterized by sadness, reduced energy, hypersomnia and weight gain that occurs in the winter and remits in the summer. We previously found that bright light exposure in the morning is an effective treatment for most patients with winter depression and that morning light exposure causes the onset of melatonin secretion to shift to an earlier time, indicating a treatment-induced advance in circadian rhythms.

During the winter of 1985-86, we conducted a study to determine the duration of morning bright light necessary for the antidepressant effect. We compared 120 to 30 minutes of morning light exposure in a group of 19 patients and 6 normal controls, using a randomized, cross-over design with a week of dim light separating the two treatment weeks. Blood was sampled in the evening (under dim light conditions) at the beginning of the study and at the end of each week to determine the onset of melatonin secretion.

The mean HAM-D rating upon entry to the study was 17.9 ± 1.4. The patients showed significant improvement with either treatment (average HAM-D was 7.7 ± 1.4 after a week of 30 min. exposure and was 6.4 ± 0.1 after a week of 120 min. exposure) although some patients experienced a distinct preference for one or the other schedules. The patients showed significantly greater phase shifts in melatonin production after morning light exposure than the controls. This finding suggests that the phase-response curve is delayed in WD patients compared to controls, which is consistent with our previous study (Lewy, et al., Science 235, 532, 1987).

NR15 **Monday, May 11, 12:00 noon–2:00 p.m.**

THE EFFECTS OF BRIGHT LIGHT IN NORMAL SUBJECTS

Siegfried F. Kasper M.D. NIMH Clinical Psycho-Biology Branch 9000 RV Pike BL10 RM4-S-239 Rockville, MD 20892, Susan Rogers, R.N., Patricia M. Schulz, M.S.W., Annette Potter, B.A., Robert G. Skwerer, M.D., Norman E. Rosenthal, M.D.

Summary:

Dramatic antidepressant and energizing effects of bright light exposure have been widely reported to occur in patients with seasonal affective disorder (SAD). Kraepelin first noted that patients with winter depressions and spring hypomanias appear to exhibit an extreme form of the seasonal behavior changes found in normal individuals. If seasonality is a behavioral dimension that spans both normal and affectively disturbed individuals, the question arises as to whether bright light exposure might have a mood enhancing and energizing effect in normal subjects. We have treated 11 normal subjects with two hours of bright full-spectrum light in the morning during the winter months (a treatment that has been reported to be effective in SAD) and 11 others with dim light. Neither group showed any change in mood or energy level. In a follow-up study we are investigating whether normal individuals, either with no history of seasonal changes (N = 10) or with mild SAD-type symptoms (N = 10) will respond to longer periods of bright light exposure (5 hours per day). Control groups (N = 10 for each group) will receive 2 hours of light per day. We are currently analyzing the results of this study and predict that the propensity to respond to light and the duration of treatment required to induce such a response are both continuous variables. If this is correct, this study should have practical implications for establishing optimal environmental lighting conditions for normal individuals during the winter.

NR16 **Monday, May 11, 12:00 noon–2:00 p.m.**

DAYLIGHT SAVING TIME AFFECTS PSYCHIATRIC SYMPTOMS

Peter A. Bick M.D. CNS Research Bristol-Myers Chaussee DE LA Hulpe 185 Brussels, Belgium B1170, Alison Hannah, A.B.

Summary:

A specific seasonal affective disorder has recently been described. This disorder, typically a winter depression, may be caused by changes in the period of natural daylight (photoperiod) leading to a disturbance in circadian rhythm homeostasis, resulting in the expression of a seasonal mood change. This postulate is supported by evidence that seasonal depressions can be readily treated with a 3-6 hour exposure to artificial light, which also resynchronises phase-disturbed circadian rhythms.

We wondered if a sudden change in apparent length of daylight consequent to a 1-hour time shift (caused by the Daylight Saving Time change) might lead to a phase disturbance in circadian rhythms and an associated increased incidence of affective disorders for a short time following the change.

We investigated the effect of five Daylight Saving Time changes on the incidence of psychiatric presentations before and after the time changes at a busy crisis center. 1,521 patient contacts were reviewed by a rater who was blind to the dates of the records. There were significantly more patient contacts during the week following the time changes. This increase was due to a specific rise in depression and psychosis related contacts.

NR17 **Monday, May 11, 12:00 noon–2:00 p.m.**

DIURNAL VARIATION IN SEASONAL AFFECTIVE DISORDER

Frederick M. Jacobsen M.D. NIMH B1 10 9000 Rockville Pike Bethesda, MD 20892, Adriana Dreizzen, M.D., Norman E. Rosenthal, M.D., David A. Sack, M.D., Robert G. Skwerer, M.D., Thomas A. Wehr, M.D.

Summary:

Diurnal variation of mood, energy, anxiety, and sleepiness in summer and winter was studied in 12 patients with seasonal affective disorder and in 12 normal controls. Subjects completed self-rating scales (Daily Ratings, Stanford Sleepiness Scale) every two hours from 7 a.m. to 11 p.m. for 3 consecutive days. Mean values for each time point were analysed by ANOVA.

Controls failed to show significant summer-versus winter differences in any of the variables. SAD patients, however, scored significantly higher in depression ($P<0.002$), fatigue ($P=0.001$), anxiety ($P<0.002$), and sleepiness ($P<0.001$) in the winter than in the summer. Cross-group comparisons revealed that SAD patients had significantly higher ratings of depression ($P<0.03$) and significantly lower ratings of energy ($P<0.05$) than controls in the winter, but the summer ratings of SAD patients did not differ from those of controls for any variable. Both groups showed significant diurnal variations in mood, energy, and sleepiness in both seasons which were compatible with the circadian rhythmicity of normals reported by other investigators. Unexpectedly, these diurnal variations did not differ between patients and controls, and also did not differ between summer and winter. These results provide evidence against a circadian rhythm phase-disturbance in SAD patients.

NR18 **Monday, May 11, 12:00 noon–2:00 p.m.**

PET STUDY OF SLEEP DEPRIVATION

Joseph Wu M.D. Psychiatry Univ Calif Irvine D410 Med Sci I UCI-CCM Irvine, CA 92717, Monte S. Buchsbaum, M.D., J. Christian Gillin, M.D.

Summary:

Sleep deprivation has been used as a nonphamacologic treatment for depression. We were interested in how sleep deprivation affects regional metabolic activity in the brain as assessed by Positron Emission Tomography (PET) scans. Change in normal controls were studied initially to provide a baseline for comparison. Preliminary results for the normal control group will be presented. Studies are ongoing for depressed subjects.

Four normal controls (4 males, $x=25.3 + 6$ yr) were studied. The normal controls had no personal or family psychiatry history or significant medical illness. The normal controls were scanned twice. The subjects were in a normal waking state on the first occasion and had slept the night before. The subjects were sleep deprived for the entire night on the second occasion and then scanned. The normal subjects felt moderately dysphoric after sleep deprivation. The subjects performed the Continous Performance Test, a vigilance test, during the thirty-minute uptake after injection of 4 to 5 mCi of 18 fluorodeoxyglucose for both scans. Nine slice images were obtained on the CTI NeuroEcat IV scanner with an in-plane resolution of 7.6 mm. Glucose metabolic rates for the scar were derived according to the model of Sokoloff.

Normal controls showed a significant decrease in relative caudate metabolic rates on the left side only using paired t-tests ($p<.05$, 1 tailed). Relative right caudate metabolic rates did not show significant change. Sleep deprivation may affect activity of dopamine rich areas in the brain.

NR19 **Monday, May 11, 12:00 noon–2:00 p.m.**

TSH RESPONSE TO SLEEP DEPRIVATION IN DEPRESSION

David A. Sack MD. CPB 10 4S239 NIMH 9000 Rockville Pike Bethesda, MD 20892, Siegfried Kasper, M.D., Thomas A. Wehr, M.D., Robert G. Skwerer, M.D., Hermes Kick, M.D., Gabrielle Voll, M.D.

Summary:

The secretion of the pituitary hormone thyrotropin (TSH), exhibits a circadian rhythm which peaks during the night. This nocturnal surge in TSH secretion is believed to be mainly responsible for the trophic support of the thyroid gland. Sleep partially suppresses the nocturnal rise of TSH, and sleep deprivation stimulates TSH secretion. Thus, sleep deprivation is a physiological challenge to TSH secretion. In a previous investigation we found that the nocturnal rise in TSH was deficient in rapid-cycling bipolar patients, and that sleep deprivation failed to increase their TSH levels compared with controls. The purpose of the present study was to determine whether a blunted TSH response to sleep deprivation was characteristic of other sub-groups of depressed patients. As part of ongoing research, we measured TSH levels in 32 unipolar patients and 9 normal controls at 2 a.m. during a normal night's sleep and during a night of sleep deprivation. On the baseline night, depressed patients had lower TSH levels compared with controls (mean = 1.60 μU/ml, controls; mean = 1.22μU/ml, patients). Sleep deprivation increased TSH levels in the controls by 100% compared with baseline, but TSH levels increased by only 30% in the depressed patients (mean = 3.21 μU/ml, controls; mean = 1.44 μU/ml, patients). These data provide additional evidence that the sleep dependent regulation of thyrotropin is disturbed in patients with major depression, and that a blunted TSH response to sleep deprivation challenge is not restricted to a particular subgroup of depressed patients.

NR20 **Monday, May 11, 12:00 noon–2:00 p.m.**

POSTPARTUM DEPRESSION AND THYROID AUTOIMMUNITY

Nelson B. Freimer M.D. Psychiatry UCSF 401 Parnassus Avenue San Francisco, CA 94143, Victor I. Reus, M.D., Luisa Manfredi, B.A.

Summary:

The role of endocrine and immune systems in postpartum depression is unclear, although both fluctuate considerly during the postpartum period. Recent studies indicate that a significant subset of postpartum women is at risk for autoimmune endocrine syndromes particularly of the thyroid. Previous studies on our unit have documented a high prevalence of antithyroid antibodies among hospitalized depressed women. We have prospectively studied 40 unselected postpartum women as part of an ongoing study. Depressed women and consecutive age-matched controls, were identified through Zung & Hamilton Depression Scales. Twenty percent of depressed women demonstrated elevated antithyroid, antibody titer compared to 5% of controls. There were no significant intergroup differences for functional thyroid indices (T_3, T_4, TSH). The personal and family histories of the depressed women were significant for high prevalence of pre-menstrual and autoimmune syndromes including asthma, diabetes mellitus and rheumatoid arthritis. We will discuss these findings in terms of possible mechanisms for postpartum depression.

NR21 **Monday, May 11, 12:00-2:00**

HLA, DEPRESSION, AND AUTOIMMUNE THYROIDITIS

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Summary:

Although several cross sectional and pedigree studies have reported a linkage between the HLA locus and the syndrome of depressive illness, many other studies have failed to find such a relationship. This may be due in part to sole dependence on behavior as the independent variable identifying pedigrees of interest. Recently we have shown a significantly increased prevalence of antithyroid antibodies in euthyroid female depressed inpatients. Because certain HLA haplotypes have been found to be significantly associated with autoimmune thyroiditis, we have assessed the distribution of class I and class II MHC antigens on lymphocytes obtained from sequential depressed female inpatients who have elevations in antibody titer. Thus far 70% of the women studied have shown the presence of A2 and several haplotypes thought to be involved in the genesis of autoimmune disease, i.e., A2-B8, A26, B38 have been identified. In addition we have identified a pedigree in which major mood disorders appear to be coinherited with autoimmune thyroid disease. Although these data are preliminary, it would appear that genetic studies of the inheritance of psychiatric illness would be strengthened through the identification of heritable disease markers of interest.

NR22 **Monday, May 11, 12:00 noon–2:00 p.m.**

THYROIDITIS IN AFFECTIVE AND NON-AFFECTIVE PSYCHIATRIC DISORDERS

John J. Haggerty, Jr. M.D. Univ of N. Carolina Dept. of Psychiatry Chapel Hill, NC 27514, Dwight L. Evans, M.D., Robert N. Golden, M.D., Cort Pederson, M.D.

Summary:

Symptomless autoimmune thyroiditis (SAT) has been reported to be prevalent in psychiatric patients with depressive symptoms; however it is not known if SAT is specifically linked to affective disorders as opposed to other forms of psychopathology. Lithium use can induce thyroiditis, and thus might increase the prevalence of SAT detected in patients with affective disorders. Therefore we determined diagnosis specific rates of SAT by means of antithyroglobulin and antimicrosomal antibody testing in 153 consecutively admitted psychiatric inpatients with no history of prior lithium ingestion. We found antithyroid antibodies in 8% (5/62) of patients with DSM-III major depression, 15% (3/20) with bipolar disorder, 0% (0/4) with schizoaffective disorder, and 5.6% (1/18) in patients with adjustment disorder with depressed mood. The overall rate of SAT in patients with DSM-III affective disorder, 9.5% (8/84), did not differ from that in patients with non-affective disorders, 10.8% (7/65). Our findings confirm earlier repots that thyroid disorders may be particularly common in bipolar affective disorder, even in the absence of lithium. However, since SAT also occurred at a greater than expected rate in nonaffective disorders, its possible psychiatric effects do not appear to be limited to affect dysregulation.

NR23 **Monday, May 11, 12:00 noon–2:00 p.m.**

SLEEP EEG IN MANIA

James I. Hudson M.D. McLean Hospital 115 Mill Street Belmont, MA 02178, Joseph F. Lipinski, M.D., Frances R. Frankenburg, M.D., Victoria J. Grochocinski, Ph.D., David J. Kupfer, M.D.

Summary:

Although disturbance of sleep is one of the cardinal features of mania, no systematic study of sleep EEG in a series of manic patients has been published. In a collaborative study, sleep EEG recordings were obtained on 9 unmedicated manic inpatients (4 males, 5 females; mean age 28.5 yrs, SD 7.8, range 18-40), 5 of whom had psychotic symptoms, for 2-4 consecutive nights at McLean Hospital. Age- and sex-matched normal control subjects were studied at Western Psychiatric Institute and Clinic (8 males, 10 females; mean age 28.3 yrs, SD 7.5, range 18-40). High inter-center reliability of scoring was achieved.

Compared to controls, manic patients exhibited significantly decreased total recording period, decreased time spent asleep, increased time awake in the last 2 hours of recording, shortened REM latency, and increased REM density. These results suggest that mania is associated with marked disturbances of sleep continuity and REM measures, similar to those reported in major depression and delusional depression. Of note, however, is that unlike depressed patients, manic patients did not show reduced slow-wave sleep.

In conclusion, it is possible that various forms of affective disorder—or psychotic disorders—share common sleep EEG abnormalities. These results have implications regarding pathophysiologic mechanisms responsible for affective and psychotic disorders.

NR24 **Monday, May 11, 12:00 noon–2:00 p.m.**

BIPOLAR ILLNESS IN PATIENTS WITH ENDOMETRIOSIS IMPLICATIONS

Dorothy Otnow Lewis M.D. Psychiatry New York Univ Sch of Med 550 First Avenue New York, NY 10016, Florence Comite, M.D., Catherine Mallouh, B.A., Laura Zadunaisky, M.S., Karen Hutchinson, M.D., Bruce Cherksey, Ph.D.

Summary:

This study sprang from the clinical observation that, among 8 female bipolar patients seen in a small private psychiatric practice, 3 had been told by gynecologists that they suffered from endometriosis. We, therefore, studied a consecutive sample of 17 women evaluated in a Women's Clinic who, on laparoscopy, were found to have endometriosis. Symptoms of mood disorder were determined using a semistructured interview based on relevant parts of the Hamilton Depression Scale, the S.A.D.S., and DSM -III criteria for unipolar and bipolar mood disorders.

FINDINGS: Of the 17 subjects, 9 had histories of both severe incapacitating depressive episodes and manic or hypomanic episodes; 1 had a history of severe depressive episodes only; 3 had histories of manic or hypomanic episodes only; in 2 cases, findings were equivocal; 2 had no symptoms of mood disorder. The onset of depressive and/or manic episodes antedated the diagnosis of endometriosis. Of the 13 subjects with clearcut major mood disorders, 9 had first degree relatives with well documented severe mood disorders. Symptoms upon which diagnoses were based, and family psychopathology in each case are presented in tabular form. These findings are preliminary. They require replication and comparison with a control sample. They are worth reporting, however, because of their possible implications for increased understanding of the genetics, endocrine physiology, and neurochemistry of bipolar mood disorder. The findings are discussed in terms of fruitful areas of future research.

NR25 **Monday, May 11, 12:00 noon–2:00 p.m.**

RECEPTOR DYSREGULATION IN PSYCHIATRIC DISORDERS

Bruce D. Perry, M.D. Psychiatry West Haven VA MC West Spring Street West Haven, CT 06516, Steven M. Southwick, M.D., Earl L. Giller, Jr., M.D.

Summary:

CNS receptor (R) regulation may be related to the pathophysiology of certain psychiatric disorders (1). Platelet (P) α_2- and lymphocyte (L) β-adrenergic R have been used to test R-dysregulation hypotheses. The results have been inconsistent but suggestive. The current studies utilized a novel paradigm (Soc. neuros. Abst. 8, 414, 1986) to examine directly the dynamics of P and L adrenergic-R regulation by measuring the rate and extent of R changes following "in vitro" incubation with agonist. Intact P and L were isolated from subjects (SADS/RDC diagnoses) and volunteers meeting study criteria. Intact P and L were incubated at 37° C in physiological buffer with agonist, e.g., P 10^{-4} M (-)epinephrine; L 10^{-5} M isoproterenol. At Time = 0, and 6 hours, intact P were removed, lysed, washed extensively and radioligand binding sites (extended 12 point competition and saturation) were performed (P ^{3}H-rauwolscine; L,^{125}Iodocyanopindodolol) to assess high and low affinity states of the membrane (2). At ~15 min intervals, aliquots of incubate were removed for single point binding assays to determine the rate of loss of R from the membrane. Data were analyzed using LIGAND (Anal. Biochem., 107, 220, 1980). The results demonstrate that the dynamics of receptor (both α_2 and β) regulation in some psychiatric disorders may be altered (dysregulation?). For example, Pα_2-R in PTSD subjects "down regulate" 4 times faster than controls. This paradigm offers significant advantages over previous assays and can be utilized to further elucidate the pathophysiological role of receptor "regulation" in clinical populations.

Supported by VA funds.

NR26 **Monday, May 11, 12:00 noon–2:00 p.m.**

DEPRESSION WITH/WITHOUT PANIC: NEUROENDOCRINOLOGY

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Summary:

Numerous studies have found blunted TSH response to TRH in depression. This phenomenon remains unexplained mechanistically and uncharacterized clinically. Recent case history, genealogic and neuropharmacologic research suggests biological similarity between panic disorder and depression. Three studies have reported TSH blunting (33-40%) in nondepressed panic patients. To investigate the influence of coexisting panic disorder on neuroendocrine findings in depressed patients we studied TSH response in 49 patients with RDC primary unipolar minor and minor depression, subtyping them by presence (10 female, 5 male) or absence (19 female, 15 male) of current panic attacks. We compared patients with 112 normals. Using Δ TSH at 30 minutes post-infusion of 500 ug TRH as a response measure, we found that depressives without panic resemble normals in mean and median Δ TSH and in % subjects with "blunting" (Δ TSH $<$ 7.0 uU/ml). Depressives with panic had significantly lower mean Δ TSH ($p \leq 0.027$). For females, the prevalence of blunting in normals, depressives without and depressives with panic were 17.9, 15.8 and 40% respectively; for males: 24.3, 26.7 and 60%. We are currently analyzing prolactin response and HPA axis measures. The data suggest that panic alters the neuroendocrine profile in depression.

NR27 **Monday, May 11, 12:00 noon–2:00 p.m.**

EFFECT OF DEXAMETHASONE HALF-LIFE ON DST RESPONSE

Peter E. Stokes M.D. Psychiatry Payne Whitney Clinic 420 East 68th St RM 277 New York, NY 10021, Peter M. Stoll, M.A., Carolyn R. Sikes, M.A., Betty J. Lasley, Ph.D.

Summary:

Data published in the last three years suggest that plasma dexamethasone (dex) levels following oral dosing may be an important variable contributing to DST response, since significantly lower plasma dex levels have been reported in nonsuppressors. To evaluate further the relationship between plasma cortisol and plasma dex levels, we studied plasma dex pharmacokinetics in RDC-diagnosed patients with major depression. Seventeen patients (11 suppressors and 6 nonsuppressors, criterion $>$5.0 μg/dl on a standard 1 mg P.O. overnight DST) received a 1mg IV dex bolus at 9 AM, with blood samples collected at intervals over the next 14 hours. We found that compared to suppressors, nonsuppressors had significantly shorter plasma dex half-life ($p<.001$), as well as lower dex levels 10 hours following drug administration ($p<.002$). Moreoever, upon clinical improvement of patients, these differences disappeared. This was due to increases in dex half-life and 10 hour plasma dex concentrations in patients who switched from nonsuppression to suppression. These findings paralleled the results of the 1mg P.O. overnight DST performed in these same 17 patients and in 31 others. Here, we found a significant increase in dex levels 10 hours following drug administration in patients who changed from nonsuppression to suppression ($<.007$), but no significant change in suppressors who continued to suppress. Interestingly, in the few patients who switched from suppression to nonsuppression over the course of hospitalization, dex levels simultaneously dropped. These findings indicate that metabolism of dex may strongly influence the cortisol response to dex, and that dex pharmacokinetics may be a state-dependent phenomenon.

NR28 **Monday, May 11, 12:00 noon–2:00 p.m.**

PREDICTORS OF HPA AXIS DYSFUNCTION IN DEPRESSION

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Summary:

Hypothalamopituitary (HPA) dysfunction in Major Depression can be demonstrated by lack of cortisol suppression after the dexamethasone suppression test (DST). This measure of neuroendocrine abnormality has been found in 40-60% of Major Depressive Disorder (MDD) patients. Previous work using single DSTs, has shown a relationship to depressive state; but few specific clinical variables have been linked to HPA axis abnormality. Expansion from single DSTs to serial measures provides insight into the course of HPA dysfunction which might better address the relationship of individual and clinical factors to HPA function. Examination of repeated DSTs revealed a variable course of neuroendocrine recovery during treatment. This was studied in 107 inpatients with Major Depression. Various patterns of post-dex cortisol emerged during the hospital course. They were used to elucidate predictors of HPA dysregulation. The DST patterns revealed the following: 27% had suppression for all DSTs, 40% with nonsuppressive DST's which suppressed by discharge, 26% persistently nonsuppressive DSTs, 7% had nonsuppression on admission and large decreases in cortisol but did not suppress. There were significant interactions of age and number of episodes in predicting the patterns of recovery; however severity was associated only with pre-treatment DST nonsuppression, not the patterns of recovery. The patterns of serial DSTs revealed relationships to patient characteristics and history which were not evident with cross-sectional assessment, suggesting that repeated neuroendocrine measurements provide additional information in understanding HPA dysregulation.

NR29 **Monday, May 11, 12:00 noon–2:00 p.m.**

SALIVARY AND SERUM CORTISOL LEVELS IN THE DST

Robert P. Climko M.D. Fair Oaks Hospital 19 Prospect Street Summit, NJ 07901, David Martin, Donald R. Sweeney, M.D.

Summary:

Determination of cortisol levels after administration of dexamethasone is one of the neuroendocrine tests utilized in the assessment of affective disorders. Our current standard administration of this dexamethasone suppression test (DST) requires the analysis of serum cortisol levels at 8, 12, 16 and 24 hours after the ingestion of one (1) mg. at midnight. This procedure is extremely cumbersome for outpatients.

We compared salivary (nonprotein bound) and serum cortisol concentrations after administration of dexamethasone in thirty (30) patients admitted to the hospital. Patients provided 2-3 ml. of saliva in plastic tubes prior to venipuncture. Nonsuppression was defined as a concentration of greater than 5 ug/dl in serum or 90 ng/dl in saliva utilizing a standard radioimmunoassay technique. Serum and saliva correspondence, in terms of suppression versus nonsuppression, occurred in 29 of the 30 patients. The only patient showing noncorrespondence had a serum cortisol level of 5.7 ug/dl.

These data show that salivary and serum cortisol measurements result in nearly identical classification. Further, the collection of saliva is more convenient and painless compared to venipuncture and more accommodating for both inpatient and outpatient evaluation of affective illness.

NR30 **Monday, May 11, 12:00 noon–2:00 p.m.**

STUDIES OF HUMAN CSF NEUROPEPTIDES

Wade H. Berrettini M.D. Neurogenetics NIMH Bldg10 RM3N220 NIH Bethesda, MD 20892, John I. Nurnberger, Jr., M.D., Joel Gelernter, M.D., Susan Simmons-Alling, M.S.N., Owen Wolkowitz, M.D.

Summary:

Neuropeptides are a group of recently-discovered putative neurotransmitters which are being intensively studied in psychiatry disorders. We have conducted some general studies of the characteristics of neuropeptides in human CSF, as measurement of these substances in CSF has been one major approach to the study of neuropeptides in psychiatric disease. We found that CSF levels of most neuropeptides are stable characteristics of individuals over time, and can be measured in a reliably reproducible fashion. CSF levels of neuropeptide Y are heritable, while CSF levels of corticotropin releasing factor and growth hormone releasing factor are determined more by cultural/environmental factors. In general, CSF neuropeptides do not exhibit rostrocaudal gradients. Diverse neuropeptides in CSF show concentrations that are highly correlated with one another, including a number of neuropeptides involved in the regulation of the hypothalamic-pituitary-adrenal axis, suggesting that CSF levels of various neuropeptides function to transmit information to distant parts of the brain. Drug treatments can alter levels of these substances, as we have found that lithium treatment increases CSF levels of vasoactive intestinal peptide, and acute doses of physostigmine increase levels of neuropeptide Y. Similarly, chronic prednisone treatment causes a decrease in CSF levels of beta-endorphine and beta-lipotropin. These observations suggest that CSF levels of neuropeptides will be a valuable tool in the study of psychiatric diseases.

NR31 **Monday, May 11, 12:00 noon–2:00 p.m.**

INSULIN RESISTANCE AFTER ORAL GTT IN DEPRESSION

Jay D. Amsterdam M.D. Psychiatry Univ. of Penn. Hospital Gibson 1, 3400 Spruce Street Philadelphia, PA 19104, Andrew Winokur, M.D., Greg Maislin, M.S.

Summary:

An association between depression and alterations of glucose utilization has been observed. Some studies using the insulin tolerance test have shown a blunted hypoglycemic response, while others have used a glucose tolerance test (GTT) and found elevated blood sugar levels. In order to more closely examine impaired glucose tolerance in depression, we performed a 5-hour oral-GTT in 28 patients with major depression with a mean (±SD) age of 38±13 years (21 melancholic, 7 nonmelancholic), and 21 healthy volunteers aged 30±10 years.

METHODS: All subjects were given a standard diet for 3 days, and fasted 8 hours prior to oral-GTT at 0830 hours. Blood samples were obtained at baseline and then at 30-minute intervals up to 300 minutes after GTT for glucose, insulin, and glucagon levels. All baseline measurements were centered so that at "time 0" the basal value was zero.

RESULTS: The cumulative glucose response for patients (312±246 mg%) was twice that of controls (152±108 mg%) ($p = 0.004$). While basal insulin levels were similar, the insulin response to GTT was higher in patients (19.9±11.9 ng/ml) than controls (12.5±5.4 ng/ml) ($p = 0.006$). These findings were most pronounced in melancholic patients. There were no correlations between baseline cortisol, growth hormone, or age and any response parameter.

In conclusion, these findings of increased insulin output and diminished glucose utilization in depressed patients given the GTT suggests the presence of insulin resistance in depression.

NR32 **Monday, May 11, 12:00 noon–2:00 p.m.**

VASOPRESSIN TEST: EFFECT OF CLINICAL VARIABLES

Juan F. Lopez M.D. Psychiatry Univ of Michigan 205 Wastenaw Place Ann Arbor, MI 48109, Roger G. Kathol, M.D., William H. Meller, M.D., Richard S. Jaeckle, M.D.

Summary:

Arginine Vasopressin (AVP) is a peptide known to stimulate the pituitary adrenal axis in humans. Patients with Major Depression (MD) (DSM-III) have a significantly greater cortisol response to AVP than normal controls (Meller et al., J. Psych. Res., in press). To investigate if the cortisol response to AVP is influenced by clinical and demographic variables, we have analyzed the relationship of this cortisol response to age, sex, severity of depression, duration of the depressive episode, duration of the illness, age at the time of the first episode and number of depressive episodes.

We administered 0.18 pressor units/kg body weight of AVP intramuscular to 24 patients with MD (17 females, 7 males) and collected plasma cortisol at 0, 15, 30, 45, 60 and 90 minutes after injection. Six patients were dexamethasone non-suppressors (NS) and 17 were suppressors (S). A stepwise linear regression analysis revealed that the maximal cortisol increase (Δ max) was positively correlated with the length of the episode ($p < .05$) but negatively correlated with the age of the first episode ($p < .05$) and with severity of illness (Carrol's Rating Scale) ($p < .001$). Peak cortisol levels were also negatively correlated with severity ($p < .05$). Females had significantly higher cortisol peaks and Δ max than males ($p < .001$). Surprisingly, peak and Δ max cortisols were positively correlated with S rather than NS patients ($p < .05$). These findings suggest that clinical and demographic variables are important contributors to the pathophysiology of cortisol abnormalities in Major Depression.

NR33 **Monday, May 11, 12:00 noon–2:00 p.m.**

BLUNTED ORTHOSTATIC RESPONSE IN MAJOR DEPRESSIVES

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

Summary:

GOALS: We have reported blunted lymphocyte beta-adrenergic receptors in Major Depressive Disorder (MDD). We therefore measured plasma catecholamine (CA) and cardiovascular measures during an orthostatic challenge test to further assess peripheral adrenergic function in MDD. METHODS: Patients ($n = 15$) and healthy controls ($N = 13$) rested supine for 30 minutes after insertion of IV catheter. EPI, NE, BP and HR were measured supine, 3 and 5 minutes after standing. Patients met RDC criteria for MDD, endogenous subtype, were on no medications, and had no active medical illnesses. RESULTS: In both patient and control groups EPI and NE rose after the orthostatic challenge test. There was no difference in mean supine EPI levels in patients compared to controls ($P = 0.2$). On standing, patients had a greater rise in EPI at 5 minutes than controls ($P < 0.005$). There was a nonsignificant trend for higher NE in patients at 5 minutes ($P = 0.16$). Patients and controls showed the expected rise in HR upon standing but there was no statistically significant difference in HR between the two groups at any time. Patients had lower supine systolic BP and lower diastolic BP after 3 and 5 minutes ($P < 0.05$). SIGNIFICANCE: (1) At rest patients do not have elevated catecholamines; (2) BP is lower in patients than controls; (3) on standing patients show exaggerated catecholamine release, yet do not show a comparable HR or BP rise; (4) these findings suggest blunting of beta-adrenergic receptor mediated cardiac responses in MDD that may be secondary to elevated CA levels when erect.

NR34 **Monday, May 11, 12:00 noon–2:00 p.m.**

FEATURES OF EYE-TRACKING IN DELUSIONAL DEPRESSION

Stephen L. Snyder M.D. Psychiatry Payne Whitney 525 East 68th Street New York, NY 10021, John A. Sweeney, Ph.D., Margaret Rea, Ph.D., J. John Mann, M.D., Allen J. Frances, M.D.

Summary:

Introduction: Although deviant eye-tracking is a frequent finding in schizophrenia and has been proposed as a psychobiological marker, its diagnostic specificity for schizophrenia remains unclear. Method: 41 SCID-diagnosed inpatients (6 delusional depressives and 35 schizophrenia) received eye-tracking tests and were compared to 22 normals. Results. Eye-tracking of both delusionally depressed and schizophrenic patients was significantly impaired. Delusional depressives had the lowest mean tracking accuracy and significantly higher mean saccade frequency compared to both normals and schizophrenics ($P<0.05$). When saccades were differentiated by size, delusional depressives had a signficantly higher number of large saccades ($\geqslant 8$ degrees of visual angle) than schizophrenics ($P<0.05$). ECT substantially improved eye-tracking in 2 delusional depressives but caused tracking to deteriorate in 2 others. Significance: The severe eye-tracking deficits in delusional depressives raise questions about the diagnostic specificity of eye-tracking deficits for schizophrenia in acutely psychotic patients. Large saccades, which may reflect the problems in attention, were even more frequent in delusionally depressed than schizophrenic patients and may help distinguish the two groups. Further analysis of specific eye-tracking characteristics is indicated to identify components of eye-tracking abnormality specific to different diagnostic groups.

NR35 **Monday, May 11, 12:00 noon–2:00 p.m.**

NATURAL KILLER CELL ACTIVITY AND AGE IN DEPRESSION

Steven J. Schleifer M.D. Psychiatry Mount Sinai Sch. Med. One Gustave L Levy Place New York, NY 10029, Steven E. Keller, Ph.D., Ronald N. Bond, Ph.D., Jacob Cohen, Ph.D., Marvin Stein, M.D.

Summary:

Natural killer (NK) cells play an important role in immune surveillance against viruses and neoplasia distinct from traditional lymphocyte functions. To determine if NK cell activity (NKCA) is altered in major depressive disorder (MDD), we measured NKCA in 88 patients with MDD, unipolar subtype, studied on the same day with age- and sex-matched controls. Subjects were in good health and had not received antidepressant treatment for 3 months. Hierarchical regressions revealed age-related effects on NKCA but no effects in relation to sex, severity (Hamilton Depression Scale) or hospitalization. There was a significant ($p<0.01$) increase in NKCA with advancing age in the healthy controls and no relationship between age and NKCA in depressed patients. The slopes of the regression lines of NKCA on age of the patients and controls were significantly different ($p<0.05$). We found similar age-related differences in mitogen-induced lymphocyte proliferation. The comparable age-related immune alterations in two distinct aspects of immunity, lymphocyte function and NKCA, suggests that MDD may be associated with a fundamental defect in immunoregulatory mechanisms common to these immune processes. Altered interleukin processes, which are subject to corticosteroid-induced inhibition, may be involved in these effects. Investigation of immune mechanisms in MDD may help to elucidate the pathophysiology of depressive states.

NR36 **Monday, May 11, 12:00 noon–2:00 p.m.**

PLASMA TRANYLCYPROMINE AND ANTIDEPRESSANT ACTION

Alan G. Mallinger M.D. Western Psych Inst 3811 O'Hara Street Pittsburgh, PA 15213, Jonathan M. Himmelhoch, M.D., Michael E. Thase, M.D., David J. Edwards, Ph.D., Steven Knopf, B.S., Carilyn Z. Fuchs, Ph.D.

Summary:

Clinical effects of psychotherapeutic agents can be substantially influenced by their pharmacokinetics and biological disposition. Thus, we investigated the relationship of plasma tranylcypromine (TCP) measurements to antidepressant action in 20 patients with bipolar depression. Subjects were treated in a double-blind protocol, and depressive symptoms were rated using the Hamilton score (HRS-D). For the plasma TCP measurements (performed between weeks 6 and 8), fasting subjects ingested a 20 mg oral TCP dose, and blood samples were collected during the postabsorptive phase (5, 6, 7, and 8 hours). Elimination half-lives ($t_{1/2}$) were then calculated from the log plasma concentration vs. time plots. Values of $t_{1/2}$ were unrelated to clinical measures. However, a consistent relationship was noted between the initial TCP concentrations measured 5 hours post-dose (^{5h}TCP) and clinical outcome. Beginning at the 3rd week of treatment (and for all 6 subsequent time points studied through 12 weeks), the log-normalized ^{5h}TCP values were significantly correlated with the observed changes from pretreatment HRS-D scores (range for r: 0.50-0.66; range for p: <0.003-<0.04). However, ^{5h}TCP was not correlated with the pretreatment HRS-D values, or the changes in HRS-D scores were measured early in treatment (weeks 1 and 2); moreoever this measure was not correlated with the elimination $t_{1/2}$ values. Based on previous TCP pharmacokinetic studies (Mallinger et al., 1986), it seems likely that elevated ^{5h}TCP values may be related to delayed TCP absorption, because of proximity of the absorption peak at this time. Thus, our present findings are consistent with an association between delayed TCP absorption and lack of responsiveness to treatment with this agent.

NR37 **Monday, May 11, 12:00-2:00**

TREATMENT-INDUCED CHANGES IN MEMBRANE LI AFFINITY

Alan G. Mallinger M.D. Western Psych Inst 3811 O'Hara Street Pittsburgh, PA 15213, Jonathan M. Himmelhoch, M.D., Michael E. Thase, M.D., Steven Knopf, B.S., Christine S. Dippold, B.S.

Summary:

Lithium (Li) is useful for treating the majority of patients with bipolar affective disorder, but for incompletely understood reasons, it is not always effective. Unlike most other psychotherapeutic agents, Li is a simple ion that is exchanged for sodium (Na) across the cell membrane via the Na-Li countertransport system (Na-Li CT). This cellular transport mechanism appears to be active in many types of tissues, and may play a major role in the biological disposition of Li that is administered clinically. We studied the effects of Li treatment on both the maximum transport rate (V_{max}) and the affinity for intracellular Li ($K_{1/2}$) of Na-Li CT. Transport measurements were performed using erythrocytes (RBCs) from 23 patients diagnosed as having bipolar affective disorder, who were studied both prior to and during Li maintenance treatment. Li pharmacotherapy had no effect on the mean ($\pm$SD) value of V_{max} (0.32 $\pm$.15 vs. 0.31 $\pm$.11 mmoles/liter RBCs/hr). However, mean $K_{1/2}$ increased significantly from 0.32 $\pm$.07 to 0.38 $\pm$.10 mmoles/liter RBCs (paired t-test, $t=3.4$, $p<0.003$), indicating reduced affinity for intracellular Li. Despite a mean increase of 22% in $K_{1/2}$ during Li treatment, there were substantial differences in this effect among individuals, ranging from -25 to 64%. Such differences were not related to serum Li levels. Reduced affinity of membrane Na-Li CT for Li could shift the distribution of this agent toward the intracellular space, thereby leading to increased tissue Li levels and possibly enhanced pharmacologic actions. Moreover, differences between individuals in the occurrence or extent of this phenomenon could contribute to individual variability in responsiveness to the clinical effects of Li.

NR38 **Monday, May 11, 12:00-2:00**

OLFACTORY DEFICITS IN SCHIZOPHRENIA

Lili C. Kopala M.D. Psychiatry University of B.C. 2255 Wesbrook Mall Vancouver, B.C. Canada V6T 2A1, Trevor A. Hurwitz, M.D., Campbell M. Clark, Ph.D., Barry D. Jones

Summary:

Olfaction, perhaps the least understood sensory system, is receiving increasing interest in the study of brain disorders. The availability of a standardised test for olfaction discrimination, the Pennsylvania Smell Identification Test (SIT) facilitates this interest. Because the olfactory tubercle is richly innervated by dopaminergic neurons of the mesolimbic system, and given the dopamine hypothesis of schizophrenia, examination of olfactory discrimination in schizophrenia may provide insights into the pathophysiological substrates of this disorder.

METHOD: The SIT was administered to eighteen acutely ill patients receiving neuroleptics and meeting DSM-III criteria for schizophrenia, eleven non-schizophrenic psychiatric control subjects who were treated with neuroleptics, and ten normal subjects. In addition, subjects were rated for overt psychopathology, and were examined neurologically to rule out traumatic and other medical causes for olfactory disturbance.

RESULTS: Schizophrenic patients had a significantly lower mean SIT score (33.4) than normals (37.7) and psychiatric controls (37.4) ($F_{2,37} = 4.90$, $P < .02$). Performance was not found to be related to age, gender, smoking habit, duration of neuroleptic exposure, fatigue or severity of psychopathology.

DISCUSSION: These results suggest a primary deficit in olfactory discrimination in schizophrenic patients. Although other explanations will need to be examined through further research, these findings have both practical and theoretical relevance to the understanding and management of schizophrenia.

NR39 **Monday, May 11, 12:00 noon–2:00 p.m.**

FLUOXETINE PLASMA LEVELS IN TREATMENT OF DEPRESSION

R. Cameron Dorey Ph.D. Chemistry Wichita State University 1845 N. Fairmount Wichita, KS 67208, Jorge H. Beber, M.D., Sheldon H. Preskorn, M.D.

Summary:

In a random assignment double-blind, controlled trial of fluoxetine vs amitriptyline in adults with DSM-III major depressive disorder, we measured plasma levels of fluoxetine and its major metabolite, norfluoxetine. Plasma levels for thirty patients taken after six weeks on fluoxetine were compared with clinical response, as measured by the Hamilton Depression Scale. The dose was initially fixed at 20 mg/da for two weeks, and afterward could be adjusted upward to a maximum 60 mg/da, based on response. In all cases, patients were on a fixed dose for one week prior to plasma sampling.

Plasma levels after two weeks on 20 mg/da ranged from 29 to 585 ng/mL fluoxetine, 53 to 445 ng/mL norfluoxetine, and 76 to 1030 ng/mL total. There was no strong correlation between fluoxetine and norfluoxetine plasma levels.

Plasma levels at the end of six weeks on fluoxetine ranged from 30 to 808 ng/mL fluoxetine, 98 to 1266 ng/mL norfluoxetine, and 175 to 1953 ng/mL total. We found no significant correlation between either two week or six week plasma levels of either compound or the total of the two with any of the following measures of clinical response: (1) final Ham-D score, (2) improvement in Ham-D score (final score-score post one week placebo), (3) "% improvement" in Ham-D score (final-post placebo)/(post placebo)*100), or (4) clinical global impression.

NR40 **Monday, May 11, 12:00-2:00**

HYDROXYMETABOLITIES OF TRICYCLIC ANTIDEPRESSANTS

Bruce G. Pollock M.D. Psychiatry WPIC 3811 O'Hara Street Pittsburgh, PA 15213, James M. Perel, Ph.D., John P. Foglia, M.S., Lori A. Birder, M.S.

Summary:

Patients treated with nortriptyline (NT), imipramine (IMI) or clomipramine (CMI) also have considerable plasma levels of pharmacologically active hydroxymetabolites. Hydroxylation controls the clearance of tricyclics; 2-hydroxyimipramine (2-OH-IMI) and 8-hydroxyclomipramine (8-OH-CMI) each comprise about 30% of their respective parent drug levels, whereas E-10-hydroxynortriptyline (E-10-OH-NT) constitutes approximately 150-300% of NT levels. A systematic examination of the direct pharmacological properties of these metabolites is therefore of paramount importance. We recently completed experiments in 70 domestic swine that reveal important cardiotoxic and pharmacokinetic differences between tricyclics and their hydroxymetabolites; the latter having been synthetized and administered de novo. 2-OH-IMI was found to be exceedingly cardiotoxic when compared to IMI, CMI, and 8-OH-CMI as determined by profound hemodynamic changes and the generation of ventricular arrhythmias. In contrast, E-10-OH-NT and its isomer Z-10-OH-NT produced less hemodynamic and EKG change than NT at comparable doses. The half-lives of hydroxymetabolites were shorter compared to their parent compounds with smaller volumes of distribution—these results were because of their single step elimination and increased polarity. It is notable that CNS penetrance (CSF/Plasma ratios) was greater for 2-OH-IMI (0.19 ± 0.05) and E-10-OH-NT (0.36 ± 0.06) than their respective parents IMI (0.09 ± 0.04) and NT (0.13 ± 0.05). Our data contribute to the interesting possibility that E-10-OH-NT and 8-OH-CMI may be potentially useful antidepressants and that 2—OH-IMI may significantly amplify the cardiotoxicity of IMI overdose.

NR41 **Monday, May 11, 12:00 noon–2:00 p.m.**

VARIABILITY OF PLASMA LEVELS OF ANTIDEPRESSANTS IN THE ELDERLY: A POSSIBLE MECHANISM

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Summary:

The blood levels of tricyclics obtained in the elderly have been reported as highly variable with some findings that absorption was very poor. It is postulated that this may be due to local muscarinic blockade in the gut and that therefore antidepressants with higher anticholinergic activity would be more variably absorbed than those with less.

The steady state plasma levels were done on 57 patients on doxepin, trimipramine, desipramine or trazodone. The average age of 30 females and 27 males was 73.7 (range 67-88). The correlation coefficient (Pearson's r) was calculated for oral dose and steady state plasma level for each drug and the results are as follows:

	N	r	p
Doxepin	18	+0.2	NS
Trimipramine	8	−0.15	NS
Desipramine	19	+0.6	<0.01
Trazodone	12	+0.91	<0.001

These data support the hypothesis that the variable absorption of antidepressants may be in part related to their anticholinergic activity, with doxepin and trimipramine steady state plasma levels having no correlation with oral dose, desipramine with less anticholinergic activity having some correlation and trazodone with the least anticholinergic activity having a highly significant relationship of oral dose to plasma level.

NR42 **Monday, May 11, 12:00 noon–2:00 p.m.**

10-HYDROXY-NORTRIPTYLINE INHIBITS EFFICACY IN ELDERLY?

Robert C. Young M.D. Psychiatry NY Hosp. Cornell Med. 21 Bloomingdale Road White Plains, NY 10605, George S. Alexopoulos, M.D., Richard D. Shindledecker, M.A., Amiya K. Dhar, D.Sc., Henn Kutt, M.D., Charles A. Shamoian, M.D.

Summary:

In geriatric patients treated with nortriptyline (NT), plasma unconjugated 10-hydroxy-NT (10-OH-NT) is more than 2-fold higher than in younger patients receiving equivalent doses. 10-OH-NT-/NT ratios vary more than 50-fold between individuals. 10-OH-NT is less protein-bound than NT, and it is phramacologically active.

Geriatric (age $\geq$ 60 yrs.) inpatients (N = 40) with major depression by DSM-III criteria and 21-item Hamilton Depression Rating Sacle (HDRS) scores $\geq$ 18 were treated with NT at stable doses of 40 to 125 mg/day. After four weeks, the HDRS was repeated (HDRS4) and change (Δ HDRS) was calculated; plasma NT and 10-OH-NT were determined. HDRS4 was positively correlated with plasma 10-OH-NT and with the 10-OH-NT/NT ratio ($r = .43$, $p < .005$; $r = .39$, $p < .04$, respectively), and ΔHDRS was negatively correlated with plasma 10-OH-NT and with 10-OH-NT/NT ratio ($r = -.47$, $p < .002$; $r = -.32$, $p < .04$, respectively). Neither was correlated with plasma NT ($r = -.08$; $r = -.03$) or with dose.

In the elderly, high 10-OH-NT may inhibit therapeutic response, at least when plasma NT is moderate. This might be because 10-OH-NT is less potent than NT, and may reflect a general mechanism underlying the reduced efficacy associated with high plasma concentrations in mixed-age patient samples chronically treated at one NT dose. Together with evidence linking 10-OH-NT, and hydroxylated metabolites of other tricyclics, with toxicity, these findings suggest a role for monitoring plasma 10-OH-NT in geriatric patients.

NR43 **Monday, May 11, 12:00 noon–2:00 p.m.**

FLUVOXAMINE IN REFRACTORY DEPRESSION

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

Summary:

Ten-30% of depressed patients are refractory to antidepressant drugs. Some antidepressants may exert their therapeutic effect by altering central serotonergic (5HT) functioning. This study investigated the efficacy of the potent and selective unicyclic 5HT reuptake inhibitor, fluvoxamine, in depressed patients refractory to standard antidepressants.

METHOD: Thirty-eight consecutively admitted depressed patients, judged refractory to standard antidepressants using operationalized criteria, were treated in a placebo-controlled protocol involving $\geq$ 2 weeks of placebo and 4–6 weeks of active fluvoxamine. Ten patients did not complete protocol: 5 worsened and one spontaneously remitted during placebo and 4 had adverse reactions to fluvoxamine. The 28 patients who completed protocol had previously failed a mean of 4.1 ± 3.1 antidepressant trials; 39% had also failed lithium augmentation. Depression was diagnosed using DSM-III criteria and symptoms were assessed weekly by blind raters using the Hamilton Depression Rating Scale. Previously published criteria were used to assess treatment response.

RESULTS: Of protocol completers, 9 (32%) were judged responders to fluvoxamine alone, 9 (32%) eventually responded to fluvoxamine plus lithium, and 2 (7%) to fluvoxamine, lithium, and perphenazine. Eight patients (29%) had no response to fluvoxamine.

CONCLUSION: Fluvoxamine is an effective drug in depressed patients refractory to available antidepressants and lithium augmentation of available antidepressants. These data suggest that selective and potent 5HT reuptake inhibitors may be effective in patients refractory to generally available antidepressant medications.

NR44 **Monday, May 11, 12:00 noon–2:00 p.m.**

AFTER LITHIUM AUGMENTATION: A RETROSPECTIVE STUDY

Andrew A. Nierenberg M.D. Psychiatry, McLean Hosp., 115 Mill St. Belmont, MA 02178, L.H. Price, M.D., D.S. Charney, M.D., G.R. Heninger, M.D.

Summary:

Although adding lithium to an antidepressant has been shown to be effective for treatment resistant depression, longitudinal outcome of such patients has not been reported. We retrospectively studied 76 DSM-III major depression patients who received lithium augmentation (Li+) after non-response to at least one adequate antidepressant trial. A rater blind to clinical status at discharge obtained information on 67 patients (87%) using a modified Longitudinal Interval Evaluation (LIFE) scale. Life table analysis showed that 75% of this group experienced neither a re-hospitalization nor suicide attempts 36 months after discharge. Stratifying by response to Li+ at discharge revealed that after 36 months full responders had an 88% non-recurrence rate, while rates for partial and non-responders were 70% and 74% respectively with non-significant differences between groups. An additional 35% were either chronically depressed or had mild/moderate recurrences managed as outpatients. Only 40% had no recurrence and only half of these remained on medication up to 4 years after discharge.

We conclude that (1) despite the severe spectrum of depression in this sample, 40% of these treatment resistant patients experienced sustained improvement and (2) response to Li+ did not predict subsequent course probably reflecting the efficacy of alternative treatments (e.g., lithium-traylcypromine or ECT) in Li+ non-responders.

NR45 **Monday, May 11, 12:00 noon–2:00 p.m.**

PSYCHOPATHOLOGY IN PARASUICIDE AND FAILED SUICIDE

John G. Keilp M.A. Psychiatry Payne Whitney Clinic 525 East 68th Street New York, NY 10021, Catherine Raduns, M.A., Susan Evans, B.S., Richard P. Brown, M.D., P. Anne McBride, M.D., J. John Mann, M.D.

Summary:

INTRODUCTION: Empirical support has accrued for the distinction between parasuicide and failed suicide, a distinction with implications for clinical management of and research on self-harm.
METHOD: We examined the validity of this model in 45 psychiatric inpatients admitted after a recent suicide atttempt who were classified according to their parasuicidal/failed status, and evaluated on interview and self-report measures of Borderline Personality (Structured Interview for Borderlines), impulsivity (Zuckerman Sensation Seeking Scale, MMPI Psychopathic Deviate subscale), and aggressivity (Aggression History Questionnaire, Buss-Durkee Hostility Inventory).
RESULTS: Stepwise discriminant analysis revealed that our para/failed classification could be reproduced with 92.5% accuracy using only a patient's age, an objective rating of the medical dangerousness of their attempt, and a rating of behaviors indicating that their attempt was planned. These 3 predictive variables in turn discriminated a population of parasuicides who had a significantly greater degree of Borderline Personality characteristics ($p<.001$), greater history of aggressive behavior ($p<.006$), and higher self-report ratings of undirected hostility ($p<.02$), suspiciousness ($p<.013$), and MMPI Psychopathic Deviancy ($p<.002$). Moreover, measures of impulsivity/agressivity were positively related to the medical dangerousness of parasuicides' attempts, but negatively related to the dangerousness of failed attempts.
DISCUSSION: Data provide support for the proposed two-population model of suicidal populations, and suggest potential diagnostic differences between the two groups.

NR46 **Monday, May 11, 12:00 noon–2:00 p.m.**

FAMILY VARIABLES RELATED TO SUICIDALITY AND VIOLENCE

Robert Plutchik Ph.D. Psychiatry Albert Einstein Coll of Medicine Jacobi Hosp 133 Bronx, NY 10461, Herman M. Van Pragg, M.D., Hope R. Conte, Ph.D., Susan Picard, M.A.

Summary:

This study was concerned with identifying family and personality variables that correlate with the risk of suicidal or violent behavior. It is based upon the authors' previous research that led to a two-stage model of countervailing forces. A battery of tests measured psychiatric patients' memories of their parents' interactions with them in the areas of sociability, inconsistency, rejection, etc., and such adult personality dimensions as submissiveness, depression, aggressiveness, and conflict. Other variables included ego strength, social network, family problems and family violence. This battery of tests was administered to 60 inpatients diagnosed mainly as affective disorders or schizophrenic spectrum disorders. Patients whose parents were rejecting, depressed, or aggressive toward them, were likely to have a high risk of both violent and suicidal behavior. Patients whose parents were high on sociability and acceptance were not likely to be at risk for either suicide or violence. Patients who scored high on assertiveness, ego strength and social network were not likely to be at risk for suicide. In contrast, patients who scored high on ego strength and assertiveness tended to be high on risk for violence. The data support the concept of countervailing forces that interact to produce overt suicidal or violent behavior.

NR47 **Monday, May 11, 12:00 noon–2:00 p.m.**

OXFORD RECORD-LINKAGE STUDY: DIAGNOSIS AND MORTALITY

John C. Simpson Ph.D. Psychiatry Brockton-WROX VAMC 940 Belmont Street, 116A Brockton, MA 02401, Ming T. Tsuang, M.D.

Summary:

Despite repeated evidence of excess mortality in psychiatric patients, few studies have examined in detail the importance of diagnosis for specific mortality risks. We utilized psychiatric hospital records and death certificates—assembled over sixteen years by the Oxford Record Linkage Study—to compare observed and expected deaths from major cause in schizophrenia (n = 3,040), affective disorders (n = 8,195) and four surgical control groups (total n = 26,921). As expected, schizophrenics of both sexes and all ages were at significantly increased mortality risk for unnatural deaths (primarily suicides), though the relative risks were greater for patients with ICD-8 depressive psychoses and nonpsychotic depression; controls were not at increased risk. Schizophrenics and affective disorder patients had similar increased risks for deaths from respiratory diseases and from cardiovascular system diseases, although middle-aged and elderly female patients with affective disorders had noticeably higher risks for cardiovascular system disease deaths. No groups had significantly increased or decreased cancer mortality. Future analyses of these data will examine the effects of length of hospitalization, socioeconomic variables, and physical diseases at admission. However, the study reaffirms the importance of diagnosis in determining the risk of unnatural deaths in psychiatric patients.

NR48 **Monday, May 11, 12:00 noon–2:00 p.m.**

LIFETIME COURSE OF ILLNESS IN CHRONIC DEPRESSION

Robert M. Rohrbaugh M.D. Psychiatry West Haven VA MC West Spring Street West Haven, CT 06516, Diane E. Sholomskas, Ph.D., Earl L. Giller, Jr., M.D.

Summary:

Knowledge of the lifetime course of illness in chronic depression is limited. We examined the course of illness in 16 male chronic depressives using the SADS-L. All subjects met RDC for either anxiety disorder (88%) or cyclothymia (12%) before age 35; these disorders preceded the initial onset of major depressive disorder (MDD) by at least 6 months. The age of onset of first MDD was bimodally distributed with 75% having onset before age 35 and 25% after age 50. Anxiety disorder symptoms continued from age 35 to 50 though depressive symptoms were relatively mild (25% with intermittent depressive disorder (IDD) and none with MDD). Moreover, anxiety disorder symptoms continued after age 50 when subjects began to experience "double depression" (IDD with superimposed episodes of MDD) despite adequate pharmacologic treatment. The bimodal distribution by age at onset of MDD, and differences in the course of IDD leads us to identify three distinct patterns of illness in "anxiety disorder associated chronic depression"; (1) "chronic dysthymia"; (2) "episodic dysthymia"; and (3) "late onset dysthymia". While supporting some current theories of anxiety and depression, these data also suggest a new conceptualization of the relationship between anxiety disorder and the other psychiatric (depression, alcoholism) and medical (ulcer disease) disorders in the population.

NR49 **Monday, May 11, 12:00 noon–2:00 p.m.**

UNIPOLAR DEPRESSION: ADOLESCENT VERSUS ADULT ONSET

Thomas H. McGlashan M.D. Research Institute Chestnut Lodge 500 West Montgomery Avenue Rockville, MD 20850

Summary:

Recent family study[1] suggests age of onset, comorbid anxiety disorder, and comorbid alcoholism each define homogeneous sybtypes of unipolar depression (UNI). If early age of onset identifies a UNI cohort that "breeds true" in families, might that cohort also be distinctive in its clinical profile and long-term outcome? We test this using long-term (average 15 years) follow-up data on DSM-III UNI patients from the Chestnut Lodge follow-up study.[2]

METHOD: Outcome data were collected by interview with adequate reliability between 2-32 years post discharge. Diagnostic, predictor, and demographic assessment involved independent (and also reliable) rating of the patients' abstracted medical records. Analyses used t-tests and chi-square tests.

RESULTS: At baseline, adolescent onset patients (<19 years old, N = 20) were significantly inferior to adult onset patients (>20 years old, N = 38) on premorbid social, sexual, and occupational functioning. They were similar symptomatically except for more alcohol abuse in the adult onset cohort. At outcome, the adolescent onset group proved superior in occupational and global functioning while the adult onset patients continued their problems with alcohol.

SIGNIFICANCE: Follow-up of early versus late onset bipolar patients demonstrates a similar reversal of baseline differences; this is the first such report for UNI patients. Our data also strongly suggest that age of onset defines UNI cohorts with distinctive longitudinal clinical profiles, thus supporting the validity of Weissman et al's early age of onset depressive subtype.

NR50 **Monday, May 11, 12:00 noon–2:00 p.m.**

SOCIAL ZEITGEBERS AND BEREAVEMENT

Joseph A. Flaherty Psychiatry Univ of Illinois 912 S. Wood Chicago, IL 60612, Judith A. Richman, Ph.D., Ellen Frank, Ph.D., David J. Kupfer, M.D., K. Hoskinson, M.S.

Summary:

Fifty-six recent (within 5 weeks of spouses' death) widows and widowers were interviewed to test the hypothesis that disruptions in social zeitgebers results in depression. Social zeitgebers were defined as daily and weekly routines and activities that orient the individual to time and provide organization of their life and entrainment to their carcadian rhythms. A preliminary instrument for assessing social zeitgebers disruption consequent to bereavement was developed after initial testing on a student population. Depression was determined by the Schedule for Affective Disorders and Schizophrenia-Lifetime version and the Center for Epidemiologic Studies-Depression Scale. Three personality factors hypothesized to be intermediary variables were also measured: neuroticism (Eysenk) self-esteem (Rostenberg) and flexibility (Wheaton). Analysis of variance showed significant main effects for personality and zeitgeber disruption on CES-D scores as well as categories of depression; interactive effects reached trend ($p = .1$) significance. Changes in the people involved in daily routine without replacement was the key zeitgeber variable accounting for the variance in depressive outcome.

NR51 **Monday, May 11, 12:00 noon–2:00 p.m.**

THE PSYCHOLOGY OF HELPLESSNESS

Marian L. Fitzgibbon Ph.D. 420 East 70th St. Apt. 7J New York, NY 10021, John A. Sweeney, Ph.D., David F. Cella, Ph.D.

Summary:

Learned helplessness (LH) is commonly seen in depression, but the components of the process have not been adequately characterized. The purpose of this study was to further validate the model within clinical populations and show the specificity of different features of depression in three distinct groups.

METHOD: Subjects were psychiatric inpatients with a diagnosis of major depession ($N = 36$), medical inpatients on a renal unit ($N = 36$), and age matched healthy controls ($N = 36$). They were given a problem solving task during which they received contingent or noncontingent feedback (always correct or incorrect). Affect, motivation, and cognition were measured before and after the task.

RESULTS: Contingent feedback had a positive and similar effect on affect and cognition (problem solving) for all groups ($p < .01$). Depressed patients were most reactive to the impact of environmental contingencies in regard to changes in affect ($p < .01$), while renal patients were most responsive in terms of changes in motivation ($p < .01$). Depressives became more depressed when given noncontingent positive feedback (always correct), whereas the renal patients had a classic response to the LH paradigm by becoming more depressed after noncontingent failure (always incorrect).

SIGNIFICANCE: These findings highlight the different components of helplessness in depression and chronic renal disease. To be optimally effective, psychological interventions may need to focus on the affective and motivational deficits seen in these groups.

NR52 **Monday, May 11, 12:00 noon–2:00 p.m.**

PROBLEM-SOLVING IN PARASUICIDES AND OUTCOME

Isaac Sakinofsky M.D. Psychiatry St. Michaels Hospital 30 Bond St. Toronto, Ont. Canada M5B 1W8

Summary:

Parasuicide (deliberate self-harm, attempted suicide) is common and high in risk for future suicide. To prevent suicide we need to understand underlying determinants. A prospective study was carried out of 228 consecutive cases who presented in a Canadian city. Initial demographic, clinical, and role functioning data were collected, together with measures of depression, self-esteem, sensitivity to criticism, hostility, alienation (powerlessness, normlessness, isolation), life events, locus of control, and severity of presenting problems. Three months later these measures were repeated on 187 (82.02%) and a further 14 were also reached subsequently (88.17% in total). The sample was then split into an improved group in whom the severity of presenting problems had improved by a criterion of at least 50% and the remainder (unimproved). Antecedent factors found to predict poor outcome at three month follow-up were prior history of adolescent neurotic disturbance, duration of presenting problems, number of previous suicide attempts, initial powerlessness, hostility and social maladjustment. At follow-up the unimproved group were rated more depressed and hostile and locus of control scores had moved toward the "external" pole. They had experienced a greater ratio of negative over positive life events. Despite these differences the surprising finding was that each group experienced a similar incidence (16%) of new parasuicidal acts.

NR53 **Monday, May 11, 12:00 noon–2:00 p.m.**

DSM-III AXIS II AND MEDICAL UTILIZATION

William R. Yates M.D. Psychiatry University of Iowa 50 Newton Road Iowa City, IA 52242, James H. Reich, M.D., Mary Nduaguba, Ph.D.

Summary:

A community survey of 401 randomly selected subjects yielded 249 responses to a standardized DSM-III, Axis II self-report instrument. Of these, 26 were diagnosed as personality disordered (PD) and 167 as having no significant pathological personality traits (controls). PD's differ from controls in having more hospitalizations in the last year (38% vs 17% $p = .006$) and in that more saw a mental health professional in the last year (35% vs 10%, $p = .002$). When number of pathological answers on the personality instrument are correlated with utilization measures for the entire sample ($N = 249$), many significant associations are found. These differ by the DSM-III personality disorder Cluster from which the questions are chosen and by sex. The most striking finding was a .50 correlation by DSM-III Cluster B questions (narcissistic, histrionic, antisocial and borderline) and family doctor visits in females ($p < .001$).

NR54 **Monday, May 11, 12:00 noon–2:00 p.m.**

PSYCHOSOCIAL SEQUELAE OF MARIJUANA USE

David W. Brook M.D. Psychiatry Mt. Sinai Medical Center 55 East 87th Street New York, NY 10128, Judith S. Brook, Ed.D.

Summary:

This prospective, longitudinal study examines the impact of marijuana use on adolescent personality and behavior, parent-adolescent relations, and peer factors. High school students filled out questionnaires voluntarily in their classrooms when they were in the ninth and tenth grades and two years later when they were in the eleventh and twelfth grades. The sample consisted of 292 black and 401 white middle class males and females. Regular use of marijuana leads to lower achievement, increased tolerance of deviance and deviant behavior, and greater rebelliousness, has a detrimental effect on parent-adolescent relationships, and leads to associating with more deviant and drug-using friends. There is a decrease in personal and social responsibility, consistent with the presence of an "amotivational syndrome," noted in the past by some investigators. Regular users appear to "exhaust" their families, leading to maternal overpermissiveness and lower family expectations, which may in turn lead to even heavier marijuana use. The effects of marijuana use for intrapersonal and interpersonal functioning were for the most part similar in different sex, age, and social class groups although there were some ethnic differences, with marijuana use having a greater impact on whites than on blacks. Implications for prevention and treatment are discussed.

NR55 **Monday, May 11, 12:00 noon–2:00 p.m.**

EPIDEMIOLOGY OF ALCOHOL DEPENDENCE SYNDROME IN U.S.

Alan J. Romanoski M.D. Psychiatry Johns Hopkins Univ 600 N Wolfe St. Meyer BL4-119 Baltimore, MD 21205, Gerald Nestadt, M.D. James C. Anthony, Ph.D., Marshal F. Folstein, M.D., Ernest M. Gruenberg, M.D., Paul R. McHugh, M.D.

Summary:

This paper describes the distribution of the Alcohol Dependence Syndrome of Edwards and Gross in an adult household population in Eastern Baltimore. These findings are different from other available data on the distribution of alcoholism in the United States in that they are based on standardized clinical examinations performed by psychiatrists and they are based on the diagnosis of the Alcohol Dependence Syndrome (ADS) as a discrete clinical entity, as opposed to data based on questionnaires or criteria based upon the quantity, frequency, or consequences of drinking.

Four specially selected and trained research psychiatrists examined a multi-stage stratified probability sample (N = 810) of 175,000 Eastern Baltimore residents over 18 years of age. Their mission was to identify each subject's DSM-3-defined disorder and the presence or absence of ADS after conducting a standardized psychiatric examination which averaged two hours in duration. The Standardized Psychiatric Examination (SPE) format and record was developed as a validation study of the NIMH Diagnostic Interview Schedule in the Eastern Baltimore site of the Epidemiologic Catchment Area studies. The SPE format also included a systematic family history and developmental history review for each study subject. The psychiatrists had no clinical responsibility for the study subjects. A 75% completion rate was attained among designated respondents.

By weighting the data on each subject according to the strata and response rates, and adjusting to the 1980 census, the authors present the first direct estimates of the age-, sex-, and race-specific rates of ADS (in contrast to DSM-3 Alcohol Use Disorders) in the U.S. and data on specific risk factors for development of ADS.

NR56 **Monday, May 11, 12:00 noon–2:00 p.m.**

DRUG ABUSE IN ALCOHOLISM

Alan C. Whitters M.D. Psychiatry University of Iowa 500 Newton Road Iowa City, IA 52242, Remi J. Cadoret.

Summary:

When drug abuse coexists with alcohol abuse, it is frequently viewed and treated as simple alcohol abuse. This study was undertaken to examine for heterogeneity by comparing 59 alcoholic inpatients with 55 patients that were diagnosed as having both alcohol and drug abuse. The Diagnostic Interview Schedule (DIS) was used to determine the diagnosis as well as examine psychiatric variables. Alcoholics with concomitant drug abuse were younger and had an earlier onset of problems due to alcohol abuse. Additionally, they had more symptoms of alcohol abuse, depression, somatization, and antisocial personality. Further, these results could not be explained merely on the basis of sociopathy alone since controlling for antisocial personality continued to show these differences in psychopathology related to drug abuse. Thus, the diagnosis of alcohol abuse complicated by drug abuse has a different natural history with additional psychopathological symptoms than alcohol abuse alone and may imply different treatment strategies.

NR57 **Monday, May 11, 12:00 noon–2:00 p.m.**

LI AND ALCOHOL: CLINICAL AND BIOLOGICAL STUDIES

Jack Hirschowitz M.D. Psychiatry Suny-Stony Brook HSC-T10 Suny/Stony Brook Stony Brook, NY 11794, Robert J. Hitzemann, Ph.D., Beatrice Kovasznay M.D., Howard LaGrone, M.D., Gail Broggini, R.N., Richard Smith, M.S.W.

Summary:

This ongoing study aims at measuring the clinical effects of Lithium on alcohol intoxication, with special emphasis on level of intoxication, recovery, craving and performance. At the same time potential biological correlates are being studied with a view to understanding the mechanism of action of Lithium in these patients and the identification of biological markers.

Drug free male detoxified alcoholics were included. After one week observation blood samples were drawn for biological studies. Patients were entered in a split half crossover design with randomization of Lithium and Placebo. Lithium was maintained at 0.9 to 1.1 meq per liter. 1.32 ml/kg 95% alcohol was administered by mouth in 4 doses over 60 minutes. Self report analog scales were used for measuring craving and intoxication while cognitive functions were measured using speed of closure test, Minnesota Clerical Test and trail marking.

Our preliminary results show that peak intoxication is not affected by Lithium but recovery is significantly enhanced. At 120 minutes after the first dose of alcohol the average intoxication score for placebo was 5.5 (out of 10) while on Lithium the score was 1.5. We have also found that Lithium significantly attenuates the alcohol induced rise in serum prolactin, and using fluorescence polarization techniques in natural and model membranes we have shown that 3mM Lithium antagonizes the ethanol induced decrease in membrane order.

NR58 **Monday, May 11, 12:00 noon–2:00 p.m.**

PLATELET SEROTONIN UPTAKE IN CHRONIC ALCOHOLICS

Jan L. Campbell M.D. Psychiatry VA Medical Center 4801 Linwood BLVD Kansas City, MO 64128, Thomas L. Kent, M.D., Thomas L. Pazdernik, Ph.D., Elizabeth C. Penick, Ph.D., Barbara J. Powell, Ph.D., Donald W. Goodwin, M.D.

Summary:

We previously reported diminished blood platelet serotonin uptake in alcoholics free of alcohol for 10 days, compared to an age and sex-matched non-alcoholic control group studied simultaneously. This finding was not due to depression, medical illness, or nutritional status. We wished to know if diminished serotonin uptake could be a remote effect of alcohol on platelet or bone marrow precursors, or might be a characteristic persisting into sobriety (or perhaps a "marker" for alcoholism).

We performed platelet serotonin uptake for alcoholics sober at least 2 months, insuring that the megaloblast would not have been exposed to alcohol during its lifespan (6 weeks). Platelet serotonin uptake was significantly ($<.001$) lower than the matched non-alcoholic control group.

The alcoholics were all taking disulfiram. We therefore studied platelet serotonin uptake prior to, and after 2 weeks, of disulfiram administration, compared to alcoholics not taking disulfiram and to non-alcoholic controls, over the same period to control for seasonal change. We found that disulfiram does not appear to affect platelet serotonin uptake.

The results suggest that persistent diminished platelet serotonin uptake in alcoholics may reflect a trait of the individual, rather than a direct effect of alcohol upon the marrow.

NR59 **Monday, May 11, 12:00 noon–2:00 p.m.**

ALCOHOLISM IN HOMELESS PEOPLE

William R. Breakey M.B. Psychiatry Johns Hopkins University Meyer 144 600 N Wolfe St. Baltimore, MD 21205, Pamela J. Fischer, Ph.D.

Summary:

As part of an epidemiological study of homeless people in Baltimore, an extensive database relating to alcohol use and abuse in this population is being collected. Preliminary analysis of 300 cases indicates that, using the Short Michigan Alcoholism Screening Test to make the diagnosis, the prevalence of alcoholism in homeless men is 68% and in women is 41%. While alcoholism is prevalent in all age, race and sex groups, the highest rates are in men over the age of 45. Alcoholics scored higher than nonalcoholics on the General Health Questionnaire, but not on the Mini Mental State examination. The alcoholics rated their own health worse than nonalcoholics and reported more accidents and injuries; however, they made less use of health services. On the other hand, their extensive experience with alcoholism treatment programs suggests that existing treatment programs had not been successful for this population. The authors comment that the recent prominence given to mental illness among homeless people has distracted public and professional attention away from alcoholism, the behavioral disorder of greatest prevalence. Health services for homeless people must strongly emphasize the importance of treatment and rehabilitation for alcoholics.

NR60 **Monday, May 11, 12:00 noon–2:00 p.m.**

AMANTADINE TREATMENT OF COCAINE ABUSE

Leonard Handelsman M.D. Psychiatry Albert Einstein Com Div Subst. Abuse 1500 Waters PL Bronx, NY 10461, Teresita P. Quesada, M.D., Prakash L. Chordia, M.D., Ira J. Marion, M.A., Joyce H. Lowinson, M.D.

Summary:

Behavioral pharmacology studies of cocaine suggest that dopamine (DA) agonists attenuate cocaine craving and self-administration. Based on this evidence, an open trial of the DA agonist, amantadine, was initiated to attenuate cocaine abuse in Methadone maintenance patients. Inclusion criteria were male or infertile female Methadone maintenance patients, age 21-50, who met DSM-III criteria for cocaine abuse for 3 months, confirmed by urine reports. Exclusion criteria were schizophrenia, bipolar disorder, epilepsy or current medical illness requiring chronic medication. Amantadine 200 mg po daily was administered for 3 weeks, then increased to 200 mg po BID for 3 weeks more; ingestion of 200 mg was observed 5 days per week by a nurse. Methadone dose was unchanged throughout. Cocaine use and craving scales and the Beck Depression Index were administered weekly; urine drug tests were obtained twice weekly. To date, 13 patients have begun treatment: 12 men, 1 woman; age range 25-40; range of maximum daily expense for cocaine $30-700 (mean = $205); initial Beck score mean = 13; route of cocaine use 2 IV, 8 freebase, 3 IN. Of 8 patients who completed 3 weeks' treatment or more, 5 reported clearcut curtailment of cocaine use and decrease in craving, which was generally confirmed by urine testing. Beck scores showed modest improvement as well. Only 1 patient discontinued treatment due to frustration with his poor outcome. Side effects of amantadine were minimal. Data for more patients will be presented. These findings are promising and support the need for blind, controlled studies to test the efficacy of amantadine in the treatment of cocaine abuse.

NR61 **Monday, May 11, 12:00 noon–2:00 p.m.**

PERSISTENT NEUROCHEMICAL DEFICIT IN COCAINE ABUSE

Irl Extein M.D. Fair Oaks Hospital 5440 Linton BLVD Delray Beach, FL 33445, William Z. Potter, M.D., Mark S. Gold, M.D. Pierre Andre, M.D., William A. Rafuls, M.D., David A. Gross, M.D.

Summary:

Cocaine euphoria is thought to be mediated through blockade of reuptake of brain dopamine (DA) and possibly norepinephrine (NE). The hypothesis that chronic use leads to DA and NE deficits has been supported by elevated prolactin levels and utility of the dopamine agonist bromocriptine and the noradrenergic tricyclic desipramine in cocaine withdrawal and craving. In order to study more directly changes in DA and NE systems in cocaine abusers we measured plasma levels of the DA metabolite homovanillic acid (HVA) and the NE metabolite 3-methoxy-4-hydroxyphenylglycol (MHPG) in 5 hospitalized young adult male chronic crack cocaine abusers and 5 age and sex matched normal volunteer controls. Plasma was obtained from patients during acute withdrawal two days after admission, and then post-detoxification, free of medication after 30 days of supervised abstinence documented by urine tests. Blood samples were obtained from patients in the morning, at bedrest and before breakfast. Plasma was frozen prior to assay for HVA and MHPG by HPLC with internal standards, expressed as pmol/ml ± SEM. HVA of 41.5 ± 4.7 and MHPG of 14.3 ± 2.0 post-detoxification were significantly lower than control HVA of 75.5 ± 10.4 and MHPG of 20.9 ± 3.0, and than HVA of 69.5 ± 7.1 and MHPG of 19.1 ± 2.7 in acute withdrawal. The lack of significant decrease in HVA or MHPG in acute withdrawal may represent acute compensatory neuromechanisms counteracting chronic changes. These data suggest deficits in brain DA and NE systems that persist following cessation of cocaine use and may contribute to persistent cocaine craving and relapse into cocaine abuse. Such neurochemical deficits support further research into the efficacy of bromocriptine, desipramine, and other agents in maintaining cocaine abstinence.

NR62 **Monday, May 11, 12:00 noon–2:00 p.m.**

NEUROPSYCHOLOGICAL FUNCTIONING IN COCAINE ABUSERS

Kenneth J. Krajewski M.D. Psychiatry UT. Medical School P.O. Box 20708 Houston, TX 77225, Heather Doering, B.S.N.

Summary:

There has been a dramatic rise in cocaine abuse as well as the availability and use of more potent preparations (e.g., "crack"). Previous investigations have focused on psychiatric disorders, personality and psychodynamic characteristics, and abstinence symptomatology associated with cocaine abuse; however, neuropsychological evaluation has been sparse. The Luria-Nebraska Neurological Battery (LNNB), claiming to offer standardized evaluation of all major neuropsychological functions, consists of 248 items; 11 scales purporting to access: (1-4) motor, rhythm and visual functions; (5-6) receptive and expressive speech; (7-9) reading, arithmetic and writing skills; (10) memory and (11) intellectual process. Therefore, in an attempt to access neuropsychological functioning in cocaine abusers, the LNNB was administered to hospitalized patients undergoing treatment for cocaine abuse. Eight consecutive right-handed patients, 7 men and 1 woman, 27 ± 6 years of age, who consumed a mean of .6 ± .2 grams of cocaine daily for 30 days prior to admission were included. Polyabuse and/or the consumption of greater than 6 oz. of alcohol per week were excluded. Sobriety was monitored with inpatient structure and urine drug screens. Administration was 10 ± 3.4 days from the time of admission. Critical level values, adjusted for age and education were computed.

RESULTS: Percent of patients demonstrating pathological elevations beyond critical levels: scales (1-4), 25%; scales (5-6), 50%; scales (7-9), 37.5%; scale (10), 100%; scale (11), 37.5%.

CONCLUSION: The LNNB demonstrated the existence of neurologically-based deficits in cognitive functioning in cocaine abusers which persisted 10 days post-intoxication. All patients demonstrated memory impairment; 25% had evidence suggesting pre-existing learning disabilities.

NR63 **Monday, May 11, 12:00 noon–2:00 p.m.**

MORPHINE EFFECT ON BRAIN METABOLISM IN POST-ADDICTS

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Summary:

Regional cerebral metabolic rates for glucose ($rCMR_{glu}$), which can be measured in human subjects by the [^{18}F]fluorodeoxyglucose (FDG) method using positron emission tomography (PET), provide an index of local brain function. To further clarify brain mechanisms or pathways mediating opioid effects, we initiated a double-blind, cross-over, placebo-controlled study of morphine's effect on $rCMR_{glu}$. Six men (21-45 yr) with no current drug dependencies but a history of opioid dependence completed the study. Electroencephalographic and subjective responses (self- reports on questionnaires, visual analogue scale) to 15 and 30 mg morphine and placebo, injected intramuscularly, were recorded on four test days during the two weeks before PET scanning. The subjects underwent two FDG scans, with either 30 mg morphine or placebo administered 15 min before FDG. Rates of $rCMR_{glu}$ were measured in the cingulate and temporal cortices, amygdalohippocampal complex, parahippocampal gyrus, caudate nucleus, and medial thalamus.

Morphine reduced mean $rCMR_{glu}$ in the six regions by 8–14% of placebo values. With $\underline{n}=6$, only the effect in the cingulate cortex was significant ($p<.05$, Bonferroni $\underline{t}$ test). The results suggest that opioids reduce cerebral oxidative metabolism, notably in the limbic cortex, which is involved in emotional and cognitive function.

NR64 **Monday, May 11, 12:00 noon–2:00 p.m.**

DOXEPIN IN DETOXIFYING DEPRESSED OPIATE ADDICTS

Steven L. Batki M.D. Psychiatry UCSF-SF General Hospital 1001 Potrero Ave San Francisco, CA 94110, Scott M. Wheeler, Ph.D., James L. Sorensen, Ph.D., Reese T. Jones, M.D., Michael Rowbotham, M.D., Kathy Brennan, M.A.

Summary:

Eighty-one opiate addicts with DSM-III Major Depressive Disorder underwent 21-day outpatient methadone detoxification and were concurrently treated with a seven-week course of doxepin or placebo in a double-blind randomized clinical trial. Preliminary analysis of the full sample showed differences in treatment outcome between the doxepin and placebo groups. Addicts treated with doxepin improved more than those receiving placebo. Improvement was consistently greater in the doxepin group in depression, opiate use, opiate withdrawal symptoms, and craving for opiates. These outcome differences approached statistical significance for most of the measures. Improvement in the doxepin group began to reach statistically significant differences over placebo at Week 3, when methadone detoxification was completed. This pattern of improvement is consistent with the expected onset of antidepressant treatment effectiveness. Attrition was similar in both the doxepin and control groups. Approximately half of subjects completed the seven weeks of treatment and reached the final 12-week follow-up. While serum doxepin levels were low in the subsample of subjects in whom this measure was obtained, medication compliance was judged to be satisfactory as measured by the consistently higher levels of antidepressant side effects reported by the doxepin group.

NR 65 **Monday, May 11, 12:00 noon–2:00 p.m.**

CANNABIS AND HIGHER FUNCTION: LONGITUDINAL STUDY

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Summary:

In the on-going debate on its effects of long-term heavy cannabis use on cognitive functions, contradictory results have been reported by various workers. One approach to resolve this issue could be a longitudinal study of the identified users over a course of time which was the strategy used in the present study.

Out of 25 each of long-term, heavy Bhang (marihuana) ingestors and Charas (Hashish) smokers and 25 matched non-user controls earlier studied and reported by us, 11 Bhang users, 19 Charas smokers and 15 controls could be re-studied after a lapse of 9-10 yrs. All the users had continued the use during the intervening years. Tests of intelligence, memory and perceptuo-motor tasks earlier administered to the subjects were repeated. This showed a significant additional deterioration in case of the users on a number of psychological measures, i.e., on digit span, speed and accuracy tests, reaction time and Bender visuo-motor gestalt test. The deterioration in case of the cannabis users was significantly greater than in the case of the non-users controls. The study thus further corroborates our earlier findings of impairment of cognitive functions associated with long-term, heavy cannabis use.

NR66 **Tuesday, May 12, 9:00 a.m.–10:30 a.m.**

BIOLOGICAL/CLINICAL SUBTYPE OF ALZHEIMER'S DISEASE

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Educational Objectives:

At the end of the program, the learner should be able to recognize that biological alterations outside the CNS may be useful in defining clinically distinct subtypes of Alzheimer's disease.

Summary:

Double-blind, fluorescence studies of membrane fluidity were conducted at 37° C with platelet membranes prepared from 51 patients with Alzheimer-type dementia, along with 25 nondemented, depressed patients and 50 neurologically-healthy subjects. The three diagnostic groups were similar in age and sex ratio, and patients receiving drugs that affect the fluorescence measurements were excluded. The fluidity of the hydrocarbon region of platelet membranes from the demented group, as reflected by the anisotropy of the fluorescent probe DPH, was significantly increased compared to that for the depressed or normal controls. Within the demented group, platelet membrane fluidity was significantly correlated with dementia severity, but not duration of illness or age at the onset of symptoms. This distribution of platelet membrane fluidity values for the demented group appeared bimodal, with one subgroup overlapping entirely with the value for the control groups ("normal" fluidity) and a second subgroup that showed little overlap with the control groups ("increased" fluidity). The subgroup of demented patients with "increased" platelet membrane fluidity had an earlier onset of symptoms, was more severely demented, and suffered a more rapid deterioration. In addition, preliminary results suggest that familial forms of dementia were more common in this group.

References:

[1]Zubenko GS, Cohen BM, Reynolds CF, Boller F, Malinakova I, Keefe N: Platelet Membrane Fluidity In Alzheimer's Disease And Major Depression. *Am J Psychiatry*, In press.

[2]Zubenko GS, Malinakova I, Chojnacki B: Proliferation Of Internal Membranes In Platelets From Patients With Alzheimer's Disease. *J Neuropath Exp Neurol*, In press.

NR67 **Tuesday, May 12, 9:00 a.m.–10:30 a.m.**

50% RISK IN ALZHEIMER FAMILIES AT ALL PROBAND AGES

John C. S. Breitner M.D. ACOS/EDUC. 11A Bronx VA Med Ctr. 130 W. Kingsbridge Road Bronx NY 10468, Richard C. Mohs, Ph.D., Marshal F. Folstein, M.D., Jeremy M. Silverman, M.A., Kenneth L. Davis, M.D.

Educational Objectives:

To instruct participants in familial risks for Alzheimer's Disease as a function of age at onset in the proband, and as a function of gender and relationship to proband.

Summary:

The 90-year lifetime risk of Alzheimer's Disease (AD) has been reported previously to approach 50% among parents and sibs of probands in an ongoing longitudinal study of AD. The study sample now comprises 379 parents, sibs and offspring aged 45+ of 79 probands. Aggregate risk among relatives is 49 ± 8% by age 87. Risk does not differ significantly among 129 relatives of senile-onset probands vs. 250 relatives of pre-senile-onset cases (56 ± 14% vs. 38 ± 9%; Mantel-Haenszel log rank $\chi^2 = 0.17$, $p > .5$), or among 117 parents vs. 247 sibs (61 ± 24% vs. 43 ± 8%; $\chi^2 = 0.68$, $.25 < p < .5$). Risks among female and male relatives also do not differ significantly (54 ± 10% vs. 34 ± 13%; $\chi^2 = 1.89$, $.1 < p < .25$), but there is a trend for females to develop diseases several years earlier, producing higher age-specific risks (suggested also by epidemiologic surveys). A separate series (collected by MFF) of 119 relatives of 24 autopsy-verified probands shows lifetime risk of 41 ± 14%, but 271 relatives of 61 controls (studied blindly to status of index subject) show risks of only 10% (relative risk of proband vs. control relatives 5; $\chi^2 = 18.12$, $p < .001$). The finding that risks do not decline in late-onset proband families differs from results of Heston, who relied primarily on autopsy diagnosis. This disparity may suggest a possible lack of etiologic specificity in the diagnosis of late-onset AD by neuropathology alone.

References:

[1]Breitner, JCS, and Folstein, MF, Familial Alzheimer dementia: a prevalent disorder with specific clinical features. *Psychological Medicine* 14:63-80 (1984).

[2]Chase, GA, Folstein, MF, Breitner, JCS et al., The use of lifetables and survival analysis in testing genetic hypotheses, with an application to Alzheimer's disease *Am J Epidemiol* 117:590-597.

NR68 **Tuesday, May 12, 9:00 a.m.–10:30 a.m.**

FUNCTIONAL DEFICITS IN ALZHEIMER'S DISEASE

Jeffrey Borenstein, M.D. Psychiatry NYU Medical Center 550 First Avenue, HN 314 New York, NY 10016, Barry Reisberg, M.D.

Educational Objectives:

To describe clinically identifiable progressive functional impairments in Alzheimer's disease (AD) which can be useful in differential diagnosis and predictions of the course of this major disorder of late life.

Summary:

Functional deficits are known to occur with the progression of Alzheimer's disease (AD). We hypothesize that a characteristic pattern of functional impairment occurs with the progression of the disease. Specifically, we have previously adumbrated 16 characteristic stages of functional impairments from normal aging to most severe AD, including impairments in handling personal finances, choosing and putting on clothing, bathing, continence, speech ability, and ambulatory ability[1,2]. In this study we prospectively examined the degree to which AD patients manifested the hypothesized functional impairments. Fifty-six patients, mean age 77.1 $\pm$ 8.3 years, consisting of 14 men and 42 women, with AD were studied. Information was obtained as to the presence of all functional impairments on the 16-point scale. Fifty patients manifested the ordinal pattern predicted. The six exceptions were of a magnitude of one to two points on this 16-point scale.

This study provides evidence that AD patients present with a characteristic pattern of functional deficits. Most patients demonstrated deficits consistent with functional assessment staging (FAST) predictions and no patients demonstrated major variation from FAST predictions. This characteristic pattern of functional deficits in AD has implications with respect to the diagnosis of AD, differential diagnosis, tracking the course of the illness process, and identifying remediable complications.

References:

[1]Reisberg, B., Ferris, S.H., Anand, R., de Leon, M.J., Schneck, M.K., Buttinger, C. and Borenstein, J. Functional staging of dementia of the Alzheimer's type. *Annals of the NY Academy of Sciences*, 435:481-483, 1984.

[2]Reisberg, B., Ferris, S.H. and Franssen, E. An ordinal functional assessment tool for Alzheimer's dementia. *Hospital & Community Psychiatry*, 36:593-595, 1985.

NR69 **Tuesday, May 12, 9:00 a.m.–10:30 a.m.**

AGE OF ONSET IN GERIATRIC DEPRESSION WITH DEMENTIA

George S. Alexopoulos M.D. Psychiatry Cornell UN. MED. College 21 Bloomingdale Road White Plains, NY 10605, Robert C. Young, M.D., Barry S. Meyers, M.D., Robert C. Abrams, M.D., Charles A. Shamoian, M.D.

Educational Objectives:

Geriatric patients with depression and dementia may have later age of illness onset than cognitively unimpaired depressives. Later age of onset has also been observed in depressives with a reversible dementia (DRD). The late onset of DRD may be related to the observation that 39% of the DRD patients eventually develop irreversible dementia.

Summary:

Late onset depressives may have a different presentation, more relapses, and less genetic loading of psychiatric disorders than early onset depressives. We hypothesized that dementia occurs more frequently in patients with late onset depression which may explain in part these differences.

We studied prospectively 126 geriatric inpatients who met DSM-III criteria for major depression and had no disorders or received drugs known to lead to depression or dementia. Depression was rated with the Hamilton scale (HDRS) and cognitive dysfunction with the Cognitive Capacity Screening Examination (CCSE). Depressed patients who also met DSM-III criteria for dementia ($N=53$) had their first depressive episode later (64.7 years $\pm$ 15.4) than patients with depression alone ($N=73$) (56.2 years $\pm$ 19.1) ($t=2.80$, $P < 0.006$). Patients with major depression and dementia whose affective (Δ HDRS $>$ 10 or final HDRS $<$ 12) and cognitive symptoms improved (Δ CCSE $\geqslant$ 3, final CCSF $\geqslant$ 24) were classified as depression with reversible dementia (DRD). DRD patients ($N=30$) had a trend towards later onset of first episode (61.1 years $\pm$ SD: 14.2) than patients with depression alone (56.2 years $\pm$ SD: 19.2) ($t = 1.44$, $P < 0.15$).

DRD patients were contacted 32 months (median time) after discharge. 30% of them had died and 39% had developed dementia (22% moderate or severe, 17% mild). The late onset of DRD may be related to the observation that DRD is often a prelude to irreversible dementia.

References:

[1]Malhendra B: Depression and dementia: the multi-faceted relationship. *Psychol Med* 15:227-236, 1985.

[2]Caine ED: Pseudodementia. Current concepts and future directions. *Arch Gen Psychiatry* 38:1359-1364, 1981.

NR70 **Tuesday, May 12, 9:00 a.m.–10:30 a.m.**

LATE-ONSET PSYCHOSIS AND STRUCTURAL BRAIN INJURY

Ira M. Lesser M.D. Psychiatry Harbor-UCLA, Med Ctr 1000 West Carson Street Torrance, CA 90509, Bruce L. Miller, M.D., Mark Goldberg, M.D., Elizabeth Hill, R.N., Kyle Boone, Ph.D., Milton H. Miller, M.D.

Educational Objectives:

To teach the clinician that there may be a relationsip between the onset of psychosis in the elderly patient and structural brain injury. CT and MRI are useful in identifying these brain abnormalities which often are not detected in routine clincal exainations.

Summary:

Many patients presenting with psychosis after the age of 45 have no obvious organic etiology detected upon routine clinical examinations. With recent neuroimaging techniques, however, structural brain disease can be documented in many of these patients. Delineation of a structural abnormality in these individuals has potential implications for a neuroanatomical basis of delusions. We have studied 30 patients with late-onset psychosis, and major depression with psychotic features, compared to age matched control subjects with the following protocol: physical, neurological, psychiatric, and laboratory examinations, magnetic resonance imaging, computerized axial tomography, electroencephalography and an extensive neuropsychological test battery with a concentration on memory and frontal lobe function. Binswanger's disease, tumor, strokes, and early dementias of the Alzheimer type, none of which were diagnosed in routine clinical care, have been identified in the two patient groups at a statistically higher frequency ($p < .01$) than in the control population. In addition, sub-frontal white matter lesions were particularly prominent in these patients. The late-onset group, currently classified in DSM-III as atypical psychosis, may, in large part, be a group of patients with identifiable brain injury. In the elderly, delusions as part of a depressive syndrome also may be a sign of organic pathology.

References:

[1]Miller BL, Benson, F, Cummings JL, Neshkes R: Late-life paraphrenia: an organic delusional syndrome. *J Clin Psychiatry2 47:204-207, 1986.*

[2]*Bridge PT, Wyatt RJ: Paraphrenia: paranoid states of late life. I. European research. J Am Geriatr Soc* 28:193-200, 1980.

NR71 **Tuesday, May 12, 9:00 a.m.–10:30 a.m.**

NEUROPSYCHOLOGY AND MRI IN HIV INFECTED GROUPS

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Educational Objectives:

To alert clinicians that brain involvement is prevalent in AIDS and ARC, and that there may be subtle neuropsychological changes in other HIV infected groups as well.

Summary:

Whereas initially brain involvement in acquired immune deficiency syndrome (AIDS) and AIDS-related complex (ARC) were thought to represent the effects of secondary infection in the immuno compromised host, recent evidence suggests that human immunodeficiency virus (HIV) is capable itself of invading the CNS. Recently, an AIDS dementia complex has been described by Price et al. Our purpose has been to characterize the neuropsychological and MRI features of HIV associated organicity. We examined the following four groups of homosexual men with comprehensive neuropsychological testing. 1) AIDS ($N = 15$); 2) ARC ($N = 13$); 3) other HIV seropositive ($N = 16$); 4) seronegative ($N = 11$). Groups 1 and 2 patients also received MRI scanning. **RESULTS:** The rates of NP abnormality: Group 1-87%; Group 2-54%; Group 3-44%; Group 4-9%. MRI was abnormal in 77% of Group 1 and 50% of Group 2. Deficits were noted in speeded information processing, abstraction, and memory. MRI abnormalities included atrophy and bilaterally placed multiple high intensity lesions in the white matter. The data suggest that there may be a progression of CNS involvement which first manifests itself as subtle cognitive change even in those groups which are infected with HIV but do not meet criteria for AIDS or ARC.

References:

[1]Perry S, Jacobsen P: Neuropsychiatric manifestations of AIDS-spectrum disorders. *Hospital and Community Psychiatry* 37:135-142, 1986.

[2]Navia BA, Jordan BD, Price RW: The AIDS dementia complex: I. clinical features. *Annals of Neurology* 19:517-524, 1986.

NR72 **Tuesday, May 12, 9:00 a.m.-10:30 a.m.**

INCIDENCE OF TD WITH INTERMITTENT PHARMACOTHERAPY

William T. Carpenter, Jr. M.D. Psychiatry MD Psych Res Center Box 21247 Baltimore, MD 21228, Douglas W. Heinrichs, M.D., Thomas E. Hanlon, Ph.D., Ann T. Summerfelt, B.A.

Educational Objectives:

Learn effects of a neuroleptic drug reduction strategy on the incidence of tardive dyskinesia in schizophrenic outpatients.

Summary:

One hypothesized significance of neuroleptic drug reduction strategies is a decrease in the incidence, or delay in the onset, of tardive dyskinesia (TD). It is difficult to evaluate this hypothesis empirically since sustained observation on a large cohort is required for adequate statistical power. Nonetheless, a preliminary analysis from a continuous vs intermittent (targeted) drug study supports the contention that targeted medication is associated with reduced incidence of tardive dyskinesia. Subjects were outpatients meeting DSM-III and RDC criteria for schizophrenia who were randomly assigned to either continuous or targeted medication for a two-year treatment course. Manifestations of TD were charted routinely by means of the *Abnormal Involuntary Movement Scale* (AIMS). In determining incidence of "probable TD," the following criteria were required: 1) no global rating above 2 on the AIMS prior to or during the first month of the study (which included a drug withdrawal period); and 2) at least two successive global ratings of 2 or more on the AIMS during experimental treatment. These criteria were applied to 55 patients randomly assigned to continuous medication and 41 assigned to the targeted strategy. Twenty-four new cases of TD were identified, 18 on continuous and six on targeted medication (chi square = 3.19, $p<.05$, one-tailed test of hypothesis). In terms of the odds ratio, the odds of a continuous drug patient developing abnormal movements were 2.83 times those of a targeted drug patient developing such symptoms. Within the targeted sample, those patients who developed TD were characterized by more days on medication and a higher cumulative dose than the remainder of the group.

References:

[1]Carpenter, W.T., Heinrichs, D.W.: Early intervention, time-limited targeted pharmacotherapy in schizophrenia. *Schizophrenia Bulletin*, 9:533-542, 1983.

[2]Baldessarini, et al.: Tardive Dyskinesia (Task Force Report 18), Washington, D.C.: American Psychiatric Association, 1978.

NR73 **Tuesday, May 12, 9:00 a.m.–10:30 a.m.**

PLASMA HVA: PHYSIOLOGIC AND PSYCHIATRIC CORRELATES

Kenneth L. Davis M.D. Psychiatry VA Medical Center 130 W. Kingsbridge RD Bronx, NY 10468, Michael Davidson, M.D., Richard C. Mohs, Ph.D., Anne Girodani, Ph.D., Thomas B. Horvath, M.D.

Educational Objectives:

To review the sources of pHVA, the behavior and drugs that can affect it, and to demonstrate its relationship to the symptoms of schizophrenia.

Summary:

Plasma levels of the dopamine metabolite, homovanillic acid (pHVA) reflect CNS dopamine activity, and hence have obvious implications for elucidating the biology of schizophrenia. To this end, the effects of diet, activity, benztropine, and smoking on pHVA were assessed in normal controls, and the effects of haloperidol and cortical atrophy in schizophrenics. Diet, ($p < .001$) though not activity, smoking, or benztropine, significantly elevated pHVA levels ($p < .001$). Schizophrenics with marked cortical atrophy, had significantly lower pHVA than other schizophrenics ($p < .005$). The acute administration of haloperidol significantly elevated pHVA within 24 hours ($p < .01$), but this effect was entirely gone after 6 weeks of continuous treatment. Debrisoquin, a peripheral MAO inhibitor, reduces the peripheral contribution of HVA to the plasma pool. Ten mg bid for 6 days significantly decreased pHVA ($p < .001$). The addition of haloperidol to debrisoquin again produced a significant increment in pHVA concentrations ($p < .003$) 24 hours after the initiation of haloperidol (10 mg bid), that was no longer apparent by 2 weeks of continuous treatment. The haloperidol induced change in pHVA did not correlate with symptom improvement. However, there was a robust correlation between baseline pHVA and the severity of schizophrenic symptoms in 35 patients ($p < .003$).

References:

[1]Davis, KL, et al.: Science, 227:1601-1602, 1985.

[2]Davidson, M, et al.: *Arch Gen Psychiatry* 44:189 (ltr), 1986.

NR74 **Tuesday, May 12, 9:00 a.m.–10:30 a.m.**

FRONTAL ATTENTION DEFICITS IN SCHIZOPHRENIA

Lewis L. Judd M.D. Psychiatry Univ of California M-003 La Jolla CA 92093, Byron Budnick, B.S., Lou Ann McAdams, Ph.D., David L. Braff, M.D.

Educational Objectives:

To teach the audience about frontal lobe and dopamine function in schizophrenia; to present relevant animal model data, data from neuropsychology, and information processing tests, and new sensory gating and P300 event related potentials in schizophrenia; to discuss the relationship of these data in schizophrenia.

Summary:

The symptoms and deficits of schizophrenic patients have been attributed to attentional/information processing dysfunction and hypofrontality. Few investigations have measured information processing and frontal lobe functions in the same group of patients. For this study, subjects consisted of 20 RDC-diagnosed schizophrenic patients and 20 demographically matched normal controls. The schizophrenic patients were characterized by psychopathology rating scales (BPRS, GAS), demographic variables, specific symptom rating scales (Andreasen's Scales for Assessment of Negative and Positive Symptoms), and amount of neuroleptic medications. Information processing was measured using a visual backward masking task (VBM). Attention was measured using the Wisconsin Card Sorting Task (WCS), and by Freedman et al's sensory gating (conditioning test) P50 event related potential (ERP) and Hillyard's P300 "odd ball" ERP paradigms. The two ERP paradigms were assessed in a frontal to occipital gradient. Schizophrenics showed normal information processing on the VBM, WCS, and both ERP paradigms. The sensory gating P50 ERP deficts were most signficant in the frontal regions, and the P300 deficits most significant in the parietal region. These data plus related research support the hypothesis of a neurobiologically important, putatively dopamine-mediated hypofrontality in schizophrenic patients. Still, the schizophrenic patients have regionally widespread abnormalities in attention and information processing, and the hypofrontality hypothesis alone cannot account for all of the data.

References:

[1]Braff DL: Attention, habituation, and information processing in psychiatric disorders. In, *Psychiatry III*, Lippincott Co: Philadelphia, Chapter 65, pp 1-14, 1986.

[2]Braff DL, Stone C, Callaway E, Geyer MA, et al: Prestimulus effects on human startle reflex in normals and schizophrenics *Psychophysiology* 15:339-343, 1979.

NR75 **Tuesday, May 12, 9:00 a.m.–10:30 a.m.**

AUTOSOMNAL ABNORMALITY LINKED TO SCHIZOPHRENIA

Anne S. Bassett M.D. Psychiatry University of B.C. 2255 Wesbrook Mall Vancouver BC, Canada V6T2A1, Barry D. Jones, M.D., Barbara C. McGillivray, M.D., J. Tapio Pantzar, M.D.

Educational Objectives:

Demonstrate how a chromosomal abnormality could be associated with a schizophrenic phenotype.

Summary:

Genetic factors are important contributors to the etiology of schizophrenia. We report the first cases of schizophrenia associated with a distinct autosomal abnormality in two related mildly dysmorphic individuals. The proband, a college student, and his maternal uncle showed remarkably similar clinical features of schizophrenia (DSM-III) in terms of age of onset, symptom profile and rapid response to neuroleptic medication. They also shared identical subtle craniofacial and skeletal abnormalities. No other family members had any history of mental illness or dysmorphic features. Cytogenetic analysis was performed using standard early metaphase trypsin-giemsa banding techniques in high resolution chromosome preparations. Analyzed metaphases of the proband revealed a male karyotype with extra chromosomal material on the long arm of chromosome 1, making the proband trisomic for part of the long arm of chromosome 5. The extra chromosomal material represented a 1;5 inverted insertion. At the available band resolution (400-500) there was no loss of chromosome 1 material. The karyotype of the maternal uncle was identical to that of the proband. The proband's mother had a female karyotype with a balanced (no extra-chromosomal material) 1;5 inverted insertion. Other family members had normal karyotypes with no chromosomal structural rearrangements. The most parsimonious explanation for these findings is that the partial trisomy of chomosome 5 is causally linked to the schizophrenic illness and other structural anomalies. The rapid drug response further suggests a possible link to the dopamine system in the mechanism of schizophrenia. The potential importance of this finding will be discussed in terms of eventual location of a gene, whether structural, regulatory or functional, that is causally linked to a schizophrenic phenotype.

References:

[1]Epstein, C J: The Consequences of Chromosome Imbalance. Cambridge, Cambridge University Press, 1986.

[2]McGue M, Gottesman I I, Rao D C: Resolving genetic models for the transmission of schizophrenia. *Genet Eipidemiol* 2:99-110, 1985.

NR76 **Tuesday, May 12, 9:00 a.m.–10:30 a.m.**

LATE ONSET SCHIZOPHRENIA: NEUROPSYCHOLOGY AND MRI

Dilip Jeste M.D. Psychiatry VA Medical Center V-116A 3350 La Jolla Drive San Diego, CA 92161, Jackuelyn Harris, M.D., C. Munro Cullum Ph.D., Mark Zweifach, M.D., Leon J. Thal, M.D., Igor Grant, M.D.

Educational Objectives:

We believe that this is the first study of neuropsychological performance and MRI scans in late onset schizophrenics. The audience will learn about our new research findings in this area. Implications of these results for differential diagnosis and for pathophysiology of late onset psychosis will be discussed.

Summary:

Schizophrenia with onset after age 45 has been poorly studied. We have found no published studies of neuropsychological performance or MRI scans in these patients.

METHODS: We are following 15 patients who meet DSM-III-Revised criteria for late-onset schizophrenia. The patients receive a battery of selected neuropsychological tests. We also obtain MRI scans of brain. We compare the patients to normal controls matched for age, gender and education level.

RESULTS: (1) Schizophrenics show a much greater variability in neuropsychological performance and MRI patterns than controls. As a group, schizophrenics are similar to normals in tests of general cognitive abilities (WAIS-R, Mini-Mental State and Trail Making), but significantly worse on tests of abstraction (Similarities), concept formation and problem solving (Categories Test). (2) A majority of schizophrenics have abnormalities in MRI including right temporal signal hyperintensity in T2 indicating encephalomalacia, reduced gray-white matter differentiation, increased signal intensity of basal ganglia on T2, and white matter changes suggestive of Binswanger's subcortical encephalopathy. A quantitative densitometric analysis of MRI scans is under way. (3) One-third of schizophrenics have gross impairment on specific neuropsychological tests and abnormal MRI scans.

COMMENT: Our results will be compared to the data in younger schizophrenics. Implications for differential diagnosis of late-onset psychosis will also be discussed.

References:

[1]Rabins P, Pauker S, Thomas J (1984). Can schizophrenia begin after age 44? *Comprehensive Psychiatry*, 25:290-293.

[2]Leuchter AF, Spar JE (1985). The late onset psychoses—Clinical and diagnostic features. *Journal of Nervous and Mental Disease*, 173: 488-494.

NR77 **Tuesday, May 12, 9:00 a.m.–10:30 a.m.**

STABLE REMISSION OF TARDIVE DYSKINESIA BY L-DOPA

Jack I. Ludatscher M.D., Psychiatry Netanya Psychiatric Hosp 46 Wingate Avenue Haifa 33531, Israel

Educational Objectives:

To learn effects of a neuroleptic drug therapy (L-DOPA), on influencing remission of Tardive Dyskinesia.

Summary:

Twenty-five adult chronic schizophrenic patients, who received long term neuroleptic therapy and were associated with severe persistent tardive dyskinesia for many years were treated with small repeated doses of L-Dopa. After four weeks of treatment, the intensity and frequency of involuntary movements decreased and after three months, the choreoathetotic movements, the protrusion of the tongue and other orofacial dyskinetic movements disappeared in all patients. Discontinuation of L-Dopa therapy in ten patients determined a relapse of involuntary dyskinetic movements after six weeks. Readministration of the same dose of L-Dopa reproduced the previous therapeutic effect in all patients. Using the Abnormal Involuntary Movement Scale of N.I.M.H. the patients were rated severe = 4 before treatment, and mild = 2 after remission. Maintenance of all twenty-five patients on daily 15 mg. Haloperidol or neuroleptic equivalent and small repeated doses of L-Dopa induced a stable remission of all involuntary dyskinetic movements for the first year. Placebo control group remained unchanged with the same severe persistent dyskinetic manifestations.

References:

[1]Friedhof AJ, Alpert M. Receptor sensitivity modification as a potential treatment. In: Lipton MA. DiMascio A. Killam KF, eds. Pyschopharmacology—a generation of progress. New York, Raven Press, 1978, pp 797-801.

[2]Jeste DV, Wyatt RJ. Understanding and treating tardive dyskinesia. The Guilford Press, New York, 1982.

NR78 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

SPECT BRAIN IMAGING IN PSYCHIATRY

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Summary:

Brain imaging with positron emission computed tomography (PET) has stimulated interest in regional cerebral blood flow (rCBF) and imaging of neurotransmitter receptors in brain. PET methodology is complicated, requiring on-site access to a cyclotron. Single photon emission computed tomography (SPECT) using the radiopharmaceutical N-isopropyl (I-123) iodoamphetamine, (IMP, I-123), permits mapping of rCBF with routinely available nuclear medicine equipment. This paper will present SPECT rCBF images and data on 64 acute psychiatric patients and controls.

SPECT scans of rCBF can be interpreted visually, and rCBF can be expressed quantitatively. Patterns of rCBF from nine loci in both hemispheres were analyzed according to diagnostic and clinical data. A significant decrease in frontal rCBF was found in major depression, which correlated with the BPRS and Hamilton. An increase in temporal rCBF was correlated with the mania rating scale. Schizophrenics had a significant increase in rCBF in the corpus striatum, which correlated with hallucinations on the BPRS and the presence of positive symptoms. Neuroleptics did not explain this increase. Clinical improvement was associated with a decrease in striatal rCBF. Lateral differences were not found. Increasing age correlated with a decrease in rCBF in all brain regions.

SPECT has potential for further studies of rCBF. New radiopharmaceuticals which image neurotransmitter receptors may have an important role in diagnosis and treatment selection.

NR79 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

PREFRONTAL COGNITIVE DYSFUNCTION IN SCHIZOPHRENIA?

Terry E. Goldberg Ph.D. WAW Building NIMH 2700 Martin Luther King Ave SE Washington, DC 20032, Daniel R. Weinberger, M.D., Karen F. Berman, M.D., N.H. Pliskin, M.A., M. Podd, Ph.D.

Summary:

The Wisconsin Card Sorting test generally elicits poor performance in schizophrenic patients. In general, it is sensitive to frontal lobe dysfunction. Recent physiological and cognitive studies of schizophrenia have indicated that dysfunction of prefrontal cortex may be a possible cause of some of the disabling intellectual and social aspects of the disease. To investigate potential reversibility of such cognitive deficits and the role of state variables (such as inattention and motivation), patients with schizophrenia were administered the Wisconsin Card Sorting test on six consecutive occasions. Two groups received incremental information regarding sorting principles and set shifting, as well as intensive and explicit card-by-card instruction. A third group served as a control. Regardless of the degree of instruction, patients who were unable to do the test could not thereafter learn it. Moreover, the deficit was not generalized as patients were able to learn word lists on the Selective Reminding memory test and were not globally demented on the Mini Mental State examination. We believe these data suggest that cognitive deficits involving prefrontal regions are more profound than generally appreciated.

NR80 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

SCHIZOPHRENIA: CT DATA AND P300/CLINICAL CORRELATES

Robert W. McCarley M.D. Psychiatry Harvard-Brockton VA 940 Belmont Street 116A Brockton, MA 02401, Steven F. Faux, Ph.D., Martha E. Shenton, Ph.D., Marjorie Lemay, M.D., Melanie Cane, A.B., Ruth Ballinger, A.B.

Summary:

This study blindly compared CT scans from 9 normal volunteers (NL) with CT scans from 9 chronic medicated, DSM-III/RDC-diagnosed schizophrenics (SZ); both groups were male, right-handed and age and WAIS-matched. The SZ group showed significant enlargement of sulci and fissures in several brain regions (p's < 0.05, Mann-Whitney U test, size rated on a 0-4 scale) while differences in ventricular system size were less prominent (e.g. VBR not significantly different). Overall, 10/18 CT measures were significantly greater in the SZ group and none in the NL group ($p < 0.001$). Of particular note was sylvian fissure enlargement (SFE), thought to reflect temporal lobe tissue changes; the SZ group showed both left SFE (NL median = 1.3, SZ = 2.0) and right SFE (NL = 1.3, SZ = 2.2) when compared with the NL group. However, in agreement with our localization hypotheses, within the SZ group only left SFE, but not right SFE, had strong correlations with the left temporal (T3) P300 electrophysiological measure (Spearman's rho = 0.74) and with positive symptoms, as measured by SAPS (rho = 0.70). Completing a three-way correlation was a rho of .61 between P300 T3 amplitude and positive symptoms (all rhos in this abstract have p's $< .05$). Frontal cortical sulcal enlargement was also prominent (NL = 2.0, SZ = 2.8), but was not correlated with P300; instead this feature was highly correlated with another electrophysiological measure, P200 amplitude at left-central locations (T3, C3, Cz, C4; rhos of .67-.86). While many previous studies have shown NL-SZ CT differences, these data are noteworthy because they suggest: (1) the presence of temporal lobe structural alterations in SZ and (2) site-specific correlations of positive symptoms and P300 left temporal amplitude and left temporal structural alterations.

NR81 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

LIMBIC SYSTEM STRUCTURAL BRAIN ABNORMALITIES IN SCHIZOPHRENIA BY MAGNETIC RESONANCE IMAGING

Deborah Dauphinais M.D. Neurogenetics NIH-NIMH Bldg 10 RM3 N218, Rockville Pike Bethesda, MD 20892, Lynne E. DeLisi, M.D., Peter Hauser, M.D., Elliot S. Gershon, M.D.

Summary:

MRI brain scans were performed on a group of RDC chronic schizophrenic patients with a family history of psychosis and normal controls. Scans were completed using a Picker Vista 0.5 tesla scanner. Twelve contiguous coronal sections were taken at 10 mm intervals beginning at the frontal pole. These were used for measurements of specific cortical regions, and structures of the limbic system. In preliminary analyses of 11 chronic schizophrenics, (7M, 4F; mean age 36.2 ± 5) and 12 controls (6M, 6F; mean age 39.2 ± 10), measurements of bilateral hippocampal areas were significantly decreased in the schizophrenics compared with controls:

	R Ant. Hippocampus	R Post. Hippocampus	L Ant. Hippocampus	L Post. Hippocampus	
Schizophrenics	1.28 ± .26	1.17 ± .30	1.37 ± .26	1.15 ± .13	*p<.03
Controls	1.61 ± .32*	1.41 ± .44	1.75 ± .37*	1.57 ± .56*	

These data are consistent with results from previously published postmortem studies. Further analyses comparing pairs of schizophrenic siblings and examining the influence of obstetrical complications on the limbic system and other structural abnormalities will be presented.

NR82 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

FUNCTIONAL CEREBRAL BLOOD VOLUME IMAGING WITH MRI

Thomas A. Kent M.D. Neurology University of Texas Medical Branch Galveston TX 77550, Eugenio Amparo, M.D., Barry Kaplan, M.D., Michael Quast, Ph.D., Ahmad Najafi, Ph.D., Robert Gevedon, B.S.

Summary:

We have developed a technique to dynamically measure cerebral blood volume (CBV) using high resolution magnetic resonance imaging (MRI) and the clinically used intravascular paramagnetic contrast agent, Gadolinium (Gd)-DTPA. This is based on the shortening of proton relaxation times which can be quantified in-vivo. Gd-DTPA and Gd-DTPA conjugated to albumin (Ogan, et al, Radiology, 1985) were used. T1 images in rabbits were obtained on a commercial 0.6T unit (Technicaire) and of rats on a 4.7T unit (GE). Calibration curves were obtained in-vitro using known Gd concentrations added to blood on the imaging units and on a 10MHz spectrometer (Radx) for use with arterial blood. The Gd complex was injected i.v. and arterial samples obtained. T1 changes observed in-vivo were then converted to [Gd]. % CBV = [Gd] (brain)/ [Gd] (blood) × 100. CBV was estimated at 8-10% using Gd—DTPA. This doubled with CO_2. CBV = approx. 2% using Gd-DTPA-alb (appropriately lower because of its impermeability into the brain) which corresponded to values obtained simultaneously with radioactive ^{153}Gd-DTPA-alb. CBV dramatically decreased in unilateral cerebral ischemia. These results demonstrate the potential of functional cerebrovascular imaging with MRI which can be correlated with localized in-vivo spectroscopy at 4.7T.

NR83 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

RE-EVALUATION OF CT IMPORTANCE IN SCHIZOPHRENIA

George Serban M.D. Psychiatry New York University 35 East 84th St. New York, NY 10028, Ajax George, M.D., Mony de Leon, Ph.D., Seymour Siegal, M.D.

Summary:

In the last decade numerous CT studies of schizophrenia have linked atrophic brain anatomical changes (BAC) with clinical signs of illness. The findings still conflict.

In a CT study done at N.Y.U. with 31 schizophrenics and matched control group we have attempted to further elucidate these issues: whether schizophrenics with enlarged ventricles comprise a special schizophrenic subgroup, and, secondly, whether the BAC is correlated to treatment response. The difficulty in assesing these events stemmed from a lack of CT normative standards for measurement of BAC, as reevaluation of the literature indicates. In addition, the selection of the control group rarely met proper research standards. In view of this, we have compared both the existing methods of measurement—linear and volumetric—to a modified volumetric one which we devised. Samples of the data were reevaluated by Drs. Weinberger and Daniel from NIMH. The findings of our study question the selection of most control groups and their results. In conclusion, we found no significant CT differences existing between normal "healthy" control and schizophrenics. However, significant correlations exist between subjective ventricular ranking and thought-disorder and anhedonia. Furthermore, CT correlated with memory scores both on linear and volumetric measurement. This finding, if replicated, may throw light on the effect of anatomical changes in schizophrenia.

NR84 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

METHODS FOR PET QUANTIFICATION OF NEURORECEPTORS

Dean F. Wong M.D. Nuclear Medicine Johns Hopkins Hospital Tower BSMT, 600 N. Wolfe St. Baltimore MD 21205, Albert Gjedde, M.D., Larry E. Tune, M.D., Godfrey D. Pearlson, M.D., Chris Ross, M.D., Henry N. Wagner, M.D.

Summary:

Important parameters for in-vivo quantification include receptor number, affinity and occupancy by therapeutic drugs. The interpretation of the images however is greatly dependant on the kinetics of the radiotracers and application of appropriate quantification methods. An earlier approach to studying the reversible binding ligand, ^{11}C-NMSP revealed no significant differences between 20 schizophrenic (SCZ) and bipolar affective patients (BP) and normal age matched controls. However, development of a more complete kinetic model and the use of pre-blocking with haloperidol has allowed quantification which is more reflective of receptor binding as opposed to more confounding issues such as blood flow. By applying this more complete approach to irreversible binding ligands, we have been able to demonstrate receptor density of approximately 18 pmoles/g which compares well to autopsy studies but also elevations in drug naive and drug treated SCZ and some BP patients with as much as 50-100% increases.

We have also developed a method for studying the ligands which equilibrate during the PET scan for S2 serotonin receptors. Estimates of receptor number in human frontal cortex has been estimated in young males as 12 pmoles/g. In summary, we have improved receptor quantification techniques in receptor systems that are important in a number of psychiatric and neurological disorders and resulted in a detection of potentially clinically relevant differences.

NR85 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

FRONTAL SYSTEM DEMENTIA IN LATE SCHIZOPHRENIA

J. Wesson Ashford M.D. Psychiatry Southern Illinois U 801 N Rutledge P.O. Box 3926 Springfield IL 62708, Robert Becker, M.D., Robert Dettling, M.S., Jerry A. Colliver, Ph.D.

Summary:

Schizophrenia, characterized by onset in early adulthood with florid psychotic ideation, frequently follows a very slow, much less flamboyant deterioration ending in old age as a "terminal dementia state" (Kraeplin, 1893; Bridge et al., 1978). We evaluated 15 elderly schizophrenic patients in a state mental hospital (mean age: 70 years; range: 53-93; mean age of onset: 23; SD: 3.6) using dementia rating scales: Mental Status Questionnaire, Mini-mental State (MMS), Clinical Dementia Rating Scale, Global Deterioration scale and the Haycox dementia scale. Scores uniformly indicated moderate to severe dementia in 8 patients (MMS = 1-19) and profound in 5 (MMS = 0), severity increasing with age. Performance proportion analysis of the MMS items showed that the schizophrenics missed items in a significantly different pattern than Alzheimer patients. Specifically, memory items were less impaired in the schizophrenics, but verbal output (oral or lexical) was more impaired. On Magnetic Resonance Image scans preliminary review indicates that schizophrenics had more ventricular enlargement (atrophy of basal ganglia) and less cortical atrophy relative to Alzheimer patients with similar degrees of dementia.

These data suggest that some schizophrenics develop a frontal system dementia primarily affecting thought and speech. Schizophrenia may be compared to Huntington's disease, manifesting acute psychotic episodes early in the course when the affected neurons of the anterior basal ganglia/nucleus accumbens develop their first pathology, progressing to a demented stage when those neurons are no longer able to interact with the frontal cortex.

NR86 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

ANTEROPOSTERIOR CALLOSAL GRADIENT IN SCHIZOPHRENIA

Henry A. Nasrallah M.D. Psychiatry Ohio State University 473 West 12th Avenue Columbus OH 43210, Nancy C. Andreasen, M.D., Jeffrey A. Coffman, M.D., Stephen C. Olson, M.D., James C. Ehrhardt, Ph.D.

Summary:

The genu, which is the first anterior portion of the corpus callosum (CC), is composed of interhemispheric fibers between the right and left frontal lobes. The splenium, which is the posterior portion of the CC, is composed of interhemispheric fibers between the right and left occipital lobes.

Several studies have suggested that there is a "hypofrontality" in cerebral blood flow or metabolism in the brain of schizophrenics. We hypothesized that if there is a "functional hypofrontality" in schizophrenia, then it may be possible to detect "neuroanatomical hypofrontality" as well, reflected in a relative reduction of anterior interhemispheric fibers (i.e., the genu) compared to posterior interhemispheric fibers (i.e., the splenium).

We conducted a magnetic resonance imaging study of 38 schizophrenics (28 males, 10 females) and 41 healthy volunteers (21 males, 20 females). The midline saggital view showing the anteroposterior profile of the CC was used for measurements. CC area was divided into four quartiles. The ratio of the genu (defined as the anterior quartile) to the splenium (defined as the posterior quartile) was calculated for all groups by diagnosis, gender and handedness.

RESULTS: Right-handed (RH) schizophrenic males were found to have a significantly smaller genu-to-splenium ratio (.91) compared to RH schizophrenic females (1.02). No such differences emerged between the RH male (.98) and female (.87) control groups, where the trend was actually in the opposite direction. The RH schizophrenic females also had a significantly higher genu-to-splenium ratio than RH control females. The data suggest either a decrease in the genu-to-splenium ratio in schizophrenic males, or an increase of this ratio in schizophrenic females. Whereas normal RH males have a genu-to-splenium ratio approximately 10% higher than normal RH females, the reverse emerged in schizophrenia. The data support the hypothesis of "neuroanatomical hypofrontality" in schizophrenic males, but may also indicate "neuroanatomical hyperfrontality" in schizophrenic females. Similar gender differences should be sought in functional brain imaging methods such as positron emission tomography or cerebral blood flow.

NR87 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

EMOTIONAL BLUNTING AND COGNITIVE DEFICITS

V. Chowdary Jampala M.D. Psychiatry Chicago Medical Sch 3333 Green Bay Road North Chicago, IL 60064, Kathryn R. Juzwyn, M.A., Michael A. Taylor, M.D., Gunnar Larson, M.D.

Summary:

Emotional blunting, in spite of being described as a core feature of schizophrenia by Kraepelin and Bleuler, remains an inadequately investigated subject. We are currently studying a group of consecutively admitted patients to an acute psychiatric unit, assessing the presence of emotional blunting (using the Emotional Blunting Scale), abnormal involuntary movements (using AIMS), cognitive abilities, and ability to recognize and discriminate between emotional stimuli.

RESULTS: Thirty patients have been enrolled in this project so far. Early data from this ongoing project suggest that compared to psychiatric patients without emotional blunting, patients with emotional blunting have significant deficits in identifying and discriminating between emotional stimuli presented auditorily, and have a difficult time identifying emotions from environmental cues. Emotionally blunted patients show significant deficits on tasks generally thought to test right cerebral hemisphere function (e.g., hidden patterns test). We, however, did not find any association between emotional blunting and abnormal involuntary movements.

DISCUSSION: These results suggest that emotional blunting is associated with a dysfunction of right hemisphere, the hemisphere thought to process and regulate emotions. These findings do not agree with the suggestion that schizophrenia is a result of left hemisphere dysfunction. Our findings also suggest the possibility that emotional blunting might have its roots in recognizing and discriminating between emotions. More research is needed to understand how these deficits lead to emotional blunting and in turn to continued social and occupational deterioration in schizophrenia. (Supported by Veterans Administration)

NR88 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

EEG COHERENCE IN UNTREATED SCHIZOPHRENICS

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

Summary:

The coherence function, a measure of covariance between two EEG signals as a function of frequency, provides an index of functional coupling between brain regions. Studies of EEG coherence in schizophrenics have yielded inconsistent results. Most are theoretically flawed because of the use of a common reference recording montage. The two studies that utilized a bipolar recording montage yielded contradictory findings within the alpha band. Both studied medicated patients and in one case used an extremely small sample.

We have measured EEG alpha coherence in 10 unmedicated schizophrenics, 8 unmedicated patients with major affective disorder, and 14 normal controls, all righthanded. Subjects were studied at rest and during active task conditions. EEGs were recorded from bilateral frontal, temporal, central, and parietal leads referenced to Fz and algebraically converted off-line to a bipolar configuration. Data were digitized at 64 samples/second, screened for artifact, and subjected to Fast Fourier Transform. Coherence functions were computed for standard wavelengths bands. Schizophrenics had higher within hemispheric alpha coherences than either control group, significantly higher than normals in one derivation ($p < 0.02$). Between hemisphere coherences also tended ($p < 0.08$) to be higher in schizophrenics. Seven schizophrenics were restudied after a period of neuroleptic treatment; there were no major changes in alpha coherence associated with medication treatment. The findings suggest topographical differences in cortical activity between schizophrenic patients and controls.

NR89 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

SCHIZOPHRENIA: P300 TOPOGRAPHY & POSITIVE SYMPTOMS

Martha E. Shenton Ph.D. Psychiatry Harvard-Brockton VA 940 Belmont Street 116A Brockton, MA 02401, Steven F. Faux, Ph.D., Robert W. McCarley, M.D., Ruth Ballinger, A.B., Michael Coleman, M.A., Frank H. Duffy, M.D.

Summary:

This study describes a topographic analysis of the auditory P300 (296-396 ms) in chronic medicated schizophrenics (Sz, $n=11$) and normal controls ($n=18$) that replicates and extends the earlier study of Morstyn et al. (1983) which showed a left temporal P300 decrement in Sz compared to normal controls. We also report a novel finding of high correlations between P300 and positive symptoms in schizophrenia. Subjects were matched for age and handedness, and Sz subjects were diagnosed by RDC and DSM III criteria. T-statistic mapping and "protected" T-squared contrasts of integrated voltages showed that the left temporal region in schizophrenics produced the greatest statistical separation between groups ($p<0.05$). A group by scalp region interaction provided statistical confirmation of these topographic differences ($p<0.05$). Within the Sz group, there were high correlations ($p<0.05$) between the left temporal region P300 amplitude and two measures of positive symptoms: the Thought Disorder Index (Spearman's rhos between .58 and .85) and the Scale for the Assessment of Positive Symptoms (rhos between .51 and .88). No such significant correlations were noted for negative symptoms (SANS). Most of these P300 correlations arose in the inattentive experimental condition where there was a pronounced asymmetry between left and right temporal waveforms. These data provide evidence for a disorder in non-voluntary attention in positive symptom schizophrenia reflected in temporal scalp region P300 voltage. They are also consistent with temporal lobe abnormalities in schizophrenia and strongly suggest a link between clinical features and electrophysiological data.

NR90 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

SCHIZOPHRENIA: P200 TOPOGRAPHY AND NEGATIVE SYMPTOMS

Steven F. Faux Ph.D. Psychiatry Harvard-Brockton VA 940 Belmont Street 116A Brockton, MA 02401, Martha E. Shenton, Ph.D., Robert W. McCarley, M.D., Ruth Ballinger, A.B., Michael Coleman, M.A., Frank H. Duffy, M.D.

Summary:

A number of studies using nontopographic analyses have reported an amplitude decrement of the auditory P200 component in schizophrenics (Sz) compared to normal controls. Here we report a topographic analysis of the auditory P200 (204-272 ms; peak to baseline) in chronic medicated Sz ($n=11$) and normal controls ($n=18$) and a high correlation between this P200 measure and negative symptoms of schizophrenia. Subjects were matched for age and handedness, and Sz were diagnosed by RDC and DSM III criteria. Exploratory T-statistic mapping (SPM) and "protected" Hotelling's T-squared contrasts of integrated voltages over the entire scalp showed that the left temporal region produced the greatest statistical separation between the two groups ($p<0.05$). A group by scalp region interaction provided statistical confirmation of topographic differences between groups ($p<0.05$). Within the Sz group, high correlations were present between the left temporal region P200 amplitude and the Scale for the Assessment of Negative Symptoms (Spearman's rhos between .53 and .82, $p<.05$). This finding complements our previous finding of a high correlation between P300 amplitude and positive symptoms in schizophrenia. P200 amplitude may be associated with more simple stimulus analysis and encoding processes than P300 and hence is correlated with more global measures of performance and symptomatology. These data thus strongly suggest a link between clinical features of schizophrenia and electrophysiological data.

NR91 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

EYE TRACKING IN SCHIZOPHRENIA: STATE AND TRAIT COMPONENTS

Margaret M. Rea Ph.D. Psychiatry NY Hospital-CUMC 525 East 68th Street New York, NY 10021, John A. Sweeney, Ph.D., Carla M. Solomon, Ph.D., Stephen Snyder, M.D., Allen J. Frances, M.D., J. John Mann, M.D.

Summary:

GOAL: Eye tracking deficit is a promising psychobiological/genetic marker for schizophrenia. This abnormality appears to be specific to schizophrenia in samples of remitted patients, and is frequently present in their first degree relatives. Characterization of possible state-related changes in eye movement activity may clarify the psychobiology of the acute phase of schizophrenia and its relationship to trait factors.
METHOD: Relationships among neuroleptic dose and blind ratings of eye tracking performance and acute clinical state (BPRS) were examined in 13 inpatient DSM III (SCID) schizophrenics on admission and weekly for four to six weeks.
RESULTS: Pursuit accuracy remained consistent across time (ICC = .86). Stability estimates (ICC) smaller saccades (3 to 5 degrees of visual angle) were greater than .60, but for larger saccades (6 to 9 degrees) less than .40. Large saccades were less frequent over the course of clinical recovery, were associated with positive family history, and may reflect problems of attention. Square wave jerks during occular fixation were observed following a major increase in neuroleptic dose in 5 of the 13 patients.
SIGNIFICANCE: For the first time, distinctive state- and trait-related components of eye movement abnormalities in schizophrenia have been demonstrated. These findings suggest specific trait components of eye tracking deficits, and that certain parameters of eye movement activity may reflect cognitive/CNS changes associated with acute episodes of illness and increases in neuroleptic dose.

NR92 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

VALIDITY OF THOUGHT DISORDER RATINGS IN SCHIZOPHRENIA

John A. Sweeney Ph.D. Psychiatry NY Hospital-CUMC 525 East 68th Street New York, NY 10021, Carla M. Solomon, Ph.D., Margaret M. Rea, Ph.D., Allen J. Frances, M.D., J. John Mann, M.D.

Summary:

GOAL: Thought disorder has traditionally been considered a cardinal characteristic of schizophrenia. However, problems demonstrating the reliability and validity of its assessment have reduced the emphasis on this feature in current diagnostic practice. Therefore, validation of new approaches to thought disorder assessment is needed for consideration of revised diagnostic criteria for schizophrenia.
METHOD: A psychological test measure of basic thinking processes of reasoning, concept formation and perceptual organization (Thought Disorder Index, TDI), and clinical ratings (SAPS) of thought disorder emphasizing deviant communication, were compared in 35 inpatient DSM-III schizophrenics (SCID).
RESULTS: Clinical ratings of thought disorder were associated with acute symptom severity (GAS, r = .51). TDI ratings of severe thought disturbance were related to avolition (SANS, r = .47) and ventricular enlargement (r = .51), and moderate thought disorder was related to global neuropsychological deficit (r = .44). Clinical and TDI rating were minimally associated (r = .21), and were unrelated to severity of hallucinations and delusions.
SIGNIFICANCE: Some components of thought disorder in schizophrenia appear related to positive symptoms, while others are associated with negative syndrome features. Psychological test ratings may be sensitive to trait-related abnormalities of thinking, while communication deviance may be a positive symptom.

NR93 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

CSF MHPG, SLEEP AND PSYCHOSIS: STATE DEPENDENT CHANGES

Daniel P. van Kammen M.D. Chief of Staff VA Medical Center Highland Drive Pittsburgh, PA 15206, Welmoet B. van Kammen, Ph.D., Jeffrey Peters, M.D., Jules Rosen, M.D., Markku Linnoila, M.D., Nancy Nugent

Summary:

Increased CSF NE levels in schizophrenics have been reported. CSF NE and MHPG have been found on different occasions to correlate with psychosis. Sleep disturbance and increased arousal which may be secondary to increased NE release are prodromal symptoms of psychotic decompensation or relapse.

We studied 28 male schizophrenic inpatients (20-50 years) who received an LP during haloperidol treatment and again 6 weeks following haloperidol withdrawal. Daily Bunney-Hamburg psychosis ratings and nightly duration of sleep were recorded. Thirteen patients were considered to have relapsed, i.e. increases over 3 days of 3 points in the Bunney-Hamburg psychosis score compared to scores of last week on haloperidol. LP's were obtained within the next 3 days. CSF MHPG, HVA and 5HIAA were measured with HPLC.

RESULTS: a) We plotted in three day running means, daily psychosis and sleep duration. Immediatey prior to meeting the relapse criteria, sleep duration decreased. After relapse criteria were met, and while psychosis ratings continued to increase, sleep duration improved. b) CSF MHPG correlated significantly with psychosis ratings (positively) and sleep (negatively) only during the drugfree condition, but not during haloperidol treatment. CSF HVA and 5HIAA did not correlate significantly with psychosis in the drugfree patients. c) CSF MHPG levels were higher ($p < .05$) in the patients who relapsed, but not HVA or 5HIAA. The data will be discussed in relationship to state dependency and NE activity increasing prior to relapse.

NR94 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

GLUCOSE INTOLERANCE IN SCHIZOPHRENIC SUBJECTS

Steven D. Roth M.D. Neuropsychiatric NYS Psych Institute 722 West 168th St. Box 72 New York, NY 10032, Giovanni Caracci, M.D., William Barr, Ph.D., Sukdeb Mukherjee, M.D.

Summary:

While abnormalities of glucose metabolism associated with schizophrenia have been long recognized, the subject has been inadequately studied. As early as 1922, Lorenz reported decreased sugar tolerance in patients with dementia praecox and, more recently, Brambilla et al reported similar abnormalities in patients on and off haloperidol. Altered dopaminergic function has been reported in alloxan-induced diabetic rats.

As part of an ongoing study of carbohydrate metabolism in psychiatric patients, 19 medically healthy DSM-III chronic schizophrenics (mean age 37.1 years, SD 6.7) underwent glucose tolerance tests (GTT). Of 18 patients studied while on haloperidol, GTT findings were normal in 10, while 5 (28%) showed glucose intolerance and 2 showed reactive hypoglycemia. While drug free, 7 of 11 (63%) patients showed impaired glucose tolerance. In total, 12 subjects had at least one GTT suggestive of impaired glucose metabolism, a prevalence far in excess of that expected for this age group. Subjects with and without an abnormal GTT did not differ on the basis of age, sex, presence of diabetes in first degree relatives, duration of illness, and WAIS-R scores. Data will be presented from a larger sample and the possible implications addressed, both in the context of neurobiology of schizophrenia and with respect to considerations of diet, exercise, and body weight in the management of psychiatric patients.

NR95 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

GROWTH HORMONE RESPONSE AND NEUROLEPTIC RESPONSE

Charles M. Beasley M.D. Psychiatry University Cincinnati Mail Loc 559; 231 Bethesda Ave Cincinnati, OH 45267, Mary Magnusson, B.S.N., David L. Garver, M.D.

Summary:

Growth hormone (GH) response to apomorphine (Apo) has been shown to demonstrate great variance within psychotic populations. The division of such populations into more homogeneous subgroups on the basis of differential response to neuroleptic drugs may aid in resolving a portion of this variance. Furthermore, the confounding effect of previous neuroleptic treatment upon this variance in neuroendocrine response can be eliminated by confining such studies to neuroleptic naive psychotics. Nineteen mood incongruent psychotic patients (Schizophreniform—8, Schizophrenia—9, Mood incongruent mania —2), never previously exposed to neuroleptic treatment were separated into three groups on the basis of latency (in days) of 55% improvement in psychotic symptoms following initiation of fixed dose haloperidol. Rapid Responders (RR) improved in the first 5 days of treatment; Delayed Responders required 8 to 54 days for such a degree of improvement; Nonresponders (NR) failed to show 35% improvement despite continued treatment. 4 RRs (Schizophreniform—3, Mood incongruent mania—1) had a mean GH response of 9.45±4.5ng/ml. 12 DRs (Schizophreniform—4, Schizophrenia—7, Mood incongruent mania—1) had a mean response of 28.55±18.94. 3 NRs (Schizophreniform—1, Schizophrenia—2) had a mean response of 32.1±15.29. The response across all groups differs significantly $p<0.05$ (Kruskal-Wallis). The difference between RR & DR responses is significant $p<0.02$ (Mann-Whitney U, two tailed). Impact of age and sex, length and severity of illness, drug dosage, and implications for further research employing the apomorphine challenge test are discussed.

NR96 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

CSF 5-HYDROXYINDOLACETIC AND SUICIDE ATTEMPTS IN SCHIZOPHRENIA

Jeffrey L. Peters M.D. Psychiatry VA Medical Center Highland Drive Pittsburgh, PA 15206, Daniel P. van Kammen, M.D., Jules Rosen, M.D., Ann V. Nugent, Markku Linnoila, M.D.

Summary:

This study examines the relationship of cerebrospinal fluid (CSF) 5-hydroxyindolacetic acid (5-HIAA), brain morphology measures, and clinical variables to a history of suicide attempts in schizophrenia.

Fifty physically healthy male patients meeting DSM-III and RDC criteria for schizophrenia consented to the study. Patients had a mean age of 34 years (range 20-51) and a mean duration of illness of 11 years. Patients were clinically stabilized on oral haloperidol alone, mean dose 13.5 mg (range 2-40), with no dose change at least two weeks before the procedure. Patients were maintained as inpatients on a low monoamine diet. CSF was obtained in standard fashion at 8 am and subsequently analyzed by HPLC with electrochemical detection for 5-HIAA. CT scans without contrast were obtained on a GE 8800 scaner and evaluated for cortical atrophy and ventricular-brain ratio (VBR) by established techniques. Based on clinical, family, prior clinician and SADS-L interviews and chart reviews, patients were classified as 1) no history of a suicide attempt 2) history of suicide gesture and 3) history of serious suicide attempt.

Preliminary analysis shows a significant difference in CSF 5-HIAA between non-attempters and serious attempters (90.9 +/−28.3 vs 71.3 +/− 24.8 pmol/ml) at $p<.05$, using the Wilcoxon two-sample rank test. There was no difference between non-attempters and those with suicide gestures only (103.6 +/− 39.9 pmol/ml). Additional analyses of the effects of age, duration of illness, cortical atrophy, VBR, haloperidol dose and blood level, clinical depression ratings, and the relationship of CSF 5-HIAA to subsequent clinical course will be provided.

NR97 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

NEW D1 DOPAMINE AND S2 SEROTONIN PET IMAGING

Dean F. Wong Nuclear Medicine Johns Hopkins Hospital Tower BSMT, 600 N. Wolfe St. Baltimore, MD 21205, John R. Lever, Ph.D., Robert Dannals, Ph.D., James Harris, M.D., Paul Hartig, Ph.D., Henry N. Wagner, M.D.

Summary:

Although numerous advances have been made with the in vivo imaging of human brain neuroreceptors in neuropsychiatric disorders, the interpretation of the studies are in part dependant upon the specificity of the ligands employed. We have developed two specific ligands for the D1 dopamine receptor, ^{11}C-SCH23390 and the S2 serotonin receptor, ^{11}C-methybromoLSD (MBL). Both have been radiolabelled with a methyiodine procedure and in vitro and in vivo animal studies have shown high specificity to their respective receptor subtypes. Blockade by D1 antagonists in mice and baboon studies have demonstrated D1 labelling. Similar studies with ^{11}C-MBL have shown high specificity to the S2 site as compared to alpha adrenergic sites, which are also in the human cortex.

Studies with the Lesch-Nyhan syndrome have been carried out, demonstrating the imaging of D1 receptors in the presence and absence of therapeutic levels of fluphenazine. Such studies will allow the examination of important receptors subsystems since animal models have shown that D1 blockage may reduce the self injury of Lesch-Nyhan. Similarly human studies are being carried out in normals and patients with ^{11}C-MBL which demonstrates specific localization to frontal and other cortical regions. These studies will be useful for the studies of depression, Alzheimer's and other neuropsychiatric disorders.

NR98 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

ELEVATED D2 DOPAMINE RECEPTORS IN SCHIZOPHRENIA

Larry E. Tune M.D. Psychiatry Johns Hopkins 600 North Wolfe Street Baltimore, MD 21205, Dean Wong, M.D., Godfrey Pearlson, M.D., Robert F. Dannals, Ph.D., Johnathan M. Links, Ph.D., Henry N. Wagner, M.D.

Summary:

We have recently demonstrated that D2 dopamine receptor densities were elevated in 10 drug naive schizophrenic patients compared to normal, age matched controls (Wong, et al, Science 234: 1558-63). Additional data from this ongoing clinical study will be presented. Correlations between these findings and clinical state will be made using the Brief Psychiatric Rating Scale (BPRS), a modified version of the Present State Examination (mini-PSE), and Schedule for the Assessment of Negative Symptoms (SANS). Of particular interest is an inverse relationship between positive symptoms of schizophrenia (as measured by the mini-PSE and D2 receptor density ($r = -.6$, p. .05). These data will be discussed in light of current theories on the psychopathology of schizophrenia.

NR99 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

CALCIUM CHANNELS ANTAGONISTS AND BRAIN D2 DOPAMINE RECEPTOR REGULATION

Richard C. Shelton M.D. Psychiatry Vanderbilt Univ Medical Center North A-2215 Nashville, TN 37232, Aaron J. Janowsky, Ph.D.

Summary:

Chronic neuroleptic treatment is known to produce up-regulation of dopamine D_2 receptors both behaviorally (increased response to agonists) and biochemically (increase in B_{max}). This change has been linked to the pathophysiology of tardive dyskinesia; as such it is probably only part of the change associated with the disease. Preliminary research demonstrated that co-administration of verapamil or diltiazem (DIL) with haloperidol (HAL) blocked the up-regulation of the behavioral response to bromocriptine (a D_2 agonist). We have now investigated the biochemical changes associated with these findings.

METHODS: Male Sprague-Dawley rats ($n = 16$ in each group) were treated for 21 days with intraperitoneal injections of the following: HAL 1.5 mg/kg; DIL 50 mg/kg; HAL 1.5 + DIL 50 mg/kg; saline control. After 5 days of washout, animals were decapitated and striata were used to measure specific binding of [^{3}H]sulpiride ([^{3}H]SUL) to D_2 receptors (B_{max} and K_d), and displacement of [^{3}H]SUL by dopamine in the presence and absence of GppNHp.

RESULTS: Chronic HAL administration produced an increase in specific [^{3}H]SUL binding (B_{max}). DIL + HAL administration produced no such change, and DIL alone produced a trend toward a decrease in B_{max}. There were no differences between HAL, DIL, and control groups for DA displacement of [^{3}H]SUL, and the shift toward a lower affinity (increase in Ki) with GppNHp was also not different among groups. In contrast, the HAL + DIL group had an increased affinity (lower Ki) for dopamine, with only a partial shift in Ki in the presence of GppNHp. These results indicate a possible relationship between calcium channels and D_2 receptor activity, possibly related to receptor coupling.

NR100 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

EFFECTS OF CAFFEINE CHALLENGE IN SCHIZOPHRENICS

Peter B. Lucas M.D. NSB NIMH BLDG 10 RM-4N214 9000 RV Pike Bethesda, MD 20892, Daniel Hommer, M.D., John Kelsoe, M.D., Mark Rapaport, M.D., Carols Pato, M.D., David Pickar, M.D.

Summary:

Uncontrolled studies show that chronic caffeine administration exacerbates symptoms of psychosis. Caffeine has also been shown to increase anxiety and induce panic attacks in patients with anxiety disorders. These findings suggest that the caffeine-induced worsening of psychosis may be a non-specific phenomenon. However, preclinical studies have demonstrated that caffeine selectively enhances dopaminergic function in mesolimbic and mesocortical systems. We hypothesized that if acute caffeine administration had a non-specific effect it would increase both psychosis and anxiety but if it had a selective effect, as suggested by preclinical studies, then only psychosis would be increased.

Eight DSM-III diagnosed schizophrenic subjects (7 treated with neuroleptics, 1 unmedicated) were administered caffeine, 10 mg/kg, in a double-blind placebo-controlled design after being free of caffeine for a minimum of 3 weeks. The BPRS was administered prior to the challenge and at 95 minutes afterwards. Change scores were derived and active and placebo conditions compared by paired t-tests.

Caffeine exacerbated symptoms of psychosis but did not increase anxiety. Significant increases were found for the BPRS total ($p<0.05$) and thought disorder ($p<0.5$) subscales but not the other subscales including anxiety-depression. There was a trend for an increase in euphoria and activation ($p<0.1$). Caffeine also produced a significant rise in serum cortisol. Changes in blood pressure and pulse correlated significantly with changes in the anxiety-depression subscale but not with changes in other subscales.

Our findings are consistent with case reports showing that caffeine worsens schizophrenic symptoms. Preclinical studies by our group have demonstrated that caffeine, administered to rodents, decreases the firing rate of mesocortical and mesolimbic neurons, perhaps by feedback-mediated inhibition secondary to release of dopamine. We therefore propose that caffeine worsens schizophrenic psychopathology through an increase in dopaminergic activity in limbic and cortical areas.

NR101 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

LOW DOSE DEPOT NEUROLEPTICS FOR PSYCHOSIS IN SDAT

Gary L. Gottlieb M.D. Psychiatry Univ Pennsylvania 3400 Spruce St 3 Piersol/4283 Philadelphia PA 19104, Thomas W. McAllister, M.D.

Summary:

Treatment of behavioral symptoms is essential to the psychiatric management of patients with Senile Dementia of the Alzheimer's Type (SDAT). While numerous agents are used to treat related psychosis and agitation, there are no studies of low dose depot neuroleptic use for these problems.

Ten older adults who met NINCDS/ADRDA criteria for probable SDAT were evaluated and behavioral symptoms were documented with the BPRS and SCAG. Ratings of extrapyramidal symptoms (EPS) and other neurologic impairments were recorded with the Simpson and AIMS. Treatment was initiated with 1.25 mg (.05 cc) of fluphenazine decanoate and titrated biweekly. Patients were reevaluated weekly.

Eight of the ten patients were stabilized with a mean dose of 3.75 mg (.15 cc) every two weeks. Mean scale scores for the group showed significant improvement at 4, 8, 12 and 16 weeks after treatment began ($p<.01$). While the two non-responders suffered significant EPS at doses of 6.25 mg (.25 cc), mean whole group EPS ratings did not change significantly during treatment ($p>.10$).

This trial suggests that depot neuroleptics can be employed safely and efficaciously in patients with psychosis and SDAT. In light of the difficulty of ensuring compliance in the treatment of these disorders, a randomized controlled trial of this intervention should be considered.

NR102 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

ETHNICITY AND NEUROLEPTIC DRUG DOSAGE

Francis G. Lu M.D. Psychiatry Univ of Calif SF 1001 Potrero Ave San Francisco, CA 94110, Ching-Piao Chien, M.D., Gertrude Heming, Ph.D., Ladson Hinton, M.D., Carol Soussain, B.A.

Summary:

Past research of ethnic differences in psychotropic drug response have primarily utilized two methodologies; (1) Retrospective record review of dosage difference; (2) Pharmacokinetic studies. Findings from these studies in relation to neuroleptic drugs among others have been conflicting and inconclusive. For example, two recent retrospective studies comparing neuroleptic dosage in Asian versus Caucasian inpatients yielded contradictory findings. In January, 1986, we began both retrospective and prospective studies at San Francisco General Hospital, a unique setting which allows for simultaneous comparison of inpatients from four ethnic groups: Asian, Latino, Black, and Caucasian. We have reviewed records of 161 inpatients treated with neuroleptic drugs who were admitted from January, 1985, to July, 1986 (Asian = 53, Latino = 37, Black = 30, Caucasian = 41). No statistical differences were found for the maximal and discharge neuroleptic dose, some demographic variables (age, sex), and some clinical variables (diagnosis, concurrent medications, length of stay, admission/discharge global assessment scale ratings, and incidence of EPs). Body weight was taken into account.

However, when the newly arrived Asian and Latino immigrant group (in U.S. less than 5 years) was compared to the other Asian/Latino groups and to the U.S.-born Caucasian group, a statistically significant difference ($P<.07$) was found in the maximum dosage; specifically, the mean maximal dose was less for the recent Asian/Latino immigrants. Implications of this study, the first to do a four-way ethnic comparison, will be discussed.

NR103 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

BENZTROPINE PROPHYLAXIS FOR HALOPERIDOL DYSTONIA

George W. Arana M.D. Psychiatry TUFTS Univ. Sch. Med. Harrison Avenue Boston, MA 02111, Donald Goff, M.D., Renee Dupont, M.D., Fred Kanter, M.D., David Greenblatt, M.D., Richard I. Shader, M.D., Marjorie Ornsteen, A.B.

Summary:

Thirty-two psychotic male inpatients were started on haloperidol (HAL) in a fixed-dose, 14-day study in which benztropine mesylate (BZM) was administered in a randomized, double-blind, placebo-controlled design for the first seven days to determine the efficacy of prophylactic anticholinergic treatment for HAL-induced dystonia. Four patients were dropped from the study because of complications. Initial mean HAL daily dose in the remaining 28 patients studied was 11.2 mg with BZM administered in a 2 mg BID schedule. Diagnoses on admission by DSM-III criteria included schizophrenia (N = 14), bipolar mania (N = 7), atypical psychosis (N = 5), and other psychotic illnesses (N = 2). Mean age was 35 years with a range of 22-54 years. A total of 10 dystonic episodes occurred, 2/14 in the first two days of BZM treatment, 5/14 in the first four days of placebo, and 3/14 between days 7-10 in patients initially on BZM who were discontinued following study protocol. Therefore, a total of eight dystonic episodes occurred when patients were BZM-free, while two dystonias occurred while patients were treated with BZM showing no significant difference between groups ($X^2 = 2.5$; df = 1; NS). Blood levels of HAL will be presented and discussed as they relate to the development of dystonia and to treatment response. The effect of BZM on HAL blood levels and the relationship of these blood levels to the development of dystonia will be discussed. Other clinical variables such as age, race, diagnosis and psychiatric history will be discussed as they relate to the development of dystonia.

NR104 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

80% NEUROLEPTIC REDUCTION IN CHRONIC PSYCHOTICS

David Shumway M.D. Psychiatry Brockton VAMC Belmont Street Brockton, MA 02401, Ming Tsuang, M.D., Paul Yin, M.D., Stephen V. Faraone, Ph.D., Walter A. Brown, M.D., Alan I. Green, M.D.

Summary:

Many schizophrenics do not show substantial improvement after a six week trial of neuroleptics. Some studies show that these treatment resistant patients achieve high serum neuroleptic levels and do not respond to "mega-doses" suggesting that patients on high doses of neuroleptics with persistent positive symptoms of psychosis should be considered for neuroleptic reduction. Forty persistently psychotic "treatment resistant" DSM-III schizophrenics are randomly being placed in two groups in a double-blind manner: 1.) reduction to 20% of current neuroleptic dosage; 2.) a control group with no reduction. For the first 14 weeks of the study (and monthly thereafter), clinical assessments are made with the Brief Psychiatric Rating Scale to determine if exacerbation of symptomatology has occurred and neuroleptic increase is necessary. All patients are followed for six months before the blind is broken. Social adjustment is assessed initially and after six months. Our preliminary results show that, of 10 patients who have completed the protocol, 1 of 6 in the reduction group and 1 of 4 controls have relapsed. These results suggest that substantial neuroleptic reduction is a viable alternative for some "treatment resistant" schizophrenic patients.

NR105 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

THE EFFICACY OF CLOZAPINE IN REFRACTORY SCHIZOPHRENIA

Jerome Costa, M.D. Research Metropolitan State Hosp 11400 Norwalk Blvd Norwalk, CA 90650, John M. Herrera, Ph.D., John Sramek, Pharm. D., J. Ananth, M.D.

Summary:

Treatment resistant schizophrenia patients make up a large proportion of our inpatient facilities, disproportionately consume mental health dollars and are perhaps the most important problem in psychiatry, today. Clozapine is a unique antipsychotic agent currently not available for clinical use in the United States; this agent is believed to have a preferential affinity for mesolimbic dopamine receptors and subsequently because of its high anticholinergic activity, extrapyramidal reactions are reportedly rare. The study examined the efficacy of clozapine the treatment of refractory schizophrenics and consisted of five experimental periods: a retrospective documentation of treatment failure (comprehensive chart review); a prospective determination of treatment failure with an established haloperidol cogentin dosage level, placebo washout, double-blind clozapine treatment period, and placebo follow-up. Included were 17 schizophrenic patients: with a mean age of 32.8, the mean age at first hospitalization was 19.2 and the mean number of prior psychiatric hospitalizations was 10.4. The assessment instruments included the BPRS, CGI, NOSIE-30, AIMS, and the Simpson-Angus Neurological Scale. In addition, the Premorbid Adjustment Scale was completed at entry, and weekly laboratory investigations were carried out. Tests of the comparative efficacy at endpoint completion of the double-blind treatment revealed that clozapine was significantly superior to chlorpromazine ($p<.05$). In addition, the data was indicative of a more rapid onset of antipsychotic activity on the part of clozapine and less extrapyramidal reactions. These results demostrate a pronounced improvement with clozapine in treatment of the most severely disturbed and refractory patient.

NR106 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

TRIFLUOPERAZINE PLASMA LEVELS AND CLINICAL RESPONSE

Philip G. Janicak M.D. IL ST Psych Inst 1601 W Taylor St Chicago, IL 60612, Javaid I. Javaid, Ph.D., Rajiv Sharma, M.D., James Peterson, B.S., David B. Bresnahan, M.D., John M. Davis, M.D.

Summary:

We investigated the relationship between trifluoperazine plasma levels and response. Thirty-one patients (male = 19; female = 12; mean age = 33 ± 13.4) who met RDC criteria for schizophrenic disorder (n = 26) or schizoaffective disorder (n = 5) were studied after the washout phase averaging 17.4 days BPRS, SNHI and GAS scores were obtained and repeated at the end of two weeks treatment with a fixed dose of trifluoperazine (5 mg PO BID). Plasma levels of the parent compound were obtained by GLC measurement on days 11 and 15 of treatment. We then averaged the two values for each patient and compared this result with clinical response as determined by a % change in scores from baseline. Plasma levels were divided into low (≤1ng/ml); medium (>1;≤2.25) or high (>2.25) categories. In comparing the low versus medium categories using Students t-test there was a greater improvement in the medium category which was highly significant for the GAS (t = 3.19; p = .007); approached significance for the SNHI (= 1.78; p = .09); and was also significant for the BPRS (t = 2.18; p = .04). A similar comparison between medium and high level categories again revealed greater improvement in the medium group which approached significance for the GAS (t = 1.84; p = .09); was significant for the SNHI (t = 2.10; p = .05); and also for the BPRs (t = 2.24; p = .04). We found a U-shaped relationship between trifluoperazine levels and response. A Multivariate analysis of variance testing this quadratic relationship was significant with a p = .01 and the univariate quadratic tests were: SNHI (t = 1.85; p = .07); BPRS (t = 2.10; p = .04) and GAS (t = 3.69; p<.001).

NR107 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

PROLACTIN SHIFTS FOLLOWING NEUROLEPTIC WITHDRAWAL

Alan I. Green M.D. Psychiatry MA Mental Health Center 74 Fenwood Road Boston, MA 02115, Stephen V. Faraone, Ph.D., Walter A. Brown, M.D.

Summary:

Neuroleptic-induced alterations in central nervous system dopamine activity may be important clinically. In this study, 21 stable schizophrenic patients, taken off their neuroleptic medication over a 3 week period, were followed for 40 weeks or until their clinical condition required reinstitution of the neuroleptic. Serum prolactin levels were measured before neuroleptic withdrawal (baseline), and during the non-neuroleptic period. When the serum prolactin values were plotted over time, 52% of the subjects showed shifting prolactin levels in the shape of a "V" following withdrawal. Those subjects who demonstrated this "V" shape had a significantly lower baseline prolactin level (6.9±5.7 ng/ml) than those without the "V" shape (17.5±12.5 ng/ml; t (12.3) = 2.44, p<.04). In previous reports, patients with low baseline serum prolactin were noted to be more likely to show early relapse with neuroleptic withdrawal and to show tolerance to the prolactin elevating effects of the neuroleptics. The pathophysiological significance of the prolactin "V" is uncertain. However, it is consistent with a hypothesis of transient dopaminergic hyperactivity following neuroleptic withdrawal, and with subsequent neuronal adaptation to compensate for this hyperactivity. Possible clinical implications of this finding will be discussed.

NR108 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

AN OPEN TRIAL OF PIMOZIDE FOR THE NEGATIVE SYNDROME

S. Shalom Feinberg M.D. Psychiatry AECOM/SVTN CMHC 1967 Turnbull Ave., Suite 28 Bronx, NY 10473, Lear Elijovich, M.D., Stanley R. Kay, Ph.D., Abraham Fiszbein, M.D., Lewis A. Opler, M.D.

Summary:

Pimozide, a neuroleptic of the diphenylbutlpiperidine (DPBP) group, has recently become available in the United States. While many American clinicians may not be familiar with pimozide, reports over the last twenty years suggest that pimozide might be helpful in the treatment of negative symptoms of schizophrenia, which are generally considered to be less responsive to standard neuroleptics. On a theoretical level research in Snyder's laboratory has suggested that neuroleptic drugs of the DPBP group uniquely possess potent calcium channel antagonism which could explain their ability to relieve negative symptoms. These earlier reports, however, use measures not specifically designed to assess the negative syndrome. The Positive and Negative Syndrome Scale (PANSS) is a recently standardized instrument specifically developed to reliably measure these dimensions in schizophrenia. Utilizing the PANSS, we studied the clinical effects of pimozide with a 6 week open clinical trial on ten neuroleptic resistent schizophrenic inpatients with prominent deficit features. Symptoms of the negative syndrome but not of the positive syndrome improved significantly suggesting the drug specifically targets the negative profile. Possible pharmacologic mechanisms for pimozide's potentially distinct clinical properties will be discussed.

NR109 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

MOLINDONE AND HALOPERIDOL: SIDE EFFECT DIFFERENCES

Barbara J. Mason Ph.D. Psychiatry Cornell U Med College 525 East 68th St New York NY 10021, J. John Mann, M.D.

Summary:

Molindone has been reported to be more selective than haloperidol for limbic versus striatal dopamine receptors in rats, and therefore may have a superior ratio of therapeutic benefits compared to severity of extrapyramidal side effects. To test this hypothesis, this double-blind study compared a new injectable form of molindone with injectable haloperidol, followed by oral forms of the assigned medications, in acutely psychotic patients.

METHOD: 31 recently admitted inpatient schizophrenics were randomly assigned to treatment with injectable molindone or haloperidol for up to 72 hours, followed by 4 weeks of oral medication. Standardized ratings of clinical response and side effects were performed.

RESULTS: Groups were equivalent on all demographic and baseline clinical measures, except that molindone patients had significantly ($p = .001$) more prior hospitalizations. Clinical improvement was equivalent in both groups during the injectable phase. However, molindone patients had significantly less ($p = .025$) akinesia and ($p = .03$) dystonia than did haloperidol-treated patients. No side effect or efficacy differences were observed in the oral phase. Mean doses of molindone and haloperidol were 92.9 mg and 11.3 mg intramuscularly, and 266.7 and 30.6 mg orally, respectively.

CONCLUSIONS: These preliminary data suggest that no efficacy differences exist between molindone and haloperidol, in both injectable and oral forms, for the treatment of acutely ill schizophrenics. However, molindone displayed an advantage in terms of less akinesia and dystonia during the injectable phase and provided support for the hypothesis. Clinically, injectable molindone may have advantages, particularly in young males who are at greater risk of dystonia.

NR110 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

A NEW TREATMENT FOR EXTRAPYRAMIDAL DISORDERS

Murray A. Cowen M.D. Psychiatry Rockland Psych Ctr and Kline Inst for Psych Research Orangeburg, NY 10962, William Sacks, Ph.D., Maurice R. Green, M.D., Aristide H. Esser, M.D., Paul Talarico, B.A., Barbara Feitel, Ph.D.

Summary:

A series of studies on the effects of acetazolamide plus thiamine administration on various groups of chronically ill and treatment-resistant mental patients was supplemented by a double blind, two-period, crossover study on the effects of these drugs on their symptoms of Tardive dyskinesia (TD) and Parkinson's disease (PD).

Sixteen subjects, 5 female and 11 male, with symptoms of both TD and PD were selected. They had a variety of psychiatric diagnoses and were on various psychotropic medications, with six being drug free. These maintenance treatments were unchanged during the four week study (two weeks on active and two weeks on placebo test drugs). Eight, ages 23 to 54, had an active treatment of 1.5 gms thiamine plus 2.0 gms acetazolamide in tid divided doses, while the remainder, ages 72 to 86, had the acetazolamide reduced to 1.5 gms total daily.

The patients were rated weekly by two independent researchers using the AIMS scale for TD and the Simpson-Angus scale for PD. All showed marked improvement on both scales during the active treatment period. The null probabilities for the change on each scale was less than 0.001. No clinically significant adverse effects were noted.

NR111 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

PROPRANOLOL AND BENZTROPINE IN AKATHISIA

Lenard Adler M.D. Psychiatry, Rm 116A New York VA Medical Ctr First Avenue & E 24th Street New York, NY 10010, Stewart Reiter, M.D., June Corwin, Ph.D., Paula Hemdal, M.A., Burt Angrist, M.D., John Rotrosen, M.D.

Summary:

Recent studies[1,2] have shown that propranolol is an effective treatment for neuroleptic-induced akathisia (NIA). We now describe data from a study assessing the comparative efficacy of benztropine versus propranolol in NIA. Measures of memory were also obtained to assess possible drug-induced dysfunction. The study was a parallel design comparison of 17 in-patients treated with propranolol (20-80 mg/day) or benztropine (1.5-4.0 mg/day).

Patients received a cognitive battery and assessments of subjective and objective NIA both at baseline and at the end of treatment. Propranolol showed greater efficacy than benztropine in treating NIA. Measures of attention and short term (immediate) memory were not significantly affected by propranolol or benztropine. Benztropine, but not propranolol, impaired most measures of long term (recent) memory. This selective effect of anticholinergic medication on recent, but not immediate memory is well known[3]. This preliminary study supports the preferential use of propranol over benztropine in the treatment of NIA.

NR112 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

RISK FACTORS FOR PARKINSONISM IN TD PATIENTS

Thomas E. Hansen M.D. Psychiatry Portland VAMC 116AP P.O. Box 1034 Portland OR 97207, Ronald M. Weigel, Ph.D., William L. Brown, B.A., Daniel E. Casey, M.D.

Summary:

We report on risk factors for drug-induced Parkinsonism (DIP) in tardive dyskinesia (TD) patients. If TD and DIP represent opposing dopamine (DA) states, then more severe TD should be incompatible with DIP, and the risk factors known for DIP (age, sex, potency, dose of neuroleptic) may be different in the presence of TD.

Psychotic TD inpatients (97% were male) were rated with the AIMS, the Sct. Hans Parkinsonism Scale, and the BPRS before receiving neuroleptics then twice weekly for a minimum of 10 days. Benztropine was used for emergent DIP, dystonia, and akathisia. Data analyses included simple correlation coefficients, logistic regression and Cox proportional hazard for risk factors.

In the 66 patients (mean age 45) studied, TD and DIP were not correlated (negative or positive). On admission, 12 (18%) had DIP coexisting with TD. Logistic regression found three risk factors: age, years of neuroleptic exposure, and use of more potent neuroleptics in the two weeks before admission (all $p \leq 0.05$). Of the remaining patients, 25 (46%) developed DIP during treatment. There were no risk factors significantly associated with earlier development of DIP in the Cox analysis.

In summary, TD did not avert DIP and known risk factors for DIP were still important at admission despite the presence of TD. The absence of identifiable risk factors for DIP during treatment may be caused by exclusion of high risk patients (those with DIP on admission). The implications of these risk factor analyses for the clinical treatment of psychotic TD patients will be discussed.

NR113 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

OBJECTIVE EVALUATION OF RESPIRATORY DYSKINESIA

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Summary:

Respiratory dyskinesia (RD), first described in 1978, is believed to be a manifestation of tardive dyskinesia (TD) involving abnormal breathing movements. To evaluate respiratory dysrhythmias occurring in patients with TD, we have compared breathing patterns in 10 subjects with moderate to severe TD with 10 subjects having a history of neuroleptic use but no TD, and with 10 normal subjects.

TD was assessed by standard rating scales (AIMS and ESRS). Breathing patterns were determined by respiratory inductive plethysmography (RIP), a non-invasive sensitive instrument for examining breathing patterns. Breathing patterns were assessed at rest, and during tasks such as leg elevation designed to elicit the involuntary movements of TD. Detailed overnight sleep studies with RIP monitoring were also performed on TD subjects.

Subjects with TD had significantly ($p < 0.02$) increased breathing frequency ($f = 17.3 \pm 1.6$) and decreased tidal volume ($VT(m1) = 483 \pm 62$) compared to normal controls ($f = 12.0 \pm 1.8$; $VT(ml) = 680 \pm 82$) during the TD activating task of leg elevation. Breathing frequency and tidal volume were also significantly more variable in TD subjects than in the other two groups. Respiratory dysrhythmias seen in awake TD subjects normalized during sleep. The group with longterm neuroleptic exposure but no TD showed a regular rhythm but increased breathing frequency compared to controls.

We conclude that RD is a respiratory musculature variant of TD. Objective measurement of RD may have potential as an early predictor of TD.

NR114 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

OBJECTIVE MEASUREMENT OF TARDIVE DYSKINESIA

C. J. Jos M.D. Psychiatry Veterans Administration Veterans Admin. Med. Cen. -JB ST. Louis MO 63125, David W. Kennard, M.D., Ludwig Heinemann, M.D. Earl Dick, M.D. Anatoly Frishberg, M.D., William True, Ph.D., Srinivas Chilakamarri, M.D.

Summary:

Regular assessment of Tardive Dyskinesia has been shown to reveal higher incidence and earlier detection. Our measurements make treatment procedures more meaningful by using instrumental methods, as opposed to general or clinical ratings. Hitherto the only scaling method which has been widely used is the AIMS Clinical Rating Scale. This takes about fifteen minutes to do by a specially trained psychiatrist. We have used an ultrasound device (1,2) to measure facial movements. This provides a digital count or readout in a period of one minute. It is appropriately calibrated. The device is mounted on a spectacle frame. The total time and conditions of measurement are similar to temperature measurement by thermometer. This research was designed to compare the AIMS Clinical Rating Scale by two psychiatrists against the ultrasound movement counts. It was done in 86 male patients at risk, of whom over 60% had taken neuroleptics for five years or more. AIMS provides assessment of several body parts, while the ultrasound only measure the lips and face. Results showed a high correlation between the two methods. Thus a powerful numerical quick and easy-to-use method seems to be available, now, for any staff to apply.

NR115 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

FREQUENCY OF LIFE EVENTS IN SCHIZOPHRENIC PATIENTS

Joseph Ventura M.A. Psychiatry ULCA 760 Westwood Plaza Box 18 Los Angeles CA 90024, Keith H. Neuchterlein, Ph.D., Jean Hardesty, Ph.D.

Summary:

Previous retrospective research has found the average rate of stressful life events to be higher in schizophrenic patients than in normal individuals. However, these studies have based the rates for patients on periods that occurred prior to episodes. Research that we presented at last year's convention reported an increase in the frequency of independent life events (but not total life events) in 11 recent-onset schizophrenic outpatients just prior to a relapse or significant exacerbation of psychotic symptomatology. A careful prospective analysis of life events frequency was conducted utilizing an expanded version of the Psychiatric Epidemiology Research Inventory for Life Events. Life event frequency for a one-month period for a group of 20 recent-onset schizophrenic outpatients was compared with 20 normal subjects matched on age, sex, ethnicity, and education. During the period assessed the schizophrenic patients were in a state of relative clinical stability. A significantly higher rate of total life events was found for normals (mean = 4.4) than for patients (mean = 2.4), $p < .003$. Normals also had a higher frequency of total negative events (mean = 2.2) than patients (mean = 1.2), $p < .03$. These results suggest that, although schizophrenic patients may experience an increase in independent stressful life events in the shortterm period just prior to episodes, their overall frequency of life events during periods of relative clinical stability is actually lower than that of normal individuals.

NR116 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

SEX DIFFERENCES OF NEUROCOGNITION OF SCHIZOPHRENIA

Gretchen L. Haas Ph.D. Psychiatry Payne Whitney 525 East 68th Street New York NY 10021, John A. Sweeney, Ph.D., Margaret M. Rea, Ph.D., Allen J. Frances, M.D.

Summary:

GOALS: Converging lines of research indicate sex-related differences in the age of onset, symptomatology, associated neurocognitive deficits, clinical course, and treatment response of schizophrenia. The purpose of this study was to compare male and female schizophrenics on basic neurocognitive, clinical, demographic and psychosocial measures to determine the nature and extent of sex differences on these dimensions and to explore possible differences in the aggregation of neuroanatomic, cognitive and clinical features across the two sexes.
METHODS: 20 male and 16 female DSM-III (SCID) schizophrenics were compared on neuroanatomic (VBR), neuropsychological, psychosocial/demographic, family history and clinical measures.
RESULTS: The indices aggregated in a systematically different fashion for the two sexes. Males demonstrated a consistent intercorrelation of deficit syndrome features, including VBR, premorbid adjustment, negative symptoms and eye tracking and cognitive deficits ($r = .51$ to .67). VBR and eye tracking deficits—measures of CNS impairment—were associated with performance on frontal cognitive tasks for men ($r = .48$ to .69), but visual right hemisphere tests for females ($r = .64$ to .77). Negative symptoms were related to cognitive deficit for males.
SIGNIFICANCE: The core deficit syndrome may be more characteristic of male schizophrenics, and the clinical and cognitive correlates of ventricular enlargement may differ for the two sexes.

NR117 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

IMPACT OF GENDER ON THE COURSE OF SCHIZOPHRENIA

Jill M. Goldstein Ph.D. Psychiatry Brockton VA Med Center 940 Belmont Street 116A Brockton MA 02401, Matthias Angermeyer, M.D.

Summary:

Past literature has suggested that the course of schizophrenia may be worse for schizophrenic men than women. Critics claim that this is due to the diagnostic inaccuracy of DSM-III criteria. This assumes that if misclassification were controlled, significant gender differences would disappear. Two studies tested the hypothesis that schizophrenic men experience a poorer course than schizophrenic women. In one study, a representative sample from Hannover, West Germany, including 278 first admission schizophrenics diagnosed by DSM-III, were followed for 3 years, regarding rehospitalizations, lengths of hospital stay, and survivorship in the community. In a second study, 91 early-break schizophrenics from NYC, diagnosed by DSM-III, were followed for 10 years regarding rehospitalizations and lengths of hospital stay. Survival analyses and multivariate multiple regression tested for gender differences in outcomes. Findings from both studies demonstrated that schizophrenic women experience fewer rehospitalizations, shorter lengths of stay, and survive longer in the community than schizophrenic men. Findings were not attributed to diagnostic misclassification, differences in subtypes, age at fist hospitalization, nor outpatient treatment prior to first hospitalization. Gender had an early effect on the premorbid period. Implications of the role of gender for understanding some of the heterogeneity of schizophrenia are suggested.

NR118 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

FIVE-YEAR OUCOME OF SCHIZOPHRENIA IN INDIA: DEMOGRAPHIC CORRELATES

Vijoy K. Varma M.B. Psychiatry Postgrad Med. Inst. Postgrad Inst. Med. Educ. Res. Chandigarh, India 160012, Bankteshwar Tripathi, M.D., Arun K. Misra, M.A.

Summary:

Two hundred and nine patients of first-onset schizophrenia were identified from a defined rural and urban catchment area over a two-year period by an active recruitment process including survey of all treatment facilities serving the area. The cases were diagnosed by rigorous operationally defined criteria as per the WHO screening schedule. Out of these, 186 patients could be fully assessed at intake by the Present State Examination (PSE) and other standardized schedules, i.e., Psychiatric and Personal History Schedule (PPHS) and Diagnostic and Prognostic Schedule (DPS) and followed up at one, two and five years using the same schedules.

Out of the 186 patients, 90%, 89% and 70% could be followed up at one, two and five years, respectively. Out of the 144 patients assessed at five years, 54% had reached and remained in almost complete or nearly complete remission, 40% had one or more relapses following remission and 5% remained continuously psychotic.

The outcome was correlated with the socio-demographic variables like urbanicity, age, sex, marital status, and socio-economic status. However, no significant relationship of any of these with the outcome was found. The outcome was found to be more favourable as compared to that reprted from the developed countries in the West.

NR119 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

FAMILIAL AND SOCIAL DETERMINANTS OF OUTCOME

Frederic J. Sautter Ph.D. Psychiatry UC Coll of Medicine 231 Bethesda Ave ML559 Cincinnati OH 45267, Barbara E. McDermott, M.A., David L. Garver, M.D.

Summary:

Current evidence suggests that two dimensions of pathology underlie schizophrenia: one dimension is characterized by positive symptoms of psychosis the other by negative symptoms. The present study evaluates the impact of genetic and psychosocial factors on both positive and negative symptoms of schizophrenia. Sixty-four patients who had received a DSM-III diagnosis of schizophrenia or schizophreniform disorder were evaluated approximately two years after index hospitalization. Patients were categorized according to family history of schizophrenia (positive or negative) and social support (high or low). A two-between analysis of variance procedure was performed on both positive and negative symptoms. With negative symptoms, there was a significant main effect for both family history ($p < .01$) and social support ($p < .02$). With positive symptoms there was a significant main effect for social support ($p < .01$). There were no significant interactions. These data indicate that schizophrenic-spectrum patients with a positive family history for schizophrenia exhibit more negative symptoms at follow-up than patients with a negative family history. They do not evidence more positive symptoms. Individuals with more social supports evidence significantly fewer positive and negative symptoms. These data indicate that both family history and social supports are important determinants of the course of schizophrenia.

NR120 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

FAMILY FACTORS PREDICTING SCHIZOPHRENIC RELAPSE

Malca B. Lebell Ph.D. Research Brentwood VA Med CTR 11301 Wilshire Boulevard Los Angeles CA 90073, Stephen R. Marder, M.D., Jim Mintz, Ph.D., Joanne McKenzie, R.N.

Summary:

Research conducted in the U.S. and England with outpatient schizophrenic populations document that certain types of stressful family environments are associated with higher relapse rates. These studies are based on the "expressed emotion" construct as derived from the Camberwell Family Interview (CFI). However, for some purposes, the CFI is too cumbersome and time-consuming an assessment instrument. This pilot study tested three more efficient alternatives for assessing familial emotional environment as predictors of relapse—the Kreisman Patient Rejection Scale, Hogarty's Global Judgment Criticism Scale, and the Gottschalk-Gleser Hostility/Anxiety Scale ratings of five-minute speech samples. Subjects were 41 patients who fulfilled DSM-III criteria for Schizophrenic Disorders and were followed systematically for two years on medication maintenance using fluphenazine decanoate. All three measurements of the emotional environment were significant predictors of relapse or psychotic exacerbation at 2 year outcome using survival analysis of (for the Kreisman Scale, $p < .01$; for the Hogarty Scale, $p < .03$; for the Gottschalk Scale $p > .01$). These findings suggest that brief interview procedures are available for assessing, familial environment and may help identify patients vulnerable to relapse.

NR121 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

SEX AND PREDICTION OF OUTCOME IN SCHIZOPHRENIA

Karen K. Bardenstein Ph.D. Research Inst Chestnut Lodge 500 West Montgomery Avenue Rockville, MD 20850, Thomas H. McGlashan, M.D.

Summary:

Are predictors of long-term outcome in chronic schizophrenia gender specific? Prior analysis[1] of largely chronic DSM-III schizophrenic patients ($N = 163$) from the Chestnut Lodge Follow-up study identified 4 baseline variables as especially robust in predicting global outcome: family history of schizophrenia, psychotic assaultiveness, depressed mood, and premorbid instrumental skills. The multiple regression equation including these and other variables correlated 0.60 with global outcome ($p < .0001$) and accounted for 35% of the outcome variance. Here, these data are reanalyzed by gender to test 1) whether overall predictive power varies with sex and 2) whether the above predictors (and others) are sex-specific.

METHOD: The sample consisted of 83 male and 80 female chronic schizophrenic patients (80% ill for more than 2 years). Medical records were retrospectively assessed for rediagnosis by DSM-III criteria and for (reliable) ratings of 150 predictors organized into four categories suggested by the literature: background, premorbid, manifest illness, and course of illness. Outcome was independently assessed by interview 15 years post-discharge (range 2–32 years). Predictor sets for each sex were identified using multiple regression of predictors on global outcome.

RESULTS: 1) Overall predictive power was higher for females (multiple $R = 0.72$, $p < .0001$; outcome variance 52%) than for males (multiple $R = 0.54$; $p < .0001$; outcome variance = 29%). 2) Some predictors were gender specific, e.g., family history of schizophrenia (among others) for males and depressed mood and assaultiveness (among others) for females. Only premorbid instrumental skills remained gender independent.

SIGNIFICANCE: Findings suggest that outcome is easier to predict for female chronic schizophrenic patients and that many individual predictors are gender specific.

NR122 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

SCHIZOPHRENIFORM DISORDER: A VALID DIAGNOSIS?

Robert K. Heinssen M.A. Research Inst. Chestnut Lodge 500 West Montgomery Avenue Rockville MD 20850, Thomas H. McGlashan, M.D.

Summary:

DSM-III classifies schizophreniform disorder (SF) outside the categories of schizophrenia (S) and affective illness. The validity of SF as an independent diagnostic entity has been questioned, however.[1] This study uses data from the Chestnut Lodge Follow-up Study to examine differences in the (1) premorbid, (2) morbid, and (3) long-term (15-year average) functioning of inpatients with SF (N = 15), S (N = 15), and unipolar affective disorder (UNI; N = 15).

METHODS: Ratings of baseline variables (premorbid functioning, illness up to and including admission, and sign and symptom variables), as well as current diagnosis, were made from patients' abstracted medical records with adequate reliability.[2] Outcome data were collected independently by interview (2–32 years post-discharge), also with adequate reliability. Five subsets of S and UNI patients were formed by random selection from larger cohorts (Ns of 163 and 44, respectively). A series of five independent data analyses compared these subsets with the sample of 15 SF patients.

RESULTS: Analysis of variance revealed tha SF patients were similar to S patients in clinical profile (presence of schizophrenic symptoms, absence of character pathology and depressive symptoms). The premorbid and long-term functioning of SF and S patients differed in several ways. SF patients reported (1) better premorbid sexual adjustment, skills and interests, (2) a later age of illness onset, and (3) greater social activity and better global functioning at follow-up. SF and UNI patients had similar long-term outcomes, but only 17% of the SF patients received a follow-up diagnosis of affective disorder while 42% received a follow-up diagnosis of S. These results indicate heterogeneity within the SF category, but generally support the validity of this disorder as a unique diagnostic entity. Its clinical picture is similar to S but not its course; its course is similar to UNI but not its psychopathologic profile.

NR123 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

INPATIENT DISCHARGE STATUS AND LONG-TERM OUTCOME

Thomas H. McGlashan M.D. Research Institute Chesnut Lodge 500 West Montgomery Avenue Rockville, MD 20850 Robert K. Heinssen, M.A.

Summary:

The prognosis of self-discharged inpatients has seldom been studied, especially by diagnosis, and is frequently assumed to be poor! This study uses data from the Chestnut Lodge Follow-up Study to evaluate the long-term (15 year average) outcome of inpatients discharged with medical advice (WMA), against medical advice (AMA), or by transfer for patients with Schizophrenia (N = 113), Schizoaffective Disorder (N = 46), Borderline Personality Disorder (N = 64), and Unipolar Affective Disorder (N = 37).

METHODS: Ratings of baseline variables (history and admission clinical picture), as well as current diagnosis, were made from patients' abstracted medical records with adequate reliability.[2] Outcome data were collected independently by interview (2–32 years post discharge), also with adequate reliability. Outcome variables were selected from six dimensions: living situation at follow-up, further treatment, employment, social activity, psychopathology, and global functioning.

RESULTS: Results show that outcome among type-of-discharge cohorts varies considerably depending upon diagnostic class. Outcome of transferred patients was poorest within each dianostic cohort. The outcome of AMA patients was poorer than the outcome of WMA patients only for the unipolar cohort. AMA unipolar patients were especially at risk for developing alcohol abuse subsequent to discharge. AMA status in schizoaffective patients correlated significantly with suicide. Regularly and irregularly discharged schizophrenic patients had virtually identical outcomes. Interestingly, AMA borderline patients functioned as well as WMA borderline patients, but managed to do so with less treatment. These findings challenge the global assumption of poorer long-term prognosis for self-discharged patients. The outcome implications of a patient's discharge decision appear to depend highly upon diagnosis.

NR124 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

INTEGRATING/SEALING OVER AND LONG-TERM OUTCOME

Thomas H. McGlashan M.D. Research Inst Chestnut Lodge 500 West Montgomery Avenue Rockville, MD 20850

Summary:

Integration (I) and sealing over (SO) are clinically distinct recovery styles from schizophrenia (1). The SO patient prefers not to think about his illness experience during recovery but adopts an attitude of "the less said the better." Integrators, by contrast, are interested in their illness experience and wish to place it into some coherent perspective. Specific definitions and scales of these styles were applied reliably to 231 patients from the Chestnut Lodge Follow-up Study (2) to delineate associations between recovery styles (I vs. SO) and long term (15 year average) functional outcome (further treatment, symptoms, social and work functioning) in schizophrenia (S) and other psychosyndromes: schizoaffective disorder (SA), unipolar affective disorder (UNI), schizotypal (SPD) and borderline personality disorder (BPD).

RESULTS: For the entire sample I correlated significantly with better functional outcome (Pearson $R = 0.49$, $p < .001$). Integrating attitudes were associated with good outcomes 77% of the time while SO attitudes were associated ubiquitously with all levels of outcome: good (31%), fair (33%), and poor (36%). By diagnosis, the recovery styles from the most I to the most SO were: UNI = SPD, BPD, SA, S. Good outcome I patients were compared with good outcome SO patients to test for differentiating characteristics. Healthy I patients had significantly ($p < .001$) higher IQ, better premorbid work/school stability, more motivation for treatment, and fewer hebephrenic-like symptoms at admission than healthy SO patients. The good outcome SO group contained more patients with S and SA and the good outcome I group more patients with UNI and SPD, with BPD patients equally distributed.

SIGNIFICANCE: I and SO are related to functional outcome. As recovery styles they appear linked to long-term trait personality characteristics as well as to type of psychopathology. They may prove useful in predicting and monitoring the recovery process of severely ill patients and useful for optimal matching of treatment strategy with individual recovery style (e.g., targeted drugs and investigative psychotherapy with I, and maintenance drugs and supportive psychotherapy with SO).

NR125 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

PREDICTING DIAGNOSTIC STABILITY IN AXIS I PSYCHOSES

Paul V. Williams M.D. Research Institute Chestnut Lodge 500 West Montgomery Avenue Rockville, MD 20850, Thomas H. McGlashan, M.D.

Summary:

We study the prediction of long term diagnostic stability and change in a cohort of Axis I schizoaffective (SA) and affectively disordered (AD) patients from the Chestnut Lodge Follow-up (FU) Study.

METHOD: FU diagnosis was assessed by interviewing patients 2–32 years post discharge (15 years average). FU diagnoses included SA, AD (bipolar and unipolar) and S (schizophrenia). Each patient's medical record was independently abstracted for baseline rediagnosis by DSM-III criteria and for ratings of multiple demographic and predictor variables. AT FU, baseline *SA* patients ($N = 60$) either retained a schizophrenic spectrum diagnosis (S or SA, $N = 45$) or changed to AD ($N = 15$). AT FU baseline AD patients ($N = 35$) either retained an AD diagnosis ($N = 21$) or changed to S or SA ($N = 14$). Separate discriminant function analyses (DFA) identified baseline variables predicting diagnostic stability and change in both of these baseline diagnostic groups (SA and AD).

RESULTS: Prediction was excellent. DFA predicted SA diagnostic stability and change with 98% sensitivity and 87% specificity, and predicted AD diagnostic stability and change with 100% sensitivity and 100% specificity. Inappropriate affect and earlier age at index admission were among the individual DFA variables predicting diagnostic stability in the SA group and diagnostic change in the AD group. Other predicting clinical variables will be presented along with the clinical implications of being able to estimate the stability of a patient's diagnosis.

NR126 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

TRAINING SCHIZOPHRENICS IN MEDICATION MANAGEMENT

Robert P. Liberman M.D. Psychiatry UCLA & VA Hospital Wilshire & Sawtelle Blvds Los Angeles, CA 90073, Thad Eckman, Ph.D., Catherine Phipps, M.S., Karen Blair, M.S.

Summary:

A structured and behaviorally-based program for training medication self-management skills in chronic schizophrenics requiring maintenance neuroleptic therapy was field tested in 28 facilities throughout the USA and Canada. The aims of the study were to determine the impact of the program—termed Medication Management Module—on patients' knowledge and use of medication as well as the fidelity with which mental health professionals could deliver the program. The Module consists of a highly prescribed Trainer's Manual, a Patient's Workbook, and a professionally made video that demonstrates the skills to be learned. The training is focused on four skill areas: identifying benefits of neuroleptic drugs; self-administration techniques; coping with side effects; and negotiating effectively with physicians. Patients learn these skills through active participation in such learning activities as modelling, role playing, problem-solving, in vivo and homework exercises. Half the field test sites received the Module in the mail and half sent two staff members to UCLA for a 2 day workshop on how to use the Module. Therapists' competency, as measured through direct observations at the field sites, was greater for those who attended the workshop, especially in conducting role plays and setting goals. Significant improvements were noted in patients performance on a behavioral role play test of generalization of skills learned in the 4 skill areas. Mean percent of skills demonstrated in the test increased from 42% to 70% from before to after the Module. The results indicated the utility and "export-ability" of a learning-based training program for independent living skills as one component in comprehensive services for the chronic mentally ill.

NR127 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

SUBSTANCE USE IN YOUNG ADULTS WITH SCHIZOPHRENIA

Mary Ann Test Ph.D. Social Work University of Wisconsin 425 Henry Mall Madison, WI 53706, Lynn Wallisch, M.A., Deborah Allness, M.S.W., William Knoedler, M.D., Katherine Ripp, M.S.W.

Summary:

This paper reports findings from a study of young adults with clearly defined schizophrenic disorders who also manifest significant use of street drugs. The purpose was to gain information from the patient's perspective about patterns, reasons for, and effects of substance use which would have treatment implications for this difficult to manage "dual problem" population.

Subjects were patients (ages 18–30) in an on-going longitudinal study of schizophrenics in an innovative community support program in Madison, WI. Case managers identified 63% of the males and 50% of the females as "significant substance users" by the criteria of current use of alcohol, marijuana, or other street drugs at least several times a week. A random sample of 29 of these "user" patients received in-depth interviews regarding their substance use.

Results revealed that substance use is heavy among this sample; that most show an early onset and a continuous pattern of use well before their first mental health contact; and that current use is maintained by powerful factors such as anxiety reduction, relief of boredom, and providing a means for social contact. Patients saw external interventions (e.g., money management) as most helpful. Providers need to assist patients in achieving the positive reinforcers they gain from drugs through other means.

NR128 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

NEGATIVE SYMPTOMS AND SOCIAL NETWORKS

N. Gregory Hamilton M.D. Psychiatry Portland VA - OHSU P.O. Box 1036 (116A-OPC) Portland, OR 97207, David L. Cutler, M.D., Catherine Ponzoha, M.A., Ronald M. Weigel, Ph.D.

Summary:

Researchers have found people with schizophrenia to have smaller, less complex, and less reciprocal social networks than non-psychiatric populations. This work, however, has not been further specified by examining positive versus negative symptoms in relation to networks. We hypothesized that among treated, chronic schizophrenic patients network variables would be abnormal when negative symtoms were prominent, but that there would be no relationship between positive symptoms and network variables.

Thirty-nine patients age 20 to 40 were studied. A DSM-III diagnosis of schizophrenia must have been present for at least two years with no diagnosis of organic mental disorder. Using Andreason's Scale for Assessment of Negative Symptoms (SANS) and Iager's Negative Symptom Rating Scale (NSRS), patients with more negative symptoms had significantly smaller social networks on Pattison's Psychosocial Kinship Inventory (rho = 0.47, P 0.05; rho = −0.64, P 0.01). Network size negatively correlated with all five SANS subscales. SANS scores also inversely correlated with all non-kin network variables such as multiplexity, instrumentality, reciprocity, and frequency. Unlike negative symptoms, positive symptoms, measured by Andreason's Scale for Assessment of Positive Symptoms, did not correlate significantly with any network variable. Neither did positive symptoms correlate significantly with negative symptoms. Eleven month follow-up confirmed these findings.

We discuss the research and treatment implications of diminished networks being associated with negative symptoms, but not with positive symptoms of schizophrenia.

NR129 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

THE NATURE OF SOCIAL SKILL IN SCHIZOPHRENIA

Alan S. Bellack Ph.D. Psychiatry Medical College PA 3200 Henry Avenue Philadelphia, PA 19129, Randall L. Morrison, Ph.D.

Summary:

Poor social competence is regarded as a hallmark of schizophrenia yet there is little data on precisely how schizophrenics perform in social encounters or why they fail to fulfill major social roles. One of the most widely accepted hypotheses is that their failure results from specific social skill deficits, but this contention has not yet received adequate empirical support. A more parsimonious explanation might be that the interpersonal difficulties result from more primary positive or negative symptoms. This research was designed to systematically study the social performance of schizophrenics in order: a) to determine whether they have specific and differential behavioral deficits, and b) to examine the validity of the social skill hypothesis.

Sixty carefully diagnosed (SADS) DSM-III schizophrenics were compared to matched groups of patients with Major Affective Disorder (25 bipolar, 5 major depression) and non-patient controls. Subjects were assessed on a battery of measures, including the BPRS, SANS, SAS-II, and a behavioral test of social skill. The results indicate that social competence is correlated with other symptoms, but is not a secondary manifestation. Both MAD patients and schizophrenics without negative syndrome had marked deficits in social skill. They scored significantly worse than non-patients on every measure of social functioning.

NR130 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

REHABILITATING SCHIZOPHRENICS IN A RURAL REGION

Hugues J. Cormier M.D. Ctr Hosp. Univ. Laval 2705 Boul. Laurier Bureau 4211A Sante-Foy, Que., Canada G1V 4G2, Gaston Guimond, M.D., Luc Allard, MP.s.

Summary:

This study aims to measure the effects of a rehabilitation program on 28 schizophrenic patients living in Portneuf, a vast rural region in Quebec. The major therapeutic and rehabilitation ingredients of this geographically decentralized program are services like case management, psychopharmacology, patient and family psychoeducation, and social skills training. The outpatients referred to the program and who met the DSM-III criteria of schizophrenic disorders were included in the study ($N = 28$). These patients were evaluated by a trained interviewer, independent of the clinical team. The evaluations were performed at the time of admission (T-0) and one year later (T-12). The effects of the program have been measured on three categories of outcomes: 1) the concordance between the need and use of 23 mental health services (measured for each service by the ratio: number of patients needing and using a service/number of patients needing that service); 2) community tenure the year before vs after the admission to the program; and 3) the level of disability on each of 14 items measured by the Disability Assessment Schedule of the WHO. The most important positive effects of the program were: 1) the improvement in the concordance between the need and use of psychosocial services like case management, social skills training and family support (respective concordance ratios of 0.11, 0.11 and 0.06 at T-0, compared to 1.00, 1.00 and 0.75 at T-12; $p < .001$); 2) the mean community tenure, which was 363 days the year after the admission compared to 334 days the year before ($p < .001$); and 3) the improvement in disability scores for self care, communication and underactivity. The implications of these findings for the organization of rural psychiatric services will be discussed.

NR131 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

WHAT DIFFERENCE DOES CASE MANAGEMENT MAKE?

Paula N. Goering, Ph.D. Social & Community Psych Clarke Institute 250 College Street Toronto Ont., Canada M5T 1R8, Donald Wasylenki, M.D., Marianne Farkas, Sc.D., William J. Lancee, MS.c, Ron Ballantyne, M.S.W.

Summary:

Case management has been defined as one of the essential elements of a community support system and there are now large numbers of mental health programs and workers with this title and function. Although studies have shown the positive impact of case management upon service utilization, client benefit has not been documented. This report describes the results of a 2 year follow-up study of client outcome for a rehabilitation case management program in Toronto. The program utilizes community-based practitioner's trained in Psychiatric Rehabilitation to do discharge planning and community service co-ordination. The study design is a comparison of the 24 month post-hospital outcome of 82 severely disabled clients with that of carefully matched historical controls from the same treatment settings. The Brief Follow-up Rating Scale is the data collection instrument. The experimental group differs significantly from controls with regard to occupational functioning, independent living situation, and social isolation. There is no difference in recidivism. Indications of improved quality of life for clients of a case-management program are no important validation of the effectiveness of this approach to service delivery. Even though short-term improvement may be unrealistic with such a severely disabled population, the long-term outlook is more optimistic.

NR132 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

PERCEPTUAL ABNORMALITIES OF ALZHEIMER PATIENTS

Richard C. Mohs Ph.D. Psychiatry VA Medical Center 130 W. Kingsbridge Road Bronx NY 10468, Bruno Giordani, Ph.D., John C.S. Breitner, M.D., Michael Davidson, M.D., Thomas B. Horvath, M.D., Kenneth L. Davis, M.D.

Summary:

Cognitive abnormalities observed in patients with Alzheimer's disease (AD) include memory loss, dysphasia and dyspraxia. Deficits in visual and auditory perception have rarely been described. As part of an ongoing longitudinal study of patients with AD and matched controls we have measured both visual and auditory thresholds using the method of limits. Patients were 38 males and 20 females, aged 55 to 89 years ($\bar{x}$ = 67 yrs) with an average of 12 years of education; controls were 45 males and 30 females aged 52 to 86 years ($\bar{x}$ = 65) with an average 14 years of education. For visual thresholds both one and two syllable words were presented tachistoscopically for durations of 1, 1/10, 1/25, 1/50 and 1/100 sec. Subjects tried to read each word presented. Although both patients and controls were able to read nearly all words presented for 1 sec. detection rates declined for briefer presentations and declined much more rapidly for AD patients than controls. This indicates that, although able to read the words, AD patients processed the visual stimuli at a much slower rate than did the controls. For auditory thresholds a pure tone of 750 hz. was presented at intensities from 70 db to below threshold in 5 db steps. Both ascending and descending orders were used and the subjects' task was to indicate whether they heard the tone on each trial. Both patients and controls detected all tones presented at 70 db; for softer tones detection rates decline and did so faster for patients than controls. These results indicate that on tasks requiring minimal memory, language and praxis skills, perceptual abilities of AD patients are impaired. These results, together with recent neuropathologic indicators of retinal impairment in AD pts., suggest that perceptual abnormalities may be an important and possibly specific, indicator of AD.

NR133 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

CSF BIOLOGICAL MEASURES IN ALZHEIMER'S DISEASE

Nunzio Pomara M.D. Clinical Division Nathan S. Kline Inst Orangeburg NY 10962, Peter A. Lewitt, M.D., Michael Stanley, Ph.D., Matthew Galloway, Ph.D., Garth Bissette, Ph.D., Carol Tamminga, M.D.

Summary:

Data from our previous work suggesting an increase in the activity of the hypothalamic-pituitary Adrenal Axis (HPA) in Alzheimer's disease together with reports of reductions in corticotropin-releasing factor (CRF)-like activity in cerebral cortex in AD, prompted us to do a study to determine whether alterations in CSF levels of CRF and cortisol occurred in AD. Additionally, because of relationships between adenohypophyseal hormone secretion, central nervous system monoaminergic activity, and melatonin secretion from the pineal, we also measured CSF levels of 5HIAA, HVA, MHPG, and melatonin as indirect indices of brain and pineal activity. Twenty-five individuals were included (forming two groups of 10 elderly controls and 15 with AD). All received diagnostic evaluations according to DSM III criteria. The two groups were of comparable age (controls 64.4 = 11.26, 7F; AD, 61.35 = 10.56, 8F). Fasting L.P.'s were done at approximately 9:00 a.m.

RESULTS: 1) CSF levels of CRF, melatonin, MHPG, cortisol showed no group differences. 2) CSF:5HIAA was significantly lower in AD (mean level± s.d. in normals 25.46± 5.27ng/ml; in AD, 18.48 = 4.54 $p<.002$) and HVA was also significantly lower (50.57 = 15.33ng/mg, 33.03 = 15.09ng/ml $p<.02$). 3) In AD, melatonin was negatively correlated with CSF cortisol ($p<.05$) but not with 5HIAA, HVA, MHPG.

CONCLUSION: The data suggest that significant reductions in CSF:HVA, and 5HIAA occur in AD without concomittant alterations in CSF:CRF, melatonin, MHPG and cortisol.

NR134 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

TREATMENT OUTCOME IN ORGANIC MANIA

Sashi Shukla M.D. Pychiatry Suny-Stony Brook Health Sciences Ctr T-10,020 Stony Brook, NY 11794, Anne Hoff, Ph.D., Thomas Aronson, M.D., Brian L. Cook, M.D., Lina Jandorf, M.A.

Summary:

The concept of organic mania (1) established that mania is not a homogenous syndrome as is commonly believed. It also raises important treatment questions. While there have been few single case reports suggesting that Lithium is efficacious during acute manic states, no systematic studies exist to date. Furthermore, data regarding the role of Lithium as a prophylactic agent against subsequent affective episodes or its safety in these patients is absent. We examined the efficacy of Lithium during acute manic episodes, in maintaining remission and the side effect profiles in 39 organic manic patients treated at a Lithium clinic.

The data indicates that during acute manic episodes Lithium alone was efficacious in only 13% of the sample, with 73% requiring either adjunct or separate trials of Carbamazapine or neuroleptics. Neurologic side effects ranged from moderate to severe in 51% of the sample. Patients on Lithium alone, during the maintenance phase of therapy had a 33% relapse rate compared to only 11% relapse rate in patients treated with other medication combinations. Patient profiles are discussed. Our findings appear similar to treatment outcome in mixed organic manics in Himmelhoch's report (2). The use of Carbamazapine and neuroleptics in these patients is discussed.

NR135 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

ATYPICAL MENTAL DISORDER OR TEMPORAL LOBE SYNDROME?

Dietrich Blumer M.D. Psychiatry Henry Ford Hospital 2799 W. Grand Blvd. CFP-3 Detroit MI 48202, Mary Heilbronn, Ph.D., Mark W. Shatz, Ph.D., Robert T. Simkins, D.O.

Summary:

Patients with various atypical psychiatric disorders who manifest labile moods and other traits typically associated with temporal lobe epilepsy (TLE), and have not responded to conventional psychiatric treatment, may represent a subictal temporal lobe syndrome. The present study compares 15 patients of this atypical group (AT) to 15 with TLE and 15 with a dysthymic disorder (DD).

The groups did not significantly differ in sex, age, education or race. Overall, the AT patients more closely resembled the TLE group, and both groups tended to significantly differ from the DD patients. 53% of AT patients had abnormal EEGs compared to 73% of the TLE and 13% of the DD patients. Blind neuropsychological test ratings provided global judgment of impairment for 26% of the AT group, compared to 60% of the TLE patients and 7% of the DD patients. The Bear-Fedio Scale scores were similarly high for the AT and TLE groups (40.7 and 47.5) compared to the DD group (27.5). A significant degree of depression was measured on the Hamilton Scale among all three groups, but rapid mood shifts were recorded on the Himmelhoch-Blumer Mood Scale for 80% of both the AT and TLE groups and for none of the DD patients. On the Family History-Research Diagnostic Criteria the groups showed similarly high prevalence of first-degree history of mental illness.

The results support the hypothesis that certain atypical psychiatric disorders represent a temporal lobe syndrome for which carbamazepine is the treatment of choice.

NR136 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

WHITE MATTER BRAIN INJURY AND DELUSIONS

Bruce L. Miller M.D. Neurology Harbor-UCLA Med Ctr 1000 West Carson Street Torrance, CA 90509, Ira M. Lesser, M.D., Mark Goldberg, M.D., Elizabeth Hill, R.N., Kyle Boone, Ph.D., Milton H. Miller, M.D.

Summary:

Large subcortical white matter lesions of various etiologies were, until recently, considered to be a rare illness diagnosable only at pathology. In recent years both computerized axial tomography (CT) and magnetic resonance imaging (MRI) have allowed for better radiographic delineation of such lesions.

In a prospective study of patients who developed psychosis after the age of forty-five, five patients were identified with extensive subfrontal white matter abnormalities on CT and MRI. These lesions were presumed to be vascular in etiology and four patients had poorly controlled hypertension. In all, the psychosis was the dominant clinical abnormality, and both dementia and motor findings were minor or absent. Unshakable delusions were present in all although many of the other features of schizophrenia were absent. A frontal syndrome with irritability, euphoria, and behavioral disinhibition was present. These cases demonstrate that CT and MRI are helpful in diagnosing a structural basis for some patients with late-life psychosis. White matter disease is an unusual but not rare predisposing factor for psychosis in the elderly and should be suspected in patients without a previous history of psychosis who develop delusions and/or a frontal syndrome.

NR137 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

SYMPTOMS OF DEPRESSION IN SENILE DEMENTIA OF THE ALZHEIMER TYPE

William J. Burke M.D. Psychiatry Washington University 4940 Audubon St Louis, MO 63110, Eugene H. Rubin, M.D., Martha Storandt, Ph.D., John C. Morris, M.D., Leondard Berg, M.D.

Summary:

The frequency of the symptoms of depression (Feighner criteria) were evaluated in 44 subjects with mild senile dementia of the Alzheimer's type (SDAT) and 58 matched controls enrolled in a longitudinal natural history study of SDAT. All were diagnosed by strict criteria which excluded affective disorder. Analysis of data obtained from the subjects and collateral source at entry, 15 and 34 months later showed significant increases from both sources in the mean number of symptoms in those with SDAT. This increase was due primarily to marked elevations in four symptoms as reported by the collateral source: loss of interest and energy, difficulty concentrating and psychomotor disturbances. The SDAT subjects reported fewer symptoms than did their collateral source significantly underreporting loss of interest, energy and difficulty concentrating. Aphasia did not account for this reduction; on the contrary, it was associated with an increase in mean number of symptoms. Symptom frequency reported by the collateral source correlated poorly with that of the subject but was strongly related to the severity of dementia rated by the Clinical Dementia Rating (CDR) scale ($r = .70$, $p < .0001$)

We believe these symptoms in this population might best be considered symptoms of dementia rather than depression. The frequency of these four symptoms in SDAT makes their routine use inadvisable in the diagnosis of depression in the cognitively impaired. We also stress the importance of obtaining information from a collateral source when dealing with such a population.

NR138 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

DIAGNOSIS OF ALZHEIMER SUBTYPES WITH PET SCAN

Gary W. Small M.D. Psychiatry UCLA NPI 760 Westwood Plaza Angeles, CA 90024, David E. Kuhl, M.D., Walter H. Riege, Ph.D., J. Wesson Ashford, Ph.D., Denson G. Fujikawa, M.D., E. Jeffrey Metter, M.D.

Summary:

We studied local cerebral metabolic rates (MR) using positron emission tomography (PET) in 26 patients with Alzheimer disease (AD). Following extensive clinical evaluations at entry into the study, 5 persons met NINCDS-ADRDA criteria for probable AD, and 21 persons met criteria for possible AD that changed to probable AD over the subsequent 24 months. At the time of PET scanning, dementia severity was in the mild to moderate range (mean Folstein Mini-Mental State Exam = 24.4±1.8 SD).

There were no significant differences in mean MR between early-onset (< 65 years; N=15) and late-onset (> 65 years; N=11) patients in 24 local regions, nor in parietal/cerebellar and parietal/caudate-thalamus ratios. When patients were further subgrouped according to sex, significant differences were found (adjusted $p > 0.01$). Late-onset men (N=6) had significantly lower mean MR than late-onset women (N=5) in both hemispheres for low frontal, caudate nucleus, thalamic, and cerebellar regions; and in the high frontal, posteroparietal, parahippocampal, putamen and global regions on the right only. Late-onset men (N=6) also had significantly lower mean MR than early-onset women (N=6) in parahippocampal and cerebellar regions in both hemispheres.

The results implicate sex and age at onset as factors in the diagnosis of AD. Moreover, MR differences in these patient subgroups argue for a heterogeneous disorder in Alzheimer disease.

NR139 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

IV NICOTINE TREATMENT OF ALZHEIMER'S DISEASE

Paul A. Newhouse M.D. Behavioral Walter Reed Army Institute of Research Washington, D.C. 20307, Trey Sunderland, M.D., Pierre N. Tariot, M.D., Allan Mellow, M.D., Brian Lawlor, M.D., Dennis L. Murphy, M.D.

Summary:

Treatment strategies for Dementia of the Alzheimer Type (DAT), have focused primarily on muscarinic cholinergic systems. However, direct augmentation of central nicotinic cholinergic function has not been previously attempted, although deficits in central nicotinic receptors have been described in the brains of DAT patients. We elected to study the effects of administering several doses of intravenous nicotine to DAT patients in an intensively designed pilot study. 6 nonsmokers, mean age 66.8 ± 8.8, who met DSM-III criteria for PDD, received separate infusions 48 hours apart of nicotine bitartrate (0.125, 0.25, and 0.5 μ/kg/min) or placebo for 60 minutes. Cognitive functioning, measured by tests of immediate and delayed free recall, category retrieval, and continuous performance, and behavioral assessments (i.e. Brief Psychiatric Rating Scale (BPRS), observer and subject visual analogue scales, and NIMH self rating scale), were made at 0, 30, 60, 240, and 500 minutes, and 24 hours. For the cognitive data, immediate intrusion errors showed a significant ($p=.02$) decline at both 30 and 60 minutes during drug administration on mid (0.25 μg) dose compared in placebo. Immediate free recall showed a trend ($p<.12$) towards an increase from baseline on mid dose, and word recall consistency showed a 35% improvement on mid dose compared to placebo. Total (24-item) BPRS score showed a significant increase on high dose compared to placebo (mean change =9.3, $p<.01$), most evident in the Anxiety/Depression subscale ($p<.05$). Observer visual analog ratings of depression showed a marked dose related increase which was significant by ANOVA ($p<.03$). Several individuals experienced frank anxiety or depressive symptoms while on drug, which occurred only once in 24 normal controls. These results suggest that nicotinic stimulation deserves further investigation as a treatment in DAT patients, and that nicotinic mechanisms may be more important in the cholinergic dysregulation in DAT, and in mood and affect regulation than previously realized.

NR140 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

AFFECTIVE FAMILY HISTORY IN SDAT AND DEPRESSION

Godfrey D. Pearlson M.D. Psychiatry Johns Hopkins Hospital 600 N Wolfe St 279 Meyer Baltimore, MD 21205, Christopher Ross, M.D., Barry W. Rovner, M.D., Larry E. Tune, M.D., Marshal F. Folstein, M.D.

Summary:

Depression, delusions, and hallucinations commonly arise for the first time in Senile Dementia of the Alzheimer Type, (AD). Genetic predisposition may contribute to the expression of such symptoms. Using chart review, we examined the natural history of psychiatric symptoms in 350 patients with NINCDS/ADRDA probable AD. Family histories of affective disorder were assessed using interviews by a trained rater of pedigrees, blind to the presence of secondary symptoms in probands. Several family members were contacted, and information sheets were sent to relatives. Affective disorder was rated positive in first degree relatives for histories of diagnosis and treatment of affective disorders or of suicide.

Of 41 AD probands with DSM-III depression, 21 (51%) had a history of affective disorder in a first degree relative. Of 104 AD probands without depression, only 9 (8.7%) had a family history of affective disorder (Chi square 29.9, p 0.001). There was no association between depression in AD probands and a family history of dementia, between delusions or hallucinations and family history of dementia or affective disorder. There were only 5 first degree relatives with schizophrenia, and they were associated with none of the secondary symptoms of AD.

Depression, which tends to occur early in the course of AD, appears related in part to a genetic vulnerability to affective illness, unlike hallucinations and delusions. Depression and hallucinations or delusions thus may have both differing etiologies and pathophysiologies.

NR141 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

PSYCHIATRIC SYMPTOMS IN CLINICAL ALZHEIMER DISEASE

Christopher A. Ross M.D. Psychiatry Johns Hopkins Univ 600 N Wolfe St. Meyer 279 Baltimore, MD 21205, Godfrey D. Pearlson, M.D., Barry W. Rovner, M.D., Larry E. Tune, M.D., Marshal F. Folstein, M.D.

Summary:

Depression, delusions, and hallucinations are common in Alzheimer's disease (AD), but their natural history has been relatively little studied. We reviewed the charts of 150 patients referred to the Dementia Research Clinic at Johns Hopkins Hospital meeting NINCDS/ADRDA criteria for probable AD. DSM-III criteria were used for the diagnosis of depression (except for ruling out "organic mental disorder"). We recorded probable age of AD onset, age and Mini Mental Status (MMS) exam at first visit, and age and MMS at the onset of each symptom. Seventy-one had neither depression, hallucinations, or delusions. Thirty-six had hallucinations or delusions (or both) without depression. Forty-three had depression (rarely, also with hallucinations or delusions). Latency from onset of AD to onset of depression (17.4 months) was significantly shorter than latency to onset of hallucinations (52.6 months) or delusions (40.4 months) (One way ANOVA, $F = 12.0$ $p < 0.001$; $t = 5.20$ and 3.78, $p = 0.01$ and 0.02 for t-tests between group means). MMS at onset of depression (20.3), was significantly higher than at the onset of hallucinations (10.4) or delusions (14.2) ($F = 8.30$, $p < 0.001$; $t = 4.67$ and 3.03, $p < 0.01$ and < 0.05). Behavioral problems (treated with neuroleptics) were significantly associated with delusions (85% of those with, versus 30% of those without, chi square 24.7, $p < 0.001$) and hallucinations (77% of those with, versus 48% of those without, chi square 6.84, $p = 0.009$), but not with depression. Differences in the latencies to depression versus hallucinations or delusions in AD suggest differing etiologies and pathophysiologies for these symptoms. The clinical importance of recognizing these symptoms is emphasized by their strong association with treatable behavioral problems.

NR142 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

LYMPHOPENIA IN PROBABLE ALZHEIMER'S DISEASE

Gary Tollefson M.D. Psychiatry St. Paul Ramsey 640 Jackson Street St. Paul, MN 55101, Michael Garvey, M.D., Erhard Haus, M.D., J. Bryan Warren, M.D., Michel C. Godes, R.N., Michael Luxenberg, Ph.D.

Summary:

Alzheimer's disease (AD) afflicts an estimated 2.5 million Americans. The high associated morbidity and mortality includes an enhanced susceptibility to infection. The various hypothesis of AD include both infectious and/or immunogenic mechanisms. The central nervous and immune systems share a number of common properties e.g. soluble chemical messengers, neurotransmitter receptors, and common antigenic determinants. We investigated absolute lymphoctye count in 25 rigorously diagnosed and staged AD patients. This cohort was compared to age-matched 1) healthy and 2) unmedicated hypertensive controls. ANOVA ($p<0.05$) and two-tailed T-test ($p<0.005$) analyses revealed lymphocyte numbers were significantly lower in the AD group than either control group. Analysis of serum albumin and cholesterol negated a possible "starvation" effect. Patient age or AD onset-age were not predictive of lymphopenia. However, Mini-Mental Status Score was positively correlated with absolute lymphocyte number ($p<0.001$). Staging of AD further supported an inverse relationship between cognitive deterioration and reduction in total lymphocyte count (Brief Cognitive Rating and Global Deterioration Scales). Single digits modality and word fluency testing also achieved significance ($p<.04$). This study confirmed lymphopenia within some AD patients and a positive correlation with degree of dementia and employed rigorous criteria, staging, medical controls, etc. The human lymphocyte offers a potential model for studying neurochemical changes in AD patients as well as individual response to pharmacologic probes. Lymphocyte properties and cognitive deterioration may serve to mark patients at risk for secondary infection.

NR143 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

A NEW SCALE ASSESSING DEPRESSED MOOD IN DEMENTIA

Trey Sunderland M.D. NIMH Building 10-RM-3D41 Lab of Clinical Sci 9000 Rockville Pike Bethesda, MD 20892, Ina S. Alterman, M.S.W., Donna Yount, R.N., James L. Hill, Ph.D., Pierre N. Tariot, M.D., Paul A. Newhouse, M.D., Dennis L. Murphy, M.D., Robert M. Cohen, M.D.

Summary:

Depression frequently accompanies dementia of the Alzheimer's type (DAT). In fact, estimates of concurrent mood disorder have ranged as high as 30–50% in DAT. And yet, there is a general paucity of rating instruments to measure depression in this population, thus necessitating the use of clinical observations and rating scales not originally designed for cognitively impaired subjects. Because of the potential therapeutic implications of quantifying concurrent depression, we have developed an objective scale specifically for the assessment of mood in demented patients. Twenty-one subjects (mean age $=67\pm10$ yrs) with mild-to-moderate DAT were tested with this new 24-item scale. Ratings were based on direct patient observation over time as well as a semi-structured interview observed by a group of trained professionals. Interrater reliability was high with an interclass correlation of 0.74 ($p<0.0001$) among the average of 7.2 raters per subject. Attempts at external validation revealed a highly significant correlation between the instrument's 17-item depression subscale total and separate global measures of depression ($r=0.73$, $p<0.0001$) and sadness ($r=0.65$, $-<0.0001$) but not cognitive and functional impairment, suggesting that this measure is selective for depressive mood rather than simply reflecting the degree of dementia. Individual items assessing depressed appearance, self-esteem, hopelessness, sense of enjoyment, suicidality, and responsiveness correlated most highly with the global depression score. We are currently testing the sensitivity of this scale to change within individual patients over time. While not intended to be diagnostic of depression, this new rating instrument should be quite useful in quantifying the severity of depressed mood in DAT and other cognitively impaired populations.

NR144 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

CAREGIVER STRESS IN DEMENTIA: PREDICTORS OF COPING

William Borden M.A. Social Service Univ of Chicago 969 E 60th St. Chicago IL 60637, Rhoda Frankel, M.A., Benedict L. Gierl, M.D.

Summary:

While an increasing number of clinical and research reports document stress-related dysfunction in family caregivers of older adults with chronic dementia, little is known about specific variables that place family members at risk for negative outcomes. In the present study spousal caregivers of elderly dementia patients completed interviews and questionnaires assessing variables in the following areas: 1) severity of patient impairment; 2) caregiver perceptions of a) specific behavioral problems associated with dementia, b) quality of marital relationship, and c) social support; 3) caregiver coping strategies; and 4) caregiver psychological well-being.

Preliminary analysis of results shows that objective measures of severity of patient impairment, behavioral problems and length of illness are not significantly related to caregiver outcomes. However, caregivers' perceptions of the stressfulness of dementia-related symptomatology and subjective appraisals of competence in mediating problems associated with the illness experience strongly correlate with psychological well-being. Perception of high levels of social support, satisfaction in the marital relationship, and use of active, problem-solving coping strategies are also associated with adaptive caregiver outcomes. In the clinical context, the results provide a rationale for the use of cognitive approaches in brief psychotherapy of caregivers and help to confirm the potential value of supportive networks in fostering caregiver adaptation over the course of the illness experience. In the research context, the findings affirm the importance of multidimensional, person-environment models in the study of caregiver stress, coping, and adaptation.

NR 145 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

THE CEREBELLAR-VESTIBULAR BASIS OF LEARNING DISABILITIES OR DYSLEXIA

Harold N. Levinson M.D. 600, Northern Boulevard Great, Neck, NY 11021

Summary:

Four thousand consecutively referred learning disabled (LD) cases were examined for evidence of a cerebellar-vestibular (c-v) dysfunction. Many cases fit the usual definition of dyslexia. A correlation between LD or dyslexia and c-v dysfunction was initially suspected because: 1) LD and "soft" signs were highly correlated; 2) "soft" signs invariably include balance, coordination and rhythmic disturbances, signs and symptoms usually indicative of a c-v dysfunction.

METHOD: All 4000 cases were examined for c-v dysfunction by utilizing three primary diagnostic categories: neurological examination, electronystagmography and optokinetic tracking.

DIAGNOSIS: To ensure reliability, the percent abnormal was determined on the basis of two or more abnormal parameters per diagnostic category.*

RESULTS: A computer analysis revealed: Ninety-eight percent LD evidenced abnormal ENG and/or c-v neurological and/or optokinetic examinations, 92% evidenced abnormal ENG and/or c-v neurological examinations, 72% evidenced abnormal ENG's, 82% evidenced c-v abnormal neurological testing, 73.5% (84%)** evidenced abnormal optokinetics vs 7% for random controls ($p.<001$), 78% demonstrated tunnel vision or single targeting vs 12% for random controls ($p.<001$). Diagnostic parameters as functions of sex and handedness as well as the relationship between c-v mechanisms and fears/phobias will be discussed.

SUMMARY: Analysis of data highlighted a significant correlation of LD with c-v dysfunction. Moreover, c-v mechanisms can readily explain most, if not all, the signs and symptoms characterizing LD as well as current LD theories and diagnostic/treatment modalities.

*Any *one* abnormal ENG and/or c-v neurological parameter is consistent with a dysfunctioning c-v system, according to the criteria utilized by Dr. Ken Brookler, chief of neuro-otology, Lenox Hill Hospital

**upon improvement in technique

NR146 **Tuesday, May 12, 12:00 noon—2:00 p.m.**

PSYCHIATRIC ILLNESS IN HIV-INFECTED MEN AND CONTROLS

J. Hampton Atkinson M.D. Psychiatry VAMC & UCSD 3350 LA Jolla Village Drive San Diego, CA 92161, Igor Grant, M.D., Caroline J. Kennedy, M.D., Douglas D. Richman, M.D., Stephen A. Spector, M.D., J. Allen McCutchan, M.D.

Summary:

Psychiatric complications in hospitalized patients with acquired immune deficiency syndrome (AIDS) and AIDS-related complex (ARC) are widely reported, but less is known of the lifetime psychiatric status of ambulatory men with AIDS, ARC, or of men infected with HIV (human immunodeficiency virus)) not meeting criteria for either AIDS or ARC. Our aim was to describe the lifetime prevalence and characteristics of psychiatric disorder in men infected with HIV, or at risk for infection. Using the Diagnostic Interview Schedule (DIS, Version III-A), Profile of Mood States (POMS), and Symptom Checklist-90 (SCL-90), we examined four groups of homosexual men and a comparison group of heterosexual men equated for age and socioeconomic status. The groups were (1) AIDS (N = 15); (2) ARC (N = 13); (3) Other HIV seropositive (N = 16); (4) HIV seronegative (N = 11); and (5) seronegative heterosexual (N = 22).

RESULTS: Lifetime prevalence of any DIS psychiatric disorder considering groups 1–4 was 80.2%. Prevalence of lifetime major depression was 30.4%; alcohol abuse/dependence 32.1%; other substance abuse 39.3%; and anxiety disorder (excluding phobias) 39.3%. There was no significant difference among groups 1–4 in prevalence of major syndromes. Over 30.3% experienced the onset of a DIS-disorder within the previous six months. Group 5 subjects had markedly lower proportions of major depression and anxiety disorder. POMS and SCL-90 were in moderately distressed range and did not differ between groups 1–4, but significantly exceeded group 5.

CONCLUSION: Lifetime and recent prevalence of psychiatric disorder among ambulatory men infected or at high risk for infection with HIV suggests careful longitudinal assessment and early intervention may be needed.

NR147 **Tuesday May 12, 12:00 noon–2:00 p.m.**

MISDIAGNOSIS AND UNDERTREATMENT OF AIDS REFERRALS

James J. Strain M.D. Psychiatry Mt. Sinai Sch. of Med. 1 Gustave Levy Place New York, NY 10029, George Fulop, M.D., Jay Strain, B.S.

Summary:

Although many reports describe clinical phenomena and symptoms of the AIDS patient in the general hospital, no systematic study has been conducted to date to compare this unique patient group with others seen in the routine psychiatric consultation setting.

METHOD: Examination of 1367 patients in 1982–86 by the psychiatric consultation staff at the Mount Sinai Hospital was recorded by using a 384-item computerized database protocol. Initial and termination items were in 5 domains: Demographic, problem precipitating consult, Mental Status Examination, DSM-III—5 Axes diagnoses, and recommendations.

RESULTS: The AIDS patients were significantly younger ($p < .01$), more likely to be male ($p = .0001$) and from medicine ($p = .0001$) than other consult patients.They did not differ with regard to race, education, employment, living situation (alone or with another), urgency of request, or personal help available. Reasons for referral were significantly different for coping (p .01), drug (p .01), and judgment ($p < .05$). The AIDS patient was more likely to have an Organic Mental Disorder secondary to a physiologic process ($p = .01$) and substance abuse disorders ($p = .0001$). AIDS patients had psychiatric in and out patient treatment recommended less often ($p = .01$), but more limit setting ($p = .0007$), follow-up treatment (5.6 ± 9 versus 3.5 ± 5, $p = .01$) were more likely to leave against medical advice ($p = .04$), and to die (18% versus 6.7% $p = .05$).

COMMENTS: The AIDS patients were less likely to be seen as having a cognitive deficit by the consultee, who overstated the problem as behavioral management or coping. The consultee was more likely to describe the AIDS patient as depressed and suicidal, while the consultant seldom diagnosed affective disorders. Although specific psychiatric inpatient and outpatient treatment was seldom recommended, several AIDS patients required intensive follow-up while on the medical wards.

NR148 **Tuesday May 12, 12:00 noon–2:00 p.m.**

NEUROPSYCHIATRIC FINDINGS, AND DEVELOPMENTAL PROBLEMS

George U. Balis M.D. Psychiatry Univ. of Maryland 645 West Redwood Street Baltimore, MD 21201, Spyros J. Monopolis, M.D.

Summary:

This paper presents data concerning the correlation of neuropsychiatric symptoms and EEG recordings in adult psychiatric patients to developmental disturbances in childhood. We used self-reported questionnaire, physician reports and EEG recordings in a cohort of 300 subjects. Based on their history of developmental problems, they were grouped as follows: 1. No developmental disturbances (control group), 2. Hyyperactivity, 3. Learning problem, 4. Behavior problem, 5. Attention deficit and Hyperactivity, 7. Attention deficit and Hyperactivity and Learning problem, 8. Attention deficit and Hyperactivity and Behavior problem, 9. Attention deficit and Hyperactivity and Learning problem and Behavior problem. Comparisions among groups showed the following significant differences: A) *History of brain insult*—common in groups 6,7,8,9. B) *Family history of epilepsy*—frequent in groups 7,8,9. C) *Neuropsychiatric symptoms*—mainly in groups 3,6,7,8,9. D) *Neuropsychiatric deficits*—in high degree in groups 7,8,9. E) *Baseline EEG records*—primarily in groups 2,3,5,6,7. F) *a-chloralose activated EEG records*—mostly in groups 2,3,6,7 and to a smaller degree in groups 4,8.

Our findings indicate that combined developmental disturbances in childhood (behavior problem, hyperactivity, learning problem, attention deficit) correlate positively with a)prenatal, perinatal and childhood pathology, b) family history of epilepsy, c) neuropsychiatric symptoms and deficits in adulthood d) EEG findings in adulthood. However, the latter were also common among single developmental disturbances.

NR149 **Tuesday May 12, 12:00 noon–2:00 p.m.**

COGNITIVE STATE EEG AND DRUG TOXICITY IN THE AGED

Ira R. Katz M.D. Psychiatry Medical Col of PA 3200 Henry Avenue Philadelphia, PA 19129

Summary:

We have investigated the relationship between EEG occipital background frequency performance on the Blessed Test (as modified by Fuld) in a group of geriatric outpatients to establish whether there were significant relationships between EEG frequency and performance, and whether excess slowing might indicate a reversible component to impairment. There is a significanat relationship between EEG (in CPS) and errors on the Blessed Test (B) in a group of 60 patients screened to rule out metabolic causes of dementia other than medications. ($EEG = 9.52 - 0.61 \times B$; $r = 0.43$, $p<0.01$). 24 of the patients had a history or evidence of stroke; EEG and Blessed score were unrelated in this group. ($EEG = 8.73 - 0.007 \times B$; $r = 0.05$). The relationship in the remaining 36 patients, however, was highly significant. ($EEG = 9.76 - 0.084 \times B$; $r = 0.62$ $p < 0.001$). Ten patients were taking medications with anticholinergic activity. They did not differ from the remainder in cognitive performance but did have slower EEG (8.85 ± 1.10 vs 7.85 ± 1.38; $t = 2.53$, $p<0.02$). Patients with EEG background > 1 cps slower than predicated from Blessed score were significantly more likely to be taking anticholinergic medication. Thus combined measures of EEG background and cognitive state may identify a group of patients likely to have drug toxicity. Supported by CRC Grant #MH5552.

NR150 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

LATERALITY, SYMPTOMS AND DIAGNOSIS

Bruce E. Wexler M.D. Psychiatry Yale University VA Medical Center 116A West Haven, CT 06516

Summary:

Dichotic listening tests were given to RDC schizophrenics (N = 11), schizoaffectives (N = 8), bipolar manics (N = 8), and major depressives (N = 14). One test consisted of words, the other of nonsense syllables. Relationships between dichotic scores and symptoms were followed up by comparing larger groups of schizophrenic (N = 31) and depressed patients (N = 38).

In the mixed diagnostic group of 41, asymmetry on the word and nonsense tests, in step-wise regression, accounted for a significant part of the variance in hallucinations ($p<.01$) and unusual thought content ($p<.05$). Regression coefficients for the two tests were opposite in sign for these and 17 of the other 22 BPRS items and factors ($p<.003$). In contrast, asymmetry scores on the two tests when weighted in the same direction accounted for a significant part of the variance in depression ($p<.005$). Consistent with this, depressed patients had greater right ear advantages than schizophrenics on both the word and nonsense tests ($p<.01$).

Opposite signs in regression weightings on the two tests suggest an alteration within the left hemisphere. Similar signs suggest an alteration in the balance between hemispheres. This is the first study to detect both these processes within a single study group and with the same experimental measures. Moreover, the data, while consistent with symptomatic differences between major diagnoses, indicate that associations between symptoms and pathophysiological processes extend across diagnostic categories.

NR151 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

PSYCHOPATHOLOGY AND SYDENHAM'S CHOREA

James A. Wilcox D.O. Psychiatry University of Iowa 500 Newton Road Iowa City, IA 52242, Henry A. Nasrallah, M.D.

Summary:

Sydenham's chorea is a movement disorder seen in rheumatic fever with basal ganglia pathology. This disorder has been associated with an increased frequency of psychopathology in both the acute choreiform stage and later in life.

We conducted a prospective study of 29 subjects with Sydenham's chorea and 29 age and sex matched controls. The patients were rated on both the occurrence of specific psychiatric syndromes and on the total number of psychiatric symptoms.

The total number of psychiatric symptoms ten years after the initial contact was much greater in the study group than in controls ($p<.0001$). Similarly, schizophrenia was more common in the study group compared to controls ($p<.025$).

Possible neuropathological associations are discussed.

NR152 **Tuesday, May 12, 12:00 noon–2:00 p.m.**

TWO-YEAR OUTCOME OF CAREGIVERS FOR CHRONICALLY ILL

Peter V. Rabins M.D. Psychiatry Johns Hopkins Hosp. 600 N. Wolfe St. Meyer 279 Baltimore, MD 21205, Melinda Fitting, Ph.D., James Eastham, Sc. D., James Zabora, M.S.W., Maria Poggi, M.S.

Summary:

30 cancer caregivers and 32 dementia caregivers were enrolled in a prospective longitudinal study of emotional state. Over a 2-year period there were no differences in emotional state or prevalence of emotional disorder between the two groups (MANOVA). Each group suffered rates of disorder twice that reported in the normal population. No specific pattern of emotional adaptation emerged; this supports the hypothesis that some caregivers suffer a "chronic grieving" state in which anger, depression, denial and guilt fluctuate but persist. Notably, a significant minority (30%) of subjects reported positive mood states.

The demented patients who were institutionalized had larger increase in the Blessed Dementia Rating Scale (7.1 ± 3.9 to 14.6 ± 2.8) than non-placed patients (6.19 ± 3.6 to 7.96 ± 2.8). Guilt scores in the Derogatis Affect Balance Scale declined in the caregivers of the placed patients ($p = .05$) but not in those remaining at home.

Negative emotional outcome (GHQ) was predicted by neuroticism ($p = .05$) and openness to experience ($p = .05$) while positive emotional state correlated with religious faith ($p = .001$) and number of social contacts ($p = .001$). ANCOVA demonstrated that number of social contacts correlated with positive outcome when extraversion was controlled for. This relationship held up for the 2 years of the study.

NR153 **Wednesday, May 13, 9:00 a.m.–10:30 a.m.**

SEASONAL VARIATION IN CLINICAL AND LABORATORY CHARACTERISTICS OF DEPRESSION

Roger F. Haskett M.D. Univ of Michigan D9702 Box 0118 UM Hospitals Ann Arbor, MI 48109, Kevin Murphy, Ph.D., Joan Kotun, M.D., James E. Shipley, M.D., Leon Grunhaus, M.D.

Educational Objectives:

To identify those characteristics of depression that show a seasonal variation. We will discuss the clinical relevance of this information and its effect on the presentation and course of depressive disorders.

Summary:

Although several characteristics of affective disorders are reported to show a seasonal variation, this association is particularly evident in a subgroup of patients with the diagnosis of Seasonal Affective Disorder (SAD). This has prompted the suggestion that there may be a relationship between the particular cluster of clinical features described in SAD and a general phenomenon of seasonal influences on depression. To explore this question in an unselected population of depressed patients, we examined clinical, DST and sleep EEG data obtained between 1977–1986 from 350 patients with Major Depressive Disorder (RDC) and a duration of episode <12 months. Patient variables were grouped separately by season of episode onset and season of presentation, in all patients, inpatients (IP) and outpatients (OP), and by diagnosis:unipolar-single (UP-S), unipolar-recurrent (UP-R), and bipolar (BP). There was no significant seasonal variation in the frequency of presentation, severity or DST result for the total group, but OP reported a maximum frequency of episode onset in the fall and a minimum in the spring. In BP patients, winter-onset depressions were more severe than summer-onset. Seasonal variation was also evident for certain clinical features associated with melancholia or SAD. An interaction between season and features of depression in a broad clinical population suggests that this relationship may not be confined to patients with SAD.

References:

[1]Parker G and Walter S: Seasonal Variation in Depressive Disorders and Suicidal Deaths in New South Wales. Br J Psychiatry 140: 626-632, 1982.

[2]Rosenthal NE, Sack DA, Gillin C, et al: Season Affective Disorder. Arch Gen Psychiatry 41: 72-80, 1984.

NR154 **Wednesday, May 13, 9:00 a.m.–10:30 a.m.**

COGNITIVE THERAPY VERSUS TCAS IN OLDER DEPRESSIVES

Gary L. Gottlieb M.D. Psychiatry Univ Pennsylvania 3400 Spruce St, 3 Piersol/4283 Phildelphia, PA 19104, Aaron T. Beck, M.D.

Educational Objectives:

To demonstrate the utility of individual intervention strategies in conservative management of geriatric depression.

Summary:

Until the present, no randomized trials comparing individual cognitive therapy (CT) and pharmacotherapy in the geriatric population have been reported.

39 adults over age 65, meeting DSM-III criteria for Major Depressive Disorder were randomly assigned to three 12-week treatment modalities: 1) Individual CT (twenty 45-minute sessions); 2) Nortriptyline (with brief weekly medication visits); 3) Individual CT and nortriptyline.

Thirty patients (10 in each cell) completed the protocol. 7 of the 9 dropouts left the study because they could not tolerate medication side-effects. The three groups who completed the study were well matched for age, sex, cognitive function and severity of depression ($p>.10$). Treatment outcomes between groups measured by Hamilton and Beck Inventory scores were virtually identical. All groups showed significant ($p<.001$) improvement in mean rating scale scores. About half the patients in each group experienced a greater than 50 percent reduction in pretreatment scores. No significant between group differences were found.

This pilot trial is the first randomized comparison of individual CT and pharmacotherapy in geriatric depressives. Each intervention was significantly effective. These data suggest that CT may be an important alternative treatment in frail elderly, often unable to tolerate antidepressant medications.

References:

[1]Jarvic LF, Mintz J, Stever J, et al: Treating geriatric depression: A 26 week interim analysis. J. Amer. Ger. Soc. 30:713-717, 1982.

[2]Gallagher D. Thompson LW: Treatment of major depressive disorders in older outpatients with brief psychotherapies. Psychotherapy: Theory Research and Practice 19:482-490, 1982.

NR155 **Wednesday, May 13, 9:00 a.m.–10:30 a.m.**

A FAMILY STUDY OF RAPID-CYCLING BIPOLAR ILLNESS

John I. Nurnburger, Jr. M.D. Psychiatry Inst. Psych. Research 791 Un. Dr., Ind. Univ. Med Ctr, Indianapolis, IN 46223, Juliet J. Guroff, M.S., Joel Hamovit, M.S.W., Wade Berrettini, M.D., Elliot S. Gershon, M.D.

Educational Objectives:

To evaluate the genetic aspects of rapid-cycling bipolar illness.

Summary:

Rapid-cycling bipolar illness has been the subject of great theoretical and clinical interest. We reviewed family study and clinic records to identify rapid-cycling bipolar (BP) or episodic schizoaffective (SA) patients (four or more episodes of illness within a 12-month period, excluding hypomanic episodes associated with antidepressant medication). Records of 202 patients were reviewed. Of these, 29 were judged to be rapid cyclers (13%). Twenty-five of the 29 were female (86%). These patients were matched with 29 of the remaining patients on the basis of age, sex, and mode of ascertainment. The age-corrected morbid risk for major affective disorder was 23.5% (11.9% BP/SA and 11.7% unipolar) in relatives cyclers (total N = 179) and 31.0% (12.3% BP/SA and 18.7% unipolar) in relatives of non-rapid cyclers (total N-189). Thus there is not evidence for increased genetic loading in families of a rapid-cycling proband. The incidence of rapid-cycling itself was also not different in the two groups of affectively ill relatives. Thus, it does not appear that rapid-cycling affective disorder "breeds true" within families. This evidence appears to support the hypothesis that rapid-cycling arises from factors (genetic or environmental) which are separable from the genetic vulnerability to bipolar illness itself.

References:

[1]Dunner DL, Fieve RR. Clinical factors in lithium carbonate prophylaxis failure. Arch Gen Psychiat. 30 229-233, 1974; Gershon ES, Hamovit J, Guroff JJ, Dibble E, Leckman JF, Sceery W, Targum SD, Nurnberger JI, Goldin LR, Bunney WE.

[2]A family study of schizoaffective bipolar I, bipolar II, unipolar, and normal control probands. Arch Gen Psychiat. 39 1157-1167, 1982.

NR156 **Wednesday, May 13, 9:00 a.m.–10:30 a.m.**

INCREASED ADRENAL WEIGHT IN SUICIDE VICTIMS

Athanasios P. Zis M.D. Psychiatry Univ. of British Columbia Health Sciences Centre Hosp. Vancouver BC, CANADA V6T 2A1, Katerina Dorovini-Zis, M.D.

Educational Objectives:

Depression—Psychobiology.

Summary:

It has been reported that the adrenal cortisol response of depressed patients to ACTH is increased, and that depressed patients compared to controls show a greater cortisol response to a given amount of ACTH released during stimulation with CRF. To explain these observations, it has been advocated that there is a progressive hypertrophy of the adrenal cortex in response to chronic hyperstimulation by ACTH during the course of depression. We report here data consistent with this hypothesis. The experimental material consisted of adrenal glands taken at the time of autopsy from 16 subjects who committed violent suicide and died immediately and from 10 individuals who had died suddenly from violent or natural causes (controls). We found a significant difference in adrenal weight between our suicide (9.77 ± 1.74 g) and control (7.74 ± 0.82 g) groups ($\bar{x}$ q SD in g) ($p<0.001$). The adrenal weight of nine suicide victims was greater than the highest value obtained in the control group. To our knowledge, an increase in the adrenal weight of suicide victims has not been documented before. Most of the subjects who commit suicide are mentally ill. Of those with a psychiatric disturbance, 40 to 60% suffer from depression. We assume that the observed increase in adrenal weight in our suicide group is accounted for by the preexisting psychiatric morbidity. This is compatible with the well-established phenomenon of progressive hypertrophy of the adrenal gland during the course of chronic stress. Our results are also consistent with reports of an exaggerated adrenal cortisol response to exogenous or endogenous ACTH in depressed patients and with the hypothesis that during the course of depression there is hypertrophy of the adrenal gland in response to chronic hyperstimulation by ACTH.

References:

[1]Gold PW, Chrousos G, Kellner C, Post R, Roy A, Augerinos P, Schulte H, Oldfield E, Loriaux DL: Psychiatric implications of basic and clinical studies with Corticotropin-Releasing Factor. Am J Psychiatry 1984;141:619-627.

[2]Neville AM, O'Hare MJ: The Human Adrenal Cortex. Berlin, Springer-Verlag, 1982.

NR157 **Wednesday, May 13, 9:00a.m.–10:30a.m.**

PLATELET 5-HT2 RECEPTORS: DEPRESSION AND SUICIDE

P. Anne McBride M.D. Psychiatry Cornell Medical College 525 East 68th Street New York, NY 10021, Richard P. Brown, M.D., Michael Demeo, M.D., John Keilp, M.A., Michael Stanley, Ph.D., J. John Mann, M.D., Barbara Stanley, M.D., Margaret Polley, Ph.D.

Educational Objectives:

To present results of ongoing research study.

Summary:

INTRODUCTION: The 5-HT2 receptor on the human platelet membrane has highly similar binding indices and pharmacological profile to the 5-HT2 receptor in human frontal cortex, and may serve as a model for the central receptor in clinical studies.
METHODS: Binding indices and physiological responsiveness of the platelet 5-HT2 receptor were assessed in 40 patients with major depression (24 with recent suicide attempts) and 35 healthy controls. Binding studies employed [125I] ILSD as radioligand, and ketanserin to define specific binding. The "Serotonin Augmentation Index" (SAI) was used to quantify the magnitude of 5-HT-mediated platelet aggregation in the presence of threshold concentrations of ADP.
RESULTS: Depressed patients more often showed high or low values for SAI (± 1SD from mean for controls) than controls ($p<.005$); high SAI were associated with lower scores on the Schedule for Interviewing Borderlines ($p<.04$), and low SAI higher scores ($p<.003$). Suicide attempters with high SAI had higher scores on the Linehan Lethality Scale for attempt severity, and were judged less manipulative and less easily rescued on the Suicide Intent Scale (all $p<.04$); those with low SAI had lower lethality scores ($p<.01$); and greater manipulative intent ($p<.04$). Distributions for values for KD and Bmax did not differ between patients and controls. Higher values for KD were found in attempters versus nonattempters and controls ($p<.007$). Attempters with high Bmax had higher lethality scores ($p<.01$).
CONCLUSIONS: High platelet 5-HT2 receptor number and responsiveness appear associated with more serious suicide attempts in major depressives, a finding consistent with our report of increased 5-HT2 receptors in frontal cortices of suicide completers. These measures may be potential markers for suicide risk.

References:

[1]Mann, J.J., Stanley, M., McBride, P.A., and McEwen, B. Increased Serotonin-Two and Beta Adrenergic Receptor Binding in the Frontal Cortices of Suicide Victims. Arch. Gen. Psychiatry 43:954-959, 1986.

[2]McBride, P.A., Mann, J.J., Polley, M.J., Wiley, A.J., and Sweeney, J.A. Assessment of Binding Indices and Physiological Responsiveness of the 5-HT2 Receptor on Human Platelets, in press.

NR158 **Wednesday, May 13, 9:00 a.m.–10:30 a.m.**

5-HT FUNCTION AND HISTORY OF SUICIDAL BEHAVIOR

Emil F. Coccaro M.D. Psychiatry Bronx VA Medical Center 130 West Kingsbridge Road Bronx, NY 10468, Larry J. Siever, M.D., Howard Klar, M.D., Lee Harter, R.N., Kim Owen, M.D., Kenneth L. Davis, M.D.

Educational Objectives:

To present data from patients with major depressive, or personality disorder which suggest that a life history of suicide attempt may be associated with a central serotonergic abnormality which in turn may be correlated with a life history of aggressiveness and impulsiveness in these patients.

Summary:

Data from CSF, brain receptor-binding, and pharmaco-challenge studies suggest diminished central 5-HT function in patients with past or recent history of a suicide attempt. We examined the PRL response to the 5-HT releaser/agonist fenfluramine (FEN: 60 mg po) in 45 patients with: Major Affective Disorder (MAD: N = 25), assessed by SADS, or DSM-III Personality Disorder (PD: N = 20), by SIDP. 13 of the 45 patients had history of at least one suicide attempt (SA+). 2 X 2 ANOVA revealed a significant effect of suicide ($p < 0.05$), a non-significant effect of diagnostic group and a non-significant interaction between the two, on mean peak delta PRL responsiveness to FEN. While peak delta PRL responsiveness to FEN in patients with violent SA+ was not significantly different from that in patients with non-violent SA+, patients with SA+ had greater clinician-rated histories of lifetime aggression, as assessed by the Brown-Goodwin Assessment for Lifetime Aggression ($p < 0.01$), and self-rated Barratt (7b) "Impulsiveness" ($p < 0.02$), Buss-Durkee "Motor-Aggression" ($p < 0.05$), MMPI "Psychopathic Deviance" ($p < 0.07$), and Zuckerman "Sensation Seeking" ($p < 0.08$). These data provide evidence that SA+ behavior may be related to both decreased central 5-HT function and lifetime history of aggression and impulsiveness in patients with MAD and PD.

References:

[1]Asberg M, Traksman L, Thoren P. 5-HIAA in the cerebrospinal fluid: A biochemical suicide predictor? Arch General Psychiatry 33:1193-1197, 1976.

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

NR159 **Wednesday, May 13, 9:00 a.m.–10:30 a.m.**

PSYCHOSIS IN BORDERLINE PATIENTS WITH DEPRESSION

Kenneth R. Silk M.D. Psychiatry Univ of Michigan, UH-9C 9150/0120, 1500 Med. Ctr Dr., Ann Arbor, MI 48109, Naomi E. Lohr, Ph.D., Drew Westen, Ph.D.

Educational Objectives:

To further the understanding of the types and frequency of psychotic-like symptoms in patients with borderline personality disorder.

Summary:

The presence of psychotic symptoms among patients with Borderline Personality Disorder (BPD) is controversial. We compared psychotic symptoms, measured by the Diagnostic Interview for Borderlines (DIB) in 24 (71% female) prospectively identified (by DIB), BPD inpatients who also met RDC criteria for Major Depressive Disorder (MDD), and 20 (50% female) MDD (RDC) inpatient (DIB < 5) controls. BPD patients were included if their DIB score was 7 or more *without* counting points on the DIB psychosis section, since scores on that section were the dependent variable. All patients were drug-free without neurological or medical problems; none were acutely psychotic. 50% of both groups were DST positive. MDD patients were significantly older with higher HDRS scores.

BPD patients had significantly more depersonalization/derealization experiences ($x^2 = 5.14$, $p < .03$). There were no significant differences on other DIB psychosis statements, though BPD patients showed a trend toward more sustained hopelessness/worthlessness and more brief paranoid episodes ($p < .10$). No BPD inpatients reported psychotic episodes while taking street drugs or alcohol, though 63% had abused substances within the previous 2 years. 70% of MDD patients received 0 or 1 point on the DIB psychosis section, a significant difference ($p < .01$). Most points for the MDD patients came from sustained hopelessness/worthlessness. Only 7 MDD patients received points on other psychosis statements, a significant difference from the borderlines ($p < .001$).

Our sample reveals that BPD patients do have "psychotic-like" symptoms, but true hallucinations or delusions, even transitory ones, are rare. The results suggest that depersonalization/derealization in borderlines is not related to affective disorder and weakens the hypothesis that BPD is a subgroup of affective disorder.

References:

[1]Pope HG Jr, Jonas JM, Hudson JI, et al: An empirical study of psychosis in borderline personality disorder. Amer J Psychiatry 142:1285-1290, 1985.

[2]Chopra HD, Beatson JA: Psychotic symptoms in borderline personality disorder. Amer J Psychiatry 143:1605-1607, 1986.

NR160 **Wednesday, May 13, 9:00 a.m.–10:30 a.m.**

A FAMILY HISTORY STUDY IN BORDERLINE PERSONALITY

Jeremy J. Silverman Ph.D. Psychiatry VA Medical 130 W Kingsbridge Bronx, NY 10468, Larry J. Siever, M.D., Howard Klar, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

Summary:

Possible familial/genetic relationships between borderline personality disorder and major depressive disorder were examined in 22 borderline and 24 other DSM-III personality disorder probands. Blind family history interviews with multiple informants were conducted using Family History RDC to assess major affective disorders and schizophrenia, and supplementary criteria to assess affective, impulsive and schizophrenia-related personalities in 94 first degree relatives of borderlines and 122 relatives of other personality disorders. The age-corrected morbid risk to relatives of borderlines for all affective related disorders (45.0%) was significantly greater ($p < .001$) than that found in relatives of other personality disorders (18.0%). By contrast, age-corrected morbid risk for all schizophrenia-related disorders was not significantly different between relatives of borderlines (7.8%) and relatives of other personality disorders (11.2%) suggesting that increase in psychiatric diagnosis of relatives of borderlines is not diagnostically non-specific. Morbid risks for affective and impulsive personality disorders, but not schizophrenia-related personality, were greater among relatives of borderline probands (affective personality, 10.6%; impulsive personality, 11.7%) compared to those of other personality disorder probands (affective personality, 2.5%, $p < .05$; impulsive personality, 2.5%, $p < .01$). Relatives of borderlines seem to possess, more so than relatives of other personality disorders, affective and impulsive symptoms and personality characteristics.

NR161 **Wednesday, May 13, 9:00 a.m.–10:30 a.m.**

CONFIRMATION OF PSYCHOSIS IN BORDERLINES

Paul S. Links M.D. Psychiatry McMaster University 50 Charlton Avenue East Hamilton L8N 4A6 ON, Canada, Meir Steiner, M.D., Jan Mitton, R.N.

Educational Objectives:

At the end of the presentation, the learner should be able to recognize the reasons for the association between Borderline Personality Disorder and psychotic symptoms.

Summary:

Comparing a large generalizable sample of inpatients with Borderline Personality Disorder (BPD) to inpatients with borderline traits, this paper will address the hypotheses proposed by Jonas and Pope (1984) regarding the association between BPD and psychotic symptoms: 1) narrowly defined psychotic symptoms are rare in BPD, 2) psychotic symptoms are due to concomitant disorders, 3) 'broadly defined' psychotic symptoms are often reported in BPD, 4) psychotic symptoms may be factitious. Consecutive admissions to inpatient services were screened for borderline features using Gunderson's discriminative characteristics and inpatients with 3 of 7 characteristics were examined using Diagnostic Interview for Borderlines (DIB) and SADS Current and Lifetime versions. The results suggested 1) Well defined delusions, hallucinations and ideas of reference were no more common in the DIB positive ($n=88$) vs DIB negative patients ($n=42$). 2) Psychotic symptoms when found were due to concomitant disorders. 3) Distrustfulness in the past week (DIB + vs DIB −; 2.06 vs 1.56, $t=2.08$, $p=.04$) and Depersonalization/derealization (DIB + vs DIB − ; 3.23 vs 1.83, $t=4.58$, $p<.005$) were more common in BPD patients. 4) The BPD patients were judged to be as reliable informants as non BPD patients (DIB + vs DIB −, 1.45 vs 1.63, $t=1.34$, n.s.) and psychotic symptoms when present fit conventional definitions. This data generally supports the proposed explanations for the association between BPD and psychotic symptoms except that the psychotic symptoms did not appear to be factitious.

References:

[1]Jonas JM, Pope HG; Psychosis in Borderline Personality Disorder, *Psychiatry Dev.* 4:295-308, 1984.
[2]Chopra HD, Beatson JA: Psychotic Symptoms in Borderline Personality Disorder. *Am J Psychiatry* 143: 1605-1607, 1986.

NR 162 **Wednesday, May 13, 9:00 a.m.–10:30 a.m.**

PERSONALITY DISORDER AND DEPRESSION: A FAMILY STUDY

Mark Zimmerman B.A. Psychiatry University of Iowa 500 Newton Road Iowa City, IA 52242, William H. Coryell, M.D.

Educational Objectives:

This presentation will describe a family study in which the relatives of normal controls and nonpsychotic depressed inpatients were interviewed with the Diagnostic Interview Schedule (DIS) and Structured Interview for DSM-III Personality Disorders (SIDP). The findings will be discussed in terms of the current controversy of whether it is more valid to subtype depressed patients by the presence or absence of melancholic symptoms or historical neurotic features.

Summary:

We interviewed 420 first-degree relatives of depressed patients and healthy controls with the Diagnostic Interview Schedule (DIS) and Structured Interview for DSM-III Personality Disorders (SIDP). The depressed patients were also interviewed with the SIDP and subdivided according to the presence or absence of any personality disorder.

Compared to the relatives of controls, the relatives of depressed patients without a personality disorder did *not* have an increased risk for depression, personality disorder, drug use disorder, alcoholism, panic disorder or obsessive-compulsive disorder.

The relatives of depressed patients with a personality disorder were characterized by an increased frequency of personality disorder, drug use disorder, alcoholism, and phobic disorder. The overall rate of major depressive disorder was also elevated; however this was only true when the major depressive disorder coexisted with a personality disorder or with a substance or anxiety disorder. The frequency of "uncomplicated" depression was similar in the relatives of the depressed patients with a personality disorder and in the relatives of the controls.

References:

[1]Zimmerman, M., Coryell, W., Stangl, D., Pfohl, B.: Validity of an operational definition for neurotic unipolar major depression. *J Affect Dis* (in press)

[2]Pfohl, B., Stangl, D., Zimmerman, M.: The implications of DSM-III personality disorders for patients with major depression. *J Affect Dis* (1984) *7*, 309-318.

NR 163 **Wednesday, May 13, 9:00 a.m.–10:30 a.m.**

DO PERSONALITY TRAITS AFFECT ANTIDEPRESSANT RESPONSE?

Eric D. Peselow M.D. Psychiatry NYU Medical School c/o 1322 East 84th Street Brooklyn, NY 11236, Faouzia Barouche, M.D., Paul J. Goodnick, M.D., Ronald R. Fieve, M.D.,

Educational Objectives:

To determine whether outpatients with major depressive disorder who have deviant personality traits have a significantly poorer response to antidepressant therapy.

Summary:

The purpose of this paper is to evaluate whether individuals with maladaptive personality traits/disorders who are suffering from an acute major depressive episode have a poorer response to antidepressant treatment.

Over the past three years, we have examined 112 patients with major depression who agreed to participation in one of three double-blind placebo-controlled outpatient protocols. At their intitial visits, the patients were rated with a Structured Interview for DSM-III Personality Disorders (SIDP), which examined personality traits in all 11 DSM-III personality disorder diagnoses.

Following a 4-10 day single-blind placebo period, all patients with significant depressive symptoms (Hamilton $>$ 18) were randomized to antidepressants (fluoxetine, clovoxamine, or imipramine) or placebo and treated in a double-blind manner over a 3-6 week period. Of the 77 patients randomized to drug treatment, 42 improved and 35 did not.

Our analysis noted that the total personality score (more deviant personality traits) was significantly higher for the drug non-responders vs. the drug responders. In addition, with respect to specific personality disorders, drug non-responders had significantly more borderline, antisocial, and narcissistic traits than drug responders.

References:

[1]Pfohl B, Stangl D, Zimmerman M: The Structured Interview for DSM-III Personality Disorders (SIDP). Department of Psychiatry, University of Iowa, Iowa City, Iowa, 1982.

[2]Pfohl B, Stangl D, Zimmerman M: The implications of DSM-III personality disorder for patients with major depression. J Affect Dis, 7:309-318, 1984.

NR 164 **Wednesday, May 13, 9:00 a.m.–10:30 a.m.**

VALIDITY OF STRUCTURED DSM-III-R AXIS II DIAGNOSIS

Andrew E. Skodol M.D. Psychiatry NYS Psych Institute Box 8 722 W 168th Street New York, NY 10032, David Kellman, M.D., John M. Oldman, M.D., Steven E. Hyler, M.D., Lyle Rosnick, M.D.

Educational Objectives:

From this presentation the listener will learn about recent developments in the structured assessment of personality disorders and about the potential strengths and limitations of cross-sectional diagnosis.

Summary:

As part of a study of the validity of structured assessments of DSM-III-R personality disorders, 50 consecutive applicants to a long-term inpatient treatment unit were interviewed with the Structured Clinical Interview for DSM-III-R, Patient Version (SCID-P) and its section for diagnosing personality disorders, SCID-II. Twenty-two patients had previously completed the Personality Diagnostic Questionnaire, Revised (PDQ-R), and 32 patients were interviewed with the Personality Disorder Examination (PDE). Although the median kappa coefficient of agreement between the two contrasting clinician-administered instruments for individual DSM-III-R personality disorders was only .39, acceptable kappas were achieved for several important diagnostic categories, including obsessive-compulsive (.73), dependent (.67), borderline (.58), and avoidant (.55) personality disorders. Kappas were generally higher for the putative personality disorder clusters than for the individual disorders themselves. The sensitivity of the PDQ-R for individual disorders (median .90 for SCID-II and .79 for PDE diagnoses) was higher than has previously been reported. Preliminary investigation of a longitudinal expert evaluation using all data (LEAD standard), based on a mean hospital stay of 7.7 months, revealed that cross-sectional assessment of personality disorders may be valid for certain categories. The results have significance for screening for personality disorders and for developing methods for their assessment in research studies.

References:

[1]Loranger AW, Susman VL, Oldham JM, Russakoff LM: The Personality Disorder Examination: a preliminary report. J Pers Dis 1: 1-13, 1987.

[2]Reich, J: Measurement of DSM-III, Axis II. *Comp Psychiatry* 26:352-363, 1985.

NR 165 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

THE EFFICACY OF LORAZEPAM IN PANIC DISORDERS

Dennis S. Charney M.D. Psychiatry Yale University 34 Park St New Haven, CT 06508, Scott W. Woods, M.D., Wayne K. Goodman, M.D., John H. Krystal, M.D., Linda M. Nagy, M.D., George R. Heninger, M.D.

Summary:

Controversy exists as to whether benzodiazepines (BZs) as a class are effective antipanic drugs or whether alprazolam is unique in this regard. To address this question, the antipanic efficacy of lorazepam was compared to alprazolam.

METHOD: Following at least three weeks of placebo, patients meeting DSM-III criteria for Agoraphobia with panic attacks or Panic Disorder were randomly assigned to receive alprazolam or lorazepam on a double-blind basis for 6 weeks. Standard ratings of panic attack frequency, generalized anxiety, depression, and global illness severity were obtained weekly.

RESULTS: Forty-eight patients completed the study. No substantive clinical change was observed during placebo administration. Both lorazepam and alprazolam treatment, respectively, resulted in rapid reductions in panic attack frequency by the end of the first week (4.8 ± 1.5 to 1.4 ± 0.4; 4.2 ± 0.8 to 1.4 ± 0.5) which was maintained for the rest of the study. By the end of 6 weeks, lorazepam and alprazolam treatments, respectively, resulted in similar decreases in global illness severity (6.8 ± 0.4 to 5.1 ± 0.8; 6.6 ± 0.4 to 4.2 ± 0.5). The final doses of lorazepam were 6.2 ± 2.5 mg/day and alprazolam 2.7 ± 1.3 mg/day.

IMPLICATIONS: The results of this study and others investigating BZs such as clonazepam suggest that alprazolam is not unique among BZs in possessing antipanic efficacy. It is likely that most, if not all, BZs will be antipanic at high doses. Additional investigations are required to determine if alprazolam, in contrast to other BZs, has antidepressant effects.

NR 166 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

LORAZEPAM TREATMENT OF PANIC DISORDER

Elizabeth F. Howell M.D. Psychiatry Medical Univ of SC 171 Ashley Ave Charleston, SC 29425, Michele Laraia, M.S.N., James C. Ballenger, M.D., Bruce Lydiard, M.D.

Summary:

Alprazolam blocks panic attacks and decreases anticipatory anxiety and avoidance behaviors in patients with Agoraphobia with Panic Attacks. We hypothesized that lorazepam, in doses comparable to alprazolam, would treat Agoraphobia with Panic Attacks. We compared the efficacy of lorazepam, to phenelzine, a widely accepted pharmacologic treatment for Panic Disorder, in an open, flexible-dose management trial. Patients were randomly assigned to either lorazepam or phenelzine, and also attended three months of weekly behavioral group therapy sessions.

Three months of treatment have been completed by 22 patients on lorazepam doses of 1 to 7 mg/day and by 22 patients on phenelzine doses of 30 to 75 mg/day. When prescribed in a behavioral group therapy setting, both medications blocked panic attacks, and decreased anticipatory anxiety and phobia severity. Onset of anti-panic action was within 1 to 2 weeks for lorazepam and 4 to 6 weeks for phenelzine. Lorazepam side effects began rapidly and included sedation, drowsiness, and depression. Phenelzine side effects were delayed, and included muscle jerking and twitching, weight gain, swollen extremities, and sexual dysfunction.

Results will be discussed in detail at the time of presentation, using data from the completed samples, which will contain 25 to 28 subjects in each cell.

NR 167 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

ALPRAZOLAM VERSUS CLONAZEPAM IN PANIC DISORDERS

Mark Pollack M.D. Psychopharmacology Mass General Hospital 15 Parkman Street Boston, MA 02114, Jerrold F. Rosenbaum, M.D., George Tesar, M.D., John B. Herman, M.D., Gary S. Sachs, M.D., Lee S. Cohen, M.D.

Summary:

We have extensive experience using clonazepam, a high potency benzodiazepine with a long half-life (T½ 20–40 hours), in the treatment of panic attacks and have assessed its efficacy in a number of open studies. We have undertaken a double blind, random assignment (N = 60) clinical trial comparing clonazepam (0.5 mg tablets up to 5.0 mg a day), alprazolam (1.0 tablets up to 10 mg a day) and placebo.

We will briefly review our early data and present our results on the first 45 patients randomized. Diagnosis of Panic Disorder (uncomplicated, with limited, or with extensive phobic avoidance) was made with the SCID-Up (DSM III-R criteria). Patients were assessed at six weekly intervals and kept daily diaries of the severity and duration of panic attacks (limited symptoms, situational, and spontaneous attacks) and degree of anticipatory anxiety. Major outcome measures to be presented include frequency and severity of panic attacks, extent of phobic avoidance, depression ratings, patient and clinician anxiety and clinical global improvement ratings, and side effect reports.

Our initial hypotheses were that (1) there would be no significant difference in the number of patients on either alprazolam or clonazepam showing at least moderate reduction in number of panic attacks and (2) both active agents would prove superior to placebo.

NR168 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

FAILURES IN EXPOSURE, TREATMENT OF AGORAPHOBIA

Iver Hand M.D. Psychiatric Univ. Clinic Martinistr. 52 D2000 Hamburg 20, W. Germany, Martina Fischer, Jörg Angenendt

Summary:

On the 1986 APA Conference we have presented two follow-up (FU) studies with altogether 260 agoraphobics, 1–4 or 6–9 years after exposure treatment without medication. Some 30% of the patients proved to be failures at FU. We have now reanalyzed failure patients and will present data regarding the following topics: 1. Problems in operationalization of "failure". 2. Level of anxiety/depression and outcome with mere exposure. 3. Subtypes of failure: chronic failure (in treatment and FU); treatment gainer with intermittent relapses during FU; treatment gainer with chronic relapse in FU. 4. Chronic failures—are they due to endogenous panic-depression, chronic neuroses or repeated aversive life events—i.e. where is *really* a case for antidepressant or anxiolytic medication.

NR169 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

LONG-TERM EFFECTS OF BEHAVIOR THERAPY FOR GAMBLERS

Iver Hand M.D. Psychiatric Univ. Clinic Martinistr. 52 D2000 Hamburg 20, W. Germany, Rüdiger Klepsch, Aygumnt Walzlo

Summary:

Pathological gambling has become a major mental health and economical problem in several countries. The few treatment programs so far available are usually derived from an addiction-model (c.f. DSM-III), whereas we have conceptualized gambling as an unspecific symptom behavior in the context of a variety of potential causal disorders. Since 1977, we have treated more than 150 gamblers with short-term outpatient behavior therapy. For 112 of these we now have follow-up data 1–8 years after treatment. Multivariate outcome assessment will be presented, including an abstinence rate of 35% and an additional 30% "satisfactory improvement". Our program is regarded complementary, not contradictory to existing addiction-model treatments. Some ideas will be presented as to when which of the programs may be preferable to the individual.

NR 170 **Wednesday, May 13, 12:00 - 2:00**

FIVE-YEAR RELAPSE RATE AFTER PHOBIA TREATMENT

Charlotte M. Zitrin M.D. Phobia Clinic Hillside Hospital PO Box 38 Glen Oaks, NY 11004, Maryann Juliano, Ph.D., Michael Kahan, M.D.

Summary:

Phobic patients, who successfully completed a controlled treatment study comparing behavior therapy (systematic desensitization) and supportive psychotherapy, combined with imipramine or placebo (double-blind), were followed for 5 years after completion of treatment. The patient sample was 161, divided into 3 diagnostic categories: agoraphobic, simple phobic, and mixed phobic (now called panic disorder with agoraphobia). A total of 31 patients relapsed. The overall relapse rate according to diagnosis was: agoraphobic—17.5%; simple phobic—18.3%; mixed-phobic—22.7%. Overall relapse rate according to treatment was: behavior therapy + imipramine—18.2%; behavior therapy and placebo—19.2%; supportive psychotherapy and imipramine —20.4%. There were no significant differences between sexes, diagnostic groups, or treatment groups and there was no significant diagnosis x treatment interaction.

Of the 31 patients who relapsed, 45.2% (14) relapsed in the first post-treatment year and 28.5% (8) in the 2nd year. Thus, the vast majority (73.7%) of relapses occured within the first 2 post-treatment years.

Tables describing these findings will be presented, as well as details of the differences found between relapsers and non-relapsers, and details on dropouts.

NR171 **Wesnesday, May 13, 12:00 noon–2:00 p.m.**

COURSE OF PANIC DISORDER

Diana P. Sandberg M.D. Anxiety Clinic NYS Pyschiatric Inst 722 West 168th Street New York, NY 10032, Mark Gallops, M. Phil., Jack M. Gorman, M.D., Michael R. Liebowitz, M.D., Donald F. Klein, M.D., Abby Fyer, M.D.

Summary:

PURPOSE: To describe prospectively the course of medication-free, remitted panic disorder patients and to examine the relationship between course and life events using both prospective and retrospective data.

METHOD: Patients are followed at regular intervals by a research psychiatrist and measures made of panic, near panic, anticipatory anxiety, phobic avoidance, generalized anxiety, depression, alcohol and drug intake, and life events. Panic disorder and agoraphobic patients fill out a retrospective life events form at intake and on another day are administered the SADS-LA. Identical data is collected from their well siblings, and life events prior to onset of the anxiety disorder are compared in the matched proband—sibling pairs.

RESULTS: Prospective pilot data on eight patients followed from 3–18 months show several patterns: 1)Symptom free remission; 2) Symptom free remission interrupted by a burst of spontaneous panic attacks and then return to full remission; 3) Regular panic attacks without the distress or disability on initial presentation; 4) Multiple symptoms of depression and anxiety without meeting criteria for either disorder. The retrospective data on life events will be compared with pilot prospective data.

SIGNIFICANCE: The heterogeneity of course and temporal sequence of symptom formation in our sample, as well as the relationship of life events to course, will generate etiologic hypotheses for further study and provide useful information for clinicians and their patients.

NR172 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

REGIONAL CEREBRAL BLOOD FLOW IN PANIC DISORDER

Harold H. Harsch M.D. Psychiatry Medical College WI 8700 W. Wisconsin Ave Box 175 Milwaukee, WI 53226, Michael Goldstein, Ph.D., Robert S. Hellman, M.D., Laurens, D. Young, M.D., Ronald S. Tikofsky, Ph.D., B. David Collier, M.D.

Summary:

Using positron emission tomography to measure regional cerebral blood flow (rCBF), Reimann, et al, demonstrated consistent right greater than left hemispheric asymmetries in parahippocampal blood flow for subjects with lactate sensitive panic disorder. Single photon emission tomography (SPECT) with 1–123 iodoamphetamine (IMP) is another, less expensive technique for study of rCBF. We have developed a new, semiautomated SPECT/IMP method for quantification of (1) right to left hemispheric differences in rCBF and (2) the ratio of right to left hemispheric rCBF. Initially, six untreated subjects with panic disorder (DSM-III criteria, three with strong and three with weak responses to lactate infusion) were studied with SPECT/IMP. SPECT/IMP was repeated for each subject three months after successful treatment. SPECT/IMP studies for seven normal subjects were used as a control population. Unlike Reimann, et al., we failed to demonstrate any significant asymmetry in IMP uptake in the right parahippocampal area associated with the lactate sensitive panic disorder. SPECT/IMP studies for weak and strong lactate responders were indistinguishable. Difference and ratio images of rCBF showed a heterogeneous distribution of asymmetries. In conclusion, using the SPECT/IMP technique, no consistent changes in parahippocampal blood flow and metabolism were associated with lactate sensitive panic disorder.

NR173 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

CEREBRAL VENTRICULAR SITE IN PANIC DISORDER

Charles H. Kellner M.D. Psychiatry Med. Univ. of SC. Clinical Sciences Ctr Suite 604 Charleston, SC 29425, Thomas W. Uhde, M.D.

Summary:

Enlargement of the cerebral ventricles has been reported in schizophrenic and affectively ill patients. Possible neurobiological links between panic disorder (PD) and major depressive disorder have been hypothesized. For these reasons, we investigated cerebral ventricular size in patients with PD. Brain CT scans were performed in 25 PD patients (12 M, 13 FM, aged 22-48 years, mean 35.2±6.7 SD yrs). Several clinical variables and lifetime exposure to benzodiazepines (BZP) were calculated in all patients. Twenty-three patients were drug-free at the time of the study. Ventricular-brain ratio (VBR) was measured by the method of Synek and Reuben (1976).

Results: Mean VBR was 3.4±2.4 SD (range 1.0-9.0). VBR's for patients who had a history of major depression (N=7, 28%) (2.9±1.5) or severe agoraphobia (N=7, 28%) (3.2±1.5) did not differ from the patients without a history of depression (3.6±2.6, $t=0.65$, $df=23$, $p=NS$) or severe agoraphobia (2.6±3.5, $t=0.28$, $df=23$, $p=NS$). There was no significant association between VBR and age ($r=-0.06$, $p=NS$), panic attacks ($r=0.04$, $p=NS$), or state anxiety ($r+0.19$, $p=NS$). There was a significant association between VBR and duration of BZP use ($r=0.51$, $p<.02$) and percentage of time ill treated with BZP ($r=0.67$, $p<.001$), although the mean VBR (3.8±2.5) of the PD patients who had received BZP treatment was similar to the patients without previous BZP exposure (2.5±1.6; $t=1.26$, $df=23$, $p=NS$).

Discussion: The ventricular size of PD patients falls well within the normal range compared with reported VBR values for normal controls in the literature. The nature of the relationship between VBR and duration of BZP exposure remains unclear. These findings will be discussed within the context of current theories regarding the biological determinants of ventricular size.

NR174 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

CHRONIC BENZODIAZEPINE USE: ABRUPT DISCONTINUATION

Edward E. Schweizer M.D. Psychiatry U of Pennsylvania 3400 Spruce St, 203 Piersol BL Philadelphia, PA 19104, Karl Rickels, M.D., W. George Case, M.D.

Summary:

We report here preliminary results of an NIMH supported study (MH-08957) examining the effect of abrupt discontinuation of a benzodiazepine (BZ) in a cohort of patients with a chronic daily BZ use of greater than 1 year. Sixty-one patients were prospectively and blindly assigned to either continue on their BZ (N = 10) or to undergo placebo substitution (N = 51). There was no pseudowithdrawal observed in those patients continued on their BZ. Twenty-four (47%) of the abrupt withdrawal group were on short half-life compounds (mean daily dose in diazepam equivalents = 19.1 mgs; mean duration of BZ use = 4.3 years); twenty-seven (53%) were on long half-life compounds (mean daily dose = 12.1 mgs; mean duration of BZ use = 10.1 years). Twenty (83%) of the short half-life patients, and 16 (59%) of the long half-life patients reported a significant withdrawal reaction. Fifty percent of patients on short half-life BZs and 26% of patients on long half-life BZs were unable to complete 7 days of abrupt withdrawal. Maximal withdrawal occurred significantly earlier for short than for long half-life BZs ($p < .0001$). Twenty-three of 51 patients (45%) continued off all BZs for more than 4 weeks. Further aspects of BZ withdrawal will be reported on and their implications for clinical practice discussed.

NR175 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

PANIC DISORDER, VERTIGO, AND THE PROTIRELIN TEST

Cary L. Hamlin M.D. Psychiatry Morristown Hospital 100 Madison Ave. Morristown, NJ 07960

Summary:

Recent work has drawn attention to a possible vestibular problem in Panic Disorder, and has demonstrated a blunted Protirelin Test compared to controls. Twenty-three panic disorder females (DSM-III criteria) who did not also meet criteria for a major depressive episode, denied drug abuse, and were on no medications were divided into groups based upon the presence or absence of the symptoms of vertigo and visual movement illusions during their attacks. Both groups received protirelin tests, and TSH levels in plasma were drawn at 0,15, and 30 minutes after 500 micrograms of TRH given intravenously. Samples were also assayed for thyroxine and thyroid uptake by radioassay methods at Psychiatric Diagnostic Laboratories of America. The 13 Panic Disorder alone patients had a mean delta TSH of 10.72 + 3.49 (std.), and TSH of 1.68 + .71 uIU/ml. The Panic Disorder with Vertigo group of 10 patients had a mean delta TSH of 18.46 + 3.12 (std.), and TSH of 2.89 + 1.49 uIU/ml. The students "T" score on the delta TSH means difference was 6.1, $p = .01$. The "T" score on the TSH means difference was 2.6 which is also highly significant. These data support the hypothesis that panic disorder with vertigo may be neuroendocrinologically a different disease from panic disorder without vertigo. There were no significant differences between groups in panic frequency, state or trait anxiety, or Beck's Score.

NR176 **Wednesday, 13 12:00 noon–2:00 p.m.**

CORONARY-PRONE BEHAVIOR AND ADRENERGIC RECEPTORS

Jeffrey P. Kahn M.D. Psychiatry Columbia University 722 West 168th St. P.O. Box 87 New York, NY 10032, Arthur Perumal, Ph.D., Robert Gully, T. Smith, Thomas B. Cooper, M.A., Donald F. Klein, M.D.

Summary:

Coronary arterial vasospasm may be a major pathogenetic factor in the development of coronary artery disease, and is substantially regulated by alpha-adrenergic vasoconstriction and beta-adrenergic vasodilatation. Coronary-prone behavior has been reported to predict exaggerated autonomic response to stress, but has not been specifically examined in relation to alpha- and beta-adrenergic subsystems.

Under controlled conditions, blood samples were obtained from 13 healthy male subjects, ages 22 to 32, with family histories of early coronary artery disease, for determination of lymphocyte $beta_1$-adrenergic receptor density and platelet $alpha_2$-adrenergic receptor density. Subjects were given the Rosenman-Friedman Structured Interview for Type A behavior. Coronary-prone behavior correlated significantly with lymphocyte $beta_1$ receptor density ($r = +0.55$; $p = 0.026$; two-tailed) but not with platelet $alpha_2$ receptor to alpha2 receptor densities ($r = +0.74$; $p = 0.002$.)

Since receptor densities may be inversely correlated with receptor stimulation, coronary-prone behavior thus may predict a relative preponderance of peripheral alpha-adrenergic activation. Such an association would be consistent with coronary artery alpha-vasoconstrictive predominance in coronary-prone individuals. These findings await confirmation in larger populations.

NR177 **Wednesday, May 13, 12:00 noon–2:00p.m.**

IDIOPATHIC CARDIOMYOPATHY AND PANIC DISORDER

Jeffrey P. Kahn M.D. Psychiatry Columbia University 722 West 168th St. P.O. Box 87 New York, NY 10032, Ronald E. Drusin, M.D., Donald F. Klein, M.D.

Summary:

Idiopathic dilated cardiomyopathy may be the most common indication for cardiac transplantation. Though little is known about its pathogenesis, both viral and autonomic etiologies have been proposed. An increased incidence of cardiovascular death has been reported in panic disorder patients. Routine psychiatric consultation on cardiac transplantation candidates provided an opportunity to assess prevalence of panic disorder in idiopathic cardiomyopathy and other endstage cardiac diseases.

Of 35 patients with idiopathic cardiomyopathy, 82% had definite or probable panic disorder. Of 18 patients with post infarction cardiac failure, on 23% had definite a probate panic disorder (Mann-Whitney $U=530.5$; $p<0.001$); and of 7 patients with congenital or rheumatic heart disease, none had panic disorder (Mann-Whitney $U=221.5$; $p<0.01$). Eleven patients with idiopathic cardiomyopathy and panic disorder showed rapid response of panic disorder to alprazolam treatment.

Panic disorder thus may be common in endstage idiopathic cardiomyopathy, but not in other endstage cardiac disease. Neither psychological distress nor cardiovascular dysfunction are sufficient to explain this observation. Autonomic mechanisms could underly the association of panic disorder and cardiomyopathy. Panic disorder could lead to increased cardiac sympathetic tone or circulating catecholamines, with consequent myocarditis and cardiomyopathy. Further studies, blind to cardiac diagnosis, will be needed to explore these hypotheses.

NR178 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

PSYCHIATRIC MORBIDITY IN CHEST PAIN PATIENTS

Peter J. Geier M.D. Psychiatry Univ. Cinn. Coll Med. 231 Bethesda Ave ML 559 Cincinnati, OH 45267, James R. Hillard, M.D., Lawson R. Wulsin, M.D.

Summary:

It is possible that many patients seen for chest pain in medical emergency departments suffer from panic disorder or depression. These disorders may be under-recognized and untreated in this population. We examined thirty-seven patients who were not hospitalized after being seen in the University Hospital Emergency Department (ED) for a chief complaint of chest pain. They filled out the CES-D and were interviewed with the panic disorder section of the SADS, modified to reflect DSM-III-R criteria for panic disorder.

Twenty-seven patients (73%) met criteria for panic attack at the time of their ED visit. Twelve patients (32%) definitely met criteria for panic disorder and two more (5%) possible met criteria. Twelve (32%) met CES-D criteria for depression. Six of the twelve patients with definite panic disorder were also depressed. Only 9% of patients had been diagnosed in the ED as having "anxiety as a major component of chest pain."

After screening, 27% of the patients were referred for psychiatric treatment. Only 30% of those completed the referral. These results demonstrate that a small percentage of patients with panic disorder and depression are being identified in the medical ED and most of those referred for psychiatric treatment fail to follow-up.

NR179 **Wednesday, May 13, 12:00–2:00**

NEUROENDOCRINE RESPONSES TO CLONIDINE IN MENTAL ILLNESS

Patrick J. Rogue M.D. Centre Hospitalier Spec Serv DU DR Macher Rouffach 68250 France, Fabrice Duval, M.D., Jean-Luc Deliry, M.D., Marc-Antoine Crocq, M.D., Christian Beaubernard, Ph.D., Jean-Paul Macher, M.D.

Summary:

To further investigate alpha-2 adrenergic function in depression we administered, after a minimum 10 day washout, clonidine (5microg/Kg) orally to patients with either DSM-III Major Depression (MD), Schizoaffective Disorder (SZAD), or Schizophrenia, and compared their plasma ACTH, Cortisol, and GH responses. The DST, cortisol cycle (blood sampling every 3 hours), and 24-hour urinary levels of norepinephrine and its catabolites were also studied. Analysis of results for a preliminary series of 29 cases (♂/♀ = 13/16) and 7 controls ♂/♀ = 2/5; age = 34.5 yrs ± 7.6) showed:

1. A blunting of the GH response to clonidine ($F_{2,26} = 6.735$, $p < .001$) in patients with MD (n = 13, age = 38.2 yrs ± 12.4) and SZAD (n = 6, 33.2 yrs8.3) as compared to schizophrenics (n = 10, 28.3 yrs ± 7.6); the mean for the latter group did not differ significantly from that of controls. This indicates a hyposensitivity of postsynaptic alpha-2 adrenergic receptors in depression. However peak GH increase and AUC correlated with age ($r = -481$, $p < .01$), which explains part of the variance; multiple linear regression showed that they are independent of other parameters (anthropometric, rating scale scores, urinary NE and MHPG, cosinor analized cortisol cycle, DST, ACTH and blood pressure responses to clonidine).

2. There was no significant difference in the plasma cortisol decrease between the groups ($F_{2,26} = .972$, $p > .25$). Thus we could not reproduce the blunting of this response reported in depression with clonidine IV (A). It was not correlated with any of the other parameters.

These results, which point to another link between MD and SZAD, are neither incompatible nor in complete agreement with the presence in MD of a dysfunction of alpha-2 adrenergic receptors. Such a deficit has been supposed to play a crucial role in the genesis of HPA hyperactivity. The absence of a clear-cut compatibility is further evidence (B) that such a simple model, though of definite heuristic value, is insufficient. The complexity of receptor regulation, and the multifactorial nature of neuroendocrine control have to be considered when interpreting such data.

NR180 **Wednesday, May 13, 12:00 noon–2:00p.m.**

CATECHOLAMINE LEVELS AND SYMPTOMS OF ANXIETY

Monica N. Starkman M.D. Psychiatry University of Mich 1500 E. Medical Ctr Drive Ann Arbor, MI 48103, Oliver G. Cameron, M.D., Randolph M. Nesse, M.D., Thomas Zelnik, M.D.

Summary:

We studied the correlation of E and NE with anxiety ratings in 3 patient groups: 1) pheochromocytoma (PH+) (n = 17),2 hypertensives with elevated catecholamines shown not to have a PH(PH−) (n = 25), 3) patients with panic disorder (PD) (n = 23). Subjects completed SCL-90R anxiety and phobic anxiety scales and Spielberger State and Trait Anxiety Inventory. None of the PH+ patients met DSM-III criteria for panic disorder. Two met criteria for generalized anxiety disorder. Of the PH− patients, 2 had PAD, 2 had GAD and 3 had both. In the PH+ group, there was no significant correlation of plasma or urine NE with any of the 4 anxiety scales. E was correlated with somatic symptoms. In the PH− group, plasma NE was significantly correlated with anxiety on all anxiety scales. ($r = .55$ to $.77$, $p < .05$). Furthermore, plasma NE was significantly correlated with 4 of the 5 items of the SCL-90 Anxiety scale related to cognitive anxiety, but only one of the 5 noncognitive items (heart racing). In PD, plasma NE showed a significant correlation with anxiety ($r = .67$, $p < .05$). Our observations suggest NE in the periphery is a measure of sympathetic nervous system stimulation by anxiety, and is a *reflection* rather than a cause of anxiety.

NR181 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

5HT AND NE BEHAVIORAL RESPONSE IN OBSESSIVE-COMPULSIVES

Eric Hollander M.D. Psychiatry Columbia University 722 West 168th Street New York, NY 10032, Michael Fay, R.N., Michael R. Liebowitz, M.D.

Summary:

A "serotonin hypothesis" has been postulated in Obsessive—Compulsive Disorder (OCD) based on pharmacologic response and CSF and peripheral measures. There is also indirect evidence of abnormalities in noradrenergic function in OCD. Behavioral responses were measured in OCD patients following m-Chlorophenylpiperazine (M-CPP), a postsynaptic serotonin receptor agonist, fenfluramine, a 5HT releaser, and clonidine, an alpha-2 agonist. Seven OCD patients received pharmacologic challenges with M-CPP (0.5 mg/kg p.o.), fenfluramine (60 mg, p.o.), clonidine (2 ug/kg IV), and placebo. Each patient was studied after a two-week drug-free interval by a clinical rater blind to the subject's challenge medication. Ratings for obsessions and compulsions, anxiety, and depression were assessed prior to, and at selected intervals following each pharmacological challenge. M-CCP caused an increase in obsessions and compulsions in the OCD patients, with the time course paralleling blood levels of the metabolite. Side effects included drowsiness, mild mood elevation, and stomach cramps in some patients. Fenfluramine did not effect obsessions or compulsions, but did cause an elevation of mood, chills, and stomach ache in some patients. Clonidine caused hypotension, increased drowsiness, a feeling of calm, and a decrease in obsessions in some patients. These preliminary findings will be presented, and their implications for a "serotonin" or "norepinephine" hypothesis of OCD will be discussed.

NR182 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

NEUROLOGIC SOFT-SIGNS IN OBSESSIVE-COMPULSIVE DISORDERS

Eric Hollander M.D. Psychiatry Columbia University 722 West 168th Street New York, NY 10032, Erica Schiffman, M.D., Michael R. Liebowitz, M.D.

Summary:

Obsessive—Compulsive Disorder (OCD) has been linked to altered neurological function following head trauma, encephalitis, abnormal birth events, Tourette's Syndrome. Abnormalities in CT, EEG, PET, and evoked-potentials have been described in this disorder. Neurological soft-signs are a particular form of deviant performance on a motor or sensory test where no other sign of a neurological lesion is present. Abnormalities include disorders of coordination, involuntary movements, and sensory signs. Previous studies have demonstrated a link between neurological soft-signs and psychiatric illness, and anxiety states in particular. We studied patients ($n=15$) with OCD who met DSM-III criteria, as well as normal controls ($n=9$). Each subject received an examination for neurological soft-signs by a trained neurologist or psychiatrist blind to the subjects diagnosis, after a two week drug free interval. Each subject was tested on 20 individual tasks involving fine motor coordination, involuntary movements, and sensory function. There was a significantly greater number of total soft-signs in the OCD group (mean = 5.9) compared to the normals (mean = 1), $t = 3.77$, $p < .01$). This consisted primarily of a significant increase in abnormalities of fine motor coordination in the OCD patients (mean = 3.43) compared to controls (mean = 0.66), ($t = 2.56$, $p < .02$). There was an equal number of right-sided and left-sided findings in both groups. These finding support the usefulness of studying neurological soft-signs in psychiatric patients, and provide additional evidence for a neurological model of obsessive—compulsive disorder.

NR183 **Wednesday, May 13, 12:00–2:00**

FLUVOXAMINE IN OBSESSIVE COMPULSIVE DISORDERS

Wayne K. Goodman M.D. Psychiatry Yale University 34 Park Street New Haven CT 06508, Dennis S. Charney, M.D., Lawrence H. Price, M.D., Steven A. Rasmussen, M.D., George R. Heninger, M.D., Pedro L. Delgado, M.D., John H. Krystal, M.D.

Summary:

Obsessive Compulsive Disorder (OCD) is often refractory to conventional therapies. The potent serotonin reuptake inhibitory action of clomipramine may be related to its apparent efficacy in OCD. However, clomipramine also blocks the reuptake of norepinephrine. To examine whether the serotonergic properties of an antidepressant drug may be associated with an antiobsessional action, the efficacy of the potent and selective serotonin reuptake inhibitor fluvoxamine was studied in OCD.
METHODS: 42 outpatients with a primary diagnosis of OCD gave informed consent and entered treatment with random, double-blind assignment to either fluvoxamine or placebo for 6 to 8 weeks. No behavioral treatment was provided. Patients were assessed weekly for symptoms of anxiety, depression, and OCD using standard self- and clinician-ratings. OCD symptom severity was also rated using the Yale-Brown Obsessive Compulsive Scale (Y-BOCS).
RESULTS: Fluvoxamine was superior to placebo on clinician-rated measures of OCD and depression. There were 9 responders (="much improved" on Y-BOCS global) out of 21 on fluvoxamine compared to 0 responders out of 21 on placebo ($p<.001$, Fisher Exact Test). Reduction in OCD symptoms did not seem to be related to baseline depression ratings. Similar findings were observed during subsequent open treatment with fluvoxamine in patients originally assigned placebo.
CONCLUSION: Fluvoxamine is effective in the treatment of OCD. Its antiobsessional effects do not seem to be dependent on the presence of depressive symptoms. These data are consistent with the hypothesis that altered serotonergic function may play a role in the treatment, and perhaps the etiology, of OCD.

NR184 **Wednesday, May 13, 12:00–2:00**

OBSESSIVE COMPULSIVE AND TOURETTE'S DISORDERS

Roger K. Pitman M.D. Research SVC VA Medical Center 718 Smyth Road, Manchester, NH 03104, Robert C. Green, M.D., Michael A. Jenike, M.D., M. Marsel Mesulam, M.D.

Summary:

It is now well established that there is a high incidence of obsessive compulsive disorder (OCD) in patients with Tourette syndrome (TS), a severe tic disorder. Tourette syndrome has been called a neurologically based model psychiatric disorder, and a genetic relationship between TS and OCD has been suggested. The occurrence of tic and related symptomatology in OCD patients has received less attention. To our knowledge, there have been no previous studies systematically comparing patients with the two disorders. In this study, 16 TS and 16 OCD outpatients and 16 healthy Controls underwent a structured interview and psychological testing. Previous findings of a high incidence of OCD in TS patients were confirmed. Certain kinds of compulsive behavior, i.e., touching and symmetry behavior, occurred more often in TS than in OCD. The TS patients were more anxious, neurotic, and compulsive on the psychometrics than the Controls, but were not as high as the OCD patients on these measures. There was a significantly increased incidence of tics in the male OCD patients, and in the relatives of both the male and female OCD probands. Both patient groups had high incidences of unipolar depressive and generalized anxiety disorders. Panic and phobic disorders were frequent in the OCD but not the TS patients, while the OCD patients showed lower occurrences of coprolalia, echo phenomena, self-destructive behavior, and childhood attention deficit. The results suggest symptomatic overlap tending to blur the two disorders, as well as symptomatic poles tending to distinguish them.

NR185 **Wednesday, May 13, 12:00–2:00**

ANTIDEPRESSANTS FOR POST TRAUMATIC STRESS DISORDERS

Julia Bess Frank M.D. Psychiatry Yale University VA Medical Center West Haven, CT 06516, Thomas R. Kosten, M.D., Earl L. Giller, M.D., Ellie Dan, B.A.

Summary:

23 veterans with PTSD have completed an 8 week, randomized, double blind outpatient trial: 11 placebo (C), 6 imipramine (I) and 6 phenelzine (P). The groups were comparable in age (mean = 37.5 years), race (17% non-white) and combat experience (mean scores = 10.9 (C) v 10.8 (I) v 8.2 (P); $F=0.8$, $P<0.5$). Baseline symptom levels were also equivalent: Covi anxiety score (5.1 (C) v 5.8 (I) v 6.0 (P); $F=0.05$, $P<0.8$ and Raskin depression score (7.6 (C) v 7.2 (I) v 9.5 (P); $F=1.0$,$P<0.3$). Raskin depression scores significantly decreased for the two medicated groups (2 pt. drop) compared to placebo (0.2 pt rise) ($F=5.46$, $P<0.03$). Covi anxiety scores decreased for both medicated groups ($P=1$ pt; $I=2$ pt) and rose for placebo (0.1 pt) $F=1.53$, $P<0.2$). The Impact of Events scale to assess PTSD symptoms showed a substantial symptom drop for both the P (43 to 22) and I (38 to 32) groups compared to the placebo group increase (35 to 37) ($F=13.95$, $P<0.001$). Thus, antidepressants were effective for veterans with PTSD, with phenelzine being particularly effective for specific PTSD symptoms.

NR186 **Wednesday, May 13, 12:00–2:00**

LACTATE INFUSION IN POST-TRAUMATIC STRESS DISORDER

Asaf Aleem M.D. Psychiatry VA Medical Center Southfield & Outer Drive Allen Park, MI 48101 John M. Rainey, M.D., Aurelio Ortiz, M.D., Vikram Yeragani, M.D., Robert Pohl, M.D., Richard Berchou, Pharm.D.

Summary:

Post Traumatic Stress Disorder (PTSD) is characterized by recurrent flashbacks, nightmares and intrusive thoughts of the traumatic events. Over 50% of PTSD patients experience panic attacks and in a recent study flashbacks occurred during panic attacks in 25/25 of PTSD patients (1). In this study seven male Vietnam veterans ranging in age from 33-44 were administered infusions of 6ml/kg of 1 Molar sodium lactate, 20 g of isoproterenolol and D_5W, double-blind in random order. During each infusion subjects were rated every 2 minutes for symptoms of PTSD and panic anxiety to determine the occurrence of flashbacks and panic attacks. All seven subjects experienced flashbacks and 6/7 had panic attacks during the lactate infusion. There were 2 flashbacks and 2 panic attacks during the isoproterenolol infusion and 1 flashback and 1 panic attack during D_5W. There was a positive correlation between the ratings of PTSD and panic anxiety (mean $r=0.79$) suggesting that there is a close relationship between flashbacks and panic attacks. Since sodium lactate infusions result in panic attacks in 80-100% of panic disorder patients but only in 0-10% of controls these findings also suggest that PTSD and panic disorder may be closely related.

NR187 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

MENSTRUAL CYCLE EFFECT ON EVOKED POTENTIAL MEASURES

Allan Tasman M.D. Psychiatry U Conn Health Center 263 Farmington Ave Farmington, CT 06032, Nancy DePalma, M.S., Victor Hesselbrock, Ph.D., Sean O'Connor, M.D.

Summary:

The influence of menstrual cycle phase on event-related potential (ERP) measures is unknown. We report the first study of the association of menstrual phase and ERP measures using a prospective design. Six women were studied following exclusionary screening for physical or psychiatric illness, menstrual difficulty or irregularity, or use of oral contraceptives. Ovulation in the cycle prior to testing was confirmed. ERP testing was begun 4-7 days after the onset of menses and continued once a week for 5 weeks. A visual stimulus target/non-target ERP paradigm was used to maximize late ERP waveform components. In order to provide an accurate definition of menstrual phase, blood samples were drawn 3 times a week beginning on the first day of menses. Sampling continued until ERP data collection was completed. Samples were assayed for LH, FSH, estradiol, and progesterone. Results of the assays indicated all women had hormonal variations commonly associated with a normal ovulatory menstrual cycle. Analysis of the ERP data showed statistically significant increases in amplitude of the P3 component of the ERP in each subject in the week preceeding onset of menses. The results will be discussed in light of understanding sensory, cognitive, and attentional changes associated with menstrual cycle phase, as well as implications for further ERP studies with female subjects.

NR188 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

EVENT RELATED POTENTIALS AND THE PHARMACODYNAMICS OF ANALGESIA

Allan Tasman M.D. Psychiatry U Conn Health Center 263 Farmington Ave Farmington, CT 06032, Sean J. O'Connor, M.D., Steven R. Cox, Ph.D., Nancy DePalma, M.S.

Summary:

Relationships between objective measures of pain and quantitative event related potential (ERP) measures associated with metabolism of analgesics offer a new method of studying pharmacokinetics. To investigate these relationships, we developed an innovative method of producing controllable nocioceptive stimuli at several intensities via electrical tooth-pulp stimulation. The apparatus, which will be described in detail in the poster presentation, provides an efficient, technically simple, and replicable methodology. Nine healthy young men participated in a double-blind Latin square cross-over design with three treatments: placebo, 400 mg ibuprofen liquid, and 400 mg ibuprofen tablets. ERP's were obtained during testing sessions in which subjects received a train of stimuli embracing 4 intensities at 15 minutes intervals for 3 hours. The stimuli were rated by each subject as sub-threshold to moderately painful. Blood samples for ibuprofen plasma level analysis were obtained via indwelling venous catheter during each block. Data analysis based on a pharmacodynamic model revealed a statistically significant reduction in ERP amplitudes that were correlated with the time course of plasma drug concentrations. Implications for research using ERP changes to monitor drug effects will be discussed.

NR189 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

PREMENSTRUAL CHANGES: PATTERNS OF DAILY RATINGS

Stephen W. Hurt Ph.D. Psychology New York Hospital 21 Bloomingdale Road White Plains, NY 10605, Richard D. Shindledecker, M.A., Sally A. Severino, M.D.

Summary:

The proposed definition for late luteal phase dysphoric disorder to be included in Appendix A of DSM-III-R stipulates that the diagnosis must be made on prospective daily ratings of symptomatology. Endicott and her colleagues have developed a daily rating form (DRF) for menstrual cycle related symptoms that is a useful instrument for gathering data related to the menstrual cycle. However, criteria for detecting significant change in daily ratings have yet to be established.

Using data on sixty women covering two consecutive menstrual cycles, we applied the spectral frequency techniques of Gottman to detect significant changes in DRF symptom ratings using the total variation in symptom scores across the two cycles as the background against which to judge significant changes in symptom severity in relation to menstrual cycle phases.

This techniques provides a more sensitive and valid procedure for detecting both circatrigantan and less than monthly changes in symptom severity. It also allows investigators to detect significant premenstrual change even in the presence of superimposed, cyclic change of periods shorter than three to four weeks.

NR190 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

STATE RELATED CHANGES IN LIFE EVENTS AND PERCEPTIONS IN MRMD

Peter J. Schmidt M.D. Biol Psychiatry NIMH 9000 Rockville Pike Bethesda MD 20892, Christine Hoban, M.S.W., David R. Rubinow, M.D.

Summary:

Much controversy exists as to the roles played by biological and psychological/social variables in the production of menstrually-related mood disorders (MRMD). One model that effectively organizes the variety of clinical and biological findings in MRMD is the state model of psychological functioning. According to this model, luteal phase related mood and behavioral disturbances are the product of a predictable biologically facilitated change of experiential state, characterized by certain recognizable affects, self-perceptions, object relations, cognitive styles, and behaviors. In order to investigate whether patients with MRMD display state-dependent alterations in perception, we studied the reporting of life events in both women with prospectively confirmed MRMD ($n=28$) and asymptomatic controls ($n=20$). During the follicular (non-symptomatic) and late luteal (symptomatic) phases of the menstrual cycle, subjects completed a schedule of life events, a 111-item self-report scale that monitors an individual's perception of (1) the frequency of occurrence of life events and (2) the degree of associated distress or pleasure. A significant increase in negative life events was seen in our patient sample compared with the control group ($p< .05$). Further, the patients with MRMD showed significantly more distress associated with events occurring premenstrually ($p< .01$); i.e., the *same* events were rated as *more* unpleasant during the luteal phase. These findings complement other evidence of luteal phase related state dependent changes in women with MRMD including significant alterations of supposed trait characteristics (MMPI), cognitive performance (Raven Matrices) and word association stability. The implications of these changes for future studies of MRMD will be discussed.

NR191 **Wednesday, May 13, 12:00-2:00**

HYPERTENSION AND IMPOTENCE

Ismet Karacan M.D. Psychiatry Baylor Coll of Med One Baylor Plaza Houston, TX 77030, Max Hirshkowitz, Ph.D., Nelda Wray, M.D., Richard E. Borreson, M.D., Patricia J. Salis, M.A.

Summary:

The disease hypertension is reportedly associated with erectile dysfunction in men. In this study we recorded nocturnal penile tumescence (NPT) and penile segmental pulsatile blood flow (SPF) in normotensive men. NPT measurement is considered by many the "gold standard" for diagnosing organic impotence in men. We have also previously reportedly SPF changes in normal men. Three groups were studied: 1) nine normotensive men with no erectile complaint, 2) nine untreated hypertensive men with no erectile complaint, and 3) nine untreated hypertensive men who reported erectile dysfunction. Average ages for the three groups were 52, 52, and 54 years, respectively. All subjects were free of sleep complaints, major medical (other than hypertension), and psychiatric conditions. Three nights of polysomnography were obtained for each man. We found diminished NPT in the impotent hypertensive patient group and normal NPT in potent men with high blood pressure. Significant SPF differences, however, were found in all three groups. Median SPF per minute of REM sleep was 7.3 mm, 3.9 mm, and 1.9 mm, for normotensive, potent hypertensive and impotent hypertensive groups, respectively. The declines in the men without erectile dysfunction may be premorbid vascular changes that signal eventual development of vasculogenic erectile dysfunction. Measurement of sleep-related penile SPF may prove useful in the early detection of impotence in men at risk for erectile dysfunction.

NR192 **Wednesday, May 13, 12:00 noon—2:00 p.m.**

SLEEP APNEA FOUND IN 38% OF ELDERLY INPATIENTS

Daniel F. Kripke M.D. Psychiatry USCD M003 LA Jolla, CA 92093 Sonia Ancoli-Israel, Ph.D., William J. Mason, M.A., Jennifer Bloomquist, R.N.

Summary:

To further explore the prevalence of sleep apnea, we have been recording randomly selected male medical patients age 60 and above on a VA Medical Service. Patients in ICU's, suffering from cancer, or too obtunded or demented to consent were excluded. Remarkably, of the first 140 patients, 38% had more than 5 apneas per hour of sleep and 85% had more than 5 apneas plus hypopneas per hour of sleep! An apnea was defined as a respiratory cessation of at least 10 seconds, and a hypopnea was a decrease in respiratory amplitude over 50% for at least 10 seconds. Those with an apnea index of 5 or more averaged 163 apneas per night. In addition, they had 210 blood oxygen desaturations exceeding 4% per night, indicating that many of the hypoventilations were physiologically significant. The percent of inpatients exceeding our apnea criteria was higher than the percent of randomly sampled independently-living elderly males. However, a similar percentage (39%) of apnea indices exceeding 5 was found in a largely female nursing home population which we have also been sampling. In the nursing home, the presence of sleep apnea is significantly correlated with increased dementia. These results indicate that sleep apnea is likely to be a complicating factor in the mental status of a high percentage of hospitalized elderly who may require psychiatric consultation.

NR193 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

DELAYED SLEEP PHASE SYNDROME REVISITED

Beth Buckwald B.S. CPB NIMH 9000 Rockville Pike B110 Rm4 S239 Bethesda, MD 20892, Norman E. Rosenthal, M.D., Shawna Murray, M.D., David A. Sack, M.D.

Summary:

Criteria for the condition of delayed sleep phase syndrome (DSPS) were defined by Weitzman et al as: 1. chronic inability to fall asleep at desired clock time; 2. once asleep, patients sleep is sound and of normal length; 3. these individuals function best and are more alert in the evening; and 4. Patients have a history of unsuccessful attempts to treat the problem. Weitzman et al reported no consistent psychopathology in their 30 patients. This group was retrospectively selected from a population of patients seen at a sleep disorder clinic and previously classified as insomniacs. They suggested chronotherapy, a process of successively delaying sleep onset time until the desired time is reached.

We identified 93 DSPS patients (diagnosed by at least the first three above criteria) by means of a newspaper article which generated over 400 responses. Clinical and demographic features were: (1) Sex distribution: female = 74%; male = 26%; (2) Age of onset: (X +/− SD) = 10 +/− 9 years. (3) Affected from birth = 22%; (4) Work schedule: regular (8,9am to 4,5pm): 28%; Unemployed = 17%; Free lance, self-employed workers = 27%; Shift work = 11% (5) Earliest time of day that the individual is alert (mean = 11:00am); (6) Previously had treatment for sleep disturbance: 55% (7) Report periods of depression: 84% (8) Treated for affective disturbance: 42%; (9) History of alcohol abuse: 13%

Our findings suggest that the prevalence of affective disturbance in DSPS may have been previously underestimated. In addition, of those subjects who reported trying chronotherapy (11%), none reported sustained benefits. The need for a lasting treatment intervention is clear. We are currently exploring alternate treatment strategies and will discuss these at the time of presentation.

NR194 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

PARENTAL PSYCHOPATHOLOGY IN ANOREXIA NERVOSA

Edward J. Schork Ph.D. Psychiatry Cornell U Med Coll 21 Bloomingdale Rd White Plains, NY 10605, Katherine A. Halmi, M.D., Elke D. Eckert, M.D., Nancy Williams, Ph.D., Louis Chavez, M.A., Tina Trudel, M.A.

Summary:

Parental psychopathology is often assumed to be associated with child and adolescent psychiatric disturbance, but there is little systematic evidence on this question in anorexia nervosa. A series of 42 anorectic adolescents (mean age 15.1) and their parents completed the MMPI at the time of the daughter's admission to inpatient treatment. Few of the parents' profiles revealed significant psychopathology. Of 38 cases where two parents responded, in only 3 instances (8%) did *both* parents have elevations in the clinical range on one or more of the MMPI clinical scales. Individually, 12 of 41 mothers (29%), 9 of 39 fathers (23%), or a total of 18 of 42 cases (43%) had one parent who met this criterion. Daughters' admission profiles did *not* show significantly more pathology when either or both parents' profiles were elevated. As a group, fathers showed a moderate tendency toward depresssive feelings, lack of insight, self-centeredness, and denial of difficulties. Mothers displayed denial and a tendency toward social introversion. Mothers' MMPI scores reflecting social introversion, passivity-compliance, acknowledgment of serious pathology, and depression, together were associated with 32% of the variance in daughters' characterological problems such as anger and impulsivity at admission ($p<.007$). Parents of anorectic restrictor vs. bulimic subtypes will be compared. The present findings do not support generalizations about parental psychopathology in anorexia.

NR195 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

EVIDENCE FOR SEROTONIN DYSREGULATION IN ANOREXIA

Timothy D. Brewerton M.D. DIRP/LCS/SBP NIMH 10/3S231 9000 Rockville Pike Bethesda, MD 20892, Edward A. Mueller, M.D., Harry A. Brandt, M.D., Michael D. Lesem, M.D., Dennis L. Murphy, M.D., David C. Jimerson, M.D.

Summary:

Studies in laboratory animals and humans implicate dysregulation of serotonin (5-HT) function in the pathophysiology of eating disorders. We have studied prolactin (PRL) responses to two serotonergic agents, L-tryptophan (L-TRP), the amino acid precursor of 5-HT, and m-chlorophenylpiperazine (m-CPP), a selective 5-HT receptor agonist. Subjects included female patients meeting DSM-III criteria for anorexia nervosa, who were studied before and 4 weeks after weight restoration (83% expected weight), and 12 healthy female controls. Active drugs or placebo were given on separate days using a randomized, double-blind design. All patients were metabolically stable and medication-free for at least 3 weeks.

Baseline PRL levels were significantly lower in both low weight and weight recovered anorexics than in controls ($p<0.05$, t-test). The PRL response to L-TRP (100 mg/kg IV) was significantly blunted in 7 low weight patients ($p<0.0001$, diagnosis (Dx) $\times$ treatment (Tx), repeated measures ANOVA (RANOVA) as was the PRL response to m-CPP (0.5 mg/kg PO) ($p<0.02$, Mann-Whitney Test). In 15 patients studied longitudinally, there was some evidence for increased PRL response following weight restoration; however, this reached statistical significance only for m-CPP ($p<0.02$, Mann-Whitney Test). Nonetheless, PRL responses in 6 weight-recovered patients were significantly blunted following L-TRP ($p<0.003$, Dx $\times$ Tx, RANOVA) and following m-CPP ($p<0.05$, Mann-Whitney Test) in comparison to controls. These findings indicate that responsiveness in hypothalamic-pituitary serotonergic pathways is blunted in both low-weight and weight-recovered anorexics, and are consistent with other evidence for serotonergic dysregulation in anorexia nervosa.

NR196 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

RISK FACTORS FOR BULIMIA AMONG HIGH SCHOOL FEMALES

Donna E. Andrews Ph.D. Psychiatry Univ of Rochester 3107 Churchill Drive Madison, WI 53713 USA, Marjorie H. Klein, Ph.D., John H. Greist, M.D., Mary Gulbrandson, R.N.

Summary:

Epidemiologic studies of bulimia estimate its prevalence at 2.5—6% of the female population (1,2). Although being female and being of late adolescent/young adult age seem to be 2 general risk factors (3,4) for developing bulimia, they are not sufficient to produce the disorder. Studies of individuals in treatment for bulimia suggest several other important risk factors—including a preoccupation with weight, the presence of depressive symptoms, self-concept disturbances. This investigation examines the relative contribution of these 3 potential risk factors to the prediction of bulimic symptomatology among a community sample. 1100 high school females were surveyed for the presence of bulimic symptomatology. The 3 risk factors were measured with previously validated instruments including the Eating Disorders Inventory, the SCL-90, and the Structural Analysis of Social Behavior (SASB) introject form. Simultaneous entry of these risk factors into a multiple regression equation indicated that preoccupation with weight was the best predictor with amount of depressive symptomatology and hostile-controlling self-concept as the next most powerful predictors. Other demographic variables such as SES, GPA and prior weight history did not predict symptomatology. Course-of-illness data revealed significant age-effects, suggesting optimal points of intervention. Additionally, prevalence rates for the full syndrome vs. individual symptoms may indicate a subclinical form of the disorder.

NR197 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

2-DEOXY-D-GLUCOSE EFFECTS ON APPETITE IN BULIMIA

Harry H. Brandt M.D. DIRP LCS SBP NIMH BLDG 10 RM 3S231 Bethesda, MD 20892, Alan Breier, M.D., Owen Wolkowitz, M.D., David Pikar, M.D., Steven M. Paul, M.D., David C. Jimerson, M.D.

Summary:

Regulation of hunger and satiety sensations may be altered in normal weight bulimia. 2-deoxy-D-glucose (2DG) is a glucose analogue which competitively inhibits glycolosis, causes intracellular glucopenia, and potently stimulates feeding in laboratory animals. As a probe of appetite regulation in bulimia, we administered 2DG (50 mg/kg) to 10 female patients meeting DSM-III criteria for bulimia and 6 age-matched female healthy volunteers. Active drug or placebo were given on separate days using a randomized, double-blind design. All subjects were metabolically stable and medication free for at least 4 weeks. Hunger was assessed at baseline and at 30 min. intervals after infusion using a 100mm analog rating scale. Subjects with marked baseline hunger rating differences (>30%) between days (3 bul.,1 volunteer) were excluded. Two hours following the infusion subjects were instructed to consume ad libitum a standardized test meal. Baseline self-ratings of hunger were nonsignificantly lower in the bulimic group (mean$\pm$S.D. = 22$\pm$23mm) as compared to controls (means$\pm$SD = 43$\pm$13mm) ($t = 1.68$, p=N.S.). The placebo corrected 2DG-induced increases in hunger were significantly blunted in bulimic patients (16$\pm$4mm) as compared to controls (37$\pm$4mm) ($t = 4.40$, $p < .002$). Caloric intake following placebo administration was similar in bulimic patients (608Cal.$\pm$114) and controls (713$\pm$323Cal.). The 2DG-induced increase in food consumption was significantly blunted in bulimic patients (164$\pm$171Cal.) as compared to controls (736$\pm$442Cal.) ($t = 2.94$, $p < .02$). This study demonstrates the potential value of 2DG as a tool for examining regulation of appetite in eating disorders. These data provide new evidence for alterations in the neurobiologic regulation of hunger and appetite in bulimia.

NR198 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

IS ANOREXIA NERVOSA OCCURRING MORE FREQUENTLY?

Alexander R. Lucas M.D. Psychiatry Mayo Clinic 200 SW 1st Street Rochester, MN 55905, C. Mary Beard, M.P.H., William O'Fallon, Ph.D., Leonard T. Kurland, M.D.

Summary:

PURPOSE: The frequency of anorexia nervosa (AN) is said to have risen markedly. Previous epidemiologic studies, however, depended on incomplete population data. We determined the incidence rates and trends for AN in Rochester, MN over the 45-yr period, 1935-79.
METHODS: This is the first population-based epidemiologic study of AN for an entire community. Using the medical record archive at Mayo Clinic we identified the records of patients diagnosed AN as well as the records of 20,000 patients who had diagnoses possibly shielding AN. Diagnosis was confirmed by DSM-III and Pathology of Eating Group criteria.
RESULTS: 140 (128 F; 12 M) residents of the community with AN were identified. Mean age for F was 21.9±8.5 yr (range 10-57 yr.). Overall incidence rate was 7.3 per 100,000 pop. Highest rate (56.7 per 100,00) was in F age 15-19 yrs. the incidence of AN was as great in 1935-49 as it it was in 1965-79. Lower rates occurred in 1950-59.
IMPORTANCE: The occurrence of AN as a disorder with highest rates in adolescent and young adult females was confirmed. It has not become more common in the Rochester, MN population in recent decades. While social influences may have an impact on its occurrence, biologic factors associated with rapid growth during puberty and developmental stresses in young adulthood may be the more powerful determinates of the illness.

NR199 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

BULIMIA ON CAMPUS: INCIDENCE AND RECOVERY RATES

Adam Drewnowski Ph.D. Psychiatry University Michigan School of Public Health M5164 Ann Arbor, MI 48109, Doris Yee, Dean D. Krahn, M.D.

Summary:

The prevalence of DSM-III-R bulimia among college women is thought to be between 1 and 5%. These data usually based on cross-sectional survey studies, reflect the number of probable bulimics in the female population at any given point. As yet, no prospective longitudinal study has documented the emergence of new (i.e. incident) cases of bulimia over a specified time period. The true incidence rate of this eating disorder thus remains unknown, and little can be said about its epidemiology or risk factors. Our Fall study surveyed 931 freshman women, 27 of whom (2.9%) fulfilled criteria for a probable diagnosis of DSM-III-R bulimia. Spring study, conducted 6 months later, re-examined 599 of these respondents (64.3% response rate). Twenty-one women (3.5%) were diagnosed as probable bulimics. However, case identity matches revealed that the majority (13/21) were new cases, not previously diagnosed as bulimic. Furthermore, over 50% of Fall bulimics no longer fulfilled diagnostic criteria in the Spring survey. The high incidence of bulimia during the freshman year (4.3 new cases per 100 women per year) appears compensated by a high spontaneous remission rate in the absence of reported physician contact. Despite stable prevalence rates, bulimia on campus may not be a chronic condition.

NR200 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

AMYLASE LEVELS IN BULIMIA

David C. Lindy M.D. NYS Psychiatric INS 722 West 168th Street New York, NY 10032, B. Timothy Walsh, M.D., Steven P. Roose, M.D., Madeline Gladis, M.A., Linda M. Wong, B.A.

Summary:

Recent evidence suggests that hyperamylasemia of salivary-gland origin is found in patients with bulimia. Although apparently related to binge-purge activity, it is unclear whether this finding is associated with bingeing or vomiting. We measured amylase levels in 22 bulimic out-patients and 12 normal controls. Hyperamylasemia (defined as serum amylase > 149 U/L) was found in 6/22 patients. (27.3%) and 0+12 controls (0%) (chi square = 3.03, $p < .10$). Mean serum amylase levels were significantly higher in patients than controls (120.23 ± 49.41 U/L vs. 79.67 ± 33.41 U/L, respectively; $t = 2.54$, $df = 36$, $p = .016$). When patients were divided into high and low amylase groups by the median amylase level (112.5 U/L), there was no difference between groups with respect to mean binge frequency. However, the mean vomiting episodes/week was significantly higher for the high amylase group (15.00 ± 11.88 vs. 4.40 ± 5.99, respectively; $t = 2.54$, $df = 19$, $p = .02$). All patients who did not vomit (4/22) were in the low amylase group. These data suggest that elevated serum amylase levels in bulimia may be associated specifically with vomiting. We are continuing to collect data from both hospitalized and out-patient populations to examine the possibility that serum amylase levels could be used clinically to follow binge-purge activity in bulimic patients.

NR201 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

PATTERN OF ONSET OF BULIMIC SYMPTOMS IN ANOREXIA

Joy A. Kassett M.S.W. Biological Psychiatry NIMH 9000 RKV Pike B10 RM 3S231 Bethesda, MD 20892, Elliot S. Gershon, M.D., Harry Gwirtsman, M.D., Walter H. Kaye, M.D., Harry A. Brandt, M.D., David C. Jimerson, M.D.

Summary:

Recently there has been increased attention to the possible etiologic relationships between bulimia and anorexia nervosa. It has been reported that approximately 50 percent of patients with anorexia develop bulimic symptoms, with the onset of these symptoms typically one year after the onset of anorexia. The present report reviews data on the sequence of the development of anorexia and bulimia in patients meeting DSM-III criteria for anorexia nervosa. Patients were interviewed between 1976 and 1987 utilizing structured interviews and were categorized into bulimic and non-bulimic subgroups using DSM-III criteria for bulimia. Preliminary analysis of data from 59 anorexic patients identified 28 patients as non-bulimic and 31 as bulimic. It was of interest that in the 19 bulimic anorexic patients studied prior to 1984, only 2 developed bulimia prior to or concurrently with the onset of anorexia. In the subjects studied since 1984, however, 6 of 12 patients developed bulimia prior to or concurrently with the onset of anorexia. The historical assignment of date of onset of symptoms meeting formal diagnostic criteria in eating disorder patients is difficult. Nonetheless, this preliminary data suggests that in recently interviewed patients, the development of bulimia prior to the onset of anorexia was not uncommon. If observed in future studies, this recent trend has implications for clinical investigative approaches to anorexia.

NR202 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

ZINC DEFICIENCY IN BULIMIA

Laurie Humphries M.D. Psychiatry U of Kentucky 820 S. Limestone St. Lexington, KY 40536, Craig McClain, M.D.

Summary:

Zinc plays an integral part in appetite regulation. Animal models of zinc deficiency (ZD) show two patterns of aberrant eating. With a diet composed of less than 20% protein, the zinc deficient rat eats very little, but if the diet contains more than 20% protein the animal alternates between eating huge amounts and eating little. Based on this, we hypothesized that ZD may be present in bulimia. To clarify this, we determined the zinc status of 55 consecutive admissions with bulimia (DSM III).

Blood samples were taken from patients in the fasting state and were collected in zinc-free plastic syringes. The 24-hour urine was collected in zinc-free plastic containers. Complete 24-hour collections were assured by stringent precautions on the Eating Disorder Service. All samples were analyzed by atomic absorption spectrophotometry. ZD was defined as a fasting serum of 70μg/dl or less and/or a 24-hour urinary zinc of less than 250 μg.

Twenty-five of fifty-five (45%) bulimics were found to be zinc deficient. This is the first report of ZD in bulimia. We propose a double blind prospective study to elucidate the role of zinc in the etiology and treatment of bulimia.

NR203 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

BULIMIA TREATED WITH CARBAMAZEPINE AND IMIPRAMINE

Allan S. Kaplan M.D. Eating Disorder Center Toronto General Hospital 200 Elizabeth St., CW1 RM 313 Toronto ON, CANADA M5G 2C4, Paul E. Garfinkel, M.D., David M. Garner, Ph.D.

Summary:

Some studies have found tricyclic antidepressants and monoamine oxidase inhibitors effective in the short term for bulimia. Carbamazepine, an anticonvulsant with thymoleptic properties, has not been rigorously investigated for this syndrome.

In a 14 week double blind placebo (P) controlled crossover study, 16 normal weight DSM-III bulimic outpatients were treated in 6 week intervals with carbamazepine (C) or imipramine (I) following a 2 week baseline period in a P-C, C-P, P-I or I-P design. 6 of 16 bulimics completed 14 week trials with both drugs. Subjects recorded the number of binges and purges daily, and completed the Eating Disorders Inventory (EDI) and the Beck Depression Inventory (BDI) in addition to other measures, at 0,8,14 weeks. Blood levels were maintained in the anticonvulsant range for carbamazepine (20-50 μmole/liter) and in the antidepressant range for imipramine (250-800 nmole/liter).

None of 11 bulimics demonstrated a decrease in binge frequency from baseline to carbamazepine greater than 75%; 3 demonstrated a greater than 50% reduction. There was no clear pattern of BDI changes in response to the drug. 3 of 11 bulimics demonstrated a decrease in binge frequency from baseline to imipramine greater than 75%. 2 of 3 bulimics who had a greater than 50% reduction in BDI scores had insignificant (<50%) reduction in binging.

This study found imipramine but not carbamazepine was clinically beneficial for a smaller subgroup of bulimics than reported in previous studies and that its antidepressant and antibulimic effects may be separate.

NR204 **Wednesday, May 13, 12:00 noon–2:00p.m.**

REDUCED RESTING METABOLIC RATE IN BULIMIC PATIENTS

Eva Obarzanek Ph.D. SBP, LCS NIMH, BLDG 10, RM 3S-231 Bethesda, MD 20892, Michael D. Lesem, M.D., David C. Jimerson, M.D.

Summary:

Recent studies based on measurement of caloric intake indicate that bulimic patients, despite being in a normal, weight range, require fewer calories to maintain their body weight than do controls. To test more directly whether bulimic patients utilize ingested calories with greater efficiency than controls, we determined resting metabolic rate (RMR) by measuring oxygen consumption in 10 female bulimics and in 7 normal-weight healthy female volunteers. RMR was significantly lower for bulimics than for controls (1019±119 vs 1152±84 kcal/day, $p<.05$). Because the relative weight of the patients was significantly lower than that of the controls (85.9±4.3 vs 98.6±9.2 percent, $p<.02$), and because RMR depends upon body weight, RMR was expressed in terms of body surface area (BSA). A strong trend toward lower RMR/BSA was still apparent in the bulimic group compared to the healthy controls (26.9±2.6 vs 29.6±2.6 kcal/m², $p<.06$). Moreover, dividing the patients into two subgroups based on relative weight still revealed reduced RMR and RMR/BSA values in the higher relative weight bulimic subgroup. These data support the observation that bulimic patients tend to have lower energy requirements than healthy volunteers. These results, taken together with evidence for alterations in sympathetic nervous system activity and in neuroendocrine regulation, suggest the possibility of hypothalamic dysfunction in bulimia. Conceivably increased energy efficiency may contribute to the onset of bulimia by promoting continual purging behavior to counteract a physiological tendency for relatively easy weight gain. Alternatively, increased energy efficiency might be a result of repeated bouts of dieting and/or weight loss.

NR205 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

ALTERED CSF NPY RELATIONSHIPS IN EATING DISORDERS

Walter H. Kaye M.D. Psychiatry University of PGH. 3811 O'Hara Street-Room 1086 Pittsburg, PA 15213, Wade H. Berrettini, M.D., Harry H. Gwirtsman, M.D., David C. Jimerson, M.D., D.T. George, M.D.

Summary:

Neuropeptide Y (NPY) is a recently discovered peptide which occurs in the mammalian brain in higher concentrations than all other peptides studied to date. Moreover, NPY is perhaps the most potent inducer of consummatory behavior yet found in animal studies. The powerful effects of NPY on feeding behavior has raised a possibility that anorectics might have reduced levels of NPY. Moreover, Gray and Morley (Life Sci., 1986) have hypothesized that NPY could be involved in the pathogenesis of bulimia. To assess brain NPY in patients with eating disorders, we measured concentrations of NPY in CSF. Contrary to our expectations, underweight anorectics had significantly elevated levels of CSF NPY compared to controls. CSF NPY levels remained significantly elevated in the same patients studied soon after weight-restoration. In contrast, CSF NPY levels in anorectics who had been long-term weight-restored and women with normal weight bulimia were similar to control women. The meaning of elevated CSF NPY in anorectics is not known. If these elevations are a homeostatic mechanism to compensate for weight loss it can be presumed to be an ineffective modifier of behavior. Moreover, it is surprising to see the persistence of elevated NPY in the short-term after weight gain. It should also be noted that NPY reduces LH secretion and suppresses lordosis in the rat raising the possibility that this peptide contributes to the amenorrhea and sexual disinterest commonly seen in anorectics. Perhaps the most interesting finding was that caloric intake and CSF NPY correlated negatively in normal control women but positively in weight-restored anorectics and normal weight bulimics. These results raise speculations that abnormal physiological relationships may exist between appetitive behavior and brain NPY systems in anorexia nervosa and bulimia. We have little understanding of why appetitive behavior is disturbed in the eating disorders. These data add to the growing body of literature suggesting that eating disorder patients have disturbances of some of the peptidergic systems implicated in appetite regulation.

NR206 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

DSM-III PERSONALITY DISORDER AMONG BULIMICS

William R. Yates M.D. Psychiatry University of Iowa 500 Newton Road Iowa City, IA 52242, Bruce Sieleni, M.D., James Reich, M.D.

Summary:

We evaluated a series of 24 normal-weight female outpatient bulimics using the Diagnostic Interview Schedule (DIS), Personality Diagnostic Questionnaire (PDQ), and a standardized eating disorder interview. The prevalence and pattern of DSM-III personality disorder among bulimics was compared to results of a community population-based survey with the same instrument (PDQ). Forty-two percent of the bulimic group met criteria for a DSM-III personality disorder compared to 11% of the community sample (odds ratio 6.0, $X^2 = 14.9$, $df = 1$, $p < .001$). Compared to the pattern of personality disorders in the community sample, bulimics were likely to have a cluster B—histrionic, borderline, narcissistic, and antisocial—personality disorder (relative risk 8.3).

Within the bulimic group we evaluated the effect of the presence of a personality disorder on various clinical parameters. Bulimics with personality disorders were more likely to have a history of major depressive disorder (80% vs 21%, Fisher's exact $p = .04$) and showed a trend toward developing the onset of bulimic behavior after age 20 (40% vs 7%, Fisher's exact $p = .075$); but they were no more likely to report previous treatment, substance abuse, or a family history of an eating disorder. This study supports previous reports of increased personality disorder among bulimics and suggests that personality disorder may affect the presentation and natural history of the disorder.

NR207 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

DSM-III PERSONALITY IN THE ELDERLY

Robert C. Abrams M.D. Psychiatry New York Hospital 21 Bloomingdale Road White Plains, NY 10605, Robert C. Young, M.D., George S. Alexopoulos, M.D., Jonathan H. Holt, M.D.

Summary:

Little is known about DSM-III personality disorders in the elderly, and the relationship of these conditions to late-life depression has not been studied. The Personality Disorder Examination (PDE), a structured interview for making Axis II diagnoses, is a recent methodological advance. Using the PDE, we report the first investigation of DSM-III personality disorders in geriatric depressives and elderly controls.

21 geriatric patients recovered from (DSM-III) major depression (mean age 70.0 years ± 6.4 S.D.) and 15 never-ill volunteers living in the community (mean age 75.9 ± 6.7) were studied. All were screened for cognitive impairment using the Mini-Mental State Examination (mean score 29.4 ± 1.2) and for residual depression using the 24-item Hamilton Depression Rating Scale (mean score 1.3 ± 1.9 for controls, 6.3 ± 3.2 for patients). Subjects were then interviewed according to the PDE format.

Two recovered depressives and no controls met DSM-III criteria for personality disorders. The patients also received higher dimensional scores for each of the personality disorders ($P<.01$) except antisocial personality. The largest differences ($P<.01$) between groups were found for the avoidant and dependent disorders.

Old age provides a unique perspective for personality study. Our data suggest an association in the elderly between personality dysfunction and major depression. Axis II criteria may prove to have implications for the pathogenesis, treatment, and outcome of late-life depression.

NR208 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

GENDER DIFFERENCES IN NARCISSISTIC STYLES

Judith A. Richman Ph.D. Psychiatry Univ of Illinois 912 S. Wood St. RM 218 Chicago IL 60612, Joseph A. Flaherty, M.D.

Summary:

The narcissistic personality style is assumed to be highly prevalent in contemporary society, but little epidemiologic attention has been directed to its actual prevalence or its relative distribution across differing social groups. This study addresses gender differences in the manifestation of narcissistic personality traits and their differential association with low self esteem and dysphoric mood. The authors developed a Narcissistic Traits Scale corresponding to DSM-III criteria and administered this scale along with measures of self esteem and depressive symptomatology to a population of medical students. The data show no sex differences in overall narcissistic styles, but do find sex differences in both the prevalence of given traits and in their differential association with low self esteem and dysphoric mood. In particular, manifestations of grandiosity, fantasies of unlimited success, and lack of empathy were significantly more prevalent in males, while feelings of distress in response to the indifference or criticism of others were more prevalent in females. These data suggest the need to take gender into account in the clinical conceptualization and empirical study of narcissistic pathology. Expanding on Kohut's imagery, a clear distinction between "Tragic Man" and "Tragic Woman" is recommended in future work on narcissism.

NR209 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

DSM-III PERSONALITY DISORDERS IN THE COMMUNITY

James H. Reich M.D. Psychiatry University of Iowa 500 Newton Road Iowa City, IA 52242, William Yates, M.D., Mary Nduaguba, Ph.D

Summary:

A sample of 1.1% of a 30,000 person population over 18 years old with a standardized DSM-III, Axis II self-report instrument yielded an age adjusted community prevalence rate for DSM-III personality disorders of 11%. Specific disorders were schizoid 0.4%, schizotypal 2.9%, paranoid 0.4%, histrionic 1.2%, narcissistic 0.2%, antisocial 0.2%, borderline 0.2%, avoidant 0, dependent 2.9%, and compulsive 3.7%. When those with personality disorders (PD's) ($N=26$) were compared to those without personality traits the PD group had less education (14.9 ± 3 years vs. 16.5 ± 3.3 years, $p = .02$), and greater degree of difficulty with alcohol (19% vs 0.6%, $p = .0001$). Of those married the PD group has a greater number of marital problems (29% vs 3.5%, $p = .002$) and there was a trend for the PD group to have greater unemployment ($p = .07$).

NR210 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

CORRELATES OF PERSONALITY DISORDERS IN THE COMMUNITY

Mark Zimmerman B.A. Psychiatry University of Iowa 500 Newton Road Iowa City, IA 52242, William H. Coryell, M.D.

Summary:

As part of a family study of nonmanic psychoses, 797 relatives of psychiatric patients and normal controls were interviewed with the SIDP and DIS and diagnosed on DSM-III axis I and II. We examined the relationship between each of the DSM-III personality disorders and age, sex, marital status and frequency of 7 axis I disorders (mania, major depression, dysthymia, alcoholism, substance abuse, phobic disorder, panic disorder).

Different personality disorders had very different demographic and diagnostic correlates. For example, young age was significantly associated only with schizotypal, antisocial, borderline, passive-agressive and mixed personality disorders. Individuals with compulsive and antisocial personality disorder were significantly more frequently men, whereas females were more frequently diagnosed as dependent personality disorder. Almost all personality disorders were associated with an increased rate of major depressive disorder, and this was strongest for schizotypal, avoidant and borderline. Suprisingly, no personality disorder was associated with dysthymia. Detailed results of the comorbidity between axis I and axis II will be presented.

NR211 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

PSYCHIATRIC MORTALITY IN THE COMMUNITY

Jane M. Murphy Ph.D. Psychiatry Harvard Medical School Massachusetts General Hospital Boston, MA 02114, Richard R. Monson, M.D., Donald C. Olivier, Ph.D. Arthur M. Sobol, M.A., Alexander H. Leighton, M.D.

Summary:

We describe an investigation (the Stirling County Study) in which psychiatric information was gathered from general physicians about a sample of a general population as well as from structured interviews with the sample members themselves. The physicians were asked to report on all types of mental disorders including organic brain syndromes, psychoses, mental retardation, personality disorders, alcohol and drug abuse, as well as depression and anxiety. Patient studies have indicated that several of these diagnoses carry an elevated risk for shortened life. Baseline prevalence rates for these disorders will be given and mortality risks related to different diagnoses will be assessed based on a 16-year follow-up study. We will also compare the results of the physician information with results based on face-to-face interviews with the subjects themselves concerning depression and anxiety. Recently we reported that subjects who gave evidence of these latter types of disorders experienced 1.5 the expected number of deaths, a risk mainly accounted for by depression. The findings will be discussed in terms of the contribution of general physicians to epidemiologic studies and the importance of investigating mortality among untreated as well as treated cases.

NR212 **Wednesday, May 13, 12:00 noon–2:00p.m.**

PERSONALITY DIMENSIONS IN CANDIDATES FOR PHOTOTHERAPY: A PILOT STUDY

Patricia M. Schulz M.S.W. Psychobiology NIMH, 4S-239, Bldg. 10 9000 Rockville Pike Bethesda, MD 20892 David A. Sack, M.D., Robert Skwerer, M.D., Beth Buckwald, B.S., Sigfried Kasper, M.D., Norman E. Rosenthal, M.D., Susan Rogers, R.N.

Summary:

It has been our clinical impression that patients with Seasonal Affective Disorder (SAD) while free of personality disorder proper, may have an abundance of personality traits which are important to the identification and treatment of the population. In order to test these hypotheses, we examined 50 consecutive admissions to NIMH Psychobiology Branch studies. The comparison groups were phototherapy candidates: with Subthreshold-SAD (S-SAD), SAD patients (N = 10), Delayed Sleep Phase Syndrome (DSPS) (N = 10) and Normal Volunteers (N = 10). Also examined were a group of Inpatients with Affective disorders (N = 10) whose depressions were not seasonal, and who were not candidates for phototherapy. Using the Structured Clinical Interview for DSM-III-R (SCID and SCID II), we generated diagnoses for all subjects. All interviews were conducted by the same interviewer, (during the winter) when the patients were symptomatic. Since we were interested in subthreshold personality disorder, and traits, we devised a scoring system for the SCID II which would preserve these data. Personality Disorder scores were analysed using Analysis of Variance. Preliminary analysis of the data suggests that candidates for phototherapy (SAD, DSPS) had elevated rates of Bipolar II disorder, compared to normals and non-phototherapy candidates. The personality traits characteristic of DSM III Cluster III (avoidant, dependent, *compulsive*, passive aggressive) and to a lesser degree Cluster I (paranoid, schizotypal, *schizoid*) were more characteristic of the candidates for phototherapy. Results of all the data of this ongoing study will be presented in detail.

NR213 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

5-HT FUNCTION IN BORDERLINE PERSONALITY DISORDERS

Emil F. Coccaro M.D. Psychiatry Bronx VA Medical Center 130 West Kingsbridge Road Bronx, NY 10468, Larry J. Siever, M.D., Howard M. Klar, M.D., Richard A. Friedman, M.D., Andrea Moskowitz, R.N., Kenneth L. Davis, M.D.

Summary:

Impulsive and aggressive behaviors are a prominent characteristic of patients with Borderline Personality Disorder (BPD) as defined by DSM-III. Since data from animal and clinical studies suggest that central 5-HT function may play a role in the modulation of such behaviors, we examined the PRL response to the 5-HT releaser/agonist fenfluramine (FEN: 60 mg po) in 20 patients with DSM-III Personality Disorder as assessed by SIDP. BPD patients had significantly reduced peak delta PRL responsiveness to FEN when compared to other non-BPD patients ($p < 0.01$). This finding was not affected by presence or absence of a current, or past, history of major affective disorder (MAD). Further, this finding was confined to only those PD patients meeting full DSM-III criteria for BPD. Similar examination of the remaining PD subtypes revealed no significant differences in peak delta PRL responsiveness to FEN between PD patients who were, or were not, Schizotypal, Paranoid, or Histrionic PD. Examination of peak delta PRL responsiveness to FEN according to the presence, or absence, of the eight individual diagnostic DSM-III BPD criteria items revealed that self-damaging acts ($p < 0.05$), impulsivity and intense anger ($p \leq 0.10$), regardless of specific PD subtype, was associated with the greatest reduction in peak delta PRL responsiveness to FEN. These data suggest that diminished PRL responsiveness to FEN may be a marker of the aggressive/impulsive behaviors clinically observed in patients with BPD.

NR214 **WEDNESDAY, MAY 13, 12:00 noon–2:00 p.m.**

MDD AND PANIC DISORDER; EFFECTS OF COMORBIDITY ON TREATMENT OUTCOME

Leon J. Grunhaus M.D. Psychiatry Univ of Michigan Hospital D 9702 Box 0118 1500 E Med Ct Ann Arbor, MI 48109, Yoseph Harel, Ph.D., Tina A. Krugler, B.A., Roger F. Haskett, M.D., John F. Greden, M.D.

Summary:

Recent research into the relationship between MDD and Panic Disorder (PD) has shown that PD may occur in up to 30% of patients with MDD, and that an episode of MDD may complicate the life course of up to 60% of patients with PD. Furthermore, patients meeting both diagnoses appear to have a more severe illness as indicated by higher ratings of distress and symptoms, worse psychosocial outcome, more frequent hospitalizations and poorer response to antidepressants. To further explore these questions we studied 41 inpatients meeting RDC diagnosis of MDD for the current episode of illness. 19 of these patients also met criteria for PD during the current episode of illness. Inclusion criteria were: 1. -HRSD score of ≥ 15; 2. -Adequate treatment (at least 3 weeks of 150 mgs Imipramine or 60 mgs of Phenelzine); 3. -Not met criteria for bipolar disorder or psychotic depression. At discharge the response to treatment was worse in patients with MDD/PD than in pure MDD, as indicated by scores on outcome variables of Global Depression, Global Assessment, Carroll Depression, and HRSD. The scores on HRSD items of depressed mood, guilt, middle and terminal insomnia, agitation, and somatic anxiety were significantly higher in MDD/PD group. A logistic regression showed that anxiety was not a significant factor in this outcome difference. Our results suggest that patients with MDD/PD are at higher risk for poorer outcome and clinicians should carefully monitor treatment response in these patients.

NR215 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

SCHIZOTYPAL PERSONALITY/BIOLOGIC CORRELATES

Zvi Zemishlany M.D. Psychiatry VA Medical Center 130 Kingsbridge Road Bronx, NY 10468, Larry J. Siever, M.D., Howard M. Klar, M.D., Miklos F. Losonczy, M.D., Stephen Greenwald, M.A., Kenneth L. Davis, M.D.

Summary:

Biologic measures, implicated as abnormal in schizophrenia, were evaluated in subsamples of 27 schizotypal personality disorder (SPD) patients and compared to subsamples of 91 schizophrenics, 22 normal controls (NC) and 20 patients with other personality disorders (PD), all diagnosed by SADS and SIDP.

Smooth pursuit eye movement (SPEM) impairment (1 sd from normal mean) was more prevalent in schizotypal patients (59.1%, $N=22$) than in normal controls (11.1%, $N=9$) (Fischer exact test, $p < .05$). Mean ventricular-brain-ratio (VBR) on CT scan in SPD (5.27 ± 2.49, $N=17$) was closer to that of schizophrenic patients (5.89 ± 2.47, $N=67$) than to other PD patients (4.47 ± 1.47, $N=8$) or NC ($4.45 \pm .2.22$, $N=20$).

Growth hormone coefficient of variation (0.77 ± 0.46) in a small sample of SPD ($N=5$) was more similar to that observed in a large sample ($N=91$) of schizophrenic patients (0.76 ± 0.39) than to that of NC (0.59 ± 0.38, $N=22$). CSF HVA concentrations in PD patients correlated positively with psychotic-like symptoms as measured by scores on the Chapman Perceptual Aberration Scale ($r=0.83$, $df=11$, $p < 0.005$) and the Physical Anhedonia Scale ($r=0.66$, $df=11$, $p < 0.01$) and the highest values were observed in SPD patients. These findings suggest that biologic abnormalities observed in chronic schizophrenia may also be observed in some patients with SPD.

NR216 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

HORMONAL RESPONSES TO FENTANYL: DIURNAL VARIATION

Ede Frecska M.D. Natl. Inst. Nerv. Men. Dis POB 1 Budapest 27, H, Hungary 1281, Mihály Arató, M.D., Csaba M. Bánki, M.D., György Bagdy, Ph.D., András Perényi, M.D. Márton I.K. Fekete, M.D.

Summary:

Opioids affect the secretion of anterior pituitary hormones and recent studies suggest that this opioid responsiveness shows circadian variation. Alterations of neuroendocrine and chronobiological functions with diurnal change of mood do appear to be characteristic features of major depression; thus opioid sensitivity measures could provide information on underlying mechanisms. We investigated the prolactin (PRL) and thyroid stimulating hormone (TSH) secretory response to the μ-receptor agonist fentanyl (0.1 mg IV) with serial blood sampling in 10 unmedicated females with major depression (DSM-III) and in 10 healthy women of similar age at 9 AM and 9 PM on different days. In 5 persons saline control trials were also performed. A repeated-measures ANOVA yielded a highly significant effect of fentanyl administration on PRL and TSH secretion ($F=42.9$, $p<0.0001$ and $F=10.7$, $p<0.0001$ respectively) but no difference was seen between healthy subjects and depressive patients. In every case there were elevated hormone responses in the evening (PRL: $F=5.18$, $p<0.05$; TSH: $F=14.87$, $p<0.001$) and more drug-related subjective symptoms were reported at this time. These findings do not support the assumption of major alteration in opioid receptor responsivity in depression concerning the regulation of pituitary hormone secretion but indicate a diurnal variation of opioid responsiveness, with the lowest sensitivity in the morning, which is congruent to the diurnal change of mood in this disorder.

NR217 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

RATING THE EXPRESSION OF FACIAL AFFECT IN CHILDREN

Kytja K.S. Voeller M.D. Psychiatry University of Florida Box J234 JHMHC Gainesville, FL 32610, Robert J. Bartucci, M.D., Christiana M. Leonard, Ph.D.

Summary:

Information crucial to normal social behavior is conveyed by specific configurations of facial muscles (Darwin, 1872; Ekman and Friesen, 1976). Primitive neural programs to process these signals are probably present at birth.

With development there is increasing cortical control characterized by conscious awareness of the production of the appropriate emotional signal. Many childhood emotional disorders involve defective social communication, perhaps due to impaired development of cortical control. We are working on an instrument designed to measure children's ability to voluntarily produce affective signals which are tied to a specific emotion.

Fifteen normal children (9 female, 6 male, mean age 8.9 years) were videotaped while (a) describing events that would make them feel happy, angry, sad or frightened and (b) producing the expression appropriate to that experience (intended). Eight frames were selected for each subject: 4 intended and 4 spontaneous expressions (foils). Two independent observers (blind to the intended affect) scored each frame for global emotion, intensity and specific configurations of facial muscles. There was substantial agreement on the global affect of intended expressions (kappa—agreement after chance agreement eliminated—=.70) but only moderate agreement for foils (kappa =.48). Thus, normal 9-year-olds can voluntarily produce appropriate affective signals. Sex and emotion-specific differences will be discussed.

NR218 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

RIGHT HEMISPHERE DYSFUNCTION AND ADD

Kytja K.S. Voeller M.D. Psychiatry Univ of Florida Box J234 JHMHC Gainesville, FL 32608, Kenneth M. Heilman, M.D.

Summary:

In a previous study on children with right hemisphere dysfunction (RHD), an unusually high incidence of Attention Deficit Disorder (ADD) was encountered. Inasmuch as there is a well-defined relationship between attentional disturbances and RHD in adults, we hypothesized that ADD might be a manifestation of RHD. To test this hypothesis, we administered a cancellation task to 9 boys with ADD and 10 without ADD, mean ages 103.2 ± 27.4 and 121.5 ± 21.9 months—not significantly different). The cancellation task requires that target letters (which occur with equal frequency on the right and left sides of the page) be crossed off. ADDs made more total errors than non-ADDs (24.6 vs 7.7, $p < .004$) as well as significantly more errors than controls on the left than right sides. Although Connors Teachers Rating (CTRF) on 6 subjects revealed large differences between ADD and non-ADD groups (mean Z-scores +1.0 for ADDs vs -0.2 S.D. for non-ADDs) this did not attain significance. Two ADDs were started on psychostimulants and the cancellation task was repeated. Total errors decreased substantially, and the left-sided preponderance of errors disappeared. If these observations are borne out by further research, it would suggest a specific neurophysiological basis for ADD and a promising avenue for further research.

NR219 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

PARENTAL VERSUS CHILD REPORT OF CHILDHOOD DEPRESSION

Mary A. Fristad Ph.D. Psychiatry Ohio State University 473 12th Avenue Columbus, OH 43210, Elizabeth B. Weller, M.D., Ronald A. Weller, M.D., Marijo Teare, B.S.

Summary:

The Children's Depression Inventory (CDI) is a modified version of the Beck Depression Inventory for use in children. This self-report instrument is one of the most commonly used and widely researched instruments available to assess childhood depression. As multiple informants are considered preferable to single informants when diagnosing childhood psychopathology, the authors developed a parent's version of the CDI (CDI-P) in which the parent reports on the child's symptoms. The purpose of this study was to: 1) compare and contrast responses to individual items and total scores between parents and children, 2) determine sensitivity (percent of depressed children correctly identified as depressed by the CDI) and specificity (percent of non-depressed children identified as non-depressed by the CDI) of the CDI-P, CDI-C and CDI-Either (CDI-E; positive if either CDI-P or CDI-C indicates depression). Subjects included 78 inpatient children who met DSM-III criteria for major depression, 34 inpatient psychiatric controls and 20 non-hospitalized normal controls. Patterns of item endorsement differed in two ways - children were more likely than parents to endorse extreme responses (i.e., scores of 0,2), and parents were more likely to endorse presence of a symptom (eq, irritability, social withdrawal, somatic complaints). Total scores did not differ between parents and children. Sensitivity was 44% for the CDI-C, 75% for the CDI-P and 87% for the CDI-E. Specificity among psychiatric controls was 67% for both the CDI-C and CDI-P, but was 24% for the CDI-E. Specificity among normal controls was 95% for the CDI-C, 100% for the CDI-P, and 95% for the CDI-E. Based on these results, diagnostic confidence (number of "correct" positive responses/all positive responses) was 37% for the CDI-C, 53% for the CDI-P, and 69% for the CDI-E.

NR220 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

LYME DISEASE: "GREAT IMITATOR" OF THE 1980'S?

Anita M. Lopker M.D. Psychiatry Yale University PO Box 12A Yale Station New Haven, CT 06520

Summary:

Lyme disease (LD) has been recognized as a multisystem infectious disorder caused by the spirochete, Borrelia burgdorferi. Its pathologic effects have been documented in skin, heart, joints and peripheral nervous system. Scattered reports exist of central nervous system involvement presenting as meningoencephalopathies, but behavioral disorders have not been recognized as potential manifestations. Unlike other spirochetal diseases, the natural history of LD bears a striking resemblance to that of Syphilis; by analogy, behavioral disorders might be expected in the course of LD. This study, from September 1985 to January 1987, of fourteen patients with LD confirmed by Rheumatologic and Neurologic evaluations including high IgG antibody titers to B. burgdorferi, documents a spectrum of behavioral disturbances associated with LD. The presence of behavioral disorders was confirmed by Psychiatric evaluation and high scores on the SCL-90. The spectrum can be divided into five groups: psychoses; dementias; chronic mood disorders, personality disturbances; and adjustment reactions. The most dramatic case presented de novo with an insidious psychosis later associated with encephalitis, serological and brain biopsy evidence of B. burgdorferi, and a marked response to penicillin. This case provides a striking model of behavioral disturbance as the initial clue to LD, and offers evidence of the spirochete's neurotropism. Clinicians should note that LD requiring antibiotics may masquerade as psychiatric illness.

NR221 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

THE ROLE OF INTERPERSONAL FUNCTIONING IN TYPE-A BEHAVIOR

Janelle M. Bessette M.A. Psychiatry NY Hospital-CUMC 525 East 68th Street New York, NY 10021, James Halper, M.D.

Summary:

GOALS: Type A behavior is a major risk factor in coronary heart disease (CHD), particularly the hostility and competitive drive components of Type A. This study investigated whether different dimensions of Type A behavior are related to current interpersonal functioning and recollections of parent child interactions.
METHODS: Two hundred seventy young males completed self-report questionnaires: The Jenkins Activity Survey-Form T, The Bell Object Relations Scale, and the Parent Behavior Form.
RESULTS: A path analysis model indicated that Type A's had poor interpersonal functioning, which was predicted by persistent patterns of parental control, hostility and achievement emphasis. Males who remembered their fathers as hostile in their use of control had poorer interpersonal functioning (Beta = .35, $p<.001$), which predicted the hostility and competitive drive components of Type A (Beta = .37, $p<.001$). Memories of mothers' emphasis on achievement predicted feelings of alienation (Beta = .17, $p<.07$), which predicted Type A hostility (Beta = .32, $p<.001$). Memories of fathers' emphasis on achievement was a direct predictor of Type A behavior (Beta = .21, $p<.05$), which was not associated with current interpersonal functioning.
SIGNIFICANCE: Results indicate that Type A hostility and hard-driveness are manifested in deviant adult interpersonal relations, which are rooted in a competitive hostile early social environment. An etiological model is suggested wherein critical, demanding child rearing practices, possibly in interaction with temperament, lead to deviant interpersonal behaviors in adult life which are major risk factors in CHD. Addressing treatment to the Type A's interpersonal environment may be an important avenue for behavioral change.

NR222 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

PSYCHOSOCIAL SEQUELAE OF BARIATRIC SURGERY

Pauline S. Powers M.D. Psychiatry USF Col of Medicine 3515 Fletcher Avenue Room 200 Tampa, FL 33613, Dale Lee Coovert, B.A., Alexander Rosemurgy, M.D., Felecia R. Boyd, ARNP

Summary:

Psychosocial problems may be frequent sequelae of bariatric surgery. Pre- and post-operative data (mean follow-up = 11.5 months) from 29 gastroplasty patients (23 female, 6 male) suggest a number of variables as potential predictors of such complications (all significant at $p < .05$). Patients with a *DSM-III* Axis I disorder (pre-operative) showed a tendency to develop surgical complications, post-operative eating problems, and social adjustment problems. Higher presurgery scores on the Beck Depression Inventory (10 or above) were associated with the development of surgical complications, eating problems, sexual adjustment problems, social adjustment problems, and psychiatric problems. Patients reporting histories of sexual abuse were more likely to develop eating and/or sexual adjustment problems. Patients reporting pre-operative social adjustment difficulties had a tendency to develop surgical complications, psychiatric problems, and sexual and/or social adjustment problems.

Our preliminary conclusion is that patients with pre-operative Axis I diagnoses, elevated Beck scores, or who report histories of sexual abuse or social adjustment difficulties are at greater risk for psychosocial complications following bariatric surgery. While bariatric surgery is an effective means of weight loss for many patients (mean weight loss at follow-up = 85.2 pounds), it is not a cure for psychiatric problems. For such patients, psychotherapy post-surgery is recommended as an adjunct to adjustment to subsequent weight loss.

NR223 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

PSYCHOLOGICAL DISTRESS IN ELDERLY HMO MEMBERS

Bentson H. McFarland M.D. Research Kaiser Permanente 4610 S.E. Belmont Street Portland, OR 97215, Donald K. Freeborn, Ph.D., Clyde R. Pope, Ph.D., John P. Mullooly, Ph.D.

Summary:

This research project examined the relationship between psychological distress and consistency of health care utilization in elderly members of a health maintenance organization (HMO). The study population was 312 adults (65 years of age and older) who had been members of Kaiser Permanente Northwest Region for the five consecutive years 1970—1974. These people were randomly selected from the HMO's total membership in 1970 for participation in an extensive "Household Interview Survey". Responses to the survey were used to construct standard measures of psychological distress such as the Langner Index and a close approximation to the DSM-III diagnostic criteria for major depressive disorder. The elderly HMO members were subsequently categorized as consistently high, consistently low, or mixed users of medical care based on their consumption of resources over the next five years. About 17 percent were classified as consistently high users, some 20 percent were consistently low, and the mixed category comprised the remaining 63 percent of the sample. Comparing the consistently high with consistently low we found that the former had much higher levels of psychological distress than did the latter. In fact, emotional problems comprised the second most common reason for seeking care among the consistently high users. Chronic medical conditions, of course, were the most frequent problem precipitating an encounter with a health care provider. Multivariate discriminant analysis indicated that psychological distress was the most important factor distinguishing consistently high from consistently low users. We discuss the mental health services provided within the HMO for these elderly beneficiaries and describe the role of psychiatrists in the organization.

NR224 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

EGO MECHANISMS OF DEFENSE AND COMPLIANCE IN DIABETES

Alan M. Jacobson M.D. Mental Health Joslin Diabetes Ctr One Joslin Place Boston, MA 02215, Elizabeth Glefand, Ed.D., Stuart T. Hauser, M.D. Joseph I. Wolfsdorf, M.D., Donald Wertlieb, Ph.D., William Beardslee, M.D.

Summary:

In order to understand the influence that diabetic patients' use of defense mechanisms has on their compliance with diabetes management, we followed an onset cohort of 57 children (9–15 y.o.) with recently diagnosed diabetes. Use of 12 defense mechanisms was assessed with scales of demonstrated reliability which were applied to clinical interview material obtained within 3 months of study entry. Compliance with the prescribed diabetes treatment regimen was evaluated quarterly by the child's health care provider over an 18 month period, during the patient's medical visits. Throughout the time patients were followed, use of immature defenses was negatively correlated with compliance. These correlations were stronger during the first half of the follow-up period (Acting-Out $r = -.55$, $p = .0001$; Avoidance $r = -.26$, $p = .05$; Displacement $r = -.37$, $p = .003$; Turning Against the Self $r = -.39$, $p = .002$; *cf.* Altruism $r = +.38$, $p = .003$) than during the second half (Acting-Out $r = -.42$, $p = .001$; Displacement $r = -.26$, $p = .05$; *cf* Altruism $r = +.26$, $p = .05$.) Stepwise regression analyses showed that age, combined with use of Acting-Out and Altruism, accounted for 46% of the variance in compliance during the first half of the follow-up period, and that age plus use of Acting-Out explained 28% of the variance in compliance during the second half. These findings provide empirical support for the utility of this system of assessing psychological defense mechanisms, and for theoretical formulations of defense mechanism hierarachies. They also suggest that defensive style can serve as an early indicator of patients who may be at risk for problems in caring for their diabetes.

NR225 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

SCREENING FOR DEPRESSIONS OF BEREAVEMENT

Selby Jacobs M.D. Psychiatry Yale University 333 Cedar Street New Haven, CT 06510, Fay Hanson

Summary:

The clinical significance of the depressions of bereavement is controversial. Evidence suggests that most of these depressions are benign; a subset of such depressions do not remit spontaneously and require professional attention. The results of a pilot study to screen for depressions of bereavement at six and twelve months after loss of a spouse using a trained, non-professional screener will be presented. The relative value of a dimensional assessment of depression (CES-D) and a structured diagnostic schedule for depression (SCID) as telephone screening measures will be evaluated. In general, the dimensional assessment overestimated the true rate of depression as determined in a subsample on the basis of a clinical diagnostic interview by a psychiatrist using the Hamilton Depression Scale. This study confirmed the existing literature on the high rate of depressions six months (over 25% of bereaved persons) and twelve months (about 15% of bereaved persons) after a loss. These depressions were more common in women than men, in contrast to previous studies, and past personal history of depression and family history of depression were not uncommon. Symptoms of anxiety were prominent, and melancholic symptoms were occasionally observed. The risk factors for this depression will be discussed briefly and criteria for differential diagnosis will be reviewed.

NR226 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

MORTALITY FOLLOWING THE LOSS OF AN ADULT SON

Itzhak Levav, Ha Das Sah University Hospital, Jerusalem, Israel, Erik Peritz, Ph.D., Jeremi Kark, M.D, Yehiel Friedlander,Ph.D.

Summary:

This epidemiological study reports parental mortality risk over a 10 - year period following the death of an adult son killed in the Yom Kippur War (N = 2,556) or due to a non-self inflicted external cause of death (N= 1,551). The role of buffering effects on the loss, such as social support in the Kibbutz, were studied. The Kaplan-Meier estimate of survivorship function was performed in both cohorts of bereaved parents. Comparison of the survival times of the two groups was performed by the log-rank test. A comparison between observed and expected deaths (calculated from a control population) was performed. The findings indicate the risk periods for elevated mortality.

NR227 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

VISITS TO OFFICE-BASED PSYCHIATRISTS: U.S., 1985

Gloria J. Gardocki Ph.D. NCHS 3700 East-West Highway, RM2-43 Hyattsville MD 20879

Summary:

Office-based psychiatrists constitute an integral segment of the mental health care sector. This presentation summarizes newly released national-level information on the number and characteristics of visits to psychiatrists.

The information examined is from the 1985 National Ambulatory Medical Care Survey (NAMCS), conducted by the National Center for Health Statistics. Data on individual visits, collected using a multistage probability sampling design, are inflated to yield national estimates. The resulting information is uniquely valuable for characterizing office-based care in terms of patient demographics and medical problems, and the clinical management of visits.

Selected highlights: In 1985 there were an estimated 18.0 million visits to office-based psychiatrists, or 77 per 1,000 population. This rate reflects an average annual increase of 2.1 percent since the last NAMCS in 1981. Females made 59 percent of the visits, and persons 25-44 years of age made 56 percent. The most common principal diagnoses were depression (18 percent of all visits), and personality disorders (18 percent) affective psychoses, including major depressive disorder (17 percent), and personality disorders (14 percent). Psychotherapy was utilized in 89 percent of the visits, and medication in 46 percent. A detailed report on these findings will be published.

NR228 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

BEYOND DRG'S: VARIABLES THAT PREDICT LENGTH OF STAY

Cynthia L. Cohen M.P.H. Psychiatry NY Hospital-CUMC 525 East 68th Street New York, NY 10021, John A. Sweeney, Ph.D., Gretchen Haas, Ph.D., Allen J. Frances, M.D.

Summary:

BACKGROUND: DRG's have been proposed for cost-containment despite few studies showing that diagnosis predicts length of stay (LOS). The current study goes beyond previous ones in evaluating the contribution of more clinical and demographic variables to the prediction of LOS.
METHODS: For 3,287 consecutive admissions to Payne Whitney Clinic, association with LOS was assessed for diagnosis, age, sex, race, marital status, income, number of people in household, age of first hospitalization, reimbursement, number of previous hospitalizations, Axes IV and V, and severity of illness.
RESULTS: Diagnosis did not correlate with LOS. For the whole sample, only severity of illness and ratio of precipitating stress to level of functioning correlated even minimally with LOS. Seven variables were weakly correlated with LOS for non-psychotic depression; four for atypical psychosis; one for psychotic depression; and none for schizophrenia or bipolar disorder. No variable predicted more than 8% of the variance in LOS for any diagnosis.
SIGNIFICANCE: Clinical and demographic variables generally did not predict LOS. Duration of hospital stay for the individual patient is not predicted by aggregate data. Therefore, the proposal to introduce DRG's for cost containment presents a problem for clinical practice.

NR229 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

RELIABILITY OF TELEPHONE INTERVIEWS

Annamarie Paulson M.D. Psychiatry University of Iowa 500 Newton Road Iowa City IA 52242, Raymond Crowe, M.D., Russell Noyes, M.D., Burce Pfohl, M.D.

Summary:

The reliability of psychiatric diagnosis using the Schedule of Affective Disorders and Schizophrenia-Lifetime Version in personal and telephone interviews with 39 subjects was assessed using a twelve-to-nineteen month test-retest design. Interrater reliability was high (Kappa 0.69–0.84) for the diagnosis of panic disorder, agoraphobia with panic attacks, probable panic disorder, major depression and alcohol abuse. The authors conclude it is possible to make these lifetime diagnoses reliably in a family study using the telephone interview.

TABLE I: Base Rates of Consensus Primary Diagnoses and K Coefficients for Specific Diagnostic Categories

I100

	Patients With Consensus Diagnosis N = 39		Diagnostic Agreement					
Diagnosis	N	%	Agree: Both: Positive	Disagree: Personal Interview Positive	Disagree: Telephone Interview Negative	Agree: Both Negative	% Agreement	K Value
Anxiety Disorders								
Panic Disorder	9	23%	9	3	0	27	92%	.81
Probable Panic Disorder	3	8%	3	0	1	35	97%	.84
Agoraphobia with Panic Attacks	6	15%	6	1	3	29	90%	.69
Agoraphobia without Panic Attacks*	0	0%	0	0	0	39	100%	—
Other Disorders								
Major Depression	6	15%	6	1	3	29	90%	.69
Alcoholism	3	8%	3	0	1	35	97%	.84
No Mental Disorder	15	38%	15	4	2	18	85%	.69

*All agoraphobics also met the criteria for panic disorder.

NR230 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

SCALING OF STRESSFUL LIFE EVENTS AMONG A GROUP OF STUDENTS IN IRAN

Morteza Mohajer M.D. Psychiatry Beheshti, U. Med. Sci., Eveen, Next To Tale Ghani Med., Tehran, Iran, Yasaman Mottaghi-Poor, Ph.D.

Summary:

Holmes and Rahe (1967) were first researchers who devised an instrument for measuring life events. Since their work different scales and measures have been developed and were used with different groups.

In our research we employed paykel (1971) Scale with few modifications to gather information in regards to life events in a completely different culture. The purpose of our research was 1) to arrive at a scaling of life events in Iranian society and 2) to compare our results with those obtained from other societies.

As initial stage 69 dental school students were asked to rank on a 0–20 scale, the degree to which 69 life events were causing stress. A short form of SCL-90 with 29 items which was previously used in Iran were also administered to assess axiety, depression and hostility among the students.

Mean and standard deviation scores were obtained for each event. Events were ranked in a meaningful way and individual variability reflected in standard deviations was moderate. Cultural differences were found in comparing our data with other data available from previous ones.

Present research is first step for future work in this area and comparison between different groups. These findings may have implications for understanding effects of culture in ranking of stressful life events and can be a positive step for future research to look into relationship between stressful life events and mental or physical health in Iran.

NR231 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

THE VALIDITY OF THE STANDARDIZED PSYCHIATRIC EXAM

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

Summary:

The Standardized Psychiatric Examination (SPE) is a structured interview intended to direct psychiatrists to make any DSM-3 diagnosis while permitting them to develop their own judgments as to the presence or absence of particular psychopathological symptoms and states. The SPE was developed at the Baltimore site of the Epidemiologic Catchment Area (ECA) study of the NIMH in response to a request for a protocol to validate the NIMH Diagnostic Interview Schedule (DIS). The SPE incorporates all 140 items found in the Present State Examination (PSE-9) and adopts a similar format for exploration of aspects of the examination of the mental state which PSE-9 lacks. The SPE combines probes for PSE-9 and adds probes similar to those in the SADS for historical and other relevant information. The scope of the SPE includes every criterion mentioned as a diagnostic criterion for DSM-3 Axes I and II. This paper reports evidence supporting both the reliability and validity of the SPE both in clinic populations and among samples of study subjects drawn from the community at large.

In reliability testing among clinic and community subjects (N = 43), kappa ranged from .71 (DSM-3 Substance Use Disorders) to .92 (DSM-3 Major Affective Disorders). PSE-9 CATEGO symptom profiles for cases of DSM-3 Schizophrenia and Major Depression identified by psychiatrists using the SPE in the Baltimore ECA study closely resemble the profiles of schizophrenics and manic-depressives identified in the International Pilot Study of Schizophrenia and the US-UK diagnostic study; moreover, nearly all SPE-identified schizophrenics and major depressives from the ECA fell into corresponding CATEGO S and D classes. In another study, 60 consecutive inpatient major depressive admissions given the SPE had CATEGO profiles identical to those in the ECA and US-UK studies.

NR232 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

ARTIFICIAL INTELLIGENCE BASED THERAPEUTIC DIALOGUE

David Servan-Schreiber M.D. Robotics Ints Carnegie-Mellon U. Schenley Park Pittsburgh PA 15213, Irving I. Binik, Ph.D.

Summary:

In several preliminary studies, computer programs compared favorably to human therapists in eliciting sensitive information from patients and on outcome measures of treatment. Examples include computer delivered systematic desensitization, behavioral treatment of agoraphobia and cognitive-behavior therapy of depression. However, these programs are limited by their inability to develop an internal model of patients (an "understanding") that would serve as a basis for their interventions. This is reflected by their dependence on continuous therapist involvement to assure compliance. We have developed a markedly different approach to computer based therapeutic dialogue, based on expert systems and intelligent tutoring research, which we have applied to the assessment and treatment of sexual dysfunctions. Our program consists of an expert system to take decisions about the couple with which it interacts and to progressively develop an internal model of their situation. Separately, a dialogue driver controls the interaction with the patients and decides on the content, appropriateness and timing of interventions, based on the model. Ten unscreened couples tried an initial consultation with the program and reported on a questionnaire that they felt "understood" and that they would feel confident enough to go through the entire treatment course with the program.

NR233 **Wednesday, May 13, 12:00 noon–2:00 p.m.**

REDUCED NOCTURNAL PENILE TUMESCENCE IN DEPRESSION

Michael E. Thase M.D. Psychiatry Western Psychiatric 3811 O'Hara Street Pittsburgh, PA 15213, Charles F. Reynolds, M.D. J. Richard Jenning, M.D., Joseph Howell, M.S., Ellen Frank, Ph.D., David J. Kupfer, M.D.

Summary:

Although depressed individuals commonly report decreased libido, it is not known if such changes are accompanied by alterations in neurophysiological processes. Preliminary studies suggest that some depressed men may manifest diminished nocturnal penile tumescence (NPT), an objective measure of erectile capacity. Results of ongoing study of NPT are reported for a sample of 34 male outpatients with major depression (DSM-III; SADS/RDC; age = 35.3 ± 10.2 years; Hamilton score: 18.6 ± 3.5) and an age-equated group of 29 healthy controls (age = 33.8 ± 12.3 years). A 3-night EEG sleep/NPT protocol was utilized, with visual estimates of fullness of erection and buckling force determined on night 3. Analysis of night 2 data by MANCOVA revealed significant effects for age, the covariate ($F = 2.86$, $p = .002$), and diagnosis ($F = 2.32$, $p = .02$). Depressed men had significantly diminished NPT time ($F = 16.8$, $p < .001$), even when adjusted for sleep time ($F = 13.4$, $p < .001$) or REM time ($F = 7.2$, $p < .01$). Diminished NPT was correlated with an EEG sleep profile characterized by a short-night's sleep and diminished generation of REM sleep. A higher proportion of depressives had buckling force ≤500-g (38% vs 12%; $p < .03$). Diminished NPT time, low buckling force, and visual inspection ratings of flaccid erection were strongly associated with a history of erectile dysfunction within the index depressive episode ($p < .001$). These findings support the hypothesis that depression in men is associated with decreased erectile capacity, which may be associated with significant sexual dysfunction. Implications for clinical practice and future research will be discussed.

NR 234 **Thursday, May 14 9:00 a.m.–10:30 a.m.**

PLASMA LEVELS OF IMIPRAMINE IN HOSPITALIZED CHILDREN

Steven J. Bupp M.D. Psychiatry University Kansas 1010 N. Kansas Wichita, KS 67214, Sheldon H. Preskorn, M.D., Elizabeth B. Weller, M.D., Ronald A. Weller, M.D.

Educational Objectives:

From this oral slide presentation participants will:
1) Understand the difficulties surrounding prediction of steady-state tricyclic antidepressant blood levels in children.
2) Appreciate the importance of blood level monitoring for treating depression in children.
3) Learn a simple method for attaining therapeutic blood levels in a safe and cost-effective way.

Summary:

The therapeutic range for imipramine in childhood depression is 125–250 ng/ml in terms of maximizing antidepressant response and minimizing adverse effects. In 68 hospitalized children (age 6-14) receiving imipramine 75 mg by mouth at bedtime, we measured steady-state plasma levels of the parent drug and its metabolites by high-pressure liquid chromotography. On this dose (FDA recommended maximum,), 67% had plasma levels below the optimum range, while 13% were above. Interindividual variability (imipramine 12-fold, desipramine 72-fold; 2-hydroxyimipramine 33-fold; 2-hydroxydesipramine 3-fold) could not be predicted by clinical or demographic data using multiple regression analysis. Despite this interindividual variability, plasma levels within a patient on a constant dose were stable (C.V. = 15%). In 51 patients who underwent subsequent dosage change, percent change in dose was linearly correlated to percent change in plasma level within a given individual ($r=76$, $p<.005$). Several clinically important findings have emerged from this work: (1) there is substantial interindividual variability in plasma drug levels, (2) almost 80% of patients on the FDA recommended maximum dose will not develop optimal plasma drug levels, (3) the interindividual variability cannot be predicted by demographic or clinical variables, (4) there is a strong linear relationship between dose and levels.

References:

[1]Preskorn, S.H.: Tricyclic antidepressant plasma level monitoring: an improvement over a dose response approach. *Journal Clinical Psychiatry* #47 (I, suppl) 24-30, 1986.

[2]Weller, E., Weller, R., Preskorn, S.H., Steady state plasma imipramine levels in prepubertal depressed children. *AM J Psychiatry* 139: 506-508, 1982.

NR235 **Thursday, May 14, 9:00 a.m.–10:30 a.m.**

SOMATIC SYMPTOMS IN BEREAVED CHILDREN

Bela Sood M.D. Psychiatry Ohio State University 473 West 12th Avenue Columbus, OH 43210, Elizabeth Weller, M.D., Ronald A. Weller, M.D., Mary A. Fristad, Ph.D., Jennifer Moye, B.A.

Educational Objectives:

To teach physical and mental health care providers about normal course of bereavement, in particular, somatic symptomatology, in children.

Summary:

Bereaved adults are reported to have increased somatic problems that lead to increased morbidity and mortality in the post-loss period. However, little is known about bereavement in children. Several variables have been hypothesized to be related to somatization in grieving children, i.e., age and sex of child, sex of living parent, type of death, and family history of somatic symptomology. In this study 39 bereaved children and their surviving parents were evaluated 8 weeks post-parental death. All were assessed with standard structured diagnostic interviews and rating scales. In general children reported few somatic complaints ($M \pm SD = .6 \pm 1.0$, and parental report of their children's complaints were even lower ($M \pm SD = .2 \pm .1$, $t = 1.91$, $p < .06$). Children who had anticipated their parents' death reported a significantly greater number of somatic symptoms than those who experienced an unanticipated loss ($t = -2.36$; $p < .03$). History of somatic complaints in a family member was also significantly associated with symptom report ($t = -2.45$; $p < .02$), while age, sex of child or living parent did not impact on presence of somatic symptoms. Thus, children with anticipated grief and family history of somatization seemed at risk to develop somatic problems. The long term health consequences of such children should be the subject of further study.

References:

[1]Clayton PJ (1973). Clinical morbidity of first year of bereavement: a review. *Comprehensive Psychiatry* Vol 4, No. 2:151-157.
[2]Higgins GL (1977). Grief reactions. *The Practitioner*, 218:689-695.

NR236 **Thursday, May 14, 9:00 a.m.–10:30 a.m.**

MOTHERS' REPORTS OF DEPRESSION IN THEIR CHILDREN

Naomi Breslau Ph.D. Psychiatry CWRU 2040 Abington Rd. Cleveland, OH 44106, Glenn Davis, M.D., Kenneth Prabucki, B.A.

Educational Objectives:

To understand the comlex effects of informant bias, in particular the potential bias of mothers' depression for family history and high risk research.

Summary:

Mothers continue to serve as important informants for diagnosing children despite the growing use of direct interviews of children. To test whether maternal depression biases the estimated risk of depression in children, when mother-informants are used, we compared mothers' and children's reports of children's depressive symptoms in an epidemiologic sample of 330 mother-child dyads. Parallel structured interviews covering DSM-III criterial symptoms of Major Depression (MDD) were used with the children and mothers about the children. The NIMH-DIS and CES-D were used to diagnose MDD and assess depressive symptoms in mothers. Mothers reported significantly fewer symptoms in their children than the children self-reported. Hierarchial regression showed that MDD (lifetime) and current depressive symptoms in a mother, each independently of the other and controlling for the child's self-reported symptoms, increased significantly a mother's rating of depressive symptoms in her child. E.g. the average child (self-rating = 15.4) was rated 8.7 by a mother negative for MDD and CES-D<16, but, at 14.0 by a mother with MDD and CES-D≥ 16. Thus, mothers' reports markedly overstate the risk of depressive symptoms in children of depressed mothers. In this study, a significant association between maternal MDD and depressive symptoms in offspring was found in the children's self-reports as well as in mothers' reports about their children, but the association was more than twice as strong in mothers' reports.

References:

[1]Weissman, MM, Orvaschel, H, and Padian, N, Children's symptoms and social functioning self report scales: comparison of mothers' and children's reports, *J. Ner. Ment. Dis.* 168:736-740, 1980.
[2]Friedland, S, Weiss, DS, and Taylor, J, Assessing the influence of maternal depression on the validity of Child Behavior Checklist, *J. Abnorm. Child Psychol.* 140:123-133, 1986.

NR237 **Thursday May 14, 9:00 a.m.–10:30 a.m.**

MOTHER/CHILD REPORTS OF CHILD PSYCHOPATHOLOGY

Alan M. Jacobson M.D. Mental Health Joslin Diabetes Ctr One Joslin Place Boston, MA 02215, Janet E. Milley, M.A., Stuart T. Hauser, M.D., Donald Wertlieb, Ph.D., Joseph I. Wolfsdorf, M.D., Raymonde D. Herskowitz, M.D.

Educational Objectives:

To further psychiatrists' understanding of the complexity of using both parent and child reports of a commonly-used measure of child psychopathology in research and clinical settings.

Summary:

In evaluating children, psychiatrists rely on information from multiple sources, including parents and children. Little is known about factors which influence the way parents and children report on child problems. To address this set of issues, mother and child reports of child symptomatology were studied using two standardized, objective instruments, the Youth Self-Report and Parent Report versions of the Child Behavior Checklist. Two groups of children, ages 9–15 were studied: patients with diabetes mellitus ($n = 57$) and a group of healthy children ($n = 61$). We examined the correspondence between mother and child reports of the child's problems. In addition, we studied the impact of specific maternal and child factors upon reports of child symptoms.

Using the kappa statistic, levels of mother-child agreement were very low ($\bar{X} = .13$). Higher mother symptom reports of children were associated with high levels of her own self-reported symptoms (SCL-90; $r = .47$, $p \leq .0001$), increased child age ($r = .28$, $p \leq .002$), lower family SES ($r = .30$, $p \leq .002$), and lower child IQ ($r = -.42$, $p \leq .0001$). No psychosocial factors were associated with child self-reported symptoms. Stepwise regression analysis showed that 32% of the variance of mother reports of child symptoms was accounted for by the level of their own symptoms and the child's IQ. These results highlight the complexity of parent reports of child behavior symptoms. Understanding factors that influence reported symptoms may facilitate clinical and research assessments with commonly-used symptom checklists.

References:

[1]Achenbach, T.M. & Edelbrock, C. Manual for the Child Behavior Checklist. Burlington: University of Vermont, 1983 Edelbrock, C., Costello, A., Dulcan, M., Conover, N.C., & Kala, R.

[2]Parent-child agreement on child psychiatric symptoms assessed via structured interview. *J. Child Psychology & Psychiatry*, 27, 1986, 181-190.

NR238 **Thursday, May 14, 9:00 a.m.–10:30 a.m.**

DOES EARLY PARENTAL LOSS CAUSE ADULT DEPRESSION?

Alan F. Breier M.D. NSB NIMH Bldg 10 RM-4N214 9000 RKV PK Bethesda, MD 20892, John Kelsoe, M.D., Stacy Beller, B.S., Paul Kirwin, B.S., Owen M. Wolkowitz, M.D.

Educational Objectives:

To examine how parental loss in childhood may lead to the development of adult psychopathology.

Summary:

Several studies have reported that parental loss during childhood is related to the development of affective disorders in adulthood. It is, however, unclear what processes may explain how early loss leads to the development of adult psychopathology. To examine the long-term effects of parental loss, we have collected diagnostic (SADS-RDC), behavioral and neuroendocrine (plasma cortisol, β-endorphin, ACTH) data in 90 adults from the general population who suffered parental loss between the ages 2 and 17 years. Behavioral assessment included results from a 32-item instrument developed by the authors that assessed the quality of home-life and personal adaptation (HAPA) during childhood subsequent to the loss.

Sixty-three percent of the sample had a history of major psychiatric disorders (primarily major affective disorder) (PATH group) and, with a few exceptions, were euthymic at the time of participation in the study. Thirty-seven percent had no history of psychopathology (NO PATH group). A stepwise discriminant function revealed that the mean HAPA score was the most powerful predictor of adult psychopathology accounting for correct categorization of 80% of the subjects into PATH and NO PATH groups. A factor analysis of the HAPA revealed that a factor reflecting a nonsupportive relationship with the surviving parent was a particularly strong predictor of adult psychopathology. PATH levels (mean ±SD) of cortisol (μg/dl) (9.0 ± 5) and β-endorphin (9.6 ± 4, $p<0.06$) levels. Moreover, mean HAPA scores significantly correlated with cortisol ($p<0.02$) and ACTH ($p<0.005$) levels.

We conclude that the quality of home life following parental loss, particularly the childhood relationship with the surviving parent may be critical in the development of adult psychopathology. The possibility that early life trauma results in long-lasting pituitary-adrenal axis activation which may lead to developing affective disorders in adulthood will be discussed.

References:

[1]Lloyd C: Life events and depressive disorder reviewed. I. Events as predisposing factors. *Arch Gen Psychiatry* 37:529-535, 1980.

[2]Roy A: Early parental separation and adult depression. *Arch Gen Psychiatry* 42:987-991, 1985.

NR239 **Thursday, May 14, 9:00a.m.–10:30 a.m.**

PERINATAL COMPLICATIONS AND PSYCHIATRIC ILLNESS

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Educational Objectives:

To review the background, rationale, design, preliminary results and future plans of a twenty-year prospective investigation of the relationships between perinatal complications and subsequent development of psychiatric illness.

Summary:

Considerable evidence has accumulated during the past thirty years regarding the relationship between pregnancy and delivery complications and a variety of psychiatric and neurologic disorders. Prior studies have suffered from major methodological problems associated with retrospective designs, most notably selection and recall biases. We are conducting a twenty-year prospective investigation of perinatal complications and psychiatric outcomes. The study cohort consists of 175 single births diagnosed as either "severe toxemia" or "breech delivery" and 175 matched control subjects, all selected from the Providence Center of the National Collaborative Perinatal Project. Extensive obstetrical, neurological, behavioral and sociodemographic information was prospectively collected for these subjects, from the perinatal period through age seven. Subjects were recontacted (ages 18–24) and administered a battery of instruments designed to assess: a) psychiatric diagnosis (using the Diagnostic Interview Schedule); b) cognitive and psychosocial functioning; and c) family history of mental disorders. 85% of the sample have been contacted and 60% successfully interviewed at this time. Preliminary analyses suggest elevated rates of substance use, antisocial personality and schizophrenia-related disorders, but not affective or anxiety disorders in association with the perinatal complications of severe toxemia and breech delivery. Further analyses will examine possible etiologic mechanisms which have been proposed to account for these associations.

References:

[1]Lilienfeld AM, Pasamanick B, Rogers M: Relationship between pregnancy experiences and the development of certain neuropsychiatric disorders in childhood. *Am J Pub Health* 45:637-643, 1955.

[2]Parnas J, Schulsinger F, Teasdale TW, et al: Perinatal complications and clinical outcome within the schizophrenic spectrum. *Brit J. Psychiatry* 140:416-420, 1982.

NR240 **Thursday, May 14, 9:00 a.m.–10:30 a.m.**

PROVOCATION OF PANIC WITH 35% CARBON DIOXIDE

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Education Objectives:

The participant will learn about a new, safe and simple method for the laboratory induction of panic and gain an understanding of the possible role of respiratory abnormalities in the pathogenesis of panic.

Summary:

GOAL: To determine the usefulness of 35% CO2 inhalation as a laboratory challenge test for panic disorder.
METHODS: In an open trial, 8 patients with DSM-III PD received 2 breaths of a 35% CO2-65% O2 mixture (compressed air). Subjects were blind to gas order; investigators were not. The acute panic inventory (API) and an anxiety self rating scale (ASR) were administered before and after inhalation of each gas. Panic determination required not only DSM-III criteria but also a subjective sense of terror, impending doom or desire to flee.
RESULTS: 5 of 8 PD patients and none of 5 normals experienced panic attacks with 35% CO2 (Fischer exact test, $p < .04$, 1-tailed). No one panicked to placebo. CO2-induced panic was described as very similar to naturally occurring panic and there was no difference between API scores for CO2-induced and retrospectively rated naturally occurring panic attacks ($t = .55$, $p = .61$). As measured by the API and ASR, patients who panicked to 35% CO2 reacted more to CO2 than placebo and more markedly to CO2 than did controls. A difference in baseline anxiety did not account for these findings.
SIGNIFICANCE: This study suggests that inhalation of 35% CO2-65% O2 provokes panic in patients with a history of spontaneous panic but not in normal controls. The CO2-induced panic closely resembles clinical panic. Although the panicogenic mechanism of CO2 is not understood, these data are consistent with the hypothesis that PD patients have abnormally sensitive CO2 receptors. The ability of CO2 to quickly induce panic raises the possibility that this sensitivity is not only related to central but also to peripheral chemoreceptors. As a method for the laboratory induction of panic, 35% CO2 is safe, simple and well tolerated. If it proves specific to patients with a history of naturally occurring panic, it will provide a valuable laboratory model for the study of panic.

References:

[1]Gorman, JM, Fyer, MR, Goetz, R. et al: Ventilatory Physiology of Patients with Panic Disorder.
[2]Arch Gen Psych (in press) Griez E and van den Hout M: Panic symptoms after inhalation of carbon dioxide. *Br J Psych* 1984, 144: 503-507.

NR241 **Thursday, May 14, 9:00 a.m.–10:30 a.m.**

COGNITIVE THERAPY OF PANIC DISORDER

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Educational Objectives:

At the end of the program, the learner should be able to evaluate the appropriateness of nonpharmacological treatments of panic disorder. The learner will be made aware of the effect of cognitive therapy on the treatment of panic.

Summary:

Twenty-five patients with panic disorder were treated with cognitive therapy. Individual therapy ranged from 10 to 44 sessions, the mean being 21. Mean number of panic attacks reduced significantly to zero by the twelfth week as measured by a self-report panic log and Zitrin's Acute Panic Inventory. Treatment results were maintained at three, six and twelve month follow-up. All patients were free of panic attacks during this period. Prior to treatment, patients reported a restricted capability to appraise their fears during the panic attacks as measured by the Cognitive Dysfunction Questionnaire. This deficit in assessing and applying information regarding the nature of the panic attacks improved significantly until panic attacks disappeared.

References

[1]Clark, D. (1986) A cognitive approach to panic. *Behavior Research Therapy,* 24 (4), 461-470.
[2]Beck, A.T., Emery, G. & Greenberg, R.L. (1985). Anxiety disorders and phobias: A cognitive perspective. New York: Basic books.

NR242 **Thursday, May 14, 9:00 a.m.–10:30 a.m.**

SIMPLE PHOBIA: EVIDENCE FOR HETEROGENEITY

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Educational Objectives:

Clarify the nosology of anxiety disorders.

Summary:

Simple phobia is a residual category in DSM-III. (1). Clinical experience suggests at least three subtypes of this group: Animal or insect; Blood and injury (BI), and "Situational" phobias. These distinctions are supported by the associations of "vasovagal" faints with blood and injury phobias (2), and of several phobias (e.g., heights, crowds, driving) with the panic/agoraphobia syndrome. In addition, some people present with circumscribed fears associated with gastroesophageal function (i.e., choking while swallowing, or vomiting). To test the validity of the subtypes, we compared patients with one of these "simple" phobias (animal = 25, BI = 9, situational = 46, eating = 8). Significant sex differences were observed ($p < .0005$); all animal and insect phobics and 7 of 8 eating phobics were female while the other two groups showed approximately equal numbers of males and females. Mean age of onset was significantly older ($p < .001$) for situational phobics (27.3 years) than animal (14.9 or BI (12.4); eating phobics were immediate (20.6). Frequency of situational phobias differed significantly among relatives of the 4 proband groups ($p < .05$). Situational phobics averaged .72 relatives with situational phobias. BI, eating, and animal phobic probands averaged .40, .25, and .06 relatives (respectively) with situational phobias. Family histories of the other three phobia subtypes did not differ significantly. Finally, endorsement of SCL-90 item 23, "suddenly scared for no reason" (presumably a panic-like episode) was less likely in animal phobics; however, these episodes were not common in any group and the differences were not significant ($p = .27$). Thus, these clinical and epidemiological variables support the separation of simple phobia into at least these four diagnostic groups.

References

[1]American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders. Edition 3. Washington, D.C., A.P.A., 1980, p. 228-230.

[2]Thyer, B.A., Himle, J., and Curtis, G.C.: Blood-Injury-Illness Phobia: A Review. *Journal of Clinical Psychology,* 41:451-459, 1985.

NR243 **Thursday, May 14, 9:00 a.m.–10:30 a.m.**

LONG TERM EFFICACY OF ALPRAZOLAM IN PANIC DISORDER

Linda M. Nagy M.D. Psychiatry Yale University 34 Park Street New Haven CT 06508 John H. Krystal, M.D., Scott W. Woods, M.D., Dennis S. Charney, M.D.

Educational Objectives:

To inform practitioners about the use of alprazolam in long term treatment of agoraphobia with panic attacks and panic disorder.

Summary:

Alprazolam has been demonstrated to be an effective treatment in Panic Disorder (PD) and Agoraphobia with panic attacks (APA). Unfortunately, little is known about the long term outcome of alprazolam treatment in these disorders.

METHODS: Fifty-five of 73 patients (75%) with DSM-III diagnosis of APA or PD treated in a placebo-controlled efficacy study of alprazolam between 8/82 and 2/85 were reinterviewed 20 to 48 months (30±8 following discharge from the study. During this time they received standard treatment in their communities. Course of illness was evaluated by two research psychiatrists using a structured psychiatric interview (46 pts) or telephone interview (9 pts). Eighteen patients were unavailable or unwilling to participate.

RESULTS: At follow-up (FU) a majority (89%) were maintained on a lower dose of alprazolam (56%) or were able to completely discontinue medication (33%). Few patients were taking the same dose (5%) or a higher dose (5%). Mean dose of alprazolam at discharge was 3.0±1.8 mg/d and at FU was 1.3±1.8mg/d. No patient switched to a different medication; only 4 patients were receiving concomitant medication. Only 56% of patients met current DSM-III criteria for APA or PD at FU. Forty-six percent reported no phobic avoidance for 6 months prior to FU. The number of panic attacks/week at discharge (1.0±2.3) and at FU (1.3±3.9) were both greatly reduced from the initial placebo treatment period (3.9±5.1).

IMPLICATION: Patients clearly do not develop tolerance to the antipanic effects of alprazolam. In addition, most patients are able to maintain improvement on a lower dose or when drug free. These results support the use of alprazolam for short and long term management of panic disorder.

References

[1]Sheehan DV, et al: Some biochemical correlates of panic attacks and their response to a new treatment.

[2]J Clin Psychopharmacol 4:66-75, 1984. Charney DS, et al: Drug treatment of panic disorder: The comparative efficacy of imipramine, alprazolam and trazodone. *J Clin Psychiatry* 47(12):5800585, 1986.

NR244 **Thursday, May 14, 9:00 a.m–10:30 a.m.**

ANTIDEPRESSANTS IN GENERALIZED ANXIETY DISORDERS

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Educational Objectives:

Benzodiazepines have long been the established treatment for clinical anxiety, yet they are not without limitations (sedation, dependence, etc.). The current report provides useful information on the benefits and risks of antidepressants as an alternative treatment option for GAD.

Summary:

The clinical utility of antidepressants in anxiety disorders has been of increasing interest lately. We report here preliminary results of an NIMH funded study (MH-40000) investigating whether antidepressants might also have a role in generalized anxiety disorder. Care was taken to exclude patients with a history of panic disorder or major depression. Ninety-seven patients were randomly assigned to one of four treatment conditions: diazepam, imipramine, trazodone or placebo. Patients were drug free and were required to have anxiety for $>$ 3 months, with HAM-A scores $>$18. Treatment was prospective and double-blind, with an acute phase lasting 8 weeks. Mean maximal daily dose for each drug was: diazepam (30.7 mgs), imipramine (158.8 mgs), trazodone (300 mgs) and placebo (6.57 pills). On the HAM-A scale only diazepam but not imipramine and trazodone differed significantly from placebo ($p<.05$). Side effects were reported by 76% diazepam, 79% imipramine, 84% trazodone and 60% placebo patients. The specific side effect sedation was reported in 57% diazepam, 63% trazodone, 39% imipramine and 7% placebo patients. Between group comparisons of HAM-A scores at endpoint showed no significant difference for any treatment group. The implications for the pharmacologic management of generalized anxiety in outpatient settings will be discussed.

References

[1]Kahn RJ, McNair DM, Lipman RS, et al.: Imipramine and chlordiazepoxide in depressive and anxiety disorders. II. efficacy in anxious outpatients. *Arch Gen Psychiatry* 43:79-85, 1986.

[2]Klein DF: Delineation of two drug-response anxiety syndromes. *Psychopharmacologia* (Berlin). 5:397-408, 1964.

NR245 **Thursday, May 14, 9:00 a.m.–10:30 a.m.**

HIGH RATES OF BEHAVIORAL INHIBITION IN CHILDREN OF AGORAPHOBICS

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Educational Objectives:

Presenting data on children at risk for panic disorder and agoraphobia from a recently completed study, we define the temperamental quality of behavioral inhibition to the unfamiliar and describe its prevalence in children of panic patients compared to comparison groups, and implications for the study of panic disorder.

Summary:

Adult agoraphobia is associated with antecedent childhood distress, particularly separation anxiety and school phobia. Studies suggest that separation anxiety and school phobia are more prevalent in children of agoraphobics who are also at risk for agoraphobia as adults. We have hypothesized that "behavioral inhibition," a temperamental quality well studied by developmental psychologists, may be evident in children of agoraphobic parents as a marker, risk factor, or precursor of childhood and adult anxiety disorders. We are presenting data comparing the frequency of "behavioral inhibition," defined according to age appropriate, standardized assessments, in children ages 2–7 of agoraphobics compared with having family members with other psychiatric illnesses. These children of well diagnosed parents were blindly assessed at the Harvard Infant Study Laboratory as to the presence or absence of behavioral inhibition, which reflects the tendency to manifest excessive withdrawal, inhibition, and physiological responses to novel stimuli and mild cognitive challenge. Fifty-three children were assessed. Children of agoraphobic parents were significantly more inhibited than children of comparison groups. The finding that close to 90% of children of agoraphobics manifested moderate to extreme behavioral inhibition as compared to about 10% of control children ($p < .001$) has important implications for the understanding of the pathogenesis of anxiety disorders.

References

[1]Kagan J, Reznick JS, Clarke et al: Behavioral inhibition to the unfamiliar. *Child Dev* 55:2212, 1984.
[2]Klein DF: Anxiety reconceptualized. *Comp Psychiatry* 21:411-427, 1980.

AUTHOR INDEX