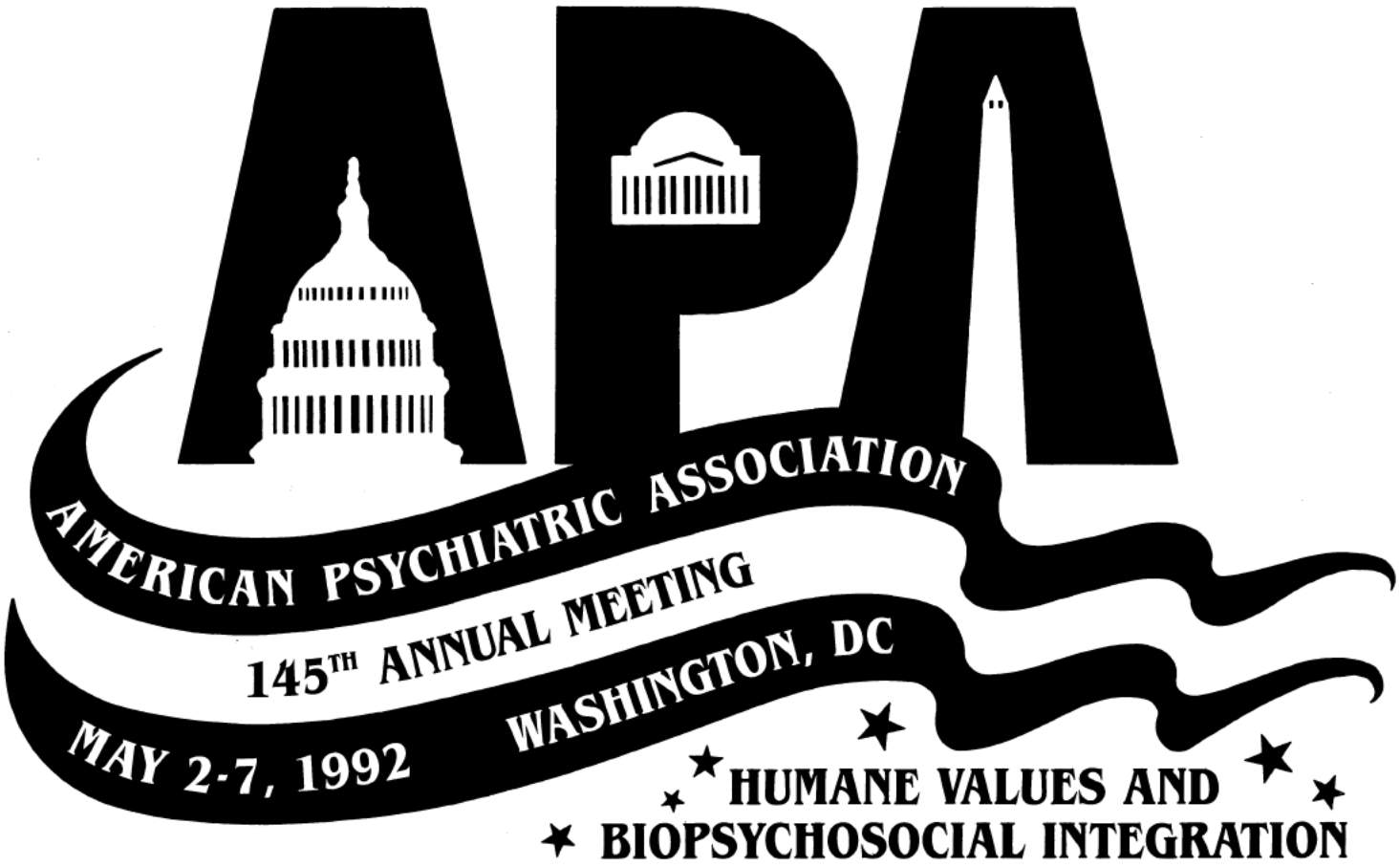
1992 New Research Program and Abstracts



PROGRAM
AND
PAPERS ON NEW RESEARCH

IN SUMMARY FORM

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

WASHINGTON, DC
May 2-7, 1992

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

American Psychiatric Association

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

May 2, 1992

Dear Fellow Research Practitioners and Consumers:

On behalf of the members and staff of the Scientific Program Committee, I would like to welcome you to the 1992 New Research Program.

This year's program reflects the increasing importance of basic and clinical neuroscience to psychiatry. The sessions are organized by topic and have been expanded to accommodate a myriad of excellent submissions.

A new Oral/Slide session for Young Investigators' has been added on Monday afternoon.

The program begins Monday, May 4, at 9:00 a.m. with the first of two Young Investigators' Poster Sessions. It continues at 10:30 a.m. with "Research Advances in Psychiatry: An Update for the Clinician," with special emphasis on the treatment of schizophrenia, differentiating organic/medical factors in mood disorders, treatment of cocaine dependence, and anxiety disorders. The Young Investigators' Oral/Slide Session will begin at 1:00 p.m. on Monday afternoon, followed by a Young Investigators' Poster Session beginning at 3:00 p.m.

The New Research Oral/Slide Sessions will be held Tuesday, May 5, through Thursday, May 7, from 9:00 a.m.-10:30 a.m. Sessions will focus on psychosis; psychotic and dissociative disorders; economic issues; and anxiety and eating disorders (Tuesday); schizophrenia and childhood and adolescent psychiatry (Wednesday); and affective disorders and substance abuse disorders (Thursday). New Research Poster Sessions will be held Tuesday and Wednesday from 12 noon-2:00 p.m. and 3:00 p.m.-5:00 p.m., and on Thursday from 12 noon-2:00 p.m. These sessions will be devoted to brain imaging; neuropsychiatry; AIDS and HIV; biological, C/L, emergency and geriatric psychiatry; organic mental disorders; and psychoimmunology; infant/childhood/adolescent disorders; alcohol and substance abuse; and eating disorders (Tuesday); schizophrenia and neuropsychiatry; anxiety, sexual, somatoform disorders; economic, diagnostic, and women's/men's issues; and forensic, community and individual psychotherapies (Wednesday); and mood disorders; psychopharmacology and other somatic therapies; and suicide (Thursday).

The 43 oral/slide papers and 548 poster presentations (including 220 Young Investigators') are a diverse and, we believe, a representative sampling of that which is new and significant in psychiatric research. We hope that you will find them informative and provocative.

Sincerely,

Susan J. Fiester M.D.

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

Outside Reviewers for the New Research Program

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B. Timothy Walsh, M.D.
Daniel R. Weinberger, M.D.
George E. Woody, M.D.
Stuart C. Yudofsky, M.D.

NEW RESEARCH

Monday, May 4, 1992, 9:00 a.m.-10:30 a.m.

New Research 1—Poster Session—Hall D, Level 1, Convention Center

YOUNG INVESTIGATORS' POSTER SESSION

Moderator: Harold Alan Pincus, M.D.

NR1 Information Processing Effect on Saccadic Reaction Time in Schizophrenia
Douglas M. Berger, M.D., Shinnichi Nezu, M.D., Tomie Iga, B.S., Takashi Hosaka, M.D., Seiro Nakamura, M.D.

NR2 Schizophrenia After Prenatal Exposure to Famine
Ezra S. Susser, M.D., Lin P. Shang, Ph.D.

NR3 Depression in First-Episode Schizophrenia
Amy R. Koreen, M.D., Jeffrey A. Lieberman, M.D., Samuel C. Siris, M.D., Miranda Chakos, M.D., Jose Alvir, Dr. P.H., David I. Mayerhoff, M.D.

NR4 Plasma HVA in First-Episode Schizophrenia
Amy R. Koreen, M.D., Jeffrey A. Lieberman, M.D., Jose Alvir, Dr. P.H., David I. Mayerhoff, M.D., Antony Loebel, M.D., Miranda Chakos, M.D., Thomas Cooper, M.A.

NR5 Schizophrenia: Correlated Onset of Comorbid Symptoms
James M. Russell, M.D., Lee N. Robins, Ph.D., John P. Rice, Ph.D.

NR6 Study of Relapse in Medication Compliant Schizophrenics
Sandra Steingard, M.D., Krishna R. Khambampati, M.D., Maureen Allen, M.P.H.

NR7 Delayed Effects of CRH and ACTH on Dopamine in Man
Joel A. Posener, M.D., Joseph J. Schildkraut, M.D., Gordon H. Williams, M.D., Melinda S. Salomon, Ph.D., Nancy L. McHale, B.S., Alan F. Schatzberg, M.D.

NR8 Comorbidity in First-Episode Psychosis
Stephen M. Strakowski, M.D., Mauricio Tohen, M.D., Andrew L. Stoll, M.D., Gianni L. Faedda, M.D., Pierre V. Mayer, M.D., Meridith L. Kolbrener, B.A., Daniel C. Goodwin

NR9 Neuroimaging in Relatives of Schizophrenics
Jeremy M. Silverman, Ph.D., Richard S.E. Keefe, Ph.D., Miklos F. Losonczy, M.D., Richard C. Mohs, Ph.D., Larry J. Siever, M.D., Kenneth L. Davis, M.D.

NR10 In Vivo Proton Magnetic Resonance Spectroscopy in Never Treated Schizophrenics
Jeff A. Stanley, M.Sc., Peter C. Williamson, M.D., Dick J. Drost, Ph.D., Tom Carr, M.D., Jane Rylett, Ph.D., Harold Merskey, D.M.

NR11 Executive Impairment in Schizophrenia and Old Age
Don R. Royall, M.D., Roderick Mahurin, Ph.D., Janet True, M.D., Brent Anderson, M.S., A. Miller, M.D.

NR12 Adjuvant to Neuroleptics in Chronic Schizophrenia
Pierre-Michel N Llorca, Marc A. Wolf, Thierry C. Bougerol, Christophe Lancon, Jean Claude Scotto

NR13 Subgroups of Schizophrenics Responding to Adjuvant Treatment
Pierre-Michel N Llorca, Thierry C. Bougerol, Marc A. Wolf, Christophe Lancon, Jean Claude Scotto

NR14 Interleukin-1 and Interleukin-2 in the CSF of Schizophrenic Subjects
Rifaat S. El-Mallakh, M.D., Richard Jed Wyatt, M.D.

NR15 Medical Education: Computer Assisted Patient Education
T. Bradley Tanner, M.D., Stuart Gitlow, M.D.

NR16 The Longitudinal Importance of Expressed Emotion
Suzanne King, Ph.D.

NR17 Remoxipride in the Treatment of Schizophrenia
Sanford Herman, M.D., Mark Weilgus, Ph.D., Carol Hermann, M.D., Andrea Berman, Ph.D., Kathleen O'Connor, B.A., John Herrera, Ph.D.

NR18 Biological Analysis in Schizophrenic Patients
Felicidad Rodriguez, M.D., Jesus Ezcurra, M.D.

NR19 Cingulate Gyrus in Schizophrenia Versus Controls
J. Thomas Noga, M.D., Elizabeth Aylward, Ph.D., Godfrey D. Pearlson, M.D.

NR20 Prolactin Decrease and Response to Haloperidol
Howard H.J. Chang, M.D., Alan I. Green, M.D., Roger A. Boshes, M.D., Mohammed Y. Alam, M.D., Joseph J. Schildkraut, M.D.

NR21 Clozapine Versus Haldol in Schizophrenia: A PET Study
Daniel Z. Press, B.A., Karen Faith Berman, M.D., Llewellyn B. Bigelow, M.D., Thomas Noga, M.D., Jill L. Ostrem, B.A., James Gold, Ph.D., Daniel R. Weinberger, M.D.

NR22 Planum Temporal in Schizophrenia: A Magnetic Resonance Study
Alessandro Rossi, Antonio Serio, M.D., Paolo Stratta, M.D., Concetta Petruzzi, M.D., Giovanni Schiazza, M.D., Massimo Casacchia, M.D.

NR23 Integrating Psychosocial Treatment on an Inpatient Schizophrenia Research Unit: A Model for Multidisciplinary Psychoeducation
Ellen Lukens, C.S.W., Kay D. Gimmestad, B.S., Helle Thorning, M.S.W., Ann Feinstein, OTR, Helen Deustch, R.N., Barbara Angell, R.N.

NR24 Information Processing Deficits in Psychoses
Esther F. Rabinowicz, Ph.D., Lewis A. Opler, M.D., David R. Owen, Ph.D., Raymond A. Knight, Ph.D.

NR25 Factor Structure of the Neurological Evaluation Scale in Schizophrenia
Laurence P. Karper, M.D., Morris Bell, Ph.D., Paul Lysaker, Ph.D., Joseph Goulet, M.S., John P. Seibyl, M.D., Joseph P. Erdos, M.D., Louise Brenner, M.S.N., John H. Krystal, M.D.

NR26 Clozapine and Slow Wave Sleep in Schizophrenia
Jon F. Chaffee, M.D., Steven G. Potkin, M.D., Joseph Wu, M.D.

NR27 Heterogeneity in Serotonin Response in Chronic Schizophrenia
Aditayanjee, M.D., Jean-Pierre Lindenmayer, M.D., Sandra Grochowski, B.A., N. Bark, M.D., N. Moynihan, B.S.N.

NR28 Comparison of Paranoid and Schizoid Personalities
Mark Fulton, M.D., George Winokur, M.D.

NR29 Abnormal Laterality in Parents and Schizophrenics
Ellen M. Smith, M.D., Nancy Docherty, Ph.D., Bruce Wexler, M.D.

NR30 PET in Frontal Head Injury and Striatal Metabolism
Stephen Lottenberg, M.D., Nicole Theuvenet, Michelle Solano, Ronald M. Ruff, Ph.D., Jill Stanley, Monte S. Buchsbaum, M.D.

NR31 Dopamine Effects on Hippocampal N-Methyl-D-Aspartate Responses
Stephen J. Schertzer, M.D., Liang Zhang, M.D., Peter L. Carlen, M.D.

NR32 Hypoxia Improves Human Cognitive Function
Thomas E. Schlaepfer, M.D.

NR33 Effects of Adinazolam and N-Desmethyl Adinazolam
Karon Dawkins, M.D., Robert P. Irwin, M.D., Richard L. Hauger, M.D., Joseph C. Fleishaker, Ph.D., William Z. Potter, M.D.

NR34 Ictal EEG Effects of ECT Stimulus Intensity
Andrew D. Krystal, M.D., Richard D. Weiner, M.D., Pamela K. Smith, Rebekka Arias, C. Edward Coffey, M.D.

NR35 Schizotypy and Right Hemisphere Function in Mescaline-Induced Psychosis
Godehard Oepen, M.D., Matthias Funfgeld, Anne Harrington, Ph.D., Gordon Claridge, Ph.D., Hanno Botsch, M.D.

NR36 Fine Motor Performance in Schizophrenia
Jay M. Griffith, M.D., Lawrence E. Adler, M.D., Robert Freedman, M.D.

NR37 Pharmacodynamic Response to Intravenous Idazoxan
Robert C. Risinger, M.D., Mark E. Schmidt, M.D., Ivan N. Mefford, Ph.D., William Z. Potter, M.D.

NR38 Relationship of Low Baseline TSH to TRH Response
Deborah Deas-Nesmith, M.D., William Carson, M.D., Shannon Little, M.D., Raymond Anton, M.D.

NR39 Ratings of Aggression in Autistic Children
Nilda M. Gonzalez, M.D., Monique Ernst, M.D., Jana Signe, B.A., Magda Campbell, M.D., Joan Welkowitz, Ph.D.

NR40 Malignant Catatonia: Sequelae and Treatment
Kemuel L. Philbrick, M.D., Teresa A. Rummans, M.D.

NR41 The Immunological Profile of Patient's with Alzheimer's Disease
Jerzy W. Leszek, M.D., August Wasik, M.D., Barbara Slesak, Ph.D.

NR42 MR Interuncal Distance in Alzheimer's and Parkinson's Disease
Bridget Early, M.A., Rodrigo Escalona, M.D., William M. McDonald, M.D., P. Murali Doraiswamy, M.D., David Axelson, B.A., K. Ranga Rama Krishnan, M.D.

NR43 Noradrenergic System Changes Induced by Electroconvulsive Shock
Stephen K. Brannan, M.D., David J. Jones, Ph.D., Alexander Miller, M.D.

NR44 The Hawaii Experience with Water Intoxication
Linda S. Godleski, M.D., Kenneth Luke, M.D., Barry Carlton, M.D.

NR45 Differential Induction of Early Genes by Neuroleptics
Patrick Rogue, M.D., Anant N. Malviya, Ph.D., Guy Vincendon, M.D.

NR46 Transcription Block and Reduced Nuclear Protein Kinase C Activation During Aging
Patrick Rogue, M.D., Guy Vincendon, M.D., Anant N. Malviya, Ph.D.

NR47 Hedonics During Amphetamine and Cocaine Withdrawal
Daniel M. Mann, Saulo C.M. Ribeiro, Ph.D., Dianne M. Camp, Ph.D., Terry E. Robinson, Ph.D., Kent C. Berridge, Ph.D.

NR48 Speech Abnormalities in Tardive Dyskinesia
Rukhsana Khan, M.D., Kathy Yedor, M.A., Chandragupta Vedak, M.D., V. Chowdary Jampala, M.D.

NR49 MRI, SPECT and Neuropsychological Testing in Psychiatric Patients
Chris A. Conway, M.D., Iqbal Ahmed, M.D., David Gansler, Ph.D.

NR50 Medial Temporal Structures on MRI in Dementia of the Alzheimer Type Offspring
Cynthia M. Churchill, M.D., James P. Fulop, B.A., Steven B. Schwarzkopf, M.D., Stephen C. Olson, M.D., Elizabeth M. Burns, Ph.D., Henry A. Nasrallah, M.D.

NR51 MRI Brain Volume and Gyral Pattern in Schizophrenics
Hiroto Hokama, M.D., Martha E. Shenton, Ph.D., Cynthia G. Wible, Ph.D., Ron Kikinis, M.D., Ferenc A. Jolesz, M.D., Robert W. McCarley, M.D.

NR52 MRI Study of Temporal Lobe Structures in OCD
Stephanie S. Richards, M.S., Elizabeth Aylward, Ph.D., Godfrey D. Pearlson, M.D.

NR53 MRI Volumetrics in Alzheimer's Disease
Andrew B. Newberg, Anand Kumar, M.D., Abass Alavi, M.D.

NR54 MRI Signals in Late-Life Depression Without Vascular Risk Factors
David Miller, M.D., Anand Kumar, M.D., David Yousem, M.D., Gary Gottlieb, M.D.

NR55 Buspirone in the Treatment of Tardive Dyskinesia
Lori E. Moss, M.D., Wayne C. Drevets, M.D., Vernon M. Neppe, M.D.

NR56 Clinical Profiles of Antidepressants: A Meta-Analysis on 400 Patients
Marie-Josee Filteau, M.D., Yvon D. Lapierre, M.D., David Bakish, M.D., Blanchard Blanchard, B.A.

NR57 Causes of Neuroleptic Discontinuation in Tourette's Syndrome
Raul R. Silva, M.D., Harry J. Magee, M.D., Arnold J. Friedhoff, M.D., Monique Ernst, M.D.

NR58 Early Onset of Lithium-Induced Hypothyroidism
Annick Vincent, M.D., Philippe Baruch, M.D., Pierre Vincent

NR59 Haloperidol: Therapeutic Window in Schizophrenia
Miguel Bernardo, Ph.D., Diego J. Palao, M.D., Alberte Arauxo, M.D., Merce Brunet, M.D., Jose Ferrer-Raldua, M.D., Enrique Gonzalez-Monclus, Ph.D.

NR60 Bipolar Disorder and Response to Valproate
Lance M. McCoy, M.D., Nicholas Votolato, R.P.H., Steven B. Schwarzkopf, M.D., Henry A. Nasrallah, M.D.

NR61 Maintenance ECT: Recipients More Severely Ill?
Teri Schwartz, M.D., Keith Isenberg, M.D., Jan Loewenstein, R.N.

NR62 Treatment of Premature Ejaculation with Prozac
Roger T. Crenshaw, M.D., Mark G. Wiesner, Ph.D.

NR63 Neuropsychiatric Functioning in Graves' Disease
Robert A. Stern, Ph.D., Lisa M. Duke, B.A., Clare E. Morey, B.A., John R. Perry, M.D., William H. McCartney, M.D., Arthur J. Prange, Jr., M.D.

NR64 Systematic Identification of Down Syndrome Genes
Adelaide S. Robb, M.D., Miles B. Brennan, Ph.D., Ute Hochgeschwender, M.D.

NR65 Morphine-Induced Delirium: A Retrospective Analysis
Kent C. Eller, M.D., Antonio C. Sison, M.D., William Breitbart, M.D., Steven Passik, Ph.D.

NR66 Depression in Alzheimer's Disease
Pedro Saz, M.D., Antonio Lobo, M.D.

NR67 Aggression and Agitation in Dementia
Jill S. Meyer, M.D., Allen Raskin, Ph.D., Jerome Levine, M.D., Michael Peszke, M.D., Paul E. Ruskin, M.D.

NR68 Treatment Outcome After Competency Determination
Jill S. Meyer, M.D., Frederick Knowles III, M.D., Joseph Liberto, M.D., Allen Raskin, Ph.D., Paul E. Ruskin, M.D., F.M. Baker, M.D.

NR69 Geriatric Depression: Screening with Two Geriatric Depression Scale Versions
Rodney L. Nitcher, D.O., William J. Burke, M.D., William H. Roccaforte, M.D., Steven P. Wengel, M.D.

NR70 ECT in Very Elderly Patients
Stephen C. Mory, M.D., Grunhaus Leon, M.D., David B. Arciniegas, B.S., Atul C. Pande, M.D., Rajiv Tandon, M.D.

NR71 Aggression in an Elderly Schizophrenic Population
Srikumar Menon, M.D., Patricia Molla, M.S.N., Linda Blake, B.S.N., Mary Rose Cordas, B.S.N., Michael Peszke, M.D., Allen Raskin, Ph.D.

NR72 Effects of Reactivating Occupational Therapy in Dementia
Doris Bach, Ph.D., Thomas Fruhwald, M.D., Franz Boehmer, M.D., Brigitte Grilc, Michael Bach, M.D.

NR73 The Pattern of Cognitive Deterioration on the Alzheimer's Dementia Assessment Scale in Patients with Alzheimer's Disease
Robert G. Stern, M.D., Richard C. Mohs, Ph.D., James Schmeidler, Ph.D., Michael Davidson, M.D., Kenneth L. Davis, M.D.

NR74 The Delirium of Trauma
Yasutaka Iwasaki, M.D., Hisashi Kurosawa, M.D., Nobuo Watanabe, M.D.

NR75 Delirium Presenting with Symptoms of Depression
Linda M. Nicholas, M.D., Byron A. Lindsey, M.D.

NR76 Psychiatric Diagnoses in Desert Storm Casualties
Charles Perrotta, Jr., M.D., Carolyn D. Randle, M.D.

NR77 Severity of Psychosocial Parameters: Young Versus Old
Ibrahim Gunay, M.D., Julia Rothe, M.Ed., Eugene Somoza, M.D.

NR78 Silent Myocardial Ischemia, Denial and Locus of Control
Christine Reynaert, Pascal Janne, Ph.D., Patrick De Coster, M.D., Rene Kremer, M.D., Edgard Coche, M.D., Leon Cassiers, M.D.

NR79 Patient Controlled Analgesia and Psychiatry
Christine Reynaert, Pascal Janne, Ph.D., Michelle Pirard, Ph.D., Vincent Delire, M.D., Edgard Coche, M.D., Leon Cassiers, M.D.

NR80 Psychiatric and Psychometric Features in Acne Excoriee
Michael Bach, M.D., Doris Bach, Ph.D.

NR81 Noncompliance in Adolescent and Young Adult Liver Transplant Recipients
Angela H. Lee, M.D., Robert G. Gish, M.D., Waldo Concepcion, M.D., Paul Nakazato, M.D., Carlos O. Esquivel, M.D.

NR82 Magnesium in Menstrual-Related Mood Disorders
Donald L. Rosenstein, M.D., Jeanette M. Hosseini, B.S., Ronald J. Elin, M.D., David R. Rubinow, M.D.

NR83 Fluoxetine Versus Placebo in Treatment of Late Luteal Phase Dysphoric Disorder
David E. Schenk, M.D., Charles Perrotta, Jr., M.D., James S. Williford, M.D., Joseph A. Whitfield, M.D., James P. Reed, M.D.

NR84 Dopamine System in Schizotypal Personality Disorder
Farooq Amin, M.D., Larry J. Siever, M.D., Robert Trestman, M.D., Jeremy Silverman, Ph.D., Peter Knott, Ph.D., George Anderson, Ph.D., Kenneth L. Davis, M.D.

NR85 Biology of Impulsivity, Suicide and MDD in Axis II
Robert L. Trestman, M.D., Emil F. Coccaro, M.D., Susan Weston, M.D., Vivian Mitropoulou, M.A., Felice Ramella, B.A., Steven Gabriel, Ph.D., Larry J. Siever, M.D.

NR86 Cognitive Processes in Borderline Personality
Kathleen T. Hamblin, Ph.D.

NR87 Diagnosis of BPD by Three Scales
Reed Goldstein, Ph.D., William G. Herron, Ph.D., Alan M. Gruenberg, M.D.

NR88 BPD at Three Sites
James J. Hudziak, M.D., Todd J. Boffeli, M.D., Samuel B. Guze, M.D., Jerold Kreisman, M.D., Marco M. Battaglia, M.D.

NR89 Personality Disorders in Atypical Depression
Ron G. Goldman, M.D., Patrick J. McGrath, M.D., Deberah S. Goldman, Ph.D., Jonathan W. Stewart, M.D., Frederic M. Quitkin, M.D.

NR90 Personality and Perceptual Asymmetry in Depression
Ron G. Goldman, M.D., Gerard E. Bruder, Ph.D., Jonathan W. Stewart, M.D., Patrick J. McGrath, M.D., Deberah S. Goldman, Ph.D., Frederic M. Quitkin, M.D.

NR91 Severity of Sleep Apnea and Degree of Psychopathology
Rocco L. Manfredi, M.D., Anthony Kales, M.D., Alexandros N. Vgontzas, M.D., Edward O. Bixler, Ph.D., David Myers, B.A.

NR92 Sleep Apnea: Cognitive Deficits are Not Mood Related
Alexandros N. Vgontzas, M.D., Ralph A.W. Lehman, M.D., Rocco L. Manfredi, M.D., Edward O. Bixler, Ph.D., Lynne Curran, B.A.

NR93 Sleep Disturbances in Chronic Fatigue Syndrome
Jon K. Zubieta, M.D., Mark A. Demitrack, M.D., Dean Krahn, M.D., N. Cary Engleberg, M.D., James E. Shipley, M.D., Alan B. Douglass, M.D.

NR94 Residents' Attitudes Toward Suicidal Patients
Helen M. Biren, M.D., William C. Wirshing, M.D., Joel Yager, M.D.

NR95 Suicide in 336 Acute Patients: A Five Year Follow-Up
Anelise Muhiebach, Ph.D., Antonio V. Andreoli, M.D., Gabriel Bittar, Ph.D.

NR96 Assaults on an Inpatients Ward
Martha L. Crowner, M.D., Brian Anderson, M.D., Menahem Krakowski, M.D., Jan Volavka, M.D.

NEW RESEARCH

Monday, May 4, 1992, 1:00 p.m.-2:30 p.m.

*New Research 2—Oral/Slide Session—Room 28, Level 1, Convention Center

YOUNG INVESTIGATORS' ORAL/SLIDE SESSION

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

NR97	Blood Pressure Change and Memory Deficit in ECT Ioannis M. Zervas, M.D., Lina Jandorf, M.A., Max Fink, M.D.	1:00 p.m.
NR98	High-Dose of Glycine in the Treatment of Schizophrenia Ilana Z. Nussenzveig, M.D., Daniel C. Javitt, M.D., Gail S. Silipo, M.A., U. Heresco-Levy, M.D., Jean-Pierre Lindenmayer, M.D., Stephen R. Zukin, M.D.	1:10 p.m.
NR99	One Hundred Years of Schizophrenia James D. Hegarty, M.D., Mauricio Tohen, M.D., Ross J. Baldessarini, M.D.	1:20 p.m.
NR100	Cocaine-Ethanol and Cocaethylene: Clinical Effects Elinore F. McCance-Katz, M.D., Lawrence H. Price, M.D., Christopher J. McDougle, M.D., Jed E. Black, M.D., Thomas R. Kosten, M.D., Peter I. Jatlow, M.D.	1:30 p.m.
NR101	Carbamazepine Use in Geropsychiatric Patients Stephen M. Aronson, M.D., Alan M. Mellow, M.D.	1:40 p.m.
NR102	Treatment of Older Depressives in a Geropsychiatry Versus General Psychiatry Clinic: A Comparison Study Nusrath Hasan, M.D., Elisse Kramer-Ginsberg, Ph.D., Blaine S. Greenwald, M.D., Jorge Ramos-Lorenzi, M.D., Peter Aupperle, M.D., Neil Kremen, M.D.	1:50 p.m.
NR103	Fluoxetine and Bupropion in Old-Old Depressives Barry Mildener, M.D., Elisse Kramer-Ginsberg, Ph.D., Blaine Greenwald, M.D., Neil Kremen, M.D., Peter Aupperle, M.D., Rosanne Leipzig, M.D.	2:10 p.m.

*offers category II.

NEW RESEARCH

Monday, May 4, 1992, 3:00 p.m.-5:00 p.m.

New Research 3—Poster Session—Hall D, Level 1, Convention Center

YOUNG INVESTIGATORS' POSTER SESSION

Moderator: Susan J. Fiester, M.D.

NR104 Effects of Depression and ECT on Subjective Memory
Eliza A. Coleman, B.A., Harold A. Sackeim, Ph.D., Joan Prudic, M.D., D.P. Devanand, M.D.

NR105 Psychodynamic Defenses in Dysthymia
Amy L. Bloch, M.D., John M. Markowitz, M.D., M. Katherine Shear, M.D., Andrew C. Leon, Ph.D., Elizabeth Winkelman

NR106 Defining Remission in Major Depression
Markus Peter Fickinger, M.D., Michael H.M. Philipp, M.D.

NR107 Elevated Platelet Membrane Phosphatidylinositol-2 in Bipolar Mania
Alan S. Brown, M.D., Alan G. Mallinger, M.D.

NR108 Clomipramine Augmentation in Resistant Depression
Martin H. Rosenzweig, M.D., Jay D. Amsterdam, M.D.

NR109 MDD State Dependent Cortisol Response to Clonidine
Julia Temple, M.D., Robert L. Trestman, M.D., Emil Coccaro, M.D., Vivian Mitropoulou, M.A., Felice Ramella, B.A., Steven Gabriel, Ph.D., Larry J. Siever, M.D.

NR110 Measures of Serotonin Function After Sleep Deprivation
Ronald M. Salomon, M.D., Pedro L. Delgado, M.D., Helen L. Miller, Julio Licinio, M.D., Dennis S. Charney, M.D., George R. Heninger, M.D.

NR111 Idazoxan: Effects on Catechols and Depression
Mark E. Schmidt, M.D., William Z. Potter, M.D., Husseini K. Manji, M.D., Karon Dawkins, M.D., Robert C. Risinger, M.D.

NR112 Fluoxetine Reduces CSF, CRH and Arginine Vasopressin in Depression
Michael D. De Bellis, M.D., Thomas D. Geracioti, Jr., M.D., Samuel J. Listwak, M.A., William T. Gallucci, M.S., David Michelson, M.D., Philip W. Gold, M.D., Mitchel A. Kling, M.D.

NR113 MRI Basal Ganglia Volumes in Bipolars
Joy Roberts, M.D., Elizabeth Aylward, Ph.D., Carol E. Peyser, M.D., Godfrey D. Pearlson, M.D.

NR114 Mixed and Dysphoric States in Bipolar Patients
Gianni L. Faedda, M.D., Stephen M. Strakowski, M.D., Mauricio Tohen, M.D., Trisha Suppes, M.D., Andrew L. Stoll, M.D., Pierre V. Mayer, M.D., Daniel C. Goodwin, Meredith L. Kolbrener, Ross J. Baldessarini, M.D.

NR115 Personality Disorders in Patients with Depression
Bonnie L. Stewart, Ph.D., Alan M. Gruenberg, M.D., Reed Goldstein, M.D., Gary S. Bruss, Ph.D.

NR116 Mood Disorder in Families with Marfan Syndrome
Francis J. McMahon, M.D., Reed E. Pyeritz, M.D., Colleen M. Dougherty, M.S., J. Raymond DePaulo, Jr., M.D.

NR117 Expressed Emotion and Siblings: Compounded Stress?
Solange Marchildon, Ph.D., Suzanne King, Ph.D., Teeya Blatt, M.A.

NR118 DST in Drug-Free Patients
Isil Vahip, M.D., Simavi Vahip, M.D., Levent Mete, M.D., Figen Toprak, M.D.

NR119 Depression and Lyme Disease: A Controlled Survey
Brian A. Fallon, M.D., Jenifer A. Nields, M.D., Donato DelBene, B.A., Jay Saoud, M.S., Kenneth Wilson, M.D., Michael R. Liebowitz, M.D.

NR120 Longitudinal Study of Women with Breast Cancer and Major Depressive Disorder
Mary L. DeFlorio, M.D., Jimmie C. Holland, M.D., Lynna Lesko, M.D., Alice Kornblith, Ph.D., Diane Baiano, R.N.

NR121 Fluoxetine Versus Desipramine in Women with Breast Cancer and Major Depressive Disorder
Mary L. DeFlorio, M.D., Jimmie C. Holland, M.D., Lynna Lesko, M.D., Alice Kornblith, Ph.D., Diane Baiano, R.N.

NR122 Hypochondriasis and Medical Illness in Depressives
Jeffrey M. Lyness, M.D., Deborah King, Ph.D., Yeates Conwell, M.D., Eric D. Caine, M.D., Christopher Cox, Ph.D.

NR123 Psychopathology in Ill Children: Discrepancies Between Parent and Child Reports
Emily S. Harris, M.D., Suzanne B. Hanser, Ed.D., Kathryn A. Shade, B.A.

NR124 Epileptoid Features in Mood Disorders
Nutan Atre-Vaidya, M.D., Michael A. Taylor, M.D., V. Chowdary Jampala, M.D., Harriett Stein, R.N.

NR125 Intravenous Haloperidol for Treatment-Resistant Mania
Atul Mahableshwarkar, M.D., Chandra Vedak, M.D., V. Chowdary Jampala, M.D., J.S.R. Van, M.D.

NR126 Social Zeitgeber Disruption in Major Depression
Martin P. Szuba, M.D., Alison Yager, Barry H. Guze, M.D., Eva M. Allen, B.A., Lewis R. Baxter, Jr., M.D.

NR127 Diurnal Mood Variation in Seasonal Affective Disorder
Elton T.C. Ngan, M.D., Raymond W. Lam, M.D., Campbell M. Clark, Ph.D.

NR128 The Brief Quality of Life Rating Scale
Ariane Rogue, M.D., Patrick Rogue, M.D.

NR129 Prospective Long-Term Follow-Up of Seasonal Affective Disorder Patients
Georg K. Leonhardt, M.D., Hans J. Haug, M.D., Peter R. Graw, Ph.D., Dorothee Wunder, Anna Wirz-Justice, Ph.D.

NR130 Psychoneuroendocrine Effects of Physostigmine
Susan G. Silva, Robert A. Stern, Ph.D., Robert N. Golden, M.D., Elizabeth J. Davidson, Ph.D., George A. Mason, Ph.D., David S. Janowsky, M.D.

NR131 Neuroleptic Exposure in Lithium-Treated Mania
Michael J. Sernyak, M.D., Robin Johnson, M.D., Ruth Griffin, R.N., H. Rowland Pearsall, M.D., Scott W. Woods, M.D.

NR132 Research Versus Clinical Diagnosis of Mood Disorders
Leah Gniwesch, B.A., James Kocsis, M.D.

NR133 Serum Chloride Levels in Agitated Depression
Cheng-Jen Chen, M.D., Elisha M. Tarlow, B.A., Herminia Ombid, B.A., Peter E. Stokes, M.D.

NR134 Comparison of Primary and Secondary Panic Disorder
Vladan Starcevic, M.D., Eberhard H. Uhlenhuth, M.D., Robert Kellner, M.D., Dorothy Pathak, Ph.D.

NR135 Effects of Desipramine on Resting Metabolic Rate in Panic Disorder
Naresh P. Emmanuel, M.D., Robert B. Lydiard, M.D., Alex W. Morton, Pharm.D., Michele T. Laraia, M.S.N., Joseph J. Zealberg, M.D., Gail W. Stuart, R.N., James C. Ballenger, M.D.

NR136 CSF, CCK and Beta-Endorphin in Panic Disorder
Richard Payeur, M.D., Robert B. Lydiard, M.D., Kathleen Brady, Ph.D., Joseph J. Zealberg, M.D., James C. Ballenger, M.D.

NR137 CSF and Beta-Endorphin in Panic Disorder and Social Phobia
Michael P. Johnson, M.D., Robert B. Lydiard, M.D., James C. Ballenger, M.D., Michele T. Laraia, M.S.N., Mark D. Fossey, M.D., Joseph J. Zealberg, M.D.

NR138 Lack of Effect of Flumazenil on CCK-4-Panic
Anne Couetoux-Dutertre, M.D., Jacques Bradwejn, M.D., Diana Koszycki, M.A., Michel Paradis, M.D., Michel Bourin, M.D.

NR139 PTSD and Hypertension
Olga Brawman-Mintzer, M.D., Thomas A. Mellman, M.D., Nelson D. Hernandez, M.D., S. George Hanna, M.D., Ramon A. Boza, M.D.

NR140 Clomipramine, Fluoxetine and Glucose Control
Lawrence Katz, M.D., Laura J. Fochtmann, M.D., Michele T. Pato, M.D.

NR141 Acute Tryptophan Depletion in Drug-Remitted OCD
Linda C. Barr, M.D., Lawrence H. Price, M.D., Christopher J. McDougle, M.D., Pedro L. Delgado, M.D., Wayne K. Goodman, M.D.

NR142 Specificity of Anger Response to m-CPP
Mark Germine, M.D., Andrew W. Goddard, M.D., Diane E. Sholomskas, Ph.D., George R. Heninger, M.D., Dennis S. Charney, M.D., Scott W. Woods, M.D.

NR143 Serotonin-3 Receptor Blockade on MCPP Response in OCD Patients
Andreas Broocks, M.D., Teresa A. Pigott, M.D., Dennis L. Murphy, M.D., Stephanie Canter, B.A., Tana A. Grady, M.D., Francine L'Heureux, M.D.

NR144 A Controlled Trial of Clonazepam Augmentation in OCD Patients Treated with Clomipramine or Fluoxetine
Teresa A. Pigott, M.D., Francine L'Heureux, M.D., Cheryl S. Rubenstein, M.A., James L. Hill, Ph.D., Dennis L. Murphy, M.D.

NR145 Dissociative Experiences Scale Scores in Patients with OCD
Teresa A. Pigott, M.D., Stephanie Canter, B.A., Frank W. Putnam, M.D., Francine L'Heureux, M.D., Dennis L. Murphy, M.D.

NR146 Neuropsychological Testing in OCD
Billinda Dubbert, R.N., Teresa A. Pigott, M.D., Irene Dalton, B.S., Francois M. Lalonde, Ph.D., Dennis L. Murphy, M.D., Alex Martin, Ph.D.

NR147 Body Dysmorphic Disorder: 50 Cases of Imagined Ugliness
Katharine A. Phillips, M.D., Susan L. McElroy, M.D., Paul E. Keck, M.D., Harrison G. Pope, M.D., James I. Hudson, M.D.

NR148 Serotonin Responses to D-Fenfluramine and Buspirone in OCD
James V. Lucey, M.B., Anthony W. Clare, M.D., Timothy G. Dinan, M.D.

NR149 Caffeine Use in Generalized Anxiety Disorder
Jeffrey N. Billett, M.D., Richard J. Maddock, M.D., Cameron S. Carter, M.D.

NR150 Soft Signs and Familial Transmission of OCD
Bonnie Aronowitz, M.A., Eric Hollander, M.D., Salvatore Mannuzza, Ph.D., Jodee Davis, M.A., Tim Chapman, M.S., Abby J. Fyer, M.D.

NR151 Symptom Progressions in OCD
David C. Rettew, B.A., Susan E. Swedo, M.D., Henrietta L. Leonard, M.D., Marge C. Lenane, M.S.W., Judith H.L. Rapoport, M.D.

NR152 A Descriptive Study of Compulsive Shoppers
Gary A. Christenson, M.D., Ronald J. Faber, Ph.D., Martina De Zwaan, M.D., Nancy C. Raymond, M.D., Sheila M. Specker, M.D., James E. Mitchell, M.D.

NR153 Psychological Symptoms in Mitral Valve Prolapse: A Control Study
Larry V. Amsel, M.D., Katherine M. Shear, M.D., Richard Devereux, M.D., Randi Kramer-Fox, M.S.

NR154 Descriptive Characteristics of Various Somatoform Disorders
Michael Bach, M.D., Detlev O. Nutzinger, M.D., Martina De Zwaan, M.D., Lydia Hartl, M.D.

NR155 Decreased Hippocampal Volume in PTSD
J. Douglas Bremner, M.D., John P. Seibyl, M.D., Tammy N. Scott, B.S., Steven M. Southwick, M.D., Dennis S. Charney, M.D., Robert B. Innis, M.D.

NR156 Deficits in Short-Term Memory in PTSD
J. Douglas Bremner, M.D., Tammy N. Scott, B.S., Richard Delaney, Ph.D., Steven M. Southwick, M.D., David R. Johnson, Ph.D., Dennis S. Charney, M.D.

NR157 The Clinician Administered Dissociative States Scale
J. Douglas Bremner, M.D., Frank W. Putnam, M.D., Steven M. Southwick, M.D., Cathryn Hansen, M.S., Glenna King, B.A., Dennis S. Charney, M.D.

NR158 Noradrenaline: Serotonin Function in Insecure Primates
Jeremy D. Coplan, M.D., Leonard A. Rosenblum, Ph.D., Steven Friedman, Ph.D., Trina B. Bassoff, M.A., Jack M. Gorman, M.D.

NR159 Noradrenaline: Serotonin Interaction in Panic
Jeremy D. Coplan, M.D., Laszlo A. Papp, M.D., Jose Martinez, M.D., Leonard A. Rosenblum, Ph.D., Jack M. Gorman, M.D.

NR160 Biogenic Amines in HIV Infection Patients
Donatella Marazziti, M.D., Pasquale Perretta, M.D., Letizia Galli, M.D., Cristiana Nisita, M.D., Antonio Scasso, M.D., Giovanni B. Cassano, M.D.

NR161 Psychiatric Morbidity and Grief in HIV Infected Men
Jacquelyn Summers, M.S.W., J. Hampton Atkinson, M.D., Sidney Zisook, M.D., Wesley W. Whitehall, M.A., J. Chandler, M.D., I. Grant, M.D.

NR162 Health Education for HIV Subjects in Clinical Setting: An Evaluation
Rao A. Venkoba

NR163 Comparison of Hemophiliacs and Gay Men with HIV
Snezana Cvejin, M.D., Jane Leserman, Ph.D., Diana O. Perkins, M.D., Carol Murphy, R.N., Kimberly Thompson, B.A., Dwight L. Evans, M.D.

NR164 Social Conflict, Depression and AIDS
Martha E. Leatherman, M.D., Jane Leserman, Ph.D., Diana O. Perkins, M.D., Carol Murphy, R.N., John Boucvalt, B.S., Dwight L. Evans, M.D.

NR165 Prevalence of Unsafe Sexual Behaviors Among Psychiatric Inpatients
Srikumar Menon, M.D., Sherry Pomerantz, Ph.D., Ernest Peacock, M.A., Corinthia Cohen, R.N., Sarahlee Horowitz, Psy.D.

NR166 Suicidality, Psychiatric Morbidity and HIV Infection
John S. McDaniel, M.D., Elisabeth Fowlie, B.S., Obo Addy, M.D., Steven A. Cohen-Cole, M.D.

NR167 A Prospective Study of HIV-Associated Psychosis
Daniel D. Sewell, M.D., Dilip V. Jeste, M.D., J. Hampton Atkinson, M.D., James L. Chandler, M.D., Igor Grant, M.D., HNRC Group

NR168 Psychological Distress of IV Drug Users with HIV Disease
Vasu Putcha, M.D., Maureen Kahn, M.D., Edward Latimer, M.D., Carol L. Alter, M.D., James Maher, M.D., Haftan Eckholdt, Ph.D., Thomas M. Sprague, D.O.

NR169 Psychiatric Symptoms and Stress in HIV Positive Women
Cheryl Ann Kennedy, M.D., Patricia Kloser, M.D.

NR170 Psychiatric Morbidity in Women Infected with HIV
Steven L. Prenzlauer, M.D., Elizabeth Getter, M.D., Philip A. Bialer, M.D., Joel J. Wallack, M.D.

NR171 Personality Disorders in HIV
Stephen J. Brown, M.D., Jacquelyn Summers, M.S.W., J. Hampton Atkinson, M.D., Wesley W. Whitehall, M.A., James L. Chandler, M.D., Igor Grant, M.D.

NR172 Personality Disorder in HIV
David F. Naftolowitz, M.D., Diana O. Perkins, M.D., Robert A. Stern, Ph.D., Jane Leserman, Ph.D., Michael A. Senger, M.A., Dwight L. Evans, M.D.

NR173 Psychiatric Referral for Substance Disorders
Iqbal Q. Sheikh, M.D., Maria L. Tiamson, M.D., Ronald C. Golinger, M.D., Ethan Kass, D.O.

NR174 Neuropsychology of Polysubstance Abuse in Dual Diagnosis: A Jacksonian Model
Godehard Oepen, M.D., Michael Levy, Ph.D., Anne Harrington, Ph.D., Meredith Handren, R.N., Linda Pinnone, Lic.SW, Ruth Saemann, PsyD.

NR175 Carbamazepine as an Aid to Smoking Cessation
Roger R. Laroche, M.D., Teresa A. Rummans, M.D., Richard D. Hurt, M.D., Gary G. Lauger, M.S., Kenneth P. Offord, M.S., Barbara K. Bruce, Ph.D.

NR176 Alcohol Use and Psychotropic Compliance of Elders
Daniel P. Chapman, Ph.D., Robert B. Wallace, M.D.

NR177 Buprenorphine and Laudanum for Opiate Maintenance
Marc Auriacombe, M.D., Denis Grabot, M.A., Jean P. Daulouede, M.D., Jean P. Vergnole, M.D., Charles P. O'Brien, M.D., Jean Tignol, M.D.

NR178 Assault, Substance Abuse and Axis II Comorbidity
Lorraine R. Dustan, M.D., Kathleen T. Brady, M.D., Dorothy E. Grice, M.D., Robert Malcolm, M.D., Dean G. Kilpatrick, Ph.D.

NR179 Assault, Substance Abuse and Axis I Comorbidity
Dorothy E. Grice, M.D., Lorraine R. Dustan, M.D., Kathleen T. Brady, M.D., Robert Malcolm, M.D., Dean G. Kilpatrick, Ph.D.

NR180 Compulsive Behaviors and Cocaine
Jed E. Black, M.D., Wayne K. Goodman, M.D., Beth K. Boyarsky, M.S.N., Lawrence H. Price, M.D.

NR181 Movement Disorders in Schizophrenic Alcoholics
Robin M. Johnson, M.D., Thomas R. Kosten, M.D., Douglas M. Ziedonis, Boris Meandzija, M.D., William M. Glazer, M.D.

NR182 Mazindol Augmentation of Neuroleptics in Cocaine Abusers
Robin M. Johnson, M.D., J. Seibyl, M.D., J. Erdos, M.D., D. Miles, R.N., D. Charney, M.D., George R. Heninger, M.D., J. Krystal, M.D.

NR183 Serotonin Drugs Slow Brain Noradrenergic Cells in Opiate Withdrawal
Gary Aston-Jones, Ph.D., Hideo Akaoka, Ph.D.

NR184 Rational Recovery as an Alternative to Alcoholics Anonymous
Ceane Willis, Ph.D., David R. Gastfriend, M.D., Stephanie E. Meyer, B.A.

NR185 Desipramine in Crack Cocaine Treatment
Elisa G. Triffleman, M.D., Kevin Delucchi, Ph.D., Sharon Hall, Ph.D., Sandra Tunis, Ph.D., Peter Banys, M.D.

NR186 The Use of Fluvoxamine in Detoxified Alcoholics
Lucien Barrelet, Claude Uehlinger

NR187 Benzodiazepine Treatment in Psychotic Disorders and Alcohol/ Substance Dependence
Mohamed Toutoungi, M.D., Anelise Muhlebach, Ph.D., Veronique Bahler, M.D., Antonio V. Andreoli, M.D.

NR188 Liver Transplantation: Effects on Psychosocial Function and Psychological Symptoms
Ondria C. Gleason, B.S., William H. Roccaforte, M.D., William J. Burke, M.D., Barbara L. Bayer, M.S.N., Carl B. Greiner, M.D.

NR189 Eating Pathology in Diabetic Children
Ann C. Childress, M.D., Timothy D. Brewerton, M.D., Christina Rock, B.S.

NR190 Ingestive Behaviors of Women with Binge Eating Disorders
Susan Zelitch Yanovski, M.D., Melissa Leet, Marilyn Flood, R.D., Philip W. Gold, M.D., H.R. Kissileff, Ph.D., B.T. Walsh, M.D.

NR191 Lifetime Prevalence of Eating Disorders in OCD
Cheryl Rubenstein, M.A., Teresa A. Pigott, M.D., Francine L'Heureux, M.D., James L. Hill, Ph.D., Dennis L. Murphy, M.D.

NR192 Eating Attitudes in Seasonal Affective Disorder and Bulimia Nervosa
Kevin G. Berman, M.D., Raymond W. Lam, M.D., Elliot M. Goldner, M.D.

NR193 Cytogenetic Study of Autism in Taiwan
Luke Y. Tsai, M.D., Joseph Y.C. Chen, M.D., Shuan-Yow Li, Ph.D., Chen-Chin Hsu, M.D.

NR194 Self-Image, Delinquency and Psychiatric Symptomatology in Normal Male and Female Adolescents
Susan K. Williams, M.D., Daniel Offer, M.D., Kenneth I. Howard, Ph.D., Kimberly Schonert-Reichl, Ph.D.

NR195 Child Psychiatry Diagnoses by Pictorial Instrument
Monique Ernst, M.D., Raul R. Silva, M.D., Jana Signe, B.A., Joan Welkowitz, Ph.D.

NR196 Stimulant Treatment of Pediatric Tourette's Syndrome and ADHD
F. Xavier Castellanos, M.D., Josephine Elia, M.D., Charles S. Gulotta, Judith H.L. Rapoport, M.D.

NR197 Effect of Quiet Room Design on Children
Carol A. Glod, M.S.N., Martin H. Teicher, M.D., Martha Butler, M.S.N., Eleanor Magnus, B.S., David Harper, B.S., Kambiz Pahlavan, M.D.

NR198 Defense Mechanisms in Latency Age Children
Marshal Blatt, M.D., Shirley Feldman, Ph.D., Afsaneh Nasserbakht, M.S., Hans Steiner, M.D.

NR199 The Longitudinal Outcomes of Regulatory Disordered Infants
Georgia A. Degangi, Ph.D., Stephen Porges, Ph.D., Ruth Sickel, Ph.D., Stanley Greenspan, M.D.

NR200 OCD Symptoms in Adults with Autistic Disorder
Susan T. Naylor, M.S.N., Christopher J. McDougle, M.D., Fred R. Volkmar, M.D., Wayne K. Goodman, M.D., Donald J. Cohen, M.D., Keith A. Hawkins, Psy.D., Lawrence H. Price, M.D.

NR201 The Prevalence of Autism in Taiwan
Yung-Cheng J. Chen, M.D., Der-Jen Lai, M.D., Chen-Chin Hsu, M.D., Luke Y. Tsai, M.D.

NR202 Auditory N100 in Conduct Disordered Adolescents
Lyndee P. Oberwetter, M.D., Martin L. Reite, M.D., Thomas J. Crowley, M.D.

NR203 Treatment of Children with Language and Behavior Disorders
Sue Batth, M.D., Gary Tait, M.A., Marjorie Button, M.Sc.

NR204 Dissociation in a Mental Health Center Population
Howard C. Wetsman, M.D., Elizabeth David, M.D., Edward Morse, Ph.D.

NR205 Dissociation in Medically Indigent Inpatients
Howard C. Wetsman, M.D., Elizabeth David, M.D., Deborah Tosh, M.D., Edward Morse, Ph.D.

NR206 A Survey of the Errors in 100 Civil Commitments
Howard C. Wetsman, M.D., Guillermo Urrutia, M.D., Margo Hammond, J.D.

NR207 Dissociation and Abuse in First-Episode Psychosis
Stephen M. Strakowski, M.D., Susan C. Batson, Ph.D., Mauricio Tohen, M.D., Shelly F. Greenfield, M.D., Meridith L. Kolbrenner, B.A.

NR208 Dissociation and Self-Destructive Behavior
Glenn N. Saxe, M.D., Bessel A. van der Kolk, M.D.

NR209 Somatization in Patients with Dissociation
Glenn N. Saxe, M.D., Gary Chinman, M.D., Bessel A. van der Kolk, M.D.

NR210 Adolescent Bereavement with Peer Death
Sherry Schachter, B.S.N.

NR211 Spinal Cord Injury and Depression
Andres Vasquez, M.D., Paul J. Goodnick, M.D.

NR212 The Firestone Voice Scale For Self-Destructive Behavior
Lisa Firestone, Ph.D.

NR213 On the Usefulness of DSM-III, Axis III
Ihsan M. Salloum, M.D., Juan E. Mezzich, M.D., Javier E. Saavedra, M.D.

NR214 Changing Office Site Lowers Therapy Compliance
Kelly L. Dunn, M.D., Paul A. Kettl, M.D.

NR215 Sitters: Substitutes for Psychiatric Consultation
Raymond R. Remmel, M.D., Francis J. Kane, M.D.

NR216 Personality Dysfunction and Outcomes in the Homeless Mentally Ill
Gavin E. Rose, M.D., Lisa Dixon, M.D., James Thompson, M.D., Marcela V. Somoza-Lennon, M.D., Bruce Warr, M.S., Anthony Lehman, M.D.

NR217 Sheltering the Homeless: Housing Patterns
Lisa Dixon, M.D., Nancy Friedman, M.S.W.

NR218 Compliance Among the Homeless Mentally Ill
Lisa Dixon, M.D., Marcela V. Somoza-Lennon, M.D., Gavin E. Rose, M.D., Kerry Petrucci, Ph.D., Bruce Warr, M.S., Anthony Lehman, M.D.

NR219 Medication Compliance Among Homeless Mentally Ill
Marcela V. Somoza-Lennon, M.D., Lisa Dixon, M.D., Peter J. Weiden, M.D., Kerry Petrucci, Ph.D., Gavin E. Rose, M.D., Anthony Lehman, M.D.

NR220 Suicidality and Final Exit
Michael Lavin, M.D., Glenn Martin, M.D., Alec Roy, M.B.

NR221 The Clinical Impact of Benzodiazepine Regulation
Donna M. Flansaas, M.D., David J. Hellerstein, M.D., Lynda D. Zweben-Howland, M.S.W., Lisa W. Samstag, M.A.

NR222 Family Problems Among Southeast Asian Refugee Patients
Hung D. Tran, M.D., James K. Boehnlein, M.D.

NR223 Psychotropics and Hispanic Nursing Home Residents
Mary Vince, M.D., Blaine S. Greenwald, M.D., Elisse Kramer-Ginsberg, Ph.D., Arthur Lennon, M.D., Robert Corcoran, M.S.

NR224 Monitoring Resident Supervision in Times of Change
Louis J. Kraus, M.D., Philip K. McCullough, M.D., John S. Lyons, Ph.D.

NR225 Predictors of Psychiatric Inpatient Length of Stay
Irvin P. Brock III, M.D., George R. Brown, M.D., Cliff Butson, Ph.D.

NR226 No Correlation Between Psychiatric Resident In-Training Examination (PRITE) and Clinical Skills
Errol M. Aksu, M.D., Edward O. Bixler, Ph.D.

NR227 Characteristics of a Forcibly Medicated Population
Safwat Attia, M.D., William M. Greenberg, M.D., Nighat Mirza, M.D.

Tuesday, May 5, 1992, 9:00 a.m.-10:30 a.m.

New Research 4—Oral/Slide Session—Rooms 23/24, Level 1, Convention Center

PSYCHOSIS, PSYCHOTIC AND DISSOCIATIVE DISORDERS; AND ECONOMIC ISSUES

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

NR228 The McLean First-Episode Psychosis Projects — 9:00 a.m.
Mauricio Tohen, M.D., Andrew L. Stoll, M.D., Stephen M. Strakowski, M.D., Gianni L. Faedda, M.D., Pierre V. Mayer, M.D., Daniel C. Goodwin

NR229 Neuroleptic Metabolism and Response in the Elderly — 9:15 a.m.
Carolyn M. Mazure, Ph.D., J. Craig Nelson, M.D., Janet S. Cellar, M.S.N., Peter I. Jatlow, M.D., Malcolm B. Bowers, Jr., M.D.

NR230 Mazindol in Negative Symptom Schizophrenia — 9:30 a.m.
John P. Seibyl, M.D., John H. Krystal, M.D., Joseph Erdos, M.D., Laurence Karper, M.D., Robin Johnson, M.D., Louise Brenner, R.N.

NR231 The Impact of Drug Abuse on Psychotic Outpatients — 9:45 a.m.
Douglas M. Ziedonis, M.D., Thomas R. Kosten, M.D., William M. Glazer, M.D.

NR232 Multisites Evaluation of VA Intensive Case Management — 10:00 a.m.
Robert Rosenheck, M.D., Michael Neale, M.S., Philip Leaf, Ph.D.

NR233 A New Screening Instrument for DSM-IV Dissociative Disorders — 10:15 a.m.
Marlene Steinberg, M.D., Bruce J. Rounsaville, M.D., Domenic Cicchetti, Ph.D.

Tuesday, May 5, 1992, 9:00 a.m.-10:30 a.m.

New Research 5—Oral/Slide Session—Rooms 25/26, Level 1, Convention Center

ANXIETY AND EATING DISORDERS

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

NR234 Comorbid Panic Disorder and Outcome in Depression — 9:00 a.m.
J. Craig Nelson, M.D., Carolyn M. Mazure, Ph.D., Peter I. Jatlow, M.D., Malcolm B. Bowers, Jr., M.D.

NR235 Maintenance/Discontinuation of Imipramine in Panic/Agoraphobia — 9:15 a.m.
Matig R. Mavissakalian, M.D., James M. Perel, Ph.D.

NR236 A Multicenter Trial of Fluvoxamine in OCD — 9:30 a.m.
Steven A. Rasmussen, M.D., John H. Greist, M.D., Michael A. Jenike, M.D., Delbert G. Robinson, M.D.

NR237 Effect of Yohimbine and Placebo in PTSD — 9:45 a.m.
Mark B. Hamner, M.D., Bruce I. Diamond, Ph.D.

NR238 The Relationship of Dieting Severity and Alcohol Use 10:00 a.m.
Dean Krahn, M.D., Candace Kurth, M.P.H., Mark A. Demitrack, M.D., Edith Gomberg, Ph.D., Adam Drewnowski, Ph.D.

NR239 Bulimic's Eating Behavior in a Feeding Laboratory 10:15 a.m.
L. K. George Hsu, M.D., Theodore Weltzin, M.D., Walter H. Kaye, M.D.

NEW RESEARCH

Tuesday, May 5, 1992, 12 noon-2:00 p.m.

New Research 6—Poster Session—Hall D, Level 1, Convention Center

BRAIN IMAGING; NEUROPSYCHIATRY; AIDS AND HIV; BIOLOGICAL, C/L, EMERGENCY AND GERIATRIC PSYCHIATRY; ORGANIC MENTAL DISORDERS; AND PSYCHOIMMUNOLOGY

Moderator: Robert W. McCarley, M.D.

NR240 Gender Related PET Differences in Normal Controls
Paul J. Andreason, M.D., Alan J. Zametkin, M.D., Alexander Guo, B.S., Paul Baldwin, RTR, Robert M. Cohen, M.D.

NR241 Dopaminergic Innervation in Human Brain
Dennis E. Schmidt, Ph.D., Robert M. Kessler, M.D., William O. Whetsell, M.D., Mohammed S. Ansari, M.S., Tomas de Paulis, Ph.D., Michael H. Ebert, M.D.

NR242 Cortical Perfusion in Frontal Lobe Type Dementia
Gene E. Alexander, Ph.D., Zafar Sharif, M.D., Isak Prohovnik, Ph.D., Yaakov Stern, Ph.D.

NR243 Temporal Lobe Abnormalities in Schizophrenia: An MRI Study
Martha E. Shenton, Ph.D., Ron Kikinis, M.D., Ferenc A. Jolesz, M.D., Seth Pollak, M.A., M. LeMay, M.D., R.W. McCarley, M.D.

NR244 Cerebral SPECT Abnormalities in Depression
Russell G. Vasile, M.D., Thomas C. Hill, M.D., B. Leonard Holman, M.D., John J. Mooney, M.D., Kerry L. Bloomingdale, M.D., Joseph J. Schildkraut, M.D.

NR245 SPECT Brain Imaging of Benzodiazepine Receptors
John P. Seibyl, M.D., Betka Sybirska, Ph.D., Andrew Goddard, M.D., Douglas Bremner, M.D., Scott W. Woods, M.D., Robert Innis, M.D.

NR246 MRI Perfusion Imaging of Brain Activity
Jeffrey R. Zigun, M.D., Fernando A. Barrios, Ph.D., Douglas W. Jones, Ph.D., Daniel Z. Press, B.S., Joseph A. Frank, M.D., Daniel R. Weinberger, M.D.

NR247 High-Resolution 18 Fluorine Deoxyglucose PET Studies in Late-Life Depression
Anand Kumar, M.D., Doug Nadel, Abass Alavi, M.D., Robin Smith, Ph.D., Martin Reivich, M.D.

NR248 Acute Effects of ECT on Memory
Avraham Calev, Ph.D., Nurith Tubi, M.A., Baruch Shapira, M.D., Bernard Lerer, M.D.

NR249 SPECT in Psychopathology Secondary to Head Injury
Zafar A. Sharif, M.D., Gene E. Alexander, Ph.D., Isak Prohovnik, Ph.D., Jonathan M. Silver, M.D.

NR250 Normal Caudate Nucleus in OCD Using MRI and SPECT
Gordon J. Harris, Ph.D., Godfrey D. Pearlson, M.D., Rudolf Hoehn-Saric, M.D., Steven R. Machlin, M.D., Elizabeth H. Aylward, Ph.D., Patrick E. Barta, M.D., Edwaldo E. Camargo, M.D.

NR251 Cerebral Metabolism by PET in Patients with Generalized Resistance to Thyroid Hormone
Alan J. Zametkin, M.D., Peter Hauser, M.D., John A. Matochik, Ph.D., Edythe Wiggs, Ph.D., Robert M. Cohen, M.D., Bruce D. Weintraub, M.D.

NR252 High-Resolution PET-FDG in Schizophrenia
Thomas E. Nordahl, M.D., Thomas Budinger, M.D., Anne Cummings, Shariar Salamet, M.D., Tasha Kusubov, B.S., William Jaqust, M.D.

NR253 Psychoeducational Testing and SPECT in Adolescents
Gregory T. Slomka, M.D., H. Jordan Garber, M.D., Mustafa H. Adatepe, M.D.

NR254 Basal Sympathoadrenal Function in PTSD
M. Michele Murburg, M.D., Miles E. McFall, Ph.D., Nancy Lewis, R.N., Eric Petrie, M.D., Richard C. Veith, M.D.

NR255 SPECT in Chronic Schizophrenia: Preliminary Findings
Robert W. Baker, M.D., Nina R. Schooler, Ph.D., Ajit N. Shah, M.D., Joyce B. Delaney, G.N., James W. Baird, Ph.D.

NR256 EEG and Electrophysiological Mapping as a Tool in Psychiatry
Remy Luthringer, Jean-Paul Macher, M.D., Richard Minot, M.D., Michel Toussaint, Ph.D., Koudou Dago Toussaint, Ph.D., Laurent Soufflet, Ph.D.

NR257 CT Prediction of Decline in Alzheimer's Disease
Elizabeth Aylward, Ph.D., Lisa Raimundo, Marshal Folstein, M.D., Godfrey Pearlson, M.D., Gary Chase, Ph.D., Kathryn Carson

NR258 SPECT and MRI in Multiple Sclerosis with Depression
H. Jordan Garber, M.D., Thomas Scott, M.D., Christopher Starratt, Ph.D., Mustafa H. Adatepe, M.D., Ziad Deeb, M.D., Gilbert H. Isaacs, M.D.

NR259 Wisconsin Card Sorting Test and Frontal Lobe Findings by MRI and SPECT
Christopher Starratt, Ph.D., H. Jordan Garber, M.D., Gerene K. Starratt, Mustafa H. Adatepe, M.D., Gilbert H. Isaacs, M.D.

NR260 WITHDRAWN

NR261 Hippocampal Kindling and Astrocyte Activation
Tom G. Bolwig, M.D., Anette Hansen, M.D., Ole Steen Jorgensen, Ph.D.

NR262 Blockade of Nicotinic Receptors Impairs Cognition
Paul A. Newhouse, M.D., Alexandra Potter, B.S., Robert Lenox, M.D.

NR263 Mood Changes and Subarachnoid 5-HIAA Levels in Temporal Lobe Epilepsy
Candace S. Brown, Pharm.D., Dietrich Blumer, M.D., Allen R. Wyler, M.D.

NR264 Physical Performance of Medicated Psychiatric Patients
Dante Robert Brebbia, Ph.D., Anne F. Brebbia, M.S., James M. Watson, B.S., Evelyn T. Pyne, R.N., Martha L. Heatley, B.A.

NR265 CSF 5-HIAA, Behavior and Tryptophan Hydroxylase Genotype
David A. Nielsen, Ph.D., David Goldman, M.D., Longina Akhtar, Matti Virkkunen, M.D., Robert Rawlings, Ph.D., Markku Linnoila, M.D.

NR266 Serotonergic Correlates of Aggressive Behavior
Avraham Molcho, M.D., Barbara Stanley, Ph.D., Ronald Winchel, M.D., Jeannine Guido, M.A., Michael Stanley, Ph.D.

NR267 Suicidal Ideation in AIDS: Roles of Pain and Mood
William Breitbart, M.D., Steven D. Passik, Ph.D., Kent Eller, M.D., Antonio F. Sison, M.D.

NR268 No Evidence of Psychophysiological Differences Between HIV-1 Infected and Noninfected Methadone Maintenance Patients
Norbert Loimer, M.D., Bettina Rauch, Ph.D., Josef Grunberger, Ph.D., Georg Pakesch, M.D.

NR269 Sex Risk Predicted by Past Sexually Transmitted Disease
Haftan M. Eckholdt, M.A., Jacqueline Bartlett, M.D., Jeanine Dasilva, B.A., Steve Schleifer, M.D., Steve Keller, Ph.D.

NR270 Cognitive Tests and HIV: The Sinai AIDS Center Cohort
David Dorfman, Ph.D., Norbert Baer, Charlene Bang, B.A., Leonard Handelsman, M.D., David Rose, M.D.

NR271 Cognitive Testing by Reaction Time of HIV Positive IV Drug Users
David Dorfman, Ph.D., Charlene Bang, B.A., Leonard Handelsman, M.D., Paul J. Rinaldi, M.A., Norbert Baer, Mary M. Schroeder, Ph.D.

NR272 Psychiatric Morbidity in HIV Infection
Diana O. Perkins, M.D., Carol Murphy, R.N., David Naftolowitz, M.D., Robert A. Stern, Ph.D., Jane Leserman, Ph.D., Dwight L. Evans, M.D.

NR273 Computerized Screening for AIDS Dementia Complex
Jonathan L. Worth, M.D., Cary R. Savage, Ph.D., Bradford A. Navia, M.D.

NR274 Risk Factors for Needle Sharing in HIV Positive and Negative Intravenous Drug Abusers
David W. Brook, M.D., Josephine Roberto, M.S.W., Joseph R. Masci, M.D., Jacques De Catalogne, M.D., Frances Amundsen, M.P.S., Judith S. Brook, Ed.D.

NR275 Risk of HIV Infection in the Mentally Ill
Barbara E. McDermott, Ph.D., Frederic J. Sautter, Ph.D., Robert M. Malow, Ph.D., Thomas Quirk, B.A., Alicia H. Borges, B.A., Daniel K. Winstead, M.D., Lee Jones, M.D.

NR276 Vitamin B12 Status and Neuropsychiatric Disorders in HIV
Robert A. Stern, Ph.D., Kevin R. Robertson, Ph.D., Diana O. Perkins, M.D., Jean W. Wilkins, Ph.D., M. Kathleen Donovan, M.D., John A. Messenheimer, M.D., Robert A. Whaley, M.D., Dwight L. Evans, M.D., Colin D. Hall, M.D.

NR277 Elderly Medical Readmissions: Psychiatric Predictors
George Fulop, M.D., David Huertas, M.D., Karen Pasternak, Peter M. Tafti, Howard Fillit, M.D., James J. Strain, M.D.

NR278 Evolution of Schizophrenia: A Psychiatric Emergency Room Perspective
Dianne Sena, M.S.W., Sean P. Stanton, Eugene Somoza, M.D.

NR279 Quality of Life Following Liver Transplantation
Esteban Cirera, M.D., Eduard Vieta, M.D., Juan De Pablo, M.D., Isabel Sanudo, M.D., Jose Visa, M.D.

NR280 Psychiatric Aspects of Angiography and Angioplasty
Pascal Janne, M.D., Christine Reynaert, M.D., Jean Costermans, Ph.D., Regnier Pirard, Ph.D., Jean Kinable, Ph.D., Xavier Renders, Ph.D.

NR281 A Most Simple Screening of Emotional Morbidity
Antonio Lobo, M.D., Maria Jesus Perez-Echeverri, M.D., Ricardo Campos, M.D., Javier Garcia-Campayo, M.D., Julian Izuzquiza, M.D., Carmen Monton, M.D.

NR282 The Role of EEG in Psychiatric Consultation
Laurens D. Young, M.D.

NR283 The Psychiatric Emergency Service Utilization
Ole J. Thienhaus, M.D.

NR284 Non-Epileptic Seizures and Sexual Abuse
Kenneth R. Alper, M.D., Orrin Devinsky, M.D., Daniel J. Luciano, M.D., Kenneth R. Perrine, Ph.D.

NR285 Psychiatric Morbidity and Length of Hospital Stay
James J. Strain, M.D., John S. Lyons, Ph.D., Jeffrey S. Hammer, M.D., Mary Eichmann, Ph.D., Marianne Fahs, Ph.D.

NR286 Fall Risk Assessment in a Psychiatric Service
Eduardo Rueda-Vasquez, M.D., Frank Tellian, M.D.

NR287 Lymphocytes in Alzheimer's Patients and Controls
Maurice W. Dysken, M.D., Marcia D. Minichiello, M.A., James L. Hill, Ph.D., Stacy S. Skare, B.A., John T. Little, M.D., Susan E. Molchan, M.D., Trey Sunderland, M.D.

NR288 Measurement of Depression in Dementia
Barry S. Fogel, M.D., Brian R. Ott

NR289 Circadian Rhythms in Alzheimer's Disease: Clinico-Neuropathology
Andrew Satlin, M.D., Edward G. Stopa, M.D., Ladislav Volicer, M.D., David Harper, B.S., Vickey Kuo-LeBlanc, B.S., Tom Edwards, Ph.D.

NR290 Telephone Screening in Alzheimer's Disease
Jeanne Radcliffe, R.N., James Hill, Ph.D., Kathleen Dietrich, R.N., Marcia Minichiello, M.A., Georgia Latham, M.D., Brian A. Lawlor, M.D., Trey Sunderland, M.D.

NR291 Age of Onset May Define a Clinical Subtype in Alzheimer's Disease
Brian A. Lawlor, M.D., Theresa Ryan, B.S., James Schmeidler, Ph.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

NR292 Life Review in Group Therapy of Demented Elderly
Rhoda R. Frankel, M.A., Karen Carlisle, M.S.W., William Borden, Ph.D., Lawrence Lazarus, M.D.

NR293 Depression: Anglo and African-American Caregivers
Jacobo E. Mintzer, M.D., Carol Macera, Ph.D.

NR294 The Geriatric Movement Disorders Assessment
Robert A. Sweet, M.D., Elizabeth De Sensi, George S. Zubenko, M.D.

NR295 Benzodiazepine Noncompliance of Older Adults
Robert B. Wallace, M.D., Daniel P. Chapman, Ph.D., Elizabeth Chrischilles, Ph.D., Janice Alexander

NR296 Temporal Stability of Tardive Dyskinesia Status in Elderly Schizophrenics Patients
Paolo Decina, M.D., Ferdinando Saraceni, M.D., Christos Hadjichristos, M.D., PierLuigi Scapicchio, M.D., Sukdeb Mukherjee, M.D.

NR297 Diazepam Induced Impairment and Cognitive Decline
Nunzio Pomara, M.D., Dennis Deptula, Ph.D., Rajkumar Singh, M.D., David J. Greenblatt, M.D.

NR298 Use of Mental Health Services Before Nursing Home Admission
Barry W. Rovner, M.D., Pearl S. German, Sc.D.

NR299 Validity of the Short Portable Mental Status Questionnaire Administered by Telephone
William H. Roccaforte, M.D., William J. Burke, M.D., Steven P. Wengel, M.D., Barbara L. Bayer, M.S.N.

NR300 Psychiatric Symptoms in Two Types of Dementia
David L. Sultzer, M.D., Harvey S. Levin, Ph.D., Michael E. Mahler, M.D., Walter M. High, Ph.D., Jeffrey L. Cummings, M.D.

NR301 Odorant Specific Hyposmia in Alzheimer's Disease
Michael J. Serby, M.D., Davina Kalkstein, B.A., Gwenn S. Smith, Ph.D., Michael Russell, M.D.

NR302 Depression Among Korean Elderly Immigrants
Keum Y. Pang, Ph.D., Guojun Cai, M.D.

NR303 TCAs, Orthostatic Monitoring and Falls in Nursing Homes
Blaine S. Greenwald, M.D., Elisse Kramer-Ginsberg, Ph.D., Susy Abraham, M.D., Richard A. Hodder, M.D.

NR304 Delirium: Detecting Mild Cases by Measuring Change
Ira R. Katz, M.D., Laura Sands, Ph.D., Richard Harner, Ph.D., Suzanne Doyle, R.N.

NR305 Serotonin in Parkinson's Disease and Depression
Lawrence H. Price, M.D., Elinore F. McCance-Katz, M.D., Kenneth L. Marek, M.D.

NR306 Access to Hospice Programs in End-Stage Dementia: A National Survey of Hospice Programs
Patricia Hanrahan, Ph.D., Daniel J. Luchins, M.D., Todd J. Segneri, B.A.

NR307 Schizophrenic Dementia Revisited
William B. Lawson, M.D., Nancy Lyon, Ph.D., Craig N. Karson, M.D.

NR308 Heritability of Personality Disorder
W. John Livesley, M.B., Douglas N. Jackson, Ph.D., Kerry L. Jang, M.A., Phillip A. Vernon, Ph.D.

NR309 Bupropion Therapy in Chronic Fatigue Syndrome
Paul J. Goodnick, M.D., Ricardo Sandoval, M.D., Andrew Brickman, Ph.D., Nancy G. Klimas, M.D.

NR310 Affective Processes, Immune Dysfunction and Health
Steven E. Keller, Ph.D., Steven J. Schleifer, M.D., Jacqueline Bartlett, M.D., Haftan Eckholdt, M.A.

NR311 Eustress of Humor Associated Laughter Modulates Immune System Components
Lee S. Berk, D.P.H., Stanley A. Tan, M.D., William F. Fry, M.D., Dottie E. Berk, R.N., William C. Eby, M.D.

NR312 Stress and Immunity in Adolescents
Jacqueline Bartlett, M.D., Steven Schleifer, M.D., Haftan Eckholdt, M.A., Melissa K. Demetrikopoulos, M.S., Steven E. Keller, Ph.D.

NEW RESEARCH

Tuesday, May 5, 1992, 3:00 p.m.-5:00 p.m.

New Research 7—Poster Session—Hall D, Level 1, Convention Center

INFANT/CHILDHOOD/ADOLESCENT DISORDERS, ALCOHOL AND SUBSTANCE ABUSE, AND EATING DISORDERS

Moderator: Gabrielle A. Carlson, M.D.

NR313 Race Bias in Child Psychiatry Versus the Juvenile Justice System?
Stuart L. Kaplan, M.D., Joan Busner, Ph.D.

NR314 Prescribing Practices of Child Psychiatrists
Stuart L. Kaplan, M.D., Robert Simms, M.D., Joan Busner, Ph.D.

NR315 Bupropion Treatment of Adolescent Depression
David E. Arredondo, M.D., Mellissa Streeter, John P. Docherty, M.D.

NR316 Conduct Disorder, Oppositional Defiant Disorder and Mood Disorder in Adolescents
David E. Arredondo, M.D., Stephen F. Butler, Ph.D.

NR317 Follow-Up of Fifty-Four Obsessive Compulsive Children
Henrietta L. Leonard, M.D., Susan E. Swedo, M.D., Marge C. Lenane, M.S.W., David C. Rettew, B.S., Judith H.L. Rapoport, M.D.

NR318 The Adult Outcome of Child Psychiatric Inpatients: Diagnosis and Mental Health Service Utilization
Michael S. Lundy, M.D., Bruce M. Pfohl, M.D.

NR319 Outcome: Home Based Child Psychiatric Treatment
Edwin J. Mikkelsen, M.D., Gerald M. Bereika, Ph.D., Wayne J. Stelk, Ph.D., Julie C. McKenzie, M.Ed.

NR320 Chronicity in Child Psychiatric Disorders
Atilla Turgay, M.D., Edward Gordon, M.D., Martin Vigdor, Ph.D.

NR321 Major Depression and Dysthymia in Children
Tova Ferro, B.A., Patricia Grayson, Ph.D., Gabrielle A. Carlson, M.D., Daniel N. Klein, Ph.D.

NR322 Axis I/II Disorders and Adolescent Sexual Behavior
Wade C. Myers, M.D., Roger C. Burket, M.D.

NR323 School Performance and Mental Health in Refugees
Cecile Rousseau, M.D., Aline Drapeau, M.S.C., Ellen Corin, Ph.D.

NR324 Mood and Altered Immunity in Adolescents
Jacqueline Bartlett, M.D., Steven Schleifer, M.D., Steven E. Keller, Ph.D.

NR325 Psychopathology and Outcome in Juvenile Offenders
Hans Steiner, M.D., William Huckaby, Ph.D.

NR326 Evidence That D2 Dopamine Receptor Alleles do not Influence Severity of Tourette's Syndrome
Joel Gelernter, M.D., David Pauls, Ph.D., James Leckman, M.D., Kenneth K. Kidd, Ph.D., Roger Kurlan, M.D.

NR327 Segregation Analysis of ADD
Stephen V. Faraone, Ph.D., Joseph Biederman, M.D., Wei Chen, M.D., Belinda R. Krifcher, B.A., Kate Keenan, B.A., Cindy Moore, B.A.

NR328 Adolescent Sex Offenders: Admitters and Deniers
Diane K. Shrier, M.D., Robert L. Johnson, M.D.

NR329 Clomipramine for Chronic Stereotypy/Self-Injury
H. Jordan Garber, M.D., John J. McGonigle, Ph.D., Gregory T. Slomka, Ph.D., Edith Monteverde, B.A.

NR330 Anabolic Steroids: Dosage and Psychiatric Effects
Donald A. Malone, Jr., M.D., Robert J. Dimeff, M.D.

NR331 Naltrexone in the Treatment of Alcohol Dependence
Joseph R. Volpicelli, M.D., Bruce J. Berg, M.D., Arthur I. Alterman, Ph.D., Motoi Hayashida, M.D., Charles P. O'Brien, M.D.

NR332 Pergolide, Bromocriptine Trial in Cocaine Addicts
Robert Malcolm, M.D., Joem Phillips, PAC, Kathleen Brady, M.D.

NR333 Ethanol Blood Levels in Older Versus Younger Males
Thomas P. Beresford, M.D., Michael Lucey, M.D., Linda Demo-Dananberg, B.S.N., Katherine Harris, B.A., Kimberly Brown, M.D.

NR334 Decreased Tolerance to Ethanol Related to Age
Thomas P. Beresford, M.D., Linda Demo-Dananberg, B.S.N., Katherine Harris, B.A., Kimberly Brown, M.D., Michael Lucey, M.D.

NR335 A New Elderly Specific Screening Test:(MAST-G) Michigan Alcoholism Screening Test
Frederic C. Blow, Ph.D., Kirk J. Brower, M.D., John Schulenberg, Ph.D., Linda Demo-Dananberg, B.S.N., James P. Young, M.S., Thomas P. Beresford, M.D.

NR336 Location of Inpatients with Comorbid Disorders
Frederic C. Blow, Ph.D., Brenda Booth, Ph.D., Cynthia Cook, Ph.D., J.C. Fortney, M.A.

NR337 Effect of Alcoholism Comorbidity on Depression
Timothy I. Mueller, M.D., Philip W. Lavori, Ph.D., Martin B. Keller, M.D.

NR338 Subject Ratings and Catecholamines During Intravenous Cocaine
Jeffery N. Wilkins, M.D., Koonlawee Nademanee, M.D., David Setoda, B.S., James Gaffield, B.S., Martin A. Josephson, M.D.

NR339 Schizophrenia and Substance Abuse Typology
Richard N. Rosenthal, M.D., David J. Hellerstein, M.D., Christian Miner, Ph.D.

NR340 Personality Disorders and Multiple Substance Use
Michael O'Boyle, M.D., Adel A. Wassef, M.D., Laurence R. Schweitzer, M.D.

NR341 Sleep, Depression and Aging in Alcoholics
James E. Shipley, M.D., Michael Aldrich, M.D., Philip Kroll, M.D., Rajiv Tandon, M.D., Kirk Brower, M.D.

NR342 Familial Alcoholism in Schizophrenia Versus Schizotypy
Leonard Handelsman, M.D., Jeremy Silverman, Ph.D., David P. Bernstein, Ph.D., Larry J. Siever, M.D., Kenneth L. Davis, M.D.

NR343 Cocaine Precipitation of Opiate Withdrawal
Susan M. Stine, M.D., Sally Satel, M.D.

NR344 Panic Disorder with Comorbid Alcohol Abuse
Juan M. Segui, M.D., Luis C. Salvador, M.D., Jaume Canet, Ph.D., Carmen Aragon, Ph.D., Cristian Herrera

NR345 Alcohol Dependence with Comorbid Panic Disorder
Juan M. Segui, M.D., Luis C. Salvador, M.D., Jaume Canet, Ph.D., Carmen Aragon, Ph.D., Cristian Herrera

NR346 Fluoxetine and Counseling in Cocaine Abuse
Lino Covi, M.D., Judy M. Hess, M.A., Charles A. Haertzen, Ph.D., Jerome J. Jaffe, M.D.

NR347 Dopamine Receptor mRNA in Prenatal Cocaine Exposure
Andrea De Bartolomeis, M.D., Mark C. Austin, Ph.D., Linda P. Spear, Ph.D., David Pickar, M.D., Jacqueline N. Crawley, Ph.D.,

NR348 Comorbidity of Alcoholism and Depression in Smokers
Kathleen N. Franco, M.D., John Hughes, M.D., Joanne Astill, M.D., Linda Inatsuka, B.A., Bettina Bailey, M.S.W., John E. Helzer, M.D.

NR349 Beer Advertising Spending Not Related to Teen Drinking
Paul A. Kettl, M.D., Michelle Sredy, B.S.

NR350 Voice-Based Computer Interview for Drug Dependence
David R. Gastfriend, M.D., Michael Brown-Beasley, M.A., Janel Hackney, Emily Gerber, B.A., Lee Baer, Ph.D., David Mee-Lee, M.D.

NR351 Comparative Validity of Five Alcoholism Typologies
William R. Yates, M.D., Ann I. Fulton, B.S.W.

NR352 Mood State Changes in Withdrawal From Methadone
Philip D. Kanof, M.D., Marvin Aronson, Ph.D., Robert Ness, Ph.D.

NR353 Schizophrenia and Drug Abuse: Clinical Correlates
William B. Lawson, M.D., Jeff Clothier, M.D., Jimo'Lea Angel, R.N., Craig N. Karson, M.D.

NR354 Predicting Antidepressant Response in Alcoholics
Edward V. Nunes, M.D., Patrick J. McGrath, M.D., Jonathan W. Stewart, M.D., Frederic M. Quitkin, M.D.

NR355 Automated Assessment of Cocaine Craving
Sharadha Raghavan, M.D., Roy King, M.D., Guenther Knoblich, B.S., Christopher Flowers, B.S., Leslie Fried-Behar, Ph.D.

NR356 Neuroendocrine Effects of Anabolic Steroids
Tung-Ping Su, M.D., Michael Pagiliaro, R.N., David Pickar, M.D., David R. Rubinow, M.D.

NR357 Evaluation of Treatments for Cocaine Abuse
Hari K. Khalsa, M.D., M. Douglas Anglin, Ph.D., Alphonso Paredes, M.D.

NR358 Biology and Phenomenology of Cocaine Withdrawal
Ananda Pathiraja, M.D., Donatella Marazziti, M.D., Bruce I. Diamond, Ph.D., Richard L. Borison, M.D.

NR359 Fluoxetine Study in Depressed Alcoholics
Jack R. Cornelius, M.D., Barry W. Fisher, M.D., Ihsan M. Salloum, M.D., Marie D. Cornelius, Ph.D., James M. Perel, Ph.D., Joan G. Ehler, M.D.

NR360 The D2 Dopamine Receptor Gene and CSF HVA
David Goldman, M.D., Michael Dean, Ph.D., Gerald L. Brown, M.D., Riitta Tokola, M.D., Matti Virkkunen, M.D., Markku Linnoila, M.D.

NR361 The Characteristics of Triply Diagnosed Patients
Eric C. Strain, M.D., Dan Buccino, M.S.W., Chester W. Schmidt, M.D., George E. Bigelow, Ph.D.

NR362 Benzodiazepine Sensitivity in Sons of Alcoholics
Deborah S. Cowley, M.D., Peter P. Roy-Byrne, M.D., Richard Ries, M.D., David J. Greenblatt, M.D., R. Dale Walker, M.D., Daniel W. Hommer, M.D., Herman H. Samson, Ph.D.

NR363 Treating the Cocaine Abusing Schizophrenic
Douglas M. Ziedonis, M.D., Ismene Petrakis, M.D., Teresa Richardson, R.N., Thomas R. Kosten, M.D.

NR364 ADHD Subgroups in Opiate Dependent Adults
Christian Y. Herrera, M.D., Juan M. Segui, M.D., Luis C. Salvador, M.D., Jaime Canet, Ph.D., Viviana Torresi, Ph.D., Isabel Rabella, Ph.D.

NR365 Social Network and Methadone Treatment Outcome
Leslie Goehl, M.A., Edward V. Nunes, M.D., Frederic M. Quitkin, M.D.

NR366 Defining Benzodiazepine Dependence
Stef M. Linsen, M.D., Christopher J. Kwik, M.D., Marinus H. Breteler, Ph.D., Frans G. Zitman, M.D.

NR367 Psychiatric Syndromes in Anabolic Steroid Users
Harrison G. Pope, M.D., David Katz, M.D., Harlyn Aizley, M.Ed.

NR368 m-CPP and Yohimbine in Alcoholics and Controls
John H. Krystal, M.D., Elizabeth Webb, M.A., Henry R. Kranzler, M.D., Ned Cooney, Ph.D., George R. Heninger, M.D., Dennis S. Charney, M.D.

NR369 Comorbid Substance Use and Psychiatric Disorders
Norman S. Miller, M.D., Beth M. Belkin, M.D., Robert Gibbons, Ph.D.

NR370 Butyrylcholinesterase Activity in Cocaine Abusers
David A. Gorelick, M.D., Linda Weinhold, Ph.D., Raymond Woosley, M.D., Fengue Du

NR371 Pica Behavior in the Mentally Retarded
Barbara C. Witkowski, Ph.D., Thomas S. Newmark, M.D.

NR372 Bright Light Therapy for Bulimia Nervosa
Raymond W. Lam, M.D., Elliot M. Goldner, M.D., Leslie Solyom, M.D., Ronald A. Remick, M.D.

NR373 Dissociation and Sexual Abuse in Eating Disorder
Kathleen Jordan, M.S.N., Mark A. Demitrack, M.D., Vivian Folsom, S.W., Dean D. Krahn, M.D., Karen Nairn, R.N., Frank W. Putnam, M.D.

NR374 Predicting Continued Abstinence in Bulimia Nervosa Over Two Years
Allan S. Kaplan, M.D., Marion P. Olmsted, Ph.D.

NR375 Open Trial of Fluvoxamine in Bulimia Nervosa
Jose L. Ayuso-Gutierrez, M.D., Monica Palazon, M.D., Jose L. Ayuso-Mateos, M.D.

NR376 Weight and Reproductive Function in Bulimia
Theodore E. Weltzin, M.D., Judy Cameron, Ph.D., Sarah Berga, M.D., Walter H. Kaye, M.D.

NR377 The Seasonality of Eating Disorders
Timothy D. Brewerton, M.D., Dean D. Krahn, M.D., Todd A. Hardin, M.D., Thomas A. Wehr, M.D., Norman E. Rosenthal, M.D.

NR378 Stimulation of the Hypothalamic-Pituitary-Adrenal Axis by Bulimic Behaviors
Margaret Altemus, M.D., Julio Licinio, M.D., Libby Jolkovsky, Philip W. Gold, M.D.

NR379 Delayed Gastrointestinal Transit Time in Eating Disordered Patients: A Radiographic Study
Arnold E. Andersen, M.D., Neel Kamal, M.D., William E. Whitehead, M.D., Twafik Chami, M.D., F.A. Rosell, R.N., M. M. Schuster, M.D.

NR380 Psychopathology and Severity of Obesity
Enos D. Martin, M.D., Tjiau-Lin Tan, M.D., Louis F. Martin, M.D., Lowell D. Mann, M.D.

NR381 Nociception in Bulimia Nervosa During Treatment
Nancy M.C. Raymond, M.D., Patricia L. Faris, Ph.D., James E. Mitchell, M.D., Elke D. Eckert, M.D.

NR382 Life Events and Anorexia Nervosa
Netta Horesh, Ph.D., Eli Lepkifker, M.D., Allen Apter, M.D.

NR383 Interhemispheric Coordination and Affect Discrimination in Disruptive Behavior Disorder
Daniel F. Shreeve, M.D.

NR384 Child/Parent Perceptions of Psychiatric Treatment
Spyros J. Monopolis, M.D., John Minas, Ph.D., John Myhill, Ph.D., Melinda B. Stein, Ph.D., Timothy Whalen, Chester W. Schmidt, M.D.

NEW RESEARCH

Wednesday, May 6, 1992, 9:00 a.m.-10:30 a.m.

New Research 8—Oral/Slide Session—Rooms 23/24, Level 1, Convention Center

SCHIZOPHRENIA

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

NR385 Brainblast: Voxel Processing for 3-D Brain Studies — 9:00 a.m.
Nancy C. Andreasen, M.D., Victor W. Swayze, M.D., Ted Cizadlo, M.S., Greg Harris, M.S., James Erhardt, Ph.D., William Yuh, M.D.

NR386 D3 Receptor Polymorphism and Schizophrenia — 9:15 a.m.
Marc-Antoine Crocq, M.D., Lars Lannfelt, M.D., Pierre Sokoloff, Ph.D., Antonia Mayer, Ph.D., Jean-Charles Schwartz, Ph.D., Jean-Paul Macher, M.D., Marie-Pascale Martres, Ph.D., Yann Hode, M.D., Fabrice Duval, M.D.

NR387 WITHDRAWN

NR388 Genetic Studies in Schizophrenia: An Update — 9:30 a.m.
Mihael H. Polymeropoulos, M.D., Hong Xiao, M.D., Timothy Crow, M.D., Lynn Delisi, M.D., Carl R. Merril, M.D.

NR389 IQ and Brain Size in Schizophrenics and Normals — 9:45 a.m.
Michael A. Flaum, M.D., Dan S. O'Leary, Ph.D., Victor W. Swayze, M.D., Randy Alliger, Ph.D., Gregg Cohen, M.S., Nancy C. Andreasen, M.D.

NR390 Obligate Carriers of Schizophrenia — 10:00 a.m.
Merilye C. Waldo, Ph.D., Alice Madison, M.D., Ellen Cawthra, R.N., William Byerley, M.D., Marina Myles-Worsley, Ph.D., Larry Adler, M.D.

NEW RESEARCH

Wednesday, May 6, 1992, 9:00 a.m.-10:30 a.m.

New Research 9—Oral/Slide Session—Rooms 25/26, Level 1, Convention Center

CHILDHOOD AND ADOLESCENT PSYCHIATRY

Chp.: Richard L. Borison, M.D.

NR391 P500 Amplitude Discriminates Between ADD Subtypes — 9:00 a.m.
R. Scott Smith, M.A., Jon F. DeFrance, Ph.D., Stephen F. Sands, Ph.D., Lloyd Smith, B.A.

NR392 Neonatal Hypoxic Exposure Results in Hyperactivity — 9:15 a.m.
Bruce I. Diamond, Ph.D., Morris J. Cohen, Ed.D., Jian Wang, B.S., Karen L. Campbell, B.A., Richard L. Borison, M.D.

NR393 Association of ADHD with Generalized Resistance to Thyroid Hormone in 18 Kindreds — 9:30 a.m.
Peter Hauser, M.D., Alan J. Zametkin, M.D., Pedro Martinez, M.D., Benedetto Vitiello, M.D., A. James Mixson, M.D., Bruce D. Weintraub, M.D.

NR394 The Continuity Between Childhood and Adult Depression: Longitudinal Study of Depressed Children as Adults — 9:45 a.m.
Christina A. Sobin, Ph.D., Jacqueline Martin, R.N., Philip Adams, Ph.D., Myrna M. Weissman, Ph.D.

NR395 Anxiety Disorders in 30 Alcoholic Adolescents — 10:00 a.m.
Duncan B. Clark, M.D., Rolf G. Jacob, M.D., Oscar Bukstein, M.D., Juan Mezzich, M.D.

NR396 Childhood Abuse and Neglect in BPD — 10:15 a.m.
Joel F. Paris, M.D., Hallie Zweig-Frank, Ph.D., Jaswant Guzder, M.D.

NEW RESEARCH

Wednesday, May 6, 1992, 12 noon-2:00 p.m.

New Research 10—Poster Session—Hall D, Level 1, Convention Center

SCHIZOPHRENIA AND NEUROPSYCHIATRY

Moderator: David Pickar, M.D.

NR397 Biochemical Effects of Clozapine and Haloperidol
Alan I. Green, M.D., Mohammed Y. Alam, M.D., Roger A. Boshes, M.D., Kathleen M. Pappalardo, B.S., Mary E. Fitzgibbon, B.S., Joseph J. Schildkraut, M.D.

NR398 Does Psychosis Contribute to Water Intoxication?
Morris B. Goldman, M.D., Daniel J. Luchins, M.D., Gary L. Robertson, M.D., Donald Hedeker, Ph.D., Javaid Javaid, Ph.D., Robert C. Marks, M.D.

NR399 Idazoxan Augmentation of Neuroleptic Therapy: Antagonist Strategies in the Pharmacotherapy of Schizophrenia
Robert E. Litman, M.D., Walter W. Hong, M.D., Rolando Gutierrez, M.D., Manji Husseini, M.D., William Z. Potter, M.D., David Pickar, M.D.

NR400 Schizophrenia: MRI Temporal Volumes and Neuropsychology
Paul G. Nestor, Ph.D., Martha E. Shenton, Ph.D., Robert W. McCarley, M.D., Jennifer Haimson, Robert S. Smith, M.A., Ron Kikinis, M.D.

NR401 Temporal Lobe in Schizophrenia
Patrick E. Barta, M.D., Godfrey D. Pearlson, M.D., Richard E. Powers, M.D., Rajiv Menon, M.B., Stephanie Richards, Larry E. Tune, M.D.

NR402 Genetic Transmission of Familial Schizophrenia
Martin Alda, M.D., Alain Labelle, M.D., Maria Dvorakova, Ph.D., Barry Jones, M.D., Petr Zvolsky, M.D., Hope Fraser, B.Sc., Jean-Michel Le Melledo, M.D., Paul Cameron, B.Sc.

NR403 Focal Temporal Lobe Abnormalities in Schizophrenia
Manuel F. Casanova, M.D., Daniel R. Weinberger, M.D., E. Fuller Torrey, M.D., Bagao Xu, Jay Sobus, Behnam Pourdeyhimi, Ph.D.

NR404 Early-Onset Temporal Lobe Lesion in Schizophrenia
Manuel F. Casanova, M.D., Denise Evans, M.D., Ramon E. Figueroa, M.D., Kathleen A. Crapanzano, M.D., Nathan DeVaughn, B.S.

NR405 Rating of Medication Influences in Schizophrenia
Tasha Mott, M.A., Peter J. Weiden, M.D., Marcella Lennon, M.D., Dodi Goldman, M.A., John Ragone, M.D., Bruce Rapkin, Ph.D.

NR406 Validity of Diagnostic Criteria for Schizophrenia
Gerhard Lenz, M.D., Kenneth Thau, M.D., Christian Simhandl, M.D.

NR407 Illness Severity and Homelessness in Schizophrenia
Carol L.M. Caton, Ph.D., Lewis A. Opler, M.D., Patrick E. Shrout, Ph.D., Boanerges Dominguez, M.P.H., Frederic I. Kass, M.D., Paula F. Eagle, M.D.

NR408 Assessing Frontal Lobe Dysfunction
Kenneth Podell, Ph.D., Michael Zimmerman, B.A., James L. Rebeta, Ph.D., Andrea Menezes, M.A., Elkhonon Goldberg, Ph.D.

NR409 Haloperidol Deconate and Nicotine Alter Cell Surface Antigens in Rats: Implications for Schizophrenia
Lauren Wing, Ph.D., Mark Coggiano, M.A., Darrell G. Kirch, M.D., Richard Jed Wyatt, M.D., Henrietta Kulaga, Ph.D.

NR410 Clozapine-Induced Changes in Liver Enzymes
Robert A. Leadbetter, M.D., Michael S. Shutty, Ph.D., Diane Pavalonis, M.S.N.

NR411 Monitoring Haloperidol Levels in Acutely Ill Schizophrenics
E. Michael Kahn, M.D., S. Charles Schulz, M.D., James M. Perel, Ph.D.

NR412 Basal Ganglia in Discordant Schizophrenic Monozygotic Twins
Katalin Vladar, Jeffrey R. Zigun, M.D., Douglas W. Jones, Ph.D., E. Fuller Torrey, M.D., Daniel R. Weinberger, M.D.

NR413 Insight and Treatment Compliance in Schizophrenia
Paul H. Lysaker, Ph.D., Morris D. Bell, Ph.D., Robert M. Milstein, M.D., Joseph B. Goulet, M.S., Gary J. Bryson, M.A.

NR414 Work Capacity in Schizophrenia
Paul H. Lysaker, Ph.D., Morris D. Bell, Ph.D., Aryeh L. Shestopal, B.A., Robert M. Milstein, M.D., Joseph B. Goulet, M.S.

NR415 Abnormal Splenial Shape in Schizophrenia
Robert M. Bilder, Ph.D., Regina Graham, Lauren Broch, Ph.D., Jeanine Springer, Jeffrey A. Lieberman, M.D.

NR416 Neuropsychological Manifestations of Hyponatremia in Chronic Schizophrenia Patients Who Exhibit Water Intoxication Syndrome
Michael S. Shutty, Ph.D., Leonard Briscoe, Ph.D., Scott Sautter, Ph.D., Robert A. Leadbetter, M.D., Walter V.R. Vieweg, M.D., Chris McDowell, Ph.D.

NR417 WITHDRAWN

NR418 Plasma Clozapine and Clinical Response in Treatment Refractory Schizophrenics
Rafael A. Munne, M.D., Sally R. Szymanski, D.O., Allan Safferman, M.D., Simcha Pollack, Ph.D., Thomas Cooper, M.A., Jeffrey A. Lieberman, M.D.

NR419 Positive and Negative Symptoms of Schizophrenia
John J. Boronow, M.D., Norman B. Ringel, M.A., Frederick Parente, Ph.D.

NR420 Neuropsychological Deficits and Withdrawal
John J. Boronow, M.D., Norman B. Ringel, M.A., Faith Dickerson, Ph.D., Frederick Parente, Ph.D.

NR421 Family History of Schizophrenia
Mary E. Kelley, B.S., Daniel P. van Kammen, M.D.

NR422 Loading Versus Standard Haloperidol Decanoate Dosing
Larry Ereshefsky, Pharm.D., Gregory B. Toney, Pharm.D., Stephen R. Saklad, Pharm.D., Cheryl Beal Anderson, Pharm.D., Donald Seidel, M.D., Tram Tran-Johnson, Pharm.D.

NR423 Neuropsychology in Schizophrenia: State or Trait?
Andrew J. Saykin, Psy.D., Derri Shtasel, M.D., Raquel E. Gur, M.D., D. Brian Kester, M.S., Lynn M. Harper Mozley, M.S., Ruben C. Gur, Ph.D.

NR424 Linkage Exclusion Between Schizophrenia and Candidates
Ann E. Pulver, Sc.D., Maria Karayiorgou, M.D., Nicola Diemarchi, M.D., Stelios Antonarakis, M.D., David Housman, Ph.D., Laura Kasch, Haig Kazazian, M.D., Malgorzata Lamacz, Ph.D., K. Lasseter, B.A., Gerald Nestadt, M.D., Paula Wolyniec, M.A., Elango Ramu, Jurg Ott, Ph.D., John McGrath, M.A., Deborah Meyers, Ph.D., Barton Childs, M.D.

NR425 Familial Risk and Mania in Schizophrenia
Ann E. Pulver, Sc.D., Kung-Yee Liang, Ph.D., Lawrence Adler, M.D., Paula Wolyniec, M.A., John McGrath, M.A., Gerald Nestadt, M.D., Barton Childs, M.D.

NR426 Neurochemistry Studies in Schizophrenic Patients
Michael Davidson, M.D., Peter Powchik, M.D., Vahram Haroutunian, Ph.D., Miklos Losonczy, M.D., Philip D. Harvey, Ph.D., Kenneth L. Davis, M.D.

NR427 Diazepam Binding Inhibitor-Immunoreactivity and Sleep EEG in Schizophrenia
Jeffrey L. Peters, M.D., John Gurklis, M.D., Mark Gilbertson, Ph.D., Thomas Neylan, M.D., Alessandro Guidotti, M.D., Daniel P. van Kammen, M.D.

NR428 Clozapine Versus Haloperidol Blockade of m-CPP in Schizophrenia
John H. Krystal, M.D., John P. Seibyl, M.D., Laurence Karper, M.D., Joseph Erdos, M.D., Ma-Li Wong, M.D., George R. Heninger, M.D., Dennis S. Charney, M.D.

NR429 Ritanserin Blockade of m-CPP Effects in Schizophrenia
John H. Krystal, M.D., John P. Seibyl, M.D., Laurence Karper, M.D., Ma-Li Wong, M.D., Joseph Erdos, M.D., George R. Heninger, M.D., Dennis S. Charney, M.D.

NR430 Effects of the NMDA Antagonist, Ketamine in Humans
John H. Krystal, M.D., Laurence Karper, M.D., John P. Seibyl, M.D., Richard Delaney, Ph.D., Glenna Freeman, B.S., George R. Heninger, M.D., Malcolm B. Bowers, M.D., Dennis S. Charney, M.D.

NR431 Stabilization and Depot Neuroleptic Dosages
Peter J. Weiden, M.D., Nina R. Schooler, Ph.D., Joanne Severe, M.A., J. Hillary Lee, Ph.D., S. Charles Schulz, M.D.

NR432 Effects of Haloperidol on Negative Symptoms
Rodrigo Labarca, M.D., Hernan Silva, M.D., Sonia Jerez, M.D., Aida Ruiz, M.D., Katia Gysling, Ph.D., Gonzalo Bustos, Ph.D.

NR433 Neuropsychology in First-Episode Schizophrenia
Derri Shtasel, M.D., Andrew J. Saykin, Psy.D., Raquel E. Gur, M.D., David B. Kester, M.S., Lynn M. Harper Mozley, M.S., Ruben C. Gur, Ph.D.

NR434 Phenomenology and Functioning in Schizophrenia
Derri Shtasel, M.D., Raquel E. Gur, M.D., Fiona Gallacher, B.A., Carolyn Heimberg, M.D., Tyrone Cannon, Ph.D., Ruben C. Gur, Ph.D.

NR435 Predictors of Noncompliance in Schizophrenia
Annette Zygmunt, Peter J. Weiden, M.D., David Klahr, M.D., Dodi Goldman, M.A., John Ragone, M.D., Bruce Rapkin, Ph.D.

NR436 Clinical Review of Clozapine Treatment in a State Hospital
William H. Wilson, M.D.

NR437 Organic Memory Pathology and Schizophrenia
Avraham Calev, Ph.D., Donald O'Donnel, M.A., Lynn Delisi, M.D., Olga Van Iyl, M.D.

NR438 Schizophrenia Spectrum: Delusions and Diagnoses
Madeline M. Gladis, Ph.D., Douglas F. Levinson, M.D.

NR439 Schizophrenia Subtypes: Stability Over Time
Jack Hirschowitz, M.D., Daniel S. Lobel, Ph.D., Moshen Aryan, M.A., Seth H. Apter, Ph.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

NR440 Schizophrenia: Premorbid Adjustment
James J. Levitt, M.D., Martha E. Shenton, Ph.D., Robert W. McCarley, M.D., Steven F. Faux, Ph.D., Amy S. Ludwig, M.A., R. Scott Smith, M.A.

NR441 Follow-Up of Clozapine Treated Schizophrenics
Del D. Miller, M.D., Paul J. Perry, Ph.D., Remi Cadoret, M.D., Nancy C. Andreasen, M.D.

NR442 Sexual Functioning of Schizophrenic Women
Jean-Michel Darves-Bornoz, M.D., Therese Lemperiere, M.D.

NR443 Clozapine Improves Sensory Gating More Than Haldol
Joseph C. Wu, M.D., Steven G. Potkin, M.D., Diane I. Ploszaj, B.A., Vickie Lau, Jennifer Telford, B.A., Glenn Richmond, M.D.

NR444 Quantity and Quality: Work Effect on Schizophrenia
Robert M. Milstein, M.D., Morris D. Bell, Ph.D., Paul H. Lysaker, Ph.D., Joseph B. Goulet, M.S.

NR445 Cortical CSF and Neuropsychological Function
Daniel S. O'Leary, Ph.D., Nancy C. Andreasen, M.D., Michael A. Flaum, M.D., Victor Swayze, M.D., James Ehrhardt, M.D., William Yuh, M.D.

NR446 Validation of Schizophrenia Spectrum Personality
Gerald Nestadt, M.D., John Hanfelt, Kung-Yee Liang, M.D., Paula Wolyniec, M.A., John McGrath, M.A., Malgorzata Lamacz, Ph.D., Ann E. Pulver, Sc.D.

NR447 Eye Movements: Bipolar Disorder and Schizophrenia
Allen Y. Tien, M.D., Godfrey Pearlson, M.D., Milton Strauss, Ph.D.

NR448 Situational Feature Detection and Schizophrenia
Patrick W. Corrigan, Psy.D., Michael F. Green, Ph.D., Rosemary Toomey, M.A.

NR449 Patient Rejection and Relapse in Schizophrenia
Uriel Heresco-Levy, M.D., Daniel Brom, Ph.D., David Greenberg, M.D.

NR450 Modules to Train Social Skills in Schizophrenics
Robert P. Liberman, M.D., Charles J. Wallace, Ph.D., Sally J. MacKain, Ph.D.

NR451 P300 and Temporal Lobe Structures in Schizophrenia
Robert W. McCarley, M.D., Martha E. Shenton, Ph.D., Brian F. O'Donnell, Ph.D., Robert S. Smith, M.A., Ron Kikinis, M.D., Ferenc A. Jolesz, M.D.

NR452 Abnormal N2 in Schizophrenia and MRI Limbic Volumes
Brian F. O'Donnell, Ph.D., Martha E. Shenton, Ph.D., Robert W. McCarley, M.D., Dean Salisbury, Ph.D., Ron Kikinis, M.D., Ferenc A. Jolesz, M.D.

NR453 Cognitive Activated Prism SPECT in Schizophrenics
Joel L. Steinberg, M.D., Michael D. Devous, Ph.D., David L. Garver, M.D., Joachim D. Raese, M.D., Rodrick R. Gregory, M.D.

NR454 Brain Potentials to Complex Tones in Schizophrenia
Gerard E. Bruder, Ph.D., James Towey, Ph.D., Dolores Malaspina, Ph.D., Jack M. Gorman, M.D., Craig Tenke, Ph.D., Charles A. Kaufmann, M.D.

NR455 Extrapyramidal Symptom Scale: A Factor Analysis
Lawrence Annable, D.S., Guy Chouinard, M.D., Andree Ross-Chouinard, M.D.

NR456 Negative Symptoms as Medication Side-Effects
Patrick B. Johnson, Ph.D., Paul M. Ramirez, Ph.D., Robert Malgady, Ph.D., Lewis A. Opler, M.D.

NR457 Compliance in Patients with Schizophrenia
Patricia G. Carrion, M.D., Alan C. Swann, M.D., Heather Kellert, M.A.

NR458 Cyclic Nucleotides and Neurotransmitter Metabolites in CSF of Clozapine-Treated Schizophrenics and Normal Controls
Emile D. Risby, M.D., Robert Risinger, M.D., Mark Stipetic, B.S., Zachary Stowe, M.D., Samuel C. Risch, M.D.

NR459 Effects of Pay for Work on Rehabilitation Outcome
Morris D. Bell, Ph.D., Robert M. Milstein, M.D., Paul H. Lysaker, Ph.D.

NR460 Pyramidical Model of Schizophrenia: Replication
Morris D. Bell, Ph.D., Paul H. Lysaker, Ph.D., Robert M. Milstein, M.D., Joseph B. Goulet, M.A.

NR461 Genetic and Social Influences on Schizophrenia
Frederic J. Sautter, Ph.D., Barbara McDermott, Ph.D., John Cornwell, Ph.D., Patricia Houterloot, M.S.W., Alicia Borges, B.A.

NR462 Cognitive Deficits in Familial Schizophrenia
Frederic J. Sautter, Ph.D., Barbara McDermott, Ph.D., F. William Black, Ph.D., Alicia Borges, B.A., Patrick O'Neill, M.D., Joanne Lucas, M.D.

NR463 Neuropsychology in Relatives of Schizophrenics
Stephen V. Faraone, Ph.D., William S. Kremen, Ph.D., Larry J. Seidman, Ph.D., John Pepple, Ph.D., Michael Lyons, Ph.D., Ming T. Tsuang, M.D.

NR464 Long-Term Mazindol Treatment of Schizophrenia
John P. Seibyl, M.D., Joseph Erdos, M.D., Laurence Karper, M.D., Robin Johnson, M.D., Louise Brenner, R.N., George R. Heninger, M.D.

NR465 Neuropsychiatry of Impulsivity and Aggression
Maxim Frenkel, M.D., Cecile Durlach-Misteli, M.D., Bonnie Aronowitz, M.A., Eric Hollander, M.D., Michael Liebowitz, M.D., Enrico Fazzini, D.O., Lee Cohen, M.D., Andrew Levin, M.D., Lawrence Rubin, M.D.

NR466 Bupropion Use in Patients at Risk for Seizures
Ben Zimmer, M.D., H. Jordan Garber, M.D., Trevor R.P. Price, M.D., Stefan Kruszewski, M.D.

NR467 Repeated Electroconvulsive Shock in Rats Does Not Enhance Electrical Amygdala-Kindling
Tom G. Bolwig, M.D., Jorn Kragh, M.D., Torben Bruhn, M.D., David P.D. Woldbye, M.D.

NR468 Reliability of Schizophrenia Symptom Assessment
Jeremy E. Stone, B.A., Richard S.E. Keefe, Ph.D., Philip D. Harvey, Ph.D., Seth H. Apter, Ph.D., Jack Hirschowitz, M.D., Richard C. Mohs, Ph.D.

NR469 Indices of Gender Effects in New Onset Schizophrenia
Sally R. Szymanski, D.O., Jeffrey A. Lieberman, M.D., Jose M.A. Alvir, Dr. PH., Margaret Woerner, Ph.D., Miranda H. Chakos, M.D., Amy R. Koreen, M.D.

NR470 Gender Effects in Clozapine Treated Patients
Sally R. Szymanski, D.O., Jeffrey A. Lieberman, M.D., Simcha Pollack, Ph.D., Margaret Woerner, Ph.D., S. Masiar, M.D., A. Safferman, M.D.

NR471 The Positive and Negative Syndrome Scale Structure in Adult and Geriatric Schizophrenia
Leonard White, Ph.D., Michael Parrella, Ph.D., Philip D. Harvey, Ph.D., Peter Powchik, M.D., Michael Davidson, M.D.

NR472 Neuropsychobiological Correlates of Tardive Dyskinesia
Henry A. Nasrallah, M.D., Robert A. Bornstein, Ph.D., Stephen C. Olson, M.D., S.B. Schwarzkopf, M.D., G. Jurjus, M.D.

NR473 Significant Decrease in Psychopathology Within Three Days of Haloperidol Treatment in Patients with Chronic Schizophrenia
Rene S. Kahn, M.D., Robert G. Stern, M.D., Michael Davidson, M.D., Philip D. Harvey, Ph.D., Seth H. Apter, Ph.D., Kenneth L. Davis, M.D.

NR474 Placebo-Controlled Treatment of Prodromal States

William C. Wirshing, M.D., Stephen R. Marder, M.D., Theodore Van Putten, M.D., Kathleen Johnston-Cronk, M.S., Joanne MacKenzie, R.N., Jim Mintz, Ph.D., Robert P. Liberman, M.D., Malca Lebell, Ph.D.

NEW RESEARCH

Wednesday, May 6, 1992, 3:00 p.m.-5:00 p.m.

New Research 11—Poster Session—Hall D, Level 1, Convention Center

ANXIETY, SEXUAL, SOMATOFORM, AND PERSONALITY DISORDERS; ECONOMIC, DIAGNOSTIC, AND WOMEN'S/MEN'S ISSUES; FORENSIC AND COMMUNITY PSYCHIATRY; AND INDIVIDUAL PSYCHOTHERAPIES

Moderator: Raymond L. Cohen, M.D.

NR475 L-365,260: A CCK-B Antagonist Blocks CCK-4-Panic
Jacques Bradwejn, M.D., Diana Koszycki, M.A., Anne Couetoux, M.D., Hank van Megen, M.D., Johan den Boer, M.D., Herman Westenberg, Ph.D., Chris Karkanias, M.Sc., Jeremy Haigh, Ph.D.

NR476 Behavioral and Cardiovascular Effects of Four Doses of CCK-4
Jacques Bradwejn, M.D., Diana Koszycki, M.A., Anne Couetoux, M.D., Lawrence Annable, D.S., Scott Reines, M.D., Chris Karkanias, M.Sc.

NR477 Personality Disorder and OCD
Donald W. Black, M.D., Russell V.R. Noyes, M.D., Bruce M. Pfohl, M.D., Rise B. Goldstein, M.S.W., Nancee Blum, M.S.W.

NR478 A Comparison of Fluvoxamine, Cognitive Therapy and Placebo in the Treatment of Panic Disorder
Donald W. Black, M.D., Robert Wesner, M.D., Wayne Bowers, Ph.D.

NR479 Effects of Fluvoxamine on Panic Disorder
Rudolf Hoehn-Saric, M.D., Daniel R. McLeod, Ph.D.

NR480 Panic Disorder in Schizophrenic Patients
Jean M. Chignon, M.D., Patrick Hardy, M.D., D. Levy, M.D., C. Epelbaum, M.D., J. Ades, M.D., A. Feline, M.D.

NR481 Chest Pain in Generalized Anxiety Disorder
Cameron S. Carter, M.D., Richard J. Maddock, M.D.

NR482 Body Dysmorphic Disorder: Can It Be Psychotic?
Susan L. McElroy, M.D., Katharine A. Phillips, M.D., Paul E. Keck, Jr., M.D., Harrison G. Pope, Jr., M.D., James I. Hudson, M.D.

NR483 Social Phobia: Efficacy of Brofaromine Versus Placebo
Mats Humble, M.D., Tom Fahlen, M.D., Charlotte Koczkas, M.D., Heimo L. Nilsson, Ph.D.

NR484 Amine Profiles in OCD
Jose A. Yaryura-Tobias, M.D.

NR485 Social Functioning in Anxiety Disorders
Catherine Mancini, M.D., Michael Van Ameringen, M.D., David Streiner, Ph.D., Georgina Stogios, Lara Kubilius, B.A., Shirley Davies, B.Sc.N., Elizabeth Ward, Reg.N., Dorothy Donison, Reg.N

NR486 Placebo Response Rates in OCD Pharmacologic Trials
Jane L. Eisen, M.D., Steven A. Rasmussen, M.D.

NR487 Predictors of Placebo Response in Panic Disorder
Mark D. Fossey, M.D., R. Bruce Lydiard, M.D., Michele T. Laraia, M.S.N., Joseph J. Zealberg, M.D., Alex Morton, Pharm.D., James C. Ballenger, M.D.

NR488 Prevalence of Anxiety Disorders in Asthmatics
Vijaya L. Boppana, M.D., Basawaraj Karajgi, M.D., Arthur Rifkin, M.D., Jean Fleischman, M.D.

NR489 Major Depression with Panic Disorder Responds to Nefazodone
Rejean Fontaine, M.D., Benoit Dassylva, M.D., Alfonso Ontiveros, M.D., Robert Elie, M.D.

NR490 OCD in Harvard/Upjohn Anxiety Research Project (HARP)
Kerrin White, M.D., David Shera, M.S., Gail Steketee, Ph.D., Ingrid Dyck, B.A., Linda Langford, B.A., Alan Gordon, M.D.

NR491 Alprazolam Discontinuation Effects of Carbamazepine
Ehud Klein, M.D., Varda Colin, M.D., John Stolk, M.D., Robert H. Lenox, M.D.

NR492 High Prevalence of Obsessional Habits in a Cohort of Italian High School Students
Mario Guazzelli, M.D., Alfonso Ceccherini Nelli, M.D., Luigi F. Bardellini, M.D., Elisabetta L. Balsamo, M.D., Pietro Pietrini, M.D.

NR493 Risk Factors for the Incidence of Social Phobia
Jane C. Wells, M.D., Allen Y. Tien, M.D., William W. Eaton, Ph.D.

NR494 Personality and Benzodiazepine Sensitivity
Deborah S. Cowley, M.D., Peter P. Roy-Byrne, M.D., David J. Greenblatt, M.D., Daniel W. Hommer, M.D.

NR495 Hyperfrontality and Serotonin in OCD
Eric Hollander, M.D., Concetta Decaria, M.S., Lisa Cohen, M.A., Mohammed Islam, M.D., Dan J. Stein, M.D., Maxim Frenkel, M.D.

NR496 Neuropsychiatric Impairment in Social Phobia
Eric Hollander, M.D., Concetta Decaria, M.S., Sari Trungold, B.A., Lisa Cohen, M.A., Maxim Frenkel, M.D., Frank Schneier, M.D., Dan J. Stein, M.D., Michael R. Liebowitz, M.D.

NR497 Lactate Sensitivity in Sleeping Panic Patients
Harold W. Koenigsberg, M.D., Charles P. Pollak, M.D., Jeffrey Fine, M.D., Tatsu Kakuma, Ph.D.

NR498 Social Phobia, Personality Traits and Brofaromine
Tom R. Fahlen, M.D., Helmo L. Nilsson, Ph.D.

NR499 The Effects of Buspirone on Sleep, Anxiety and PTSD
Patrick E. Ciccone, M.D., Robert A. Greenstein, M.D., Marvin Weisbrot, R.Ph.

NR500 A Study of the Seasonality of OCD
Timothy D. Brewerton, M.D., James C. Ballenger, M.D.

NR501 Buspirone in Social Phobia
Franklin R. Schneier, M.D., Raphael Campeas, M.D., Brian A. Fallon, M.D., Eric Hollander, M.D., Jeremy Coplan, M.D., Michael R. Liebowitz, M.D.

NR502 Panic Disorder and Separation Anxiety Disorder: New Relationships
Juan M. Segui, M.D., Cristian Y. Herrera, M.D., Luis C. Salvador, M.D., Jaime Canet, Ph.D.

NR503 BETA Receptors in Panic Disorder: Treatment Effects
Richard J. Maddock, M.D., Cameron S. Carter, M.D., Joseph R. Magliozzi, M.D., Dorothy W. Gietzen, Ph.D.

NR504 Significance of Past Depression in Panic Disorder
Richard J. Maddock, M.D., Cameron S. Carter, M.D., K.H. Blacker, M.D., Mary Beth Logue, M.S., Ranga Krishnan, M.D., John H. Greist, M.D.

NR505 A Comparison of Trichotillomania and OCD
Joseph A. Himle, M.S.W., Patrick Bordnick, M.S.W.

NR506 Cues Which Elicit Recurrent Psychopathology
Thomas B. Mackenzie, M.D., Stephen L. Ristvedt, Ph.D., Gary A. Christenson, M.D., Alyson S. Lebow, M.S., James E. Mitchell, M.D.

NR507 Concurrent Panic Disorder and Social Phobia
Michael van Ameringen, M.D., Catherine Mancini, M.D., Georgina Stogios, Lara Kubilius, Shirley Davies, B.Sc.N., Dorothy Donison, Reg.N.

NR508 Regional Cerebral Blood Flow in Panic Disorder
Laura Guarneri, M.D., Alberto Bestetti, M.D., Emanuela Scuto, M.D., A. Chiti, M.D., G.L. Tarolo, M.D., Emilio Saccmetti, M.D.

NR509 Oral and Parenteral m-CPP in 12 Patients with OCD
Wayne K. Goodman, M.D., Christopher J. McDougle, M.D., Lawrence H. Price, M.D., Linda C. Barr, M.D., George R. Heninger, M.D.

NR510 Normal Alph-2 Adrenergic Functioning in OCD
William A. Hewlett, M.D., Sarah Berman, B.S., Karron Martin, R.N.

NR511 Psychiatric Diagnosis in Dental Phobic Patients
Peter P. Roy-Byrne, M.D., Peter Milgrom, D.D.S., Khoon-Mei Tay, B.D.S., Philip Weinstein, Ph.D., Wayne J. Katon, M.D.

NR512 Does Anxiety or Insomnia, as Part of Major Depression, Predict a Differential Response to the Type of Antidepressant Prescribed?
Gary D. Tollefson, M.D., Mary E. Sayler, M.S., Susan L. Holman, M.S.

NR513 Haloperidol Addition in Fluvoxamine-Refractory OCD
Christopher J. McDougle, M.D., Wayne K. Goodman, M.D., James F. Leckman, M.D., Nicole C. Lee, M.S.N., George R. Heninger, M.D., Lawrence H. Price, M.D.

NR514 Panic Disorder: Treatment with Valproate
Catherine L. Woodman, M.D., Russell V.R. Noyes, M.D.

NR515 Correlates of Dissociative Symptomatology in Patients with Physical and Sexual Abuse Histories
Janet S. Kirby, B.A., James A. Chu, M.D., Diana L. Dill, Ed.D.

NR516 Economic Methods in Cost Offset Measurement
Marianne Fahs, Ph.D., James J. Strain, M.D., John S. Lyons, Ph.D., Jeffrey S. Hammer, M.D.

NR517 Determinants of Length of Stay in Geropsychiatry
Paul S. Aisen, M.D., Donald Johannessen, M.D., Kathleen E. Giblin, C.S.W., Linda S. Packer, C.S.W., Brian A. Lawlor, M.D.

NR518 Work Loss and Depression: Impact of Fluoxetine
Eric Souetre, M.D., Patrick Martin, Pharm.D., Helene Lozet, Ph.D., J-P Lecanu, M.D., C. Blachier, M.B.A.

NR519 Methods of Funding Psychiatric Consultation Research and Teaching Services
James J. Strain, M.D., Mirjami Easton, George Fulop, M.D.

NR520 Adjustment Disorders in the Medical Inpatient Setting: A Multisite Study
Jeffrey S. Hammer, M.D., James J. Strain, M.D., Graeme C. Smith, M.D., Michael Blumenfield, M.D., Thomas Garrick, M.D., John R. Hayes, M.D., Philip R. Muskin, M.D., Joel J. Wallack, M.D., Asher Wilner, M.D.

NR521 Giftedness and Psychological Abuse in BPD
Lee C. Park, M.D., John B. Imboden, M.D., Thomas J. Park, Ph.D., Stewart H. Hulse, Ph.D., H. Thomas Unger, M.D.

NR522 Validity of Self-Defeating Personality Disorder
Charlotte Copas, Ph.D.

NR523 Eye Tracking Impairment and Deficit Symptoms
Jackie Moskowitz, M.A., Sonia Lees, B.A., Lee Friedman, Ph.D., Richard S.E. Keefe, Ph.D., Richard C. Mohs, Ph.D., Larry J. Siever, M.D.

NR524 Fluoxetine in BPD
Carl Salzman, M.D., Alan F. Schatzberg, M.D., Edison Miyawaki, M.D., M. Albanese, M.D., A. Wolfson, A.B., J. Looper, M.D.

NR525 Comparing Self-Defeating and Masochistic Criteria
Ross A. McElroy, Jr., M.D., Linda Lefler, M.D., Roger K. Blashfield, Ph.D.

NR526 A Study of Anger as a Personality Trait
Abelardo Pena-Ramos, M.D., Denise K. Gross, Psy.D.

NR527 Impaired Vigilance in Borderline Personality
Anselm George, M.D., Paul H. Soloff, M.D., Stuart R. Steinhauer, Ph.D., Jack R. Cornelius, M.D.

NR528 Unconscious Information Processing and Repression
Bruce Wexler, M.D., George Bonano, Ph.D.

NR529 Patient Versus Family Informant Derived Diagnoses
Delbert G. Robinson, M.D., Jose Alvir, Dr.PH

NR530 SCID and SCID-D Interviews of Dissociative Patients
Robert G. Lussier, M.D., Marlene Steinberg, M.D., Domenic Cicchetti, Ph.D.

NR531 A Comparison of Comorbid Axis I Diagnoses in Stimulant Dependent and Depressed Research Subjects
Mark H. Rapaport, M.D., John R. Kelsoe, M.D., Shah Golshan, Ph.D., J. Christian Gillin, M.D.

NR532 Conflict with Physician Pregnancy: Revisited
Kathleen N. Franco, M.D., Nancy B. Campbell, M.D., Cynthia L. Evans, M.D., Stephen G. Jurs, Ph.D., Marijo B. Tamburrino, M.D.

NR533 Battered American Indian Women
Ilena M. Norton, M.D., Spero M. Manson, Ph.D.

NR534 Gay and Lesbian Issues in United States Psychiatric Training
Mark H. Townsend, M.D., Mollie M. Wallick, Ph.D., Karl M. Cambre, M.S.

NR535 Response to Fenfluramine in Premenstrual Syndrome
Margaret L. Moline, Ph.D., Sally K. Severino, M.D., Daniel R. Wagner, M.D., Steven Zendell, RP.SGT., Stephen W. Hurt, Ph.D.

NR536 The New Woman: Psychosocial and Sexual Aspects
Samuel S. Janus, Ph.D., Cynthia L. Janus, M.D.

NR537 Cost of Intensive Care Community Treatment
Kathleen Degen, M.D., Carolyn Harmon, Ph.D.

NR538 Medical Complaints and the Homeless Mentally Ill
Kerry Petrucci, Ph.D., Lisa Dixon, M.D., Jean Hyde, M.S., Carol Lindes, M.S., David Stuart, M.D., Jan Wemmer, R.N.

NR539 Economic Social Network: A New Model for Homelessness
Martin Korn, M.D., Isora C. Bosch, Ed.D., Frederick D. Greene, Ph.D., Vera Zilzer, A.T.R., Herman M. van Praag, M.D.

NR540 Disability Determinations: A Reliability Study
Samuel O. Okpaku, M.D., Amy E. Sibulkin, Ph.D., Christoph Schenzler, M.A.

NR541 Continuity of Care by Means of Psychoeducational Therapy
Avner Elizur, Enav Karniel-Layer, Henry Szor

NR542 Gender and Patients' Initiation of Complaints
Thomas Gift, M.D.

NR543 Humane Values and Mental Health in Quebec, 1950-1990
Hughes J. Cormier, M.D.

NR544 Implementing a Ten-Step Study for Monitoring Tardive Dyskinesia
Bradford Frank, M.D., Kathleen Degen, M.D., Roger Adams, Ph.D., Maureen Hazleton, R.N., Tom Wellington, M.P.H., Gary Nemergut, B.S.

NR545 Receiver Operating Characteristic and the Accuracy of Violence Prediction
Douglas Mossman, M.D., Roberta Schaffner, M.D.

NR546 Violence and Civil Commitment: A Study of Attitudes
Douglas Mossman, M.D., Kathleen J. Hart, Ph.D.

NR547 Patients Characteristics and Brief Therapy Outcome
John J. Sigal, Ph.D., Marianne E. Kardos, M.D., Gilbert Zimmerman, M.D., Michael Buonvino, B.Sc.

Thursday, May 7, 1992, 9:00 a.m.-10:30 a.m.

New Research 12—Oral/Slide Session—Rooms 23/24, Level 1, Convention Center

AFFECTIVE DISORDERS

Chp.: Raymond L. Cohen, M.D.

NR548	Psychobiology of Response to Inpatient Cognitive Therapy Michael Thase, M.D.	9:00 a.m.
NR549	Those Intolerant to One Selective Serotonin Reuptake Inhibitor May Tolerate Another Walter A. Brown, M.D.	9:15 a.m.
NR550	ECT Schedule: Therapeutic and Cognitive Implications Baruch Shapira, M.D., Avraham Calev, Ph.D., Bernard Lerer, M.D.	9:30 a.m.
NR551	Depression, Cognitive Impairment and Mortality Gary J. Kennedy, M.D., Howard R. Kelman, Ph.D., Cynthia Thomas, Ph.D.	9:45 a.m.
NR552	Biochemical Measures in Dysthymic Disorder Arun Ravindran, Robert J. Bialik, Ph.D., Gregory M. Brown, M.D., Yvon D. Lapierre, M.D.	10:00 a.m.
NR553	Antidepressant Treatment of Chronic Tinnitus: An RCT Mark D. Sullivan, M.D., Wayne J. Katon, M.D., Joan Russo, Ph.D., Robert A. Dobie, M.D., Connie S. Sakai, MSPA	10:15 a.m.

Thursday, May 7, 1992, 9:00 a.m.-10:30 a.m.

New Research 13—Oral/Slide Session—Rooms 25/26, Level 1, Convention Center

SUBSTANCE ABUSE DISORDERS

Chp.: Markku I. Linnoila, M.D.

NR554	Late-Onset Alcohol Use Disorders in Older Men Roland M. Atkinson, M.D., Robert L. Tolson, M.S.W.	9:00 a.m.
NR555	Thirty-Year Follow-Up of Sons of Alcoholics Donald W. Goodwin, M.D., Elizabeth Penick, Ph.D., William Gabrielli, M.D., Per Jensen, M.D., Joachim Knop, M.D., Fini Schulsinger, M.D.	9:15 a.m.
NR556	Dopaminergic Therapy for Cocaine Withdrawal in Rats Ronald P. Hammer, Ph.D., Shay J. Lee, M.D., Blanche B. Young, B.A.	9:30 a.m.
NR557	Fluoxetine for Cocaine Abuse: Psychiatric Factors Steven L. Batki, M.D., Luisa Manfredi, B.A., Reese T. Jones, M.D., Laura Goldberger, B.A., Jennifer M. Murphy, B.A.	9:45 a.m.

NR558 Opiate Detoxification: An Indication for Serotonin-3 Receptor Antagonists 10:00 a.m.
Norbert Loimer, M.D., Peter Hofmann, M.D., Haroon Chaudhry, M.D.

NR559 Amphetamine Sensitizes c-fos Expression in Brain 10:15 a.m.
Andrew B. Norman, Ph.D., Sunny Y. Lu, M.D., Jennifer M. Klug, B.S., Eugene Somoza, M.D., Robert B. Norgren, Ph.D.

NEW RESEARCH

Thursday, May 7, 1992, 12 noon-2:00 p.m.

New Research 14—Poster Session—Hall D, Level 1, Convention Center

MOOD DISORDERS, PSYCHOPHARMACOLOGY AND OTHER SOMATIC THERAPIES, AND SUICIDE

Moderator: Trey Sunderland, M.D.

NR560 Drug Abuse/Dependence in Early-Onset Depression
Kimberly C. Burke, M.S., Jack D. Burke, Jr., M.D., Donald S. Rae, M.S.

NR561 Relapse Following Cognitive Therapy of Depression
Michael E. Thase, M.D., Anne Simons, Ph.D., Edward Friedman, M.D.

NR562 Depression and Lymphocyte Function in Adolescents
Steven J. Schleifer, M.D., Jacqueline Bartlett, M.D., Steven E. Keller, Ph.D.

NR563 Carbamazepine Induces Bupropion Metabolism
Terence A. Ketter, M.D., Janice Barnett, Pharm.D., David H. Schroeder, Ph.D., Melvin L. Hinton, B.S., John Chao, M.S., Robert M. Post, M.D.

NR564 Increasing Rates of Adolescent Depression
Andrew C. Leon, Ph.D., Gerald L. Klerman, M.D., Myrna M. Weissman, Ph.D., Priya Wickramapaine, Ph.D.

NR565 Bipolar Disorder in Infancy
Clifford H. Siegel, M.D., Pamela McBogg, M.D.

NR566 The Effectiveness of Drug Treatment in Depressed Patients
Avner Elizur, Zipora Bar, Henry Szor

NR567 Cognitive Subtypes of Depression in Adolescents
John B. Jolly, Psy.D., Janet M. Jolly, Balkozar Adam, M.D., Doug Reed, M.Ed.

NR568 Differentiating Anxiety and Depression in Youths
John B. Jolly, Psy.D., Ross A. Dykman, Ph.D., David S. McCray, M.D., Janet M. Jolly, Melanie Wheeler, B.S., Rebecca Bregy, R.N.

NR569 Depression in Schizophrenia: Self Versus Observer Report
Donald E. Addington, M.D., Jean Addington, Ph.D., Eleanor Maticka-Tyndale, Ph.D.

NR570 Moclobemide in Major Depression and Dysthymia
Jorge Nazar, M.D.

NR571 Paroxetine in the Prevention of Depression
Geoffrey C. Dunbar, M.D., Dusan Petrovic, M.D.

NR572 Effects of Paroxetine on Sleep EEG
L. Staner, M.D., J. Mendlewicz, M.D., M. Kerkhofs, M.D., D. Detroux, M.D., E. Bouillon, M.D., Prof Juan Ramon de la Fuente, M.D.

NR573 Thyroid Hormones and TSH Response to TRH
Marie-Claude Mokrani, Ph.D., Fabrice Duval, M.D., M. Antoine Crocq, M.D., Juarez Oliveira Castro, M.D., Sergio Valdivieso, M.D., Jean-Paul Macher, M.D.

NR574 TRH-TSH Test, DST and Prognosis of Depression
Fabrice Duval, M.D., Juarez Oliveira Castro, M.D., Sergio Valdivieso, M.D., Marie-Claude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Jean-Paul Macher, M.D.

NR575 Life Events at Onset of Bipolar Disorder in Pedigrees
Victor I. Reus, M.D., Mitzi Spesny, M.S., Michael Escamilla, M.D., Alvaro Gallegos, M.D., Pedro Leon, M.D., Nelson Freimer, M.D.

NR576 Lithium and Tardive Dyskinesia in Affective Disorder
Abdu'L-Missagh Ghadirian, M.D., Lawrence Annable, D.S., Guy Chouinard, M.D., Marie-Claire Belanger, R.N.

NR577 Prevalence and Onset of Bipolar Illness in Adolescent Inpatients
Abdu'L-Missagh Ghadirian, M.D., Normand Roux, M.D.

NR578 Desipramine Levels After Sertraline or Fluoxetine
Sheldon H. Preskorn, M.D., Jeffrey Alderman, Ph.D., Michael Messig, Ph.D., Stuart Harris, M.D., Menger Chung, Ph.D.

NR579 Long-Term Treatment of Major Depressive Disorder with Paroxetine
Eugene A. DuBoff, M.D.

NR580 Paroxetine is a Selective Serotonin Reuptake Inhibitor in Man
D. R. Nelson, Katharine J. Palmer, B.Sc., Tim C. Tasker, M.B., Ian F. Tulloch, Ph.D.

NR581 Symptom Profiles of Abnormal DST and Clonidine Test
Sergio Valdivieso, M.D., Fabrice Duval, M.D., Marie-Calude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Nicolas Schaltenbrand, Ph.D., Jean-Paul Macher, M.D.

NR582 Sex in the State of Depression
Eric A. Nofzinger, M.D., Michael E. Thase, M.D., Charles F. Reynolds, M.D., Ellen Frank, Ph.D., J. Richard Jennings, Ph.D., David J. Kupfer, M.D.

NR583 Gender and Outcome of Major Depression
Christine Ryan, Ph.D., Gabor Keitner, M.D., Ivan Miller, Ph.D.

NR584 Chronicity in Geriatric Depression
George S. Alexopoulos, M.D., Barnett S. Meyers, M.D., Robert C. Young, M.D., Tatsuyuki Kakuma, Ph.D., Janis Chester, M.D., Eileen Rosendahl, Ph.D.

NR585 Sleep Deprivation Hormonal Response in Depression
Richard C. Shelton, M.D., Peter T. Loosen, M.D., David N. Orth, M.D.

NR586 The Effects of Antidepressants on the Thyroid Axis
Richard C. Shelton, M.D., Peter T. Loosen, M.D.

NR587 Efficacy of the Medical Outcomes Study Questionnaire as an Outpatient Screen for Dysthymic Disorder
Mary E. Moran, M.Ed., John C. Markowitz, M.D., James H. Kocsis, M.D.

NR588 Critical Flicker Fusion as a Measure of Antidepressant Efficacy
Ian Hindmarch, Ph.D., John Kerr, Ph.D., Alex Alexander, M.D.

NR589 Mechanisms Underlying Antidepressant Action
Pedro L. Delgado, M.D., George R. Heninger, M.D., Helen L. Miller, M.D., Lawrence H. Price, M.D., Ronald S. Salomon, M.D., Julio Licinio, M.D., Dennis S. Charney, M.D.

NR590 Diurnal Variation of CSF CRH in Major Depression
Mitchel A. Kling, M.D., Thomas D. Geracioti, M.D., Michael D. DeBellis, M.D., Samuel J. Listwak, M.S., Daniel K. O'Rourke, M.D., Edward H. Oldfield, M.D., Philip W. Gold, M.D.

NR591 Depression, Cardiac Regulation and Sudden Death
Gregory W. Dalack, M.D., Steven P. Roose, M.D., Alexander H. Glassman, M.D., Sally Woodring, R.N., Thomas J. Bigger, M.D.

NR592 Euthymia, Major Depression and Fluoxetine Response
Gregory W. Dalack, M.D., Alexander H. Glassman, M.D., Sarah Rivelli, Lirio S. Covey, Ph.D., Fay Stetner, M.S., Jill Becker, M.A.

NR593 Validation of a New Mania-Depression Scale
Verinder Sharma, M.B., Dwight S. Mazmanian, Ph.D., Emmanuel Persad, M.B., Karen Kueneman, B.A., Janice Burnham, B.Scn.N., Julie Franklin, RNA, Gloria Leiska, R.N., Mark Hemmings, R.N.

NR594 oCRH Stimulation in Anxious Depression
William H. Meller, M.D., Paula J. Clayton, M.D., Roger G. Kathol, M.D., Stephen D. Samuelson, M.D., Timothy L. Gehris, B.S., Andrew F. Pitts, M.D.

NR595 Characterizing Organic Mood Syndrome: Depressed Type
Jack R. Cornelius, M.D., Juan E. Mezzich, M.D., Horacio Fabrega, M.D., Marie D. Cornelius, Ph.D., Nancy L. Day, Ph.D., Richard F. Ulrich, M.S.

NR596 Early Pharmacokinetic Targeting of Tricyclic Doses
William A. Kehoe, Pharm.D., Arthur F. Harralson, Pharm.D., John J. Jacisin, M.D., M.J. Hetnal, M.D.

NR597 Family Treatment of Bipolar Disorder
Ivan W. Miller, Ph.D., Gabor I. Keitner, M.D., Nathan B. Epstein, M.D., Duane S. Bishop, M.D., Christine E. Ryan, Ph.D.

NR598 Signs of Dyscontrol and Responsiveness to Fluoxetine in Major Depressives
Giovanni Conte, M.D., Alessandro Calzeroni, M.D., Laura Guarneri, M.D., Ambrogio Pennati, M.D., Giuseppe Russo, M.D., Emilio Sacchetti, M.D.

NR599 Efficacy of Fluoxetine in Psychotic Depression
Anthony J. Rothschild, M.D.

NR600 Rubidium Normalizes Split Rhythms in Hamsters
John D. Hallonquist, Ph.D.

NR601 Immunity in Drug-Naive Major Depressive Episode Patients
Steven E. Keller, Ph.D., Antonio A. Andreoli, M.D.

NR602 Interpersonal Deficits and TCA Response in Dysthymia
John C. Markowitz, M.D., James H. Kocsis, M.D., Mary E. Moran, M.Ed.

NR603 Psychoeducation for Mood Disorder
Ira Glick, M.D., Lorenzo Burti, M.D., Keigo Okonogi, M.D.

NR604 Double Blind, Placebo Controlled Comparative Study of Levoprotiline and Amitriptyline in Patients with Moderate to Severe Depression
Ram K. Shrivastava, M.D., S.S. Shrivastava, M.D., Norbert Overweg, M.D., Richard Katz, Ph.D., Diane Romley, B.A.

NR605 Core Symptoms of Depression
James R. Moeller, Ph.D., Eric Rubin, M.D., Harold A. Sackeim, Ph.D.

NR606 Use of Postnatal Depression Scale
Alec Roy, M.B., Peggy Gang, R.N., Karyl Cole, M.D., Monica Rutsky, C.S.W., Joann Weisbord, C.S.W., Leslie Reese, C.S.W.

NR607 Onset of Antidepressant Action with S-Adenosylmethionine: A Controlled Clinical Trial
Carlos Leon-Andrade, M.D., Hector Ortega-Soto, M.D., Prof Juan Ramon de la Fuente, M.D.

NR608 Long-Term Valproate Prophylaxis in Refractory Affective Disorders
Stephen Hayes, M.D.

NR609 ECT and Twin Pregnancy
Ray Walker, M.D.

NR610 Treatment of Psychotic Depression in Late-Life
Benoit H. Mulsant, M.D., Robert A. Sweet, M.D., George S. Zubenko, M.D., James M. Perel, Ph.D., Charles F. Reynolds III, M.D.

NR611 Sleep, Depression and Fibromyalgia in Fatigue
Peter Manu, Thomas J. Lane, M.D., Dale A. Matthews, M.D., Robert K. Watson, Ph.D., Richard J. Castriotta, M.D., Micha Abeles, M.D.

NR612 Psychobiologic Predictors of Reattempted Suicide
Kevin M. Malone, M.D., Joyce M. Myers, M.D., Gretchen L. Haas, Ph.D., Tammy A. Mieczkowski, M.A., John A. Sweeney, Ph.D., J. John Mann, M.D.

NR613 Low Association Between Childhood Trauma and BPD
Carl Salzman, M.D., Judith P. Salzman, Ed.D., Abbie Wolfson, A.B., E. Miyawaki, M.D., M. Albanese, M.D., J. Looper, M.D.

NR614 Comparison of Venlafaxine, Trazodone and Placebo in Major Depression
Lynn A. Cunningham, M.D., Richard L. Borison, M.D., John Carman, M.D., John Crowder, M.D., Bruce I. Diamond, Ph.D.

NR615 Lithium, RBC Levels and Renal Side Effects
Simavi Vahip, M.D., Hakan Coskunol, M.D., Evert J.D. Mees, M.D., Ali Basci, M.D., Oya Bayindir, M.D., Isik Tuglular, M.D.

NR616 Fluoxetine Blood Levels and Clinical Response
Paul J. Goodnick, M.D.

NR617 Psychogeometry: The Dynamic Analysis of Mood
Hector C. Sabelli, M.D., Linnea Carlson-Sabelli, Ph.D., Minu Patel, M.S., Nancy Hein, A.S., Erika Harris

NR618 Family and Population Studies of Affective Disorders with 11p15.5 DNA Markers
Francis Gheysen, M.D., Alain Malafosse, M.D., Mokran Abbar, M.D., Marion Leboyer, M.D., Stephan Amadeo, M.D., Prof. E. Zarifian, M.D.

NR619 Imipramine Maintenance in Postpsychotic Depression
Samuel G. Siris, M.D., Paul C. Bermanzohn, M.D., Susan E. Mason, Ph.D., Mitchell A. Shuwall, Ph.D.

NR620 Predictors of Suicide in the Consultation Population
James J. Strain, M.D., Yasutaka Iwasaki, M.D., Jeffrey S. Hammer, M.D., Hwai-Tai C. Lam, Ph.D.

NR621 Imitation Suicides After a Live Televised Suicide
Paul A. Kettl, M.D., Michael J. Christ, B.S., Edward O. Bixler, Ph.D.

NR622 Economic Growth and Rise of Youth Suicide
Paul A. Kettl, M.D., Michelle Sredy, B.S.

NR623 Suicidal Youth: Resident Hospitalization Decisions
Robert Dicker, M.D., Richard Morrisey, Ph.D., Howard Abikoff, Ph.D., Harold S. Koplewicz, M.D., Kimberly Weissman, B.A.

NR624 Effects of Mints on Medication-Induced Xerostomia
Patrick E. Ciccone, M.D., Roy S. Feldman, D.D.S., Ralph S. Richter, B.S., Jack Vincent, D.M.D., Michael L. Barnett, D.D.S.

NR625 Quality of Life: Assessment in Drug Development
Richard L. Rudolph, M.D., Albert T. Derivan, M.D., Ronald Pederson, M.S.

NR626 A Trial of Lithium Citrate for the Management of Acute Agitation of Psychiatric Patients
Hyung K. Lee, M.D., Tarakumar Reddy, M.D., Sheldon Travin, M.D., Harvey Bluestone, M.D.

NR627 Antibodies to Heat Shock Protein in Schizophrenia
Konstantinos Kilidireas, M.D., Saud A. Sadiq, M.D., David H. Strauss, M.D., Jack M. Gorman, M.D., Norman Latov, M.D.

NR1 Monday May 4, 9:00 a.m.-10:30 a.m.

Information Processing Effect on Saccadic Reaction Time in Schizophrenia

Douglas M. Berger, M.D., Psychiatry, Einstein College of Med., 1155 Warburton Avenue 12Y, Yonkers, NY 10701; Shinnichi Nezu, M.D., Tommie Iga, B.S., Takashi Hosaka, M.D., Seiro Nakamura, M.D.

Summary:

Information processing was tested by comparing saccadic reaction times of 13 schizophrenics and 13 normal controls under conditions where there was information provided about the duration of a warning signal to those where there was not. Saccadic reaction time measured by electro-oculogram was studied in order to minimize complicating variables associated with prior studies using manual reaction time. Supporting prior research, this study found that schizophrenics do worse when there is prior information about warning signal duration than when there is not, while in controls this was reversed. Significant enhancement of this effect with increasing age and a possible normalizing effect with greater neuroleptic dose were also found. The major limitations of this study, however, included a small N and uncontrolled medication. The authors conclude that (a) there is a schizophrenic deficit in the processing of information in order to establish a mental set necessary for preparation, (b) this deficit may be useful in confirming the diagnosis of schizophrenia in older age groups, and (c) effects of antipsychotic medication on information processing warrant further study. They hypothesize that effects of neurotransmitters on information processing and time perception, abnormalities in the frontal lobes, and information processing steps measured by evoked potential may play a role in impaired information processing in schizophrenia.

NR2 Monday May 4, 9:00 a.m.-10:30 a.m.

Schizophrenia After Prenatal Exposure to Famine

Ezra S. Susser, M.D., NY State Psch Inst., 722 W. 168th St. Box 24, New York NY 10032; Lin P. Shang, Ph.D.

Summary:

We tested the hypothesis that first trimester exposure to acute famine is a risk factor for schizophrenia. A sharp and time-limited decline in the food intake of the Dutch population following a Nazi blockade in 1944-45 created a unique, if tragic, natural experiment in which to test this hypothesis. In each of three regions of Holland (West, North, South), birth cohorts exposed to acute food deprivation in the first trimester showed a substantial increase in hospitalized schizophrenia in women, and no increase in men. In the West or Famine region, statistically significant relative risks for women were 2.17 for "broad" schizophrenia and 2.56 for "restricted" schizophrenia. In the North and South, relative risks for women—based on smaller numbers—were of the same magnitude and in the same direction but not statistically significant. The threshold for an association between first trimester food deprivation and risk of schizophrenia in women was an average daily ration under 1000 Kcalories in the Famine region and under 1500 Kcalories in the North and South regions. These findings give plausibility to three propositions: 1) early prenatal factors can have a large effect on the risk of schizophrenia; 2) prenatal nutritional deprivation can play a role in the etiology of schizophrenia; and 3) the effect of prenatal nutritional deprivation on the risk of schizophrenia is greater in women than in men.

NR3 Monday May 4, 9:00 a.m.-10:30 a.m.

Depression in First-Episode Schizophrenia

Amy R. Koreen, M.D., Research, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004; Jeffrey A. Lieberman, M.D., Samuel C. Siris, M.D., Miranda Chakos, M.D., Jose Alvir, Dr. P.H., David I. Mayerhoff, M.D.

Summary:

Depresstion is known to occur in patients with schizophrenia and influences its course and treatment. However, previous studies of depression in schizophrenia have been limited by the effects of chronic neuroleptic treatment. Data were therefore obtained from 70 first episode schizophrenic patients (RDC) in an ongoing prospective study of psychobiology in order to examine the prevalence and prognostic significance of depressive symptoms. Clinical assessments (SADS, SANS, CGI + SAEPS) were done at baseline and then biweekly. Extracted Hamilton scores (HAM) and a syndromal definition of depression were obtained from the SADS. Depressive symptoms were defined as having a HAM $\geq$15 and a syndromal depression.

At baseline 66 percent had depressive symptoms by one set of criteria and 23 percent by both sets of criteria. Most depressive symptoms occurred concurrently with psychosis and resolved as the psychosis remitted. HAM scores were correlated with both negative and positive symptoms. Depressive symptoms were prodromal to only 5 percent of the observed psychotic relapses. Depressed patients were not different diagnostically, demographically, or premorbidly or in baseline psychopathology or risk for EPS from nondepressed patients but did have a lower incidence of family history of schizophrenia and tended to have a better global outcome.

NR4 Monday May 4, 9:00 a.m.-10:30 a.m.

Plasma HVA in First-Episode Schizophrenia

Amy R. Koreen, M.D., Research, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004; Jeffrey A. Lieberman, M.D., Jose Alvir, Dr. P.H., David I. Mayerhoff, M.D., Antony Loebel, M.D., Miranda Chakos, M.D., Thomas Cooper, M.A.

Summary:

Plasma homovanillic acid (pHVA) may reflect brain dopamine activity making it a useful tool for studying schizophrenia. However, a concern in intrepreting previous studies are the effects of long-term treatment. Data were therefore obtained from 41 neuroleptic naive schizophrenic patients diagnosed according to RDC who participated in an ongoing study on the psychobiology of first-episode schizophrenia. Plasma HVA was drawn at baseline and then weekly during standardized open neuroleptic treatment. Clinical assessments (SADS, SANS + CGI) were done at baseline and then weekly during standardized open neuroleptic treatment. Clinical assessments (SADS, SANS + CGI) were done at baseline and biweekly during acute treatment. Remission was defined as when patients received a CGI global improvement rating of $\leq$2 and had $\leq$3 on any psychotic item of the SADS.

Overall group mean showed a significant increase in pHVA at week 1 before declining towards baseline by week 4. Gender differences were observed with females having higher pHVA concentrations at all time points. Baseline pHVA and week 1 pHVA levels were negatively correlated with time to reach remission. When response was stratified by gender, responders had higher baseline values, a greater increase at week one and higher post-treatment values than nonresponders. These and additional analyses wil be presented.

NR5 Monday May 4, 9:00 a.m.-10:30 a.m.

Schizophrenia: Correlated Onset of Comorbid Symptoms

James M. Russell, M.D., Psychiatry, Washington University, 4940 Audubon Road Box, 8134, St. Louis, MO 63110; Lee N. Robins, Ph.D., John P. Rice, Ph.D.

Summary:

In a community sample of 19,640 U.S. residents, 305 individuals with a diagnosis of DSM-III schizophrenia were identified. A total of 91 percent of these individuals met criteria for another psychiatric disorder at sometime during their life. On average schizophrenics met criteria for 2.3 comorbid psychiatric disorders. Without exception, our data showed that increasing severity of schizophrenia, defined by number of symptoms, was associated with higher rates of comorbidity. The onset of the comorbid psychiatric disorder was highly correlated with the onset of the schizophrenic disorder. A total of 42 percent of schizophrenics with mania, 28.3 percent of schizophrenics with depression, 24 percent of schizophrenics with panic, 23 percent of schizophrenics with obsessive-compulsive disorder, and 17 percent of schizophrenics with phobia recalled the onset of both disorders in the same year. These findings confirm previous clinical studies indicating a significant syndromal overlap between schizophrenia and other psychiatric disorders, underscoring the complexity of the schizophrenic syndromes. Clinicians should expect the presenting schizophrenic patient to have a complex constellation of symptoms that cross many diagnostic boundaries. Cross sectional diagnosis of schizophrenia may therefore be difficult and result in significant diagnostic heterogeneity. Modeling for this comorbidity may reduce this heterogeneity and result in reliable and replicable research findings.

NR6 Monday May 4, 9:00 a.m.-10:30 a.m.

Study of Relapse in Medication-Compliant Schizophrenics

Sandra Steingard, M.D., Psychiatry, Univ of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213; Krishna R. Khambampati, M.D., Maureen Allen, M.P.H.

Summary:

Although studies of maintenance neuroleptic treatment demonstrate a substantial rate of relapse in compliant patients, appropriate treatment for these patients has not been well studied.

Method. This pilot investigation included 32 patients admitted to hospital with an exacerbation of schizophrenia despite medication compliance. In addition to their pre-admission neuroleptics, subjects were randomly assigned either to additional fluphenazine (FPZ) or placebo (PBO) for ten days. Ratings of psychopathology, EPS, and stress were completed. Medication was administered double blind in a flexible dose schedule ranging from 2.5-10 mg./day (1 cap = 2.5 mg of FPZ).

Results. Fifteen subjects received FPZ, 17 PBO. There were no differences between the groups in age, gender, or race. The PBO group was less ill on the BPRS psychosis factor ($p<.03$) at baseline. No other measures differed.

The mean dose/day ± SD was 1.5 ± caps (3.75 mg) for the FPZ group and 1.4 ± 0.46 for the PBO group ($p=0.33$).

After ten days, there were no differences between groups with one exception—the FPZ group showed more improvement in BPRS Hostility ($p=02$). For all subjects, higher baseline depression predicted greater improvement.

Conclusion. This study supports the hypothesis that increasing the dose of neuroleptic does not improve short term outcome for schizophrenic patients who relapse despite having been compliant with treatment.

NR7 Monday May 4, 9:00 a.m.-10:30 a.m.

Delayed Effects of CRH and ACTH on Dopamine in Man

Joel A. Posener, M.D., Psychiatry, Mass Mental Health, 74 Fenwood Road, Boston, MA 02115; Joseph J. Schildkraut, M.D., Gordon H. Williams, M.D., Melinda S. Salomon, Ph.D., Nancy L. McHale, B.S., Alan F. Schatzberg, M.D.

Summary:

The hypothalmic-pituitary-adrenal (HPA) axis may be an important regulator of dopamine systems. This presentation reports new results from our ongoing studies of HPA axis—dopamine interactions in healthy humans. Synthetic adrenocorticotropic hormone (ACTH), co-syntropin 0.25 mg IV, was administered to 12 subjects at 8:35 a.m. Contrary to expectations, plasma levels of homovanillic acid (pHVA), the main dopamine metabolite, did not increase over the following 3.5 hours. However, we also measured baseline pHVA in the morning (8-9:30 a.m.) and afternoon (3-6:30 p.m.) before co-syntropin and at the same times for each of the two days after co-syntropin in a subgroup of six subjects, and we observed a small, statistically significant rise in pHVA 31 and 55 hours after co-syntropin ($p.<.05$). One week later, ovine corticotropin-releasing hormone (oCRH) 1 μ g/kg was administered to 10 subjects at 7 p.m. While pHVA did not change during the first four hours after oCRH, significant changes were observed the next day. In a subgroup of five subjects, mean ± SD baseline pHVA was 11.8 ± 3.9 ng/ml in the morning and 10.3 ± 3.1 ng/ml in the afternoon on a day prior to oCRH, and 15.4 ± 3.2 ng/ml in the morning and 23.1 ± 7.2 ng/ml in the afternoon the day after oCRH. This represented a significant change over time ($p<.02$), with pHVA in the afternoon following oCRH (i.e., 20 hours later) significantly greater than at baseline ($p.<.05$). Implications of these findings for the pathophysiology of psychosis in schizophrenic and affective disorders are discussed.

NR8 Monday May 4, 9:00 a.m.-10:30 a.m.

Comorbidity in First-Episode Psychosis

Stephen M. Strakowski, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Mauricio Tohen, M.D., Andrew L. Stoll, M.D., Gianni L. Faedda, M.D., Pierre V. Mayer, M.D., Meridith L. Kolbrener, B.A., Daniel C. Goodwin

Summary:

The authors studied medical and psychiatric comorbidity in a cohort ($n=102$) of patients hospitalized with a first episode of psychosis. Patients were diagnosed using *DSM-III-R* criteria. Outcome variables at discharge were final symptom rating scale scores, length of hospitalization, and recovery using operationalized criteria. Comorbid diagnoses were present in 52.2 percent ($n=53$) of these patients including 40.2 percent ($n=41$) with psychiatric comorbidity, and 17.6 percent ($n=18$) with medical illnesses. Twenty (37.7) percent of patients had multiple comorbid diagnoses. The most common comorbid diagnosis was that of substance abuse (22.5 percent of total). Patients with affective psychoses were significantly more likely than those with nonaffective psychoses to have a comorbid substance abuse diagnosis. Patients diagnosed with delusional disorder were significantly less likely to have a comorbid diagnosis than other subjects with nonaffective psychosis. Patients with psychiatric comorbidity demonstrated poorer initial outcome, while those with medical comorbidity were less symptomatic at discharge. Comorbidity is common and may be a useful predictor of outcome in first-episode psychosis.

NR9 Monday May 4, 9:00 a.m.-10:30 a.m.

Neuroimaging in Relatives of Schizophrenics

Jeremy M. Silverman, Ph.D., Psychiatry 116A, Bronx VA Med. Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Richard S.E. Keefe, Ph.D., Miklos F. Losonczy, M.D., Richard C. Mohs, Ph.D., Larry J. Siever, M.D., Kenneth L. Davis, M.D.

Summary:

The evidence for a genetic relationship between schizotypal personality disorder (SPD) characteristics, especially deficit symptoms such as social isolation, and schizophrenia suggests that SPD features may help to characterize a schizophrenia-related phenotype. In addition, the neuro-anatomical factors associated with schizophrenia, e.g., frontal cortical dysfunction, may also characterize some of the relatives of schizophrenic probands, especially those with prominent SPD characteristics. This possibility was investigated with 86 nonpsychotic 1° relatives of 23 schizophrenic probands who have to date been assessed for SPD symptoms and all other *DSM-III* axis II characteristics. The diagnostic assessment on each relative was conducted using both face-to-face and informant structured personality disorder interviews. In addition, frontal horn size and other ventricular measures, assessed by CT scan, as well as neuropsychological measures sensitive to frontal dysfunction, such as the Wisconsin Card Sort Test (WCST) and the Trailmaking Test Part-B (TMT-B), have been obtained on most of these subjects (n = 55). Significant correlations have been observed between frontal size and perseverative errors on the WCST ($r = .46$, $p < .001$) and TMT-B scores ($r = .38$, $P = .01$). In addition, frontal horn size in relatives who met criteria for SPD (mean = 2.52; m = 8) was significantly larger ($t = 2.09$, d.f. = 37, $p < .05$) than that observed in relatives with ≤1 SPD symptom (mean = 1.80; n = 31). Finally, modest but significant relationships were observed between social isolation and frontal horn size ($r = .22$, $p = .05$). The results suggest that SPD characteristics, perhaps especially deficit symptoms, in relatives of schizophrenic probands may be associated with structural brain abnormalities similar to those found in schizophrenia. Furthermore, these structural abnormalities, especially when present in conjunction with SPD deficit features, may aid in the more accurate identification of a schizophrenia-related phenotype.

NR10 Monday May 4, 9:00 a.m.-10:30 a.m.

In Vivo Proton Magnetic Resonance Spectroscopy in Never Treated Schizophrenics

Jeff A. Stanley, M.Sc., Magnetic Res., St. Joseph's Hospital, 268 Grosvenor Street, London ON N6A 4L6, Canada; Peter C. Williamson, M.D., Dick J. Drost, Ph.D., Tom Carr, M.D., Jane Rylett, Ph.D., Harold Merskey, D.M.

Summary:

Cerebral metabolic compositions of amino acids, peptides, and in particular the excitatory amino acid neurotransmitter, glutamate, are accessible in defined regions with *in vivo* proton (^1H) Magnetic Resonance Spectroscopy (MRS). In this study, *in vivo* ^1H MR spectra from the left dorsal prefrontal cortex of never treated schizophrenic patients (N = 6, mean age of 20 ± 3 years) were analyzed and compared to a control group (N = 12, mean age of 34 ± 8 years). The stimulated echo sequence, STEAM, with an echo time of 20 ms and a volume-of-interest (VOI) 2x2x2 cm^3, was the localization technique used, on a 1.5 tesla Siemens MR imager. The positioning of the VOI was confirmed by coronal and sagittal MR images. All metabolite levels are expressed as a mole % (± SD) of the total observed ^1H MR signal between resonances 2.01ppm, the CH_3, resonsance of the N-acetyl-aspartate (NAA) and 3.41 ppm.

A significant decrease in glutamate (β-CH_2) mole % was observed in the never treated schizophrenics compared to the controls, (5.2 ± 2.9% vs. 15.8 ± 2.3%, $p. < 0.001$). The mole % of NAA-glutamate (-CH_3) and glutamine (β-CH_2) both significantly increased from a negligible, unmeasurable value in the control group to 4.6 ± 2.0 mole % and 8.7 ± 2.1 mole %, respectively, in the schizophrenic group ($p < 0.001$). However, no significant difference in mole % was observed for the metabolites NAA, γ-aminobutyric acid, creatine, phosphocreatine, taurine, and choline-containing compounds.

To our knowledge this is the first time that direct, non-invasive, *in vivo* results on never treated schizophrenics have shown a glutametergic function abnormality in the prefrontal cortex. In addition, there was no evidence of neuronal cell loss. No significant difference in the metabolite levels was observed due to the age differences within the control group or the schizophrenics.

NR11 Monday May 4, 9:00 a.m.-10:30 a.m.

Executive Impairment in Schizophrenia and Old Age

Don R. Royall, M.D., Psychiatry, UTHSC/SA, 8535 Tom Slick Drive, San Antonio, TX 78229; Roderick Mahurin, Ph.D., Janet True, M.D., Brent Anderson, M.S., A. Miller, M.D.

Summary:

Forty chronically ill schizophrenics (RC:S) (mean age = 33.3) from residential care units at the San Antonio State Hospital were compared with 42 elderly residential care residents (RC:E) (mean age = 86.1), 51 intermediate nursing care residents (NH:E) (mean age = 86.3) of a 537 bed comprehensive retirement community, and 21 independent elderly controls (IL:E) (mean age = 77.4) on the Executive Interview (EXIT), a bedside measure of executive impairment, and the Folstein Mini-Mental State Exam (MMSE). Scores were adjusted for age prior to analysis. The EXIT discriminated between elderly residents at each level of care ($p < .001$). Neither instrument could discriminate between schizophrenics and elderly residents at the same level of care. The MMSE also failed to discriminate between independent elderly subjects and those in the residential units. The EXIT correlated highly with the MMSE in the elderly subjects ($r = .80$, $n = 107$), but not among schizophrenics ($r = .48$, $n = 40$).

An analysis of selected EXIT items showed that the frequency of "DESIGN FLUENCY" failures increased with level of care (IL:E = 4.8 percent, RC:E = 71 percent, RC:S = 75 percent, NH:E = 88.2 percent) as did "WORD FLUENCY" failures. No difference was found on these items between schizophrenics and elderly residents receiving the same level of care. Frontal release signs, "GRASP" and "SNOUT", also rose with level of care in the elderly subjects (GRASP: IL:E = 0 percent, RC:E = 19 percent, NH:E = 45.1 / SNOUT: IL:E = 14.3 percent, RC:E = 16.7 percent, NJ:E = 53.4 percent). Schizophrenics, however, had markedly fewer frontal release signs than elderly subjects at the same level (GRASP = 2.5 percent; SNOUT = 8.0 percent).

These results suggest that the degree of executive impairment is comparable across diagnoses in patients at similar levels of care. Some EXIT items, such as "DESIGN FLUENCY," are particularly sensitive to executive dyscontrol at all levels. Frontal release signs vary across diagnosis within level of care, and may reflect disease-specific impairment. The impairments elicited by the EXIT can be divorced from the more general cognitive deficits elicited by the MMSE. The EXIT is more sensitive to mild impairment than the MMSE.

NR12 Monday May 4, 9:00 a.m.-10:30 a.m.

Adjuvant to Neuroleptics in Chronic Schizophrenia

Pierre-Michel N Llorca, Psychiatry, Ste Marguerite, 270 BD Ste Marguerite, Marseille 13274, France; Marc A. Wolf, Thierry C. Bougerol, Christophe Lancon, Jean Claude Scotto

Summary:

Carbamazepine, bromocriptine, and cyproheptadine have been proven efficient in combination to neuroleptics in chronic schizophrenia. In a double-blind, crossover study, we used carbamazepine, bromocriptine, and cyproheptadine as adjuncts to haloperidol in a sample of 24 chronic schizophrenic inpatients. Each patient

was given haloperidol (15 to 60 mg a day) and then carbamazepine (400 mg a day), bromocriptine (2.5 mg a day), cyproheptadine (24 mg a day), and placebo in a randomized order during four weeks for each drug. Every two weeks a psychiatric evaluation using BPRS, SANS, SAPS, and RSEB was done. Abnormal involuntary movements and extrapyramidal symptoms were evaluated using AIMS and SARS.

The data were analyzed using an ANOVA. None of the three drugs has shown any clinical efficacy compared to placebo on BPRS, SANS, SAPS, and RSEB. We showed a negative effect of those drugs compared to placebo for the extrapyramidal symptomatology.

NR13 Monday May 4, 9:00 a.m.-10:30 a.m.

Subgroups of Schizophrenics Responding to Adjuvant Treatment

Pierre-Michel N Llorca, Psychiatry, Ste Marguerite, 270 BD Ste Marguerite, Marseille 13274, France; Thierry C. Bougerol, Marc A. Wolf, Christophe Lancon, Jean Claude Scotto

Summary:

Carbamazepine, bromocriptine, and cyproheptadine have been proven efficient in combination to neuroleptics in chronic schizophrenia. In a double-blind, crossover study, we used carbamazepine, bromocriptine, and cyproheptadine as adjuncts to haloperidol in a sample of 24 chronic schizophrenic inpatients. Each patient was given haloperidol (15 to 60 mg a day) and then carbamazepine (400 mg a day), bromocriptine (2.5 mg a day), cyproheptadine (24 mg a day), and placebo in a randomized order during four weeks for each drug. Every two weeks a psychiatric evaluation using BPRS, SANS, SAPS, and RSEB was done. Abnormal involuntary movements and extrapyramidal symptoms were evaluated using AIMS and SARS.

Using an ANOVA, none of those drugs showed a clinical efficacy compared to placebo. We identified two subgroups of seven patients each who respond to carbamazepine and cyproheptadine respectively. We can't characterize those groups using demographic and clinical criteria.

NR14 Monday May 4, 9:00 a.m.-10:30 a.m.

Interleukin-1 and Interleukin-2 in the CSF of Schizophrenic Subjects

Rifaat S. El-Mallakh, M.D., Neuropsychiatry, NIMH Neuroscience Center, 2700 M.L. King Jr. Ave SE, Washington, DC 20032; Richard Jed Wyatt, M.D.

Summary:

Objective: Since interleukins (IL) are produced in the central nervous system and have cytokine and growth promoting properties, they may play a role in neurodegenerative, neuroplastic, or neuroimmunologic processes that have been implicated in the pathophysiology of schizophrenia. *Methods:* Cerebrospinal fluid (CSF) obtained from schizophrenic patients on and off medication and from normal controls were examined. IL-1α and Il-2 were assayed using an enzyme-linked immunoassay sensitive to 98 pg/ml. *Results:* IL-1α concentrations were below the detection limits of the assay in 46 of 50 control and schizophrenic samples. Concentrations (ng/ml $\pm$ SE) of IL-2 in medicated schizophrenics (0.451 ± 0.048, $n = 17$), unmedicated schizophrenics (0.496 ± 0.059, $n = 18$), and controls (0.416 ± 0.061, $n = 11$) were not significantly different. Similarly, values in 7 patients examined on (0.508 ± 0.096) and off (0.481 ± 0.119) psychotropic medication were not different. Duplicate samples varied by 0.066-0.512 ng/ml. *Conclusions:* We have been unable to replicate a previous report using the same assay of elevated CSF IL-2 in unmedicated schizophrenics. However, since IL levels are very close to the detection limits of current assays, it may be difficult to demonstrate a significant difference.

NR15 Monday May 4, 9:00 a.m.-10:30 a.m.

Medical Education: Computer Assisted Patient Education

T. Bradley Tanner, M.D., WPIC, Univ of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15232; Stuart Gitlow, M.D.

Summary:

The authors have created an interactive computer workshop, *MedEd: Medication Education*, designed to educate schizophrenic patients about their prescribed medications. Patient education is essential for improved health and relapse prevention. Use of MedEd should improve patients' understanding of their medication without increasing the time commitment of health care professionals. Instruction is given through use of an interactive program involving digitized video, animation, voice, and sound. Patients have the opportunity to select sequences about side effects, good effects, and general medication information. Segments may be repeated upon demand, and a summary sheet is printed for the patient when the interaction is complete. Current research is examining whether knowledge acquisition, retention, or both, is improved following computer education. A group of 50 chronic schizophrenic patients treated with haloperidol and not experiencing acute psychotic symptoms will receive either computer-based or standard verbal education regarding their medication. Instructional method efficacy will be evaluated using a comparison of written test performance both before and after education. A second posttest will be administered two weeks after the sequence to measure retention.

NR16 Monday May 4, 9:00 a.m.-10:30 a.m.

The Longitudinal Importance of Expressed Emotion

Suzanne King, Ph.D., Psychosocial, Child Research Center, 6875 Blvd LaSalle, Verdun QC H4H 1R3, Canada

Summary:

Studies have shown that risk of relapse within nine months of hospital dischrage increases significantly when a schizophrenic patient lives in a "High EE" household. While results of such studies imply that expressed emotion causes, rather than is caused by, the patient's psychopathology, the relative predictive importance of EE and patient symptoms have never been compared.

The purpose of the current study was to determine whether the severity of schizophrenic symptoms is more a function of the family's expressed emotion or of the patient's earlier symptom profile. Seventy-four young adult schizophrenic patients and 116 of the relatives with whom they live were recruited. Patients were administered the BPRS twice, nine months apart. Relatives were interviewed with the CFI to determine expressed emotion levels at about the same time as the patient's first interview. Unlike previous EE studies, interviews were only conducted when the patient was not in relapse.

Data for 53 of the subjects have been analyzed to date. The results suggest that earlier symptoms explain 34 percent, 51 percent, and 68 percent of variance in total, positive and negative symptoms at follow-up, respectively; EE scores explain less than 2 percent additional variance (n.s.). Analyses of the complete data set will be presented and implications for the meaning of EE discussed.

NR17 Monday May 4, 9:00 a.m.-10:30 a.m.

Remoxipride in the Treatment of Schizophrenia

Sanford Herman, M.D., Psychiatry, Mt. Sinai Services, 79-01 Broadway, Elmhurst, NY 11373; Mark Weilgus, Ph.D., Carol Hermann, M.D., Andrea Berman, Ph.D., Kathleen O'Connor, B.A., John Herrera, Ph.D.

Summary:

It is reported that the functional ability of chronic schizophrenics can be improved with long-term antipsychotic therapy. However, poor compliance often results from extrapyramidal side effects. EPS is thought to result from nonspecific blockage of dopamine receptors in the brain. Remoxipride, a substituted benzamide, is believed to have selective affinity for the D2 dopamine receptor. This results in preferential antipsychotic effect in the limbic system versus the nigrostriatum which mediates EPs. A Merck-sponsored multicenter triple-blind study was conducted at Mt. Sinai's Elmhurst affiliate to investigate the efficacy of two nonoverlapping dose ranges of Remoxipride in acute schizoprhenics. A total of 16 inpatients were selected, consented, and washed out for one week with placebo. They were then randomly assigned for six weeks to one of three treatment groups—Remoxipride 90 mg/day, Remoxipride 450 mg/day, or Haldol 30 mg/day which served as the control. Clinical change was assessed weekly using the BPRS, CGI, AIMS, NSA, and NOSIE scales. A repeated measures ANOVA was completed with the BPRS total score and the results revealed a significant main effect (p. .05). In order to examine the comparative rates of improvement, coefficients were determined on a weekly basis and t-tests were completed on the above scales. The results of these comparisons will be presented and the impressive extrapyramidal symptom profile of Remoxipride will be discussed.

NR18 Monday May 4, 9:00 a.m.-10:30 a.m.

Biological Analaysis in Schizophrenic Patients

Felicidad Rodriguez, M.D., C. Morfologica, Facultad Medicina, PL Fragela SN, Cadiz 12 11001, Spain; Jesus Ezcurra, M.D.

Summary:

We have analyzed the digital and palmar dermatoglyphics and some biological markers (HLA antigens, MAO and COMP activity) in a sample of 60 patients treated in the Mental Health Center Bahia de Cádiz. This sample was subdivided in two groups. One of them included 28 schizophrenics with a familiar history of the disease. The diagnosis was established by criteria in *DSM-III-R*. One control sample of 50 healthy subjects proceeding of the same geographical zone was also included. None of the biological markers showed significant differences in the three groups. Recently a significant excess of certain HLA antigens has been found among schizophrenics with a family history of the disease. However, in our study the results showed no difference in the incidence of these antigens in the whole sample, and an increase of HLA B27 antigen in the patients with a familiar history of the disease failed to reach statistical significance. In this sense, our study failed to identify an immunological marker for schizophrenia in basis to presence or absence of familiar history. In the dermatoglypic analysis, we observed a significantly higher index of symmetry in the control group in relation with the two groups of patients (the fluctuating asymmetry has been related with a polygenic inheritance). These results may indicate a relation between the fluctuating dermatoglyphic asymmetry and the genetics of liability of schizophrenia, in basis to a polygenic model of the illness, considering that a polygenic of the dermatoglyphic traits has been proposed.

NR19 Monday May 4, 9:00 a.m.-10:30 a.m.

Cingulate Gyrus in Schizophrenia Versus Controls

J. Thomas Noga, M.D., CBDB, NIMH, 2700 M.L. King Jr. Ave SE, Washington, EC 20032; Elizabeth Aylward, Godfrey D. Pearlson, M.D.

Summary:

Comparable sections of anterior (area 24) and posterior (area 23) cingulate were measured on MRI (using a method developed by the authors) in 14 patients with schizophrenia *(DSM-III-R* criteria) and 14 controls matched for age, sex, education, and parental SES. Interrater reliability exceeded .92 on all structures measured. Ratings were made blind to diagnostic status of subjects. Brain volume in the two groups differed by 2 percent. Cingulate gyri measures were smaller in the patients significantly; there was an inverse correlation between left anterior cingulate size and severity of hallucinations ($r = 0.67$, $p < .01$) but this was not significant after Bonferroni correction. Lateral asymmetry was the same in both groups.

The cingulate gyrus is of interest to schizophrenia researchers due to reports of cingulate pathology in schizophrenia; cingulate involvement in social, cognitive, sensory, and emotional functions in man and monkey; and connections with prefrontal, temporal, and parietal cortices, amygdala, nucleus accumbens, basal ganglia, and thalamus.

We demonstrate a reliable method, unreported thus far in the literature, to measure cingulate gyrus on MRI; the results suggest that cingulate gyri may be reduced in size in schizophrenia and this may be associated with severity of hallucinations.

NR20 Monday May 4, 9:00 a.m.-10:30 a.m.

Prolactin Decrease and Response to Haloperidol

Howard H. J. Chang, M.D., Harvard Med Sch/Psych., Mass Men Hlth Ctr, 74 Fenwood Road, Boston, MA 02115; Alan I. Green, M.D., Roger A. Boshes, M.D., Mohammad Y. Alam, M.D., Joseph J. Schidkraut, M.D.

Summary:

Serum prolactin (PRL) levels were evaluated during a six-week fixed dose (10 mg/day) haloperidol (HAL) study in seven schizophrenic patients, who were treated following a five to seven day drug washout period. Weekly assessments included ratings with the Brief Psychiatric Rating Scale (BPRS) and measurements of PRL levels. Clinical response (measured by percent change in BPRS from baseline to the average value of week 5/6) ranged from 32 percent to 88 percent. During constant dosing with HAL, the PRL initially increased in all patients before decreasing from the highest point during the latter weeks of the study in most patients. The percent PRL decrease (from the highest value to week 5/6) showed a meaningful inverse correlation with clinical response on the BPRS (Spearman $r = -.61$), especially for positive symptoms ($r = -.71$; $p = .07$). When week 5 was taken as the end point of the study (to eliminate an outlying value at week 6), there was an even stronger inverse correlation between PRL decrease and clinical improvement ($r = -.93$; $p < .003$). While further studies are needed to confirm these preliminary data, the findings suggest that a decrease in PRL level following an initial PRL rise during fixed-dose HAL treatment may be linked to a less favorable clinical response. The potential clinical and theoretical implications of these findings will be discussed.

NR21 Monday May 4, 9:00 a.m.-10:30 a.m.

Clozapine Versus Haldol In Schizophrenia: A PET Study

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M.D., Llewellyn B. Bigelow, M.D., Jill L. Ostrem, B.A., James Gold, Ph.D., Daniel R. Weinberger, M.D.

Summary:

Novel antipsychotic drugs such as clozapine (CLZ) differ from haloperidol (HAL) and other traditional antipsychotics in that they show efficacy in some treatment-resistant patients and have fewer extrapyramidal side-effects. Though it has been hypothesized that these drugs may have differing effects in certain cortical regions, the neurophysiological underpinning for their properties remains elusive. To investigate this further the present study compares the effects of HAL and CLZ in patients with schizophrenia using the $H_2{}^{15}O$ method for measuring regional cerebral blood flow (rCBF) with positron emission tomography (PET).

Schizophrenic subjects are studied while on HAL (0.4 mg/kg/day) and again while on CLZ (clinically optimum dose). rCBF measurements are made while the subjects perform 2 tasks: 1) a novel Delayed Alteration (DA) human analog of the classic monkey paradigm for testing dorsolateral prefrontal cortical (DLPFC) function; and 2) a sensorimotor control task. Data are collected on a 15-slice scanner with axial and in-plane resolution of 6.5mm after reconstruction. rCBF data are normalized to the whole brain mean on a pixel-by-pixel basis. Coplanar MRI's are acquired to define regions of interest.

Analysis of the data from the first three subjects shows that during DA for each patient rCBF tended to be lower on CLZ than HAL in basal ganglia (right:$t>5.1$, $p<.05$, left:$t>2.95$, $p<.10$). In contrast, rCBF was higher in left DLPFC ($t=11.8$, $p.<.01$). These effects were less consistent during the control task. These data suggest that CLZ and HAL may have differing physiologic effects in subcortical vs. cortical (specifically frontal) regions during cognitive stimulation.

NR22 Monday May 4, 9:00 a.m.-10:30 a.m.

Planum Temporal in Schizophrenia: A Magnetic Resonance Study

Alessandro Rossi, Psychiatry, University of L'Aquila, Ospedales, .M. Collemaggio, L'Aquila 67100, Italy; Antonio Serio, M.D., Paolo Stratta, M.D., Concetta Petruzzi, M.D., Giovanni Schiazza, M.D., Massimo Casacchia, M.D.

Summary:

Recently, it has been hypothesized that schizophrenia could result from an anomaly of development of cerebral asymmetry. Among the several cerebral areas studied, Planum Temporale (PT), known to be larger on the left side, has received surprisingly little attention. We report here findings of an MR study of PT in schizophrenia, using a new imaging protocol. MR imaging was performed with a 0.5 T Toshiba. 11T1-weighted sagittal SE 400-20 images were obtained after an axial slice of reference was established. A T1 weighted fast gradient echo sequence (3D fast field echo), parallel to the posterior horizontal ramus of sylvian fissure, was applied. This resulted in 29 contiguous axial slices of 2 mm thickness, to provide sufficient three-dimensional resolution for computer reformations in arbitrary planes. By using sagittal and coronal reformations to identify anatomical landmarks, a reformatted axial image of PT was obtained for each subject and for each side (left vs. right). The current sample consisted of 12 young schizophrenics (six male and six female). A two-way mixed ANOVA showed a significant sex effect with larger PT in males ($p<.01$), a significant side effect with the left side larger than the right (mean PT areas $\pm$ SD410.75 $\pm$ 165.39 vs. 332.91 $\pm$ 75.76mm2; $p<.015$) and a sex by side interaction ($p<.005$). Results from an expanded sample will be discussed in the context of the "lateralization hypothesis" and possible sex differences in schizophrenia.

NR23 Monday May 4, 9:00 a.m.-10:30 a.m.

Integrating Psychosocial Treatment On An Inpatient Schizophrenia Research Unit: A Model For Multidisciplinary Psychoeducation

Ellen Lukens, C.S.W., Clinical Psychbio, NY State Psych Inst., 722 West 168th Box 117, New York, NY 10032; Kay D. Gimmestad, B.S., Helle Thorning, M.S.W., Ann Feinstein, OTR, Helen Deustch, R.N., Barbara Angell, R.N.

Summary:

Psychosocial factors clearly play a significant role in the course and outcome of schizophrenia. However, the effectiveness of short-term interventions during inpatient hospitalization aimed at mollifying those factors have not been fully determined. The multidisciplinary study is designed 1) to compare two short-term models of psychoeducational multiple family group treatment (one with patients and one without) in terms of increased knowledge and changes in attitude and associated stigma regarding mental illness; 2) to evaluate the efficacy of recreation therapy as an intervention to improve leisure functioning among patients and family members; and 3) to test the effectiveness of social skills training with patients during the inpatient stay. Pilot data were collected for 12 families and patients on admission and discharge, approximately four months later.

Findings suggest that the knowledge base among family members increased substantially over time but did not differ between groups. Changes in attitude and stigma did not decrease significantly in either group. Preliminary data indicate an improvement from admission to discharge in the following barriers to leisure: social skills, opportunity and money.

Overall, we conclude that an inpatient unit is a critical time to effect change in the lives of both patients and their families.

NR24 Monday May 4, 9:00 a.m.-10:30 a.m.

Information Processing Deficits In Psychoses

Esther F. Rabinowicz, Ph.D., Psychiatry, Albert Einstein, Pelham Pkwy S-Eastchester Rd, Bronx, NY 10461; Lewis A. Opler, M.D., David R. Owen, Ph.D., Raymond A. Knight, Ph.D.

Summary:

Cognitive dysfunctions are fundamental to schizophrenia. Normals use a two-stage approach (global, perceptual followed by analytic, attentional processing); input dysfunctions in schizophrenics (Scs) may arise from either of these processes.

We tested these hypotheses in 24 Scs, 17 affective psychotics, and 38 controls via the *same* stimuli in number and form identification tasks, requiring analytic and holistic processing of dot patterns. Three cued delays measure temporal processing. Essential results confirm dual processing predictions for controls, and highlight specific deficits in both perceptual and attentional processes in Scs. For *number* processing, increased delay improves controls' accuracy and decreases Scs' accuracy ($p<.03$). More dots affect controls' accuracy adversely ($p<.03$), but not Scs ($p>.83$). Though Scs are twice as impaired, and bipolars four-fold worse ($p<.0001$) on form than on number; all patients improve ($p<.02$) on *form* judgments. State-trait differences may account for differential performance deficits in Scs vs affectives.

These data suggest Scs' perceptual organization deficits are not due to iconic dysfunctions, but are mediated in a feedback loop via primary Stage 2 cognitive deficits. We propose perceptual organization deficits occur as a *consequence* of Stage 2 deficits in allocation and consolidation. This impacts negatively on automatization and subsequent encoding of perceptual gestalt templates.

NR25 Monday May 4, 9:00 a.m.-10:30 a.m.

Factor Structure Of The Neurological Evaluation Scale in Schizophrenia

Laurence P. Karper, M.D., Psychiatry, West Haven VAMC, 950 Campbell Avenue 116A, West Haven, CT 06516; Morris Bell, Ph.D., Paul Lysaker, Ph.D., Joseph Goulet, M.S., Joseph P. Erdos, M.D., Louise Brenner, M.S.N., John H. Krystal, M.D.

Summary:

Buchanan and Heinrichs introduced a standardized examination for evaluating neurological "soft signs," the Neurologic Evaluation Scale (NES). The NES reliably distinguishes patients from healthy subjects. NES items were clustered into three subscales and "other items" on an a priori basis. These clusters appear to be clinically relevant and differentially related to clinical features of schizophrenic patients. The purpose of this study is to present preliminary findings of NES factors derived from an analysis of data from schizophrenic patients. *Methods:* In an ongoing study, the NES was administered to 28 stable patients meeting *DSM-III-R* (SCID) criteria for schizophrenia or schizoaffective disorder who were participating in a vocational rehabilitation research program. The version of the NES utilized in this study was modified from the initial version in order to standardize item presentation and scoring. A factor analysis with Equamax rotation was performed. *Results:* Preliminary analysis suggest the existence of four factors. Factor 1, "Sensory-Motor Disinhibition," includes: Adventitious Overflow, Synkinesis, Extinction, Romberg Test, Right-Left Confusion, Tremor, Glabellar Reflex, and Mirror Movements. Factor 2, "Sequencing and Memory," includes: Memory, Motor Sequencing Tests, Convergence, and Grasp Reflex. Factor 3, "Cross-modal Sensory Function," includes: Suck Relfex, Gaze Impersistence, A/V Integration, Rhythm Tapping A, and Graphesthesia. Factor 4, "Dexterity" includes: Stereognosis, Tandem Walk, Rhythm Tapping B, Finger-Thumb Opposition, and Rapid Altering Movements. *Implications:* These findings generally parallel the factor structure initially introduced by Buchanan and Heinrichs, with important modifications. The neurologic deficits exhibited by some schizophrenic patients may arise from discrete alterations in brain structure or function that may have important clinical or pathophysiologic significance.

NR26 Monday May 4, 9:00 a.m.-10:30 a.m.

Clozapine and Slow Wave Sleep in Schizophrenia

Jon F. Chaffee, M.D., Psychiatry, Univ of Calif. Irvine, 101 City Drive South Rt. 88, Orange, CA 92668; Steven G. Potkin, M.D., Joseph Wu, M.D.

Summary:

Various abnormalities have been described in the sleep of persons with schizophrenia, including impaired and reduced total sleep, decreased slow wave sleep, alterations in REM latency and quantity, and decreased REM rebound following REM deprivation. Recently, attention has been focused on the slow wave sleep abnormalities observed in 60 percent of schizophrenics. Patients with these slow wave sleep abnormalities may represent a distinctive subgroup of schizophrenia. The effects of the atypical antipsychotic agent clozapine on sleep in schizophrenics have not been evaluated. Clozapine is a potent serotonin antagonist. The serotonin system has been implicated in the regulation of slow wave sleep. To evaluate the effect of clozapine, we recorded sleep polygraphs on a cohort of schizophrenic patients treated with clozapine, haloperidol, and drug free. Clozapine appears to decrease the amount of slow wave sleep. The sleep parameters before and after clozapine are related to clinical symptoms and response.

NR27 Monday May 4, 9:00 a.m.-10:30 a.m.

Heterogeneity in Serotonin Response in Chronic Schizophrenia

Aditayanjee, M.D., Psychiatry, Albert Einstein Med., 1500 Waters Place, Bronx, NY 10461; Jean-Pierre Lindenmayer, M.D., Sandra Grochowski, B.A., N. Bark, M.D., N. Moynihan, B.S.N.

Summary:

This is an ongoing study on serotonergic response in chronic schizophrenia utilizing a neuroendocrine challenge paradigm with oral m-chlorophenlpiperazine (m-CPP). We are utilizing this 5HT receptor agonist based on the hypothesis that some patients may show hypersensitivity. Ten chronic schizophrenic patients *(DSM III-R)* have so far completed the challenge with oral m-CPP (0.25 mg/kg). After signing informed consent the patients undergo two weeks' drug withdrawal. Behavioral response was assessed on positive and negative symptoms (PANSS), affect (MARS) and AIMS. There was a trend toward worsening in total psychopathology ($p \leq .10$) with significant increases ($p \leq .05$) in hostility, paranoid-belligerence, mannerisms, and depression. The patients showed an increase in uncooperativeness, motor retardation, and anergia ($p \leq .10$). Hormonal data available for only eight patients so far suggests a dichotomy in response. Responders showed a significant increase in cortisol level while they exhibited decreased hallucination, increased negative symptoms and poor rapport. Implications of this herterogeneity in serotonergic response in chronic schizophrenia will be discussed.

NR28 Monday May 4, 9:00 a.m.-10:30 a.m.

Comparison of Paranoid and Schizoid Personalities

Mark Fulton, M.D., Psychiatry, Dallas VAMC, 4500 Lancaster, Dallas, TX 75216; George Winokur, M.D.

Summary:

We investigated the records of 50 probands admitted to the University of Iowa Psychiatric Hospital during the period 1953 to 1986 who met criteria for *DSM-III-R* schizoid and paranoid personality disorders. We found that schizoid personality probands as opposed to paranoid personality probands were significantly younger on index admission (age 22 vs. 41), more likely to have subsequent admissions (7/20 vs none of the paranoids), and more likely to worsen on follow-up. Schizoid traits and schizophrenia occur more commonly in the families of schizoid probands (7/31 of the schizoids had a first degree relative described as schizoid vs. none of the paranoids), while paranoid personality traits occur more commonly in the families of paranoid personality probands (3/17 vs 2/31).

We also found little overlap between these diagnoses and other Axis I or II diagnoses. In a comparison of *DSM-III* and *DSM-III-R* diagnostic systems, concordance of diagnosis was low (kappa for schizoid personality = .016, kappa for paranoid personality = .062), an indication that the monothetic structure of *DSM-III-R* is an improvement over *DSM-III.*

NR29 Monday May 4, 9:00 a.m.-10:30 a.m.

Abnormal Laterality in Parents and Schizophrenics

Ellen M. Smith, M.D., Psychiatry, Yale University, RM 203 34 Park Street CMHC, New Haven, CT 06519; Nancy Docherty, Ph.D., Bruce Wexler, M.D.

Summary:

Previous studies have found that schizophrenics do not show the normal right ear-left hemisphere perceptual advantages on dichotic tests of lateralized cerebral function. We now report preliminary evidence of a similar abnormality in nonschizophrenic parents of

schizophrenic patients. Perceptual asymmetry was first measured with the same fused, single response dichotic word test that had yielded differences between schizophrenics and controls in previous studies. The parents (n = 16) demonstrated a significantly lower right ear advantage (REA) than controls matched to the parents by age and education (n= 10, p= .04), but performed similarly to their schizophrenic children (n=9). The same subjects were then given two additional tests. Neutral words were paired with words of a positive emotional valence in one test, and with words of a negative emotional valence in the other. On these two tests, the parents exhibited a pattern of results more similar to the controls than to their schizophrenic children (p=.017). This difference arose because the schizophrenics demonstrated a significantly lower REA than their parents (p= .013) on the negative/neutral word test. These results suggest that although schizophrenics and their parents appear to have relatively similar abnormalities in cerebral hemispheric activation states in baseline conditions, when listening to words with negative emotional valence, the schizophrenic children but not their parents demonstrate a further decrease in left hemispheric activation.

NR30 Monday May 4, 9:00 a.m.-10:30 a.m.

PET in Frontal Head Injury and Striatal Metabolism

Stephen Lottenberg, M.D., Psychiatry, Univ Calif. Irvine, Brain Imaging Ctr Whitby RM164, Irvine, CA 92717; Nicole Theuvenet, Michelle Solano, Ronald M. Ruff, Ph.D., Jill Stanley, Monte S. Buchsbaum, M.D.

Summary:

Pycock suggested that an apparent supersensitive subcortical DA system may develop after lesions of the prefrontal cortex and that this may have implications for the development of schizophrenia. We have observed patients with schizophrenia to have low metabolic rates in the basal ganglia which are increased by neuroleptic administration, suggesting that frontal lobe lesions in normal individuals could be associated with similar decreases.

Twenty-four adult patients with closed head injury (16 unconscious at least two minutes), all psychiatrically normal before the automobile accident (18 male, 6 female, mean age 40.5) received PET scans with FDG and the Continuous Performance Test at least two months after the accident.

Patients were compared to 31 normal controls performing the same task. Patients with relative metabolism more than two standard deviations below the normal mean in the frontal lobe (n=16) and in the parietal, occipital and temporal lobe (n=8) were compared for basal ganglia metabolism. Twelve of 14 patients with frontal lobe injury defined by PET had significant decreases in the basal ganglia as well; only four of 10 patients with non-frontal injury had similar decreases (p=0.028, Fisher exact test). This is consistent with an association of frontal lobe injury and dysfunction.

NR31 Monday May 4, 9:00 a.m.-10:30 a.m.

Dopamine Effects on Hippocampal N-Methyl-D-Aspartate Responses

Stephen J. Schertzer, M.D., Psychiatry, Toronto Western Hospital, 399 Bathurst St. ECW-3D, Toronto Ontario M5T-2S8, Canada; Liang Zhang, M.D., Peter L. Carlen, M.D.

Summary:

There is abundance of evidence that dopaminergic hyperactivity underlies the pathophysiology of schizophrenia. The basic cellular mechanisms through which dopamine (DA) works as a neurotransmitter are poorly delineated. Excitatory amino acid neurotransmitters in general, and N-Methyl-D-Aspartate (NMDA) in particular, are critical in mediating learning and plasticity at the neuronal level. Furthermore, NMDA has recently been postulated to play a role in schizophrenia. This study used whole cell patch-clamp recordings of individual pyramidal cells in the CA1 region of the hippocampus *in-vitro* to assess the modulation by DA of NMDA synaptic transmission. Data revealed that D1 against SKF38393 in concentrations of 10uM reduced NMDA currents by greater than 50 percent. It also appeared that this inhibition was mediated by a post-synaptic mechanism through a second messenger system. This is the first report of NMDA modulation by DA and has important implications for the understanding of neural transmission, long-term potentiation and schizophrenia.

(Supported by The Canadian Psychiatric Research Foundation and the Medical Research Council of Canada.)

NR32 Monday May 4, 9:00 a.m.-10:30 a.m.

Hypoxia Improves Human Cognitive Function

Thomas E. Schlaepfer, M.D., Poliklinik, Psychiatrische Univ., Murtenstr. 21, Bern 3010, Switzerland

Summary:

Prolonged (> 10 h) exposure to hypoxia and high altitude (> 5000m) invariably has detrimental neuropsychological effects. Paradoxically, mild improvements of cognitive functions in patients with chronic obstructive pulmonary disease (COPD) after cessation of oxygen therapy have been reported.

We studied in each of ten healthy subjects the effect of an acute altitude challenge (rapid helicopter transport to the Jungfraujoch (altitude 3450m) and of an acute exposure to mild hypoxia (Fractional inspiratory oxygen concentration (FIO_2) 14.5 percent) on a simple test of cognitive performance: Under both hypoxic conditions the time needed to read briefly presented letters decreased.

Mild hypoxia induced by helicopter transport to the Jungfraujoch or by breathing a gas mixture with decreased oxygen concentration under controlled conditions increased cognitive performance, expressed as a reduction of the time needed to read briefly displayed letters from 12.1 ± SD 3.8 ms to 8.3 ± 1.5 ms in the first and from 11.9 ± 1.9 ms to 8.1 ± 1.1 ms in the second condition. A rapid hypoxic challenge paradoxically seems to improve a simple measure of cognitive performance above normal values.

The common notion that exposure to hypoxia and altitude invariably deteriorate cognitive performance may have to be reevaluated.

NR33 Monday May 4, 9:00 a.m.-10:30 a.m.

Effects of Adinazolam and N-Desmethyl Adinazolam

Karon Dawkins, M.D., Sec. Clin. Pharm., Natl. Inst. Mental Health, 9000 Rockville Pike, Bethesda, MD 20892; Robert P. Irwin, M.D., Richard L. Hauger, M.D., Joseph C. Fleishaker, Ph.D., William Z. Potter, M.D.

Summary:

Alprazolam can be used as a probe of three different biological systems thought to be dysregulated in affective illness: (ACTH/cortisol, growth hormone [GH], and norepinephrine [NE]). Adinazolam (AD) is a new triazolobenzodiazepine with similar *in vitro* characteristics to alprazolam. Both bind GABA receptors, are anxiolytic, and have been investigated clinically as antidepressants. We investigated whether AD or its active major metabolite, n-desmethyl adinazolam (NDMAD), would show differential pharmacodynamic properties. Eight healthy young male volunteers received three intravenous infusions: of placebo, 20 mg AD, and 40 mg NDMAD in a blinded random order. Each infusion was over 30 minutes and separated by at least five days. Whereas both parent drug and metabolite comparably reduced ACTH, cortisol, and plasma norepinephrine, only the metabolite produced marked sedation and stimulation of growth hormone. The dissociation between the GH and sedative from the ACTH and NE responses with

regard to AD vs NDMAD has implications for functional benzodiazepine receptor subtypes in humans which may relate to differential behavioral and clinical effects.

NR34 Monday May 4, 9:00 a.m.-10:30 a.m.

Ictal EGG Effects of ECT Stimulus Intensity

Andrew D. Krystal, M.D., Duke Univ Medical Center, Box 3309, Durham, NC 27710; Richard D. Weiner, M.D., Pamela K. Smith, Rebekka Arias, C. Edward Coffey, M.D.

Summary:

Recent data comparing right unilateral (UL) ECT administered at just above seizure threshold to higher dose UL treatments and bilateral (BL) treatments were suggestive of diminished efficacy in the low dose UL group, disproving the notion that seizure adequacy depends only on seizure duration. In light of these findings and studies reporting greater ictal EEG amplitude, regularity, symmetry and post-ictal suppression in BL then UL ECT, we performed this pilot manual analysis of the ictal EEG in depressed patients receiving UL ECT delivered at the estimated seizure threshold (T) (n = 6) vs. 2.5 times estimated threshold (2.5T) (n = 10).

Similar to that reported for BL compared to UL ECT, 2.5T subjects had seizures that were of higher ictal amplitude (mean = 361mcv vs. 297mcv), more regular in morphology (4.5 vs. 3.1 (6 point scale)), and had greater immediate post-ictal suppression (33mcv vs. 53mcv) then the T subjects. A strong inverse relationship between these EEG parameters and subject age was also found. This work supports the further study of ictal EEG parameters as markers of right UL stimulus intensity and thus, ECT seizure adequacy.

NR35 Monday May 4, 9:00 a.m.-10:30 a.m.

Schizotypy and Right Hemisphere Function in Mescaline-Induced Psychosis

Godehard Oepen, M.D., Affective Disorders, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Matthias Funfgeld, Anne Harrington, Ph.D., Gordon Claridge, Ph.D., Hanno Botsch, M.D.

Summary:

Using mescaline-induced psychosis (.5 g. mescaline-sulfate) as a model for paranoid-hallucinatory psychosis, 12 male healthy volunteers tested the hypothesis that dysfunctional right hemisphere (RH) processes play an essential role in schizophreniform psychosis. Neurometabolic activity was assessed using SPECT without mescaline and at peak of psychosis. Schizotypy was rated using a Schizotypal Questionnaire. RH neuropsychological performance in a visual half field task was studied using tachistoscopically presented face stimuli. RH capacity to identify faces was continuously reduced under mescaline, possibly because of competition between the RH demands of the tests and the RH demands on the subject imposed by drug-induced visual hallucinations. The 99m-Tc-HMPAO SPECT undertaken at the peak of psychosis revealed a marked right-sided, presumably striato-limbic increase in the marker substance uptake under mescaline in comparison with that found under control conditions. Coronal and transversal scans showed high schizotypy to be significantly correlated with a higher RH tracer uptake than low schizotypy. High schizotypy was significantly correlated with a lower tracer uptake without mescaline ($p<.011$) than low schizotypy. Correlations to psychopathy did not reach significance level. We discuss results using a dimensional model of schizotypy and schizophrenia.

NR36 Monday May 4, 9:00 a.m.-10:30 a.m.

Fine Motor Performance in Schizophrenia

Jay M. Griffith, M.D., Psychiatry, Univ of CO. Hlth Sci Ctr, Box C268-71 4200 E. Ninth Ave, Denver, CO 80262; Lawrence E. Adler, M.D., Robert Freedman, M.D.

Summary:

Fine motor performance, muscle recruitment patterns, and smooth pursuit eye movements (SPEM), were compared in schizophrenics (n = 9) and controls (n = 9). Fine motor performance was assessed through the use of a finger movement task in which the subject had to follow a visual target with sinusoidal vertical movement. The task is similar to the SPEM task used by Holtzman and others, substituting finger movement for eye movement. The result was expressed as a signal to noise ratio after Fast Fourier Transform analysis. Muscle recruitment patterns were determined by observing electromyographic recordings of individual motor units during the finger movement performance. They were quantitated by interspike interval histogram. Schizophrenics demonstrated significantly poorer finger movement performance than controls with a log log signal to noise ratio of $1.67 +/- .82$ versus $2.60 +/- .38$ ($p<.001$). There was no difference, however, in motor unit recruitment patterns between the two groups. The schizophrenics' performance were related to their score on the Smith extrapyramidal symptom scale with a Pearson correlation of -0.740.

These findings suggest that schizophrenics have deficits in fine motor control which are not based on motor unit recruitment abnormalities.

NR37 Monday May 4, 9:00 a.m.-10:30 a.m.

Pharmacodynamic Response to Intravenous Idazoxan

Robert C. Risinger, M.D., Sec. Clin. Pharm., NIMH Bldg 10 RM 2D46, 9000 Rockville Pike, Bethesda, MD 20892; Mark E. Schmidt, M.D., Ivan N. Mefford, Ph.D., William Z. Potter, M.D.

Summary:

Idazoxan (IDX) is a new selective alpha-2 antagonist of the imidazoline family. We have recently found that chronic oral administration of IDX is associated with a decrease in 24 hr urinary MHPG, CSF MHPG, and an increase in basal and post-orthostatic challenge plasma norepinephrine (NE) in depressed patients. In parallel we have modified an IV infusion method to examine the acute pharmacodynamic properties of IDX by sampling more frequently and adding an orthostatic challenge 2 hr post-infusion in order to assess the functional state of α_2 receptors prior to treatment. Subjects and Methods: Six healthy volunteers received three blinded infusions separated by at least one week in random order: 100 μg/kg IDX, 200 μg/kg, or placebo. The compound was infused at a constant rate over 30 minutes with blood samples drawn prior to infusion, then at 10, 20, 30, 40, 50, 60, 90, 150 and, for the orthostatic challenge, at 210 and 215 minutes after beginning the infusion. Blood pressure and heart rate were measured at each sampling point. Results: The NE response begins 10 minutes after the onset of infusion and reaches a peak of 100 percent over baseline 30 to 40 minutes after the onset of infusion. Orthostatic challenge results in a five-to-six-fold evaluation of NE after 200 μg/kg IDX compared to a three-fold rise with placebo. Despite these results, the cardiovascular effects are minimal. We therefore propose this protocol as a safe, effective means of testing the acute consequences of α_2 blockade.

NR38 Monday May 4, 9:00 a.m.-10:30 a.m.

Relationship of Low Baseline TSH to TRH Response

Deborah Deas-Nesmith, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; William Carson, M.D., Shannon Little, M.D., Raymond Anton, M.D.

Summary:

As many as 50 studies have found that the response of TSH to TRH stimulation is diminished in depressed, schizophreniform, and other psychiatric patients. The relationship of low baseline TSH to the response caused by TRH needs further clarification. The TRH stimulation test was administered to 11 consecutive admissions with low baseline TSH (0.3 + 0.11 U/ml). These patients were compared to ten consecutive admissions with normal baseline TSH (1.6 ± .39uU/ml) who also received a TRH test. 9/11 (82 percent) patients with low baseline TSH had a blunted TSH response (<5mU/ml). In contrast, 2/10 (20 percent) patients with normal baseline TSH had a blunted TSH response. Patients with a low baseline TSH showed statistically significant blunting when compared to patients with normal baseline TSH (chi square = 8.025,p,0.01). A total of 5/9 (56 percent) patients with a low baseline TSH had an affective diagnosis and 4/9 (44 percent) a nonaffective diagnosis. Patients with a normal baseline TSH and a blunted TSH response all had a diagnosis of depression. Low baseline TSH is a predictor of blunted TSH response to TRH. In a clinical setting, the TRH test may be more useful in identifying affective disorders, particularly depression in patients with normal baseline TSH.

NR39 Monday May 4, 9:00 a.m.-10:30 a.m.

Ratings of Aggression in Autistic Children

Nilda M. Gonzalez, M.D., Psychiatry, NYU Medical Center, 550 First Avenue, New York, NY 10016; Monique Ernst, M.D., Jana Signe, B.A., Magda Campbell, M.D., Joan Welkowitz, Ph.D.

Summary:

Preliminary data on measurement and changes in aggression against others and against self by multiple raters using an Aggression Rating Scale (ARS) (Campbell, unpublished) are presented.

Subjects were seven hospitalized male autistic children, ages 3.67 to 7.42 years (mean 5.98), participating in studies of naltrexone, pimozide, and haloperidol. Ratings were conducted during the two-week pre-treatment placebo period, the three-week treatment period and the one-week post-treatment placebo period.

Two child psychiatrists and the nursery teacher rated the children in the classroom daily, simultaneously, during three 10-minute periods; the teacher also rated the children during two three-hour periods.

The ARS measures the severity of aggressiveness against others and against self on a seven-point rating scale. The ARS was sensitive to changes due to drug. For aggressiveness against others, both rating conditions yielded the same results: it decreased from baseline during treatment and increased during post-treatment, in both ten-minute and three-hour ratings. However, aggressiveness against self increased during treatment in the ten-minute ratings and decreased during treatment in the three-hour ratings. Individual aggression scores, interrater reliability, and comparison of morning with afternoon ratings will be presented.

NR40 Monday May 4, 9:00 a.m.-10:30 a.m.

Malignant Catatonia: Sequelae and Treatment

Kemuel L. Philbrick, M.D., Psychiatry, Mayo Clinic, 200 First St. SW Desk West 9A, Rochester, MN 55905; Teresa A. Rummans, M.D.

Summary:

Malignant catatonia is a syndrome which spans psychiatry and the remainder of medicine. The diversity of its etiology, coupled with dramatic medical and neurological sequelae which often masquerade as independent phenomena, may obscure the primary diagnosis and delay definitive intervention.

We present five patients with psychogenic catatonia which progressed to near lethality. These patients were distinguished by the severity of their medical developments (including marked autonomic instability, significant electrocardiogram and echocardiogram abnormalities, disturbed parameters of endocrine function, and pronounced cortical and brainstem malfunction), all of which reversed after electroconvulsive therapy. While evaluation of such abnormalities remains necessary in the context of catatonia, the patient is served by resisting distraction and interpreting these complications through the lens of evolving malignant catatonia.

These cases illustrate the enduring presence of catatonia despite neuroleptics, the potential lethality despite transient improvement with benzodiazepines, and the life-saving efficacy of prompt electroconvulsive therapy. They also highlight the poverty of our understanding of the graduated dysfunction of the neurochemical arborizations involved in this syndrome. Serial SPECT or PET scans may prove useful in the investigation of the underlying pathophysiology.

NR41 Monday May 4, 9:00 a.m.-10:30 a.m.

The Immunological Profile of Patients With Alzheimer's Disease

Jerzy W. Leszek, M.D., Psychiatry, Medical University, Kraszewskiego 25 St., Wroctaw 50229, Poland; August Wasik, M.D., Barbara Slesak, Ph.D.

Summary:

In the course of disease resulting from autoagression there may occur morbid changes within the CNS presenting the clinical picture of some kind of senile dementia of Alzheimer's type. Diagnostic difficulties arise when the cases examined by the classical radioimmunological methods are found to be seronegative or when the changes in the CNS precede the pathology of others systems or organs. To ascertain whether there may be immunological defects in Alzheimer's disease, the patients treated in the Medical Uni. Psychiatric Clinic were given tests for the subpopulation of lymphocytes in the peripheral blood and for NK cells with the use of monoclonal antibodies. Also the ratio T_4 and T_8 cells was examined. In addition the percentage of B cells was investigated, evaluating the presence of surface immunoglobulins using the immunofluorescent test. Quantitative changes within the lymphocyte subpoulation expressed in an increase of T_4/T_8 ratio and/or a higher percentage of NK cells were found in 9 out 18 patients being examined. Besides, a positive latex reaction and the presence of antielastin antibodies of a titre above 1/8 as well as an increase in IgA immunoglobulins were found in 8 patients. The present results of the study pointing to changes in the parameters of cellular immunity.

NR42 Monday May 4, 9:00 a.m.-10:30 a.m.

MR Interuncal Distance In Alzheimer's and Parkinson's Disease

Bridget Early, M.A., Psychiatry, Duke University Med Ctr, Box 3215, Durham, NC 27710; Rodrigo Escalona, M.D., William M. McDonald, M.D., P. Murali Doraiswamy, M.D., David Axelson, B.A., K. Ranga Rama Krishnan, M.D.

Summary:

Recent reports have suggested that interuncal distance can be used in the diagnosis of Alzheimer's disease. Interuncal distance was measured on trans-axial T1-weighted MR scans in a group of 17 community controls, 11 depressed patients, 13 patients with Parkinson's disease, and 12 patients with early stage Alzheimer's disease. Amygdala hippocampal complex volumes were measured with stereological technique on coronal T1-weighted images in the group of normal controls and depressed patients. No significant correlation was found between interuncal distance and amygdala hioppocampal complex volume. There were also no significant correlation between interuncal distance and Folstein Mini-Mental Status scores in the group of Alzheimer's disease patients. The only significant difference found in interuncal distances were between Parkinson patients and normal controls. This significance disappeared when controlling for age. These data indicate that MR interuncal distance is not useful in differentiating early stage Alzheimer's disease from Parkinson's disease or normal controls.

NR43 Monday May 4, 9:00 a.m.-10:30 a.m.

Noradrenergic System Changes Induced by Electroconvulsive Shock

Stephen K. Brannan, M.D., Psychiatry, Univ of TX Hlth Sci Ctr., 7703 Floyd Curl Drive, San Antonio, TX 78284; David J. Jones, Ph.D., Alexander Miller, M.D.

Summary:

Study of the biology of electroconvulsive shock (ECS) has the potential to enhance our understanding of antidepressant mechanisms. Noradrenergic receptors have been a major focus for research into antidepressant actions. Recent studies report ECS induces an increased density of alpha-$_1$ receptors and a decreased density of alpha-$_2$ receptors in cortex, as well as behavioral evidence of alpha-$_2$ subsensitivity. Most experiments examine a single receptor subtype. We chose to examine three receptor subtypes simultaneously. Assaying cortical homogenates yielded a significant increase in alpha-$_1$ binding (^{3}H-prazosin), a significant decrease in beta binding (^{125}I-iodocyanopindolol), and a trend toward a decrease in alpha-$_2$ binding (^{3}H-paraminoclonidine) in ECS versus control rats. To characterize presynaptic alpha-$_2$ function, we measured the inhibition of potassium stimulated [^{3}H]-norepinephrine release by UK 14304 (an alpha-$_2$ agonist). There were no differences between ECS and control rats using synaptosomal preparations or slices from cortex. Our results are consistent with the observations of Vetulani and Pilc that antidepressant treatments produce alpha-$_1$ upregulation as well as beta and alpha-$_2$ downregulation in cortex. Early hypotheses postulating that antidepressant treatments correct a deficiency of noradrenergic transmission are not easily reconciled with the complex changes in receptor populations which we and others have observed.

NR44 Monday May 4, 9:00 a.m.-10:30 a.m.

The Hawaii Experience with Water Intoxication

Linda S. Godleski, M.D., Psychiatry, University of Hawaii, 1356 Lusitana St. Fourth Flr., Honolulu, HI 96813; Kenneth Luke, M.D., Barry Carlton, M.D.

Summary:

Excessive water intake by chronically mentally ill patients has been documented for some time. Altered water homeostasis leads to hyponatremia and its consequences, including seizures, coma, and death. Our poster session outlines a treatment plan for such patients and discusses its implementation in the multi-ethnic Asian/Pacific Islander population of Hawaii.

Daily 7 a.m. to 4 p.m. weight gains were correlated with serum sodium concentrations, such that we could project hyponatremic parameters based upon these weight changes. Clinical treatment in response to progressive severity of hyponatremia included water restriction, oral sodium chloride administration, lithium and phenytoin supplementation, and intravenous hypertonic saline.

In initiating such a treatment program in Hawaii, we faced many unique factors such as environmental, dietary, and cultural beliefs specific to this Asian/Pacific Island population. Water restriction in a warmer, non-air-conditioned environment, concurrent with high salt diets will be discussed. Ethnic beliefs regarding issues of behavioral control will also be considered.

NR45 Monday May 4, 9:00 a.m.-10:30 a.m.

Differential Induction of Early Genes by Neuroleptics

Patrick Rogue, M.D., LNMIC, Centre De Neurochimie, 5 Rue Blaise Pascal, Strasbourg 67084, France; Anant N. Malviya, Ph.D., Guy Vincendon, M.D.

Summary:

Chronic treatment by neuroleptics induces an up-regulation of striatal dopamine D_2 receptor mRNA. We will report the effects of acute and chronic administration of dopamine D_2 agonists and antagonists on the expression of different early genes. A single injection I.P. of haloperidol (2 mg/kg) or sulpiride (100 mg/kg) produced a rapid and transient increase in c-*fos*, c-*jun*, *jun*B and zif268 mRNA, but had no influence on the expression of ETRI or *jun*D. These inductions were specifically blocked by pretreatment with a D_2 agonist (1 mg/kg quinelorane). The effect of the NMDA antagonist MK801 will also be discussed. Emphasis will be on the significance of these specific IEG activation patterns for the mechanism of action of antipsychotics.

NR46 Monday May 4, 9:00 a.m.-10:30 a.m.

Transcription Block and Reduced Nuclear Protein Kinase C Activation During Aging

Patrick Rogue, M.D., LNMIC, Centre De Neurochimie, 5 Rue Blaise Pascal, Strasbourg 67084, France; Guy Vincendon, M.D., Anant N. Malviya, Ph.D.

Summary:

The response to a stress such as heat shock includes activation of the transcription of various genes. We studied the expression in the whole animal of the heat shock protein and c-*fos* genes. Young (2-3 months) or aged (24-25 months) Wistar rats were maintained in an incubator until their rectal temperature reached 42°C (45-60 min), then sacrificed for Northern analysis of HSP70 and c-*fos* mRNA levels. The activation of HSP-70 and of c-*fos* genes by heat shock were reduced several fold in the senescent animal. Nuclear run-off transcription assays confirmed that this phenomenon is linked to a block at the level of transcription. Protein kinase C (PKC) plays an important role in the regulation of transcription, in the response to thermal stress, and in Alzheimer's disease. We document that the activation of nuclear PKC is significantly reduced in the senescent animal. Similar results were found in the CNS and in the liver. The significance of these results for Alzheimer's disease will be discussed.

NR47 Monday May 4, 9:00 a.m.-10:30 a.m.

Hedonics During Amphetamine and Cocaine Withdrawal

Daniel M. Mann, Psychiatry, Univ of Michigan, 1500 East Medical Center Dr., Ann Arbor, MI 48109; Saulo C.M. Ribeiro, Ph.D.,

Dianne M. Camp, Ph.D., Terry E. Robinson, Ph.D., Kent C. Berridge, Ph.D.

Summary:

Anhedonia, a cardinal affective symptom in humans, has been inferred in animal models of depression. During amphetamine and cocaine withdrawal, rats show decreased intracranial self-stimulation. This has been interpreted as decreased ability to experience pleasure. To test this "anhedonia hypothesis" we used the taste reactivity test, which quantifies ingestive and aversive responses to solutions infused into the mouth through an oral cannula. This test may provide a better measure of hedonics than ICSS.

Thirty-six male rats received saline or escalating doses of cocaine or amphetamine over 42 days. On days 1, 2, 7, and 28 of withdrawal, each rat received infusions of both sweet and bittersweet solution, each given over 30 seconds. Mouth movements were videotaped and scored by a rater blind to pretreatment. Amphetamine, cocaine, and saline groups did not differ in number of ingestive responses to either solution on any test day ($p>0.10$).

The attenuation in reward during stimulant withdrawal may not be due to a decrease in hedonic capacity. Decreases in the appetitive phase of motivated behavior, or in the ability to attribute salience to neutral stimuli, are proposed as alternative hypotheses. These findings may be of significance for the neurobiological understanding of anhedonia in humans.

NR48 Monday May 4, 9:00 a.m.-10:30 a.m.

Speech Abnormalities in Tardive Dyskinesia

Rukhsana Khan, M.D., Psychiatry, Chicago Medical School, 3333 Green Bay Road, North Chicago, IL 60064; Kathy Yedor, M.A., Chandragupta Vedak, M.D., V. Chowdary Jampala, M.D.

Summary:

Few studies have examined the phenomenon of abnormal speech pattern in patients with tardive dyskinesia (TD). We evaluated 27 chronic psychiatric patients using Modified Abnormal Involuntary Movement Scale (MAIMS) and divided into two groups: those with and without TD. The two groups were similar in age and medication status. A speech therapist assessed all patients for structural and functional status of speech apparatus, and articulation. Even in the absence of significant differences between the two groups in the incidence of structural abnormalities, patients with TD had significant deficits in phonation, intelligibility of words and sentences, and the rate of speech. Total MAIMS score and orofacial dyskinesia score had significant negative correlations with phonation, intelligibility, and the rate of speech. These findings confirm the high incidence of speech abnormalities in patients with TD and suggest that these deficits occur even in the absence of major structural or functional deficits of the speech apparatus. Initiation of speech therapy in the early stages of TD may help prevent speech abnormalities in chronic psychiatric patients.

NR49 Monday May 4, 9:00 a.m.-10:30 a.m.

MRI, SPECT and Neuropsychological Testing in Psychiatric Patients

Chris A. Conway, M.D., Psychiatry, New England Medical, 52 Fenno Street, Cambridge, MA 02138; Iqbal Ahmed, M.D., David Gansler, Ph.D.

Summary:

Objective: The evaluation of psychiatric patients for brain dysfunction includes CT, MRI, Single Photon Emission Computerized Tomography (SPECT) and neuropsychological testing. Our goal was to identify which studies contribute to diagnosis and treatment decisions under what circumstances. *Method:* Over a two year period 18 patients with various DSM-III-R Axis I, II, and III diagnoses admitted to an acute psychiatry ward were evaluated with CT or MRI, SPECT and neuropsychological testing. *Results:* Generalized atrophy was found on CT or MRI and SPECT in three patients. SPECT detected cortical abnormalities in two patients where MRI was normal. In two cases SPECT showed right parietal dysfunction when white matter lesions were noted on MRI. In two patients with developmental disorders neuropsychological testing was abnormal but SPECT and MRI were normal. There was a good correlation between all modalities when focal cortical lesions were present as determined by MRI. *Conclusions:* MRI is sensitive to most acquired white and gray matter lesions. SPECT seems to be more sensitive to cortical dysfunction in the following situations: 1) MRI is normal or demonstrates only subcortical lesions, 2) Cases of right parietal dysfunction with white matter lesion on MRI and frontal subcortical abnormalities in neuropsychological testing. SPECT is however not sensitive in identifying white matter lesions. Neuropsychological testing elucidates abnormalities in both subcortical and cortical brain systems involving acquired and developmental disorders. It appears that for a comprehensive assessment of neuropsychiatric disorders these three methods, CT or MRI, SPECT and neuropsychological testing are complementary to each other.

NR50 Monday May 4, 9:00 a.m.-10:30 a.m.

Medial Temporal Structures on MRI in Dementia of the Alzheimer Type Offspring

Cynthia M. Churchill, M.D., Psychiatry, Ohio State University, 473 West 12th Avenue, Columbus, OH 43065; James P. Fulop, B.A., Steven B. Schwarzkopf, M.D., Stephen C. Olson, M.D., Elizabeth M. Burns, Ph.D., Henry A. Nasrallah, M.D.

Summary:

Atrophy of the medial temporal structure is prominent in individuals with dementia of the Alzheimer type (DAT). The hippocampal and entorhinal structures were measured on MRI in healthy, nondemented middle-aged offspring of DAT patients ($N=22$) and controls ($N=10$). Lenticular nucleus measurement was used to correct for overall brain size. The volume of the subiculum for the offspring of DAT patients was 20.3 percent smaller than for controls ($p<0.03$). The entorhinal cortex, hippocampal formation and parahippocampal gyrus had smaller mean volumes than for controls, but this difference did not reach statistical significance. This finding in offspring of DAT patients suggests that structural neuroanatomical degeneration may precede clinical DAT by almost two decades.

NR51 Monday May 4, 9:00 a.m.-10:30 a.m.

MRI Brain Volume and Gyral Pattern in Schizophrenics

Hiroto Hokama, M.D., Psychiatry, Harvard Medical School, 940 Belmont Street, Brockton, MA 02401; Martha E. Shenton, Ph.D., Cynthia G. Wible, Ph.D., Ron Kikinis, M.D., Ferenc A. Jolesz, M.D., Robert W. McCarley, M.D.

Summary:

New computer automated image processing of MR data sets affords a new opportunity to examine in vivo differences between schizophrenic patients and normal control subjects. We have applied these techniques to examine both volumetric MR brain measurements and 3D reconstructions of the gyral pattern of the cortex obtained from 15 chronic medicated schizophrenics and 15 normal controls matched for age (mean = 38 years), sex, handedness, social class of origin, and verbal IQ. MR data were acquired axially using spin echo sequences (TR = 3000, TE = 30/80msec, slice thickness = 3 – mm, #slices = 108 at 54 levels) and coronally using a 3DFT SPGR protocol (slice thickness = 1.5 – mm, #slices = 124) on a Signa GE 1.5T MR Scanner. Automated volumetric analyses

showed no overall differences between groups in gray matter, white matter, subarachnoidal CSF, or intraventricular CSF although there was a greater variance ($p = 0.001$) in the lateral ventricles of schizophrenics. A closer examination of the later ventricles revealed bilateral, though more left than right, enlargement of the temporal horns ($p = 0.028$; $p = 0.037$). A semi-automated analysis of the gyral patterns (by raters blind to diagnosis) revealed a different gyral pattern in the left temporal lobe of schizophrenic patients ($p < 0.05$) as well as preliminary indications of gyral alterations in prefrontal regions. These data suggest pattern and volume alterations in schizophrenics in the temporal and frontal lobe without gross brain volume alterations. Frontal changes suggest the possibility of associated temporal lobe-prefrontal alterations in schizophrenia.

NR52 Monday May 4, 9:00 a.m.-10:30 a.m.

MRI Study of Temporal Lobe Structures in OCD

Stephania S. Richards, M.S., Psychiatry, Johns Hopkins University, 600 N. Wolfe Street, Baltimore, MD 21218; Elizabeth Aylward, Ph.D., Godfrey D. Pearlson, M.D.

Summary:

Obsessive-compulsive disorder is thought to involve the frontal lobe-basal ganglia-limbic system as supported by cerebral blood flow, computed tomography, psychosurgical, and neuropsychological data. However, considerable evidence exists implicating temporal, especially mesial temporal lobe, including focal EEG abnormalities, association of OCD with the onset of temporal lobe epilepsy (TLE), similarities of "forced thinking" in TLE to OCD, impaired recent memory, impaired oxygen consumption in the parahippocampal gyrus in related anxiety disorders, and the simulation of OCD in the hippocampectomized rat. To date there are no neuroimaging studies of the temporal lobe in OCD.

This study is an MRI morphometric study of mesial temporal and temporal lobe structures in 23 *DSM-III-R* OCD patients and 19 normal controls matched for age, sex, and race. Volume measurements were obtained on 3mm thick T-1 weighted coronal images of the following structures: right and left anterior temporal lobes, amygdala, hippocampus, parahippocampal gyrus, anterior superior temporal gyrus, and insular cortex in addition to right and left sylvian fissures, lateral ventricles, temporal horns, and the third ventricle. Structural volumes were slightly larger in OCD patients than normal controls except bilateral hippocampi, left parahippocampal gyrus, right sylvian fissure, and right insular cortex. None of these differences approached statistical significance.

We will also examine the clinical correlation of several detailed symptom severity scales with these structural volumes.

While considerable evidence implicates temporal lobe pathology in OCD, this novel MRI study of temporal lobe and mesial temporal structures revealed no significant structural abnormalities.

NR53 Monday May 4, 9:00 a.m.-10:30 a.m.

MRI Volumetrics in Alzheimer's Disease

Andrew B. Newberg, Nuclear Medicine, Univ. of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104; Anand Kumar, M.D., Abass Alavi, M.D.

Summary:

The purpose of this study was to accurately measure the volumes of each cerebral hemisphere and its CSF spaces in 22 patients who met the NINCDS-ADRDA criteria for probable dementia of the Alzheimer type (DAT) and 27 healthy age-matched controls. Most DAT patients were mild to moderately impaired as determined by mini-mental status exam with an average score of 20.5 ± 8.3 (of possible 30). Proton density and T2 weighted MR images were obtained with a prospectively designed acquisition sequence which maximized the contrast between neural tissue and CSF. A semi-automated boundary program and segmentation algorithm was then used to differentiate brain tissue from CSF. All brain volumes were normalized to total intracranial volume to correct for different absolute volumes, although average intracranial volume was the same in patients and controls. Patients with DAT had 71 percent larger lateral ventricular volumes than controls (4.0 percent of the intracranial volume compared to 2.3 percent, $p < 0.0005$), 49 percent larger sulcal volumes than controls (20.3 percent to 13.3 percent, $p < 0.0005$), and 53 percent larger total CSF volumes than controls (16.3 percent compared to 11.0 percent, $p < 0.0005$). These changes were symmetrical with respect to the left and right hemispheres. Comparison between sexes in the DAT group showed no difference in total or sulcal CSF volumes. However, female DAT subjects had average normalized ventricular sizes 45.2 percent larger than male DAT subjects. There was no significant correlation between the duration of symptoms and ventricular, sulcal, or total CSF volumes. These findings clearly showed a significant quantitative CSF expansion in both cortical and periventricular areas in patients with DAT compared to controls suggesting wide spread neuronal involvement.

NR54 Monday May 4, 9:00 a.m.-10:30 a.m.

MRI Signals in Late-Life Depression Without Vascular Risk Factors

David Miller, M.D., Psychiatry, Univ. of Pennsylvania, 3615 Chestnut St. Ralston Penn, Philadelphia, PA 19104; Anand Kumar, M.D., David Yousem, M.D., Gary Gottlieb, M.D.

Summary:

We examined periventricular (PVWH), deep white matter (DWH), and subcortical (SCH) high intensity MRI signals in older adults (N = 14, 3M, 11W), mean age 69, (SD6) who met *DSM-III-R* criteria for Major Depressive Disorder (HRSD scores mean 22 SD 6), 16 subjects (8M, 8W) with probable Alzheimer's disease (DAT), mean age 67 (SD 8), and 23 healthy age-matched controls (11M, 12W), mean age 68 (SD 8). All subjects were healthy and free of major vascular risk factors including hypertension. MRI scans were performed using a 1.5 tesla GE signa scanner with head coil (TR = 3000, TE = 30, 80 msec) and 5mm contiguous slices were obtained. T2 and proton density images were analyzed by a neuroradiologist blind to the clinical status of all subjects. PVWH, DWH, and SCH were rated on a 0-3 severity scale (Fazekas et al, 1987, AJNR, Coffey et al. 1990 *AJP*). There were no statistically significant differences on any of the MRI indices between the three groups studied. These preliminary data demonstrate that late-life depression, like DAT, in the absence of major vascular risk factors, is not associated with a significant increase in MRI high density signals when compared to healthy controls.

NR55 Monday May 4, 9:00 a.m.-10:30 a.m.

Buspirone in the Treatment of Tardive Dyskinesia

Lori E. Moss, M.D., Psychiatry, Chicago Medical School, 3333 Greenbay Road, North Chicago, IL 60064; Wayne C. Drevets, M.D., Vernon M. Neppe, M.D.

Summary:

Eight subjects with mild to severe tardive dyskinesia were treated for 12 weeks with buspirone in dosages up to 180 mg daily in an open label, pilot study. Buspirone was well tolerated by most subjects at these doses. A within-subjects comparison of pretreated and post-treatment AIMS (Abnormal Involuntary Movement Scales) scores revealed a mean improvement of 4.35 (p 0.01). Improvement was also observed in other neuroleptic-induced extrapyramidal side effects, as reflected by reductions in Simpson-Angus Extrapyramidal Scale scores. Scores on the Hamilton Anxiety

Rating Scale and the Brief Psychiatric Rating Scale did not change during the twelve week study. These results indicate that a double-blind, placebo-controlled trial is warranted to confirm buspirone's efficacy in the treatment of tardive dyskinesia.

NR56 Monday May 4, 9:00 a.m.-10:30 a.m.

Clinical Profiles of Antidepressants: A Meta-Analysis on 400 Patients

Marie-Josee Filteau, M.D., Research, Royal Ottawa Hospital, 1145 Carling Avenue, Ottawa ON K1Z 7K4, Canada; Yvon D. Lapierre, M.D., David Bakish, M.D., Blanchard Blanchard, B.A.

Summary:

Recent years have seen the availability of several antidepressants with highly selective biochemical effects. However, their clinical specificity is still debated. Our research center has been studying depression through clinical drug trials since the beginning of the decade. From ten studies, including 400 patients, we present a meta-analysis of change under treatment by classical tricyclic antidepressants and more interestingly by specific serotonergic and noradrenergic antidepressants of behavioral dimensions in depressed patients. Five groups are considered: noradrenaline reuptake inhibitors (desipramine, maprotiline, oxaprotiline); 5HT reuptake inhibitors (fluoxetine, zimelidine, fluvoxamine, sertraline); mixed NA/5HT reuptake inhibitors (amitriptyline, imipramine); partial 5HT2 antagonists (ritanserine, nefazodone, trazodone); placebo. The patients were evaluated at least during 4 weeks of treatment using HDRS. Factorial analysis performed on differential scores of Hamilton depression rating scale (week 4–week 0) in order to define clinical dimensions selectively improved by each antidepressant group. Analyses of data are in progress and will be presented at the meeting. Our initial analysis of global scores of HDRS has shown no response selectivity in agitated or retarded depressives to NA or 5HT uptake drugs and factorial analysis of the different items of HDRS will prove more fruitful. They will offer important and heuristic avenues for a sound prescription of the right drug to the right features presented by depressed patients.

NR57 Monday May 4, 9:00 a.m.-10:30 a.m.

Causes of Neuroleptic Discontinuation in Tourette's Syndrome

Raul R. Silva, M.D., Psychiatry, NYU Medical Center, 550 First Avenue, New York, NY 10016; Harry Magee, M.D., Arnold J. Friedhoff, M.D., Monique Ernst, M.D.

Summary:

Neuroleptics are considered the mainstay of treatment in Tourette's disorder, with haloperidol deemed the treatment of choice by many. Factors such as efficacy and the development of side effects have been implicated in affecting medication compliance, though a detailed evaluation has not been undertaken in Tourette's disorder.

Subjects: Of 50 consecutive referrals to a Tourette's clinic, 47 met *DSM-III-R* criteria for Tourette's disorder; of those 27 previously received neuroleptic treatment. In this set of 27 patients, 23 (15 male, 8 female) had initially received treatment with haloperidol, and made up the present sample. Their ages ranged from 10.42 to 47.92 years (mean 25.82). Age of Tourette onset ranged from 2 to 16 years of age. *Method:* This is a retrospective study which used the Tourette Syndrome Questionnaire, clinical and family interviews, and chart reviews to gather information concerning factors that led to haloperidol discontinuation and/or noncompliance and other bothersome side effects. *Results:* Duration of treatment ranged from three days to 14 years (mean 3.7 years). Thirteen percent of this sample was still on haloperidol after an average of 8.4 years. Reasons for haloperidol discontinuation: 52 percent of cases were because of side effects, in 8 percent it became ineffective, one patient stopped medication because of the fear that certain side effects might occur. Thirteen percent discontinued medication because of combinations of the above categories. The side effects leading to discontinuation will be detailed and discussed. Intervention strategies will be delineated.

NR58 Monday May 4, 9:00 a.m.-10:30 a.m.

Early Onset of Lithium-Induced Hypothyroidism

Annick Vincent, M.D., Psychiatry, Had De Enfant-Jesus, 1401 18ieme Rue, Quebec G1J 1Z4, Canada; Philippe Baruch, M.D., Pierre Vincent

Summary:

To evaluate the critical time at which a patient receiving lithium is more at risk of developing hypothyroidism, a retrospective study has been done on 154 records of patients followed at two general hospital lithium clinics from January 1980 to August 1991.

Forty-two cases of hypothyroidism (clinical hypothyroidism and/or abnormal elevated TSH levels) have been detected. There is no significant correlation between thyroid abnormality and age, sex, menopausal status and diagnostic category.

This longitudinal study is the first to describe an evolutive outline of thyroid function in terms of long-term treatment time, lithium-induced hypothyroidism appearing above all in the first two years. Among the 42 hypothyroidism cases, 16 were diagnosed before six months (38 percent), 23 during the first year (55 percent) and 31 in less than two years (74 percent).

Since thyroid function is an important parameter in the good evolution of affective disorders, its close and frequent monitoring appears especially mandatory in the first two years of treatment.

NR59 Monday May 4, 9:00 a.m.-10:30 a.m.

Haloperidol: Therapeutic Window in Schizophrenia

Miguel Bernardo, Ph.D., Psiquiatria, Hospital Clinico, Villarroel 170, Barcelona 08036, Spain; Diego J. Palao, M.D., Alberte Arauxo, M.D., Merce Brunet, M.D., Jose Ferrer-Raldua, M.D., Enrique Gonzalez-Monclus, Ph.D.

Summary:

Clincial response of 20 schizophrenic inpatients with acute exacerbation *(DSM-III-R)* was measured on days 0, 4, 7, 14, and 21 by scales BPRS, SAPS, SANS, and Simpson for extrapiramidal symptoms. These patients had received treatment with fixed doses of haloperidol (HAL) randomly assigned (10, 20, or 30 mg/day). Plasma determination of HAL were made on days 4, 7, 14, and 21 by HPLC technique with UV detection and previous extraction. The mean HAL steady state was 11.01 ± 6.57 mg/ml. The improvement on BPRS for patients with plasma levels between 6.0 and 14.4 ng/ml was significantly greater than the rest (Mann-Whitney's U test, $p = .0014$). Only one out of the ten patients inside the interval was a nonresponder (F test, $p = .009$). When the clinical response was measured separately on SANS and SANP scales no significant correlation was found. Linear correlation was not found between HAL plasma levels and clinical response on any scale. Our results provide additional support to studies that find a curvilinear (U-shaped) relation between HAL plasma levels and clinical response measured with instruments that consider both positive and negative symptoms of schizophrenia, as the BPRS scale.

NR60 Monday May 4, 9:00 a.m.-10:30 a.m.

Bipolar Disorder and Response to Valproate

Lance M. McCoy, M.D., Psychiatry, The Ohio State University, 473 West 12th Avenue, Columbus, OH 43210; Nicholas Votolato, R.P.H., Steven B. Schwarzkopf, M.D., Henry A. Nasrallah, M.D.

perspectives outlined above, including the relationship of urgency and time lag of consult request to outcome of whether or not procedure was performed in incompetent patients. We have delineated the outcome of competency evaluations as to whether the medical procedure was actually performed, and the data help us understand why intended medical procedures for incompetent patients are not performed.

NR69 Monday May 4, 9:00 a.m.-10:30 a.m.

Geriatric Depression: Screening With Two Geriatric Depression Scale Versions

Rodney L. Nitcher, D.O., Psychiatry, Univ of NE Med. Center, 600 South 42nd Street, Omaha, NE 68198; William J. Burke, M.D., William H. Roccaforte, M.D., Steven P. Wengel, M.D.

Summary:

This study compares patient versus collateral source reports of depressive symptoms on the Geriatric Depression Scale (GDS) in cognitively intact and impaired patients.

The 30-item GDS was completed by 194 outpatients undergoing geriatric assessment while their collateral source (CS) independently completed a newly developed version of the GDS (CS-GDS). The patients were evaluated by one of three geropsychiatrists who were blind to the GDS results. These clinical diagnoses were compared to the GDS and CS-GDS results.

Data were analyzed using ROC curves, which showed good agreement between the clinical diagnosis of major depression and the results of both the GDS (AUC = 0.81) and CS-GDS (AUC = 0.75). However, while the optimal cutoff score for the GDS was 14, it was 21 for the CS-GDS, suggesting that CS's reported more depressive symptoms than the patients. The GDS predicted depression in cognitively intact and impaired patients, providing further evidence that it is an accurate screening test for depression in the elderly, regardless of cognitive status. This study provides evidence that the CS-GDS can provide similar information although at a higher cutoff point than the GDS.

NR70 Monday May 4, 9:00 a.m.-10:30 a.m.

ECT in Very Elderly Patients

Stephen C. Mory, M.D., Psychiatry, Univ of Mich. Med. Ctr., 1500 E. Med. Ctr. Dr. Bx 0840, Ann Arbor, MI 48109; Grunhaus Leon, M.D., David B. Arciniegas, B.S., Atul C. Pande, M.D., Rajiv Tandon, M.D.

Summary:

Octogenarians are referred for electroconvulsive therapy (ECT) with increasing frequency. There are very few data and studies reporting the efficacy and potential complications of ECT in this age group. We reviewed 54 charts to date of inpatients at the University of Michigan Medical Center ECT Program, comparing three age groups: 60-69 years (Group 1, N = 10), 70-79 years (Group 2, N = 33), and 80-89 years (Group 3, N = 11). The median ages for the three groups were 66, 75, and 82 years. Prior to the ECT the three groups showed no significant differences on multiple demographic and clinical variables, including severity of medical and psychiatric illnesses. ECT was performed following the 1991 APA Task Force guidelines. Post-ECT, on the Clinical Global Impression (CGI) subscale for Severity of Illness (SI), Group 1 scored a mean of 2.9 ± .738, Group 2 mean 3.76 ± 1.03, and Group 3 mean was 3.9 ± 1.04. Comparing this CGI SI factor by ANOVA, Group 1 versus Group 2 and Group 1 versus Group 3 were significantly different, at $p<.05$. ANOVA of the CGI Global Improvement variable also showed Group 1 had significantly lower scores than the other two groups at $p<.05$. The third finding was systolic blood pressure post-ECT was significantly higher in the two older groups. The systolic pressure (mm Hg) in Group 1 was 168.4 ± 14.9, Group 2 was 187.3 ± 25.2, and Group 3 was 189.8 ± 20.9, which yields significant differences between the youngest Group 1 versus Group 2 and versus Group 3 by ANOVA at $p<.05$. Our findings suggest that ECT in octogenarians is safe and reliable, but clinical response is actually better in the younger two groups.

NR71 Monday May 4, 9:00 a.m.-10:30 a.m.

Aggression In An Elderly Schizophrenic Population

Srikumar Menon, M.D., Psychiatry, Loch Raven VAMC, 3900 Loch Raven Blvd, Baltimore, MD 21218; Patricia Molla, M.S.N., Linda Blake, B.S.N., Mary Rose Cordas, B.S.N., Michael Peszke, M.D., Allen Raskin, Ph.D.

Summary:

Most studies on aggression in the elderly have centered on patients with dementia. Elderly schizophrenic patients, like patients with dementia, are another group which exhibits physically aggressive behaviors such as striking other, pushing, grabbing, and swinging at others. The Perry Point V.A.M.C. has referred many veterans who have long histories of difficult to treat agitation, including verbal and physical aggression. For this study 40 male elderly (>60 yrs) schizophrenic patients and 39 elderly male patients with other diagnosis were selected from two long-term psychogeriatric units at this center. For a two-week period, ratings of agitated behaviors for each shift were done daily by the nurse's aides on the two units. Each nurse's aide completed a 30-item checklist of agitated behaviors for the ten patients assigned to them on that shift. Results showed that during this two-week period 17 patients (21.5 percent) manifested at least one episode of physically aggressive behavior on the day shift. Verbally aggressive behaviors such as cursing, shouting angrily, or insulting and threatening others were reported for 31 patients (39.2 percent). A stastically significant association was observed between the occurrence of episodes of physically aggressive behavior and the prior occurrence of verbally aggressive behaviors on the previous day. This suggests that early interventions directed at reducing verbal aggression may prevent the later manifestation of physical aggression in this patient population.

NR72 Monday May 4, 9:00 a.m.-10:30 a.m.

Effects Of Reactivating Occupational Therapy In Dementia

Doris Bach, Ph.D., Barmherzig, Keit Inst., Haus Der, Vinzenzgasse 2-6, A-1180 Vienna, Austria; Thomas Fruhwald, M.D., Franz Boehmer, M.D., Brigitte Grilc, Michael Bach, M.D.

Summary:

In this controlled treatment study we assessed the effects of a newly developed re-activating occupational therapy (OT) on cognitive capacity, subjective well-being and social integration of long-term geriatric inpatients. Forty-four patients with a moderate dementia according to *DSM-III-R* were randomly allocated to two different treatment groups, one group (n = 22) following a reactivating OT in small groups (5-7 person/group) over 24 weeks, the other group (n = 22) following a standard OT. The following psychometric tests were carried out at baseline, after 12 and 24 weeks of treatment: the Benton-Test (BT), assessments of latent memory (LL) and of subjective well-being (BF), the Gottfried-Brane-Steen Scale (GBS), and the Sandoz Clinical Assessment Geriatric Scale (SCAG). Patients receiving re-activating OT exhibited a substantial improvement in memory capacity, subjective well-being and social integration when as there was no improvement in patients receiving standard OT. AT the end of 24-weeks treatment phase patients in the re-activating OT group scored significantly better in all parameters tested as compared to controls ($p<0.05$ for BT, $p<0.01$ for LL, BF, GBS and SCAG). These results suggest that OT, particularly

focusing an activation is significantly superior to a standard OT in geriatric inpatients.

NR73 Monday May 4, 9:00 a.m.-10:30 a.m.

The Pattern Of Cognitive Deterioration On The Alzheimer's Dementia Assessment Scale In Patients With Alzheimer's Disease

Robert G. Stern, M.D., Psychiatry, Bronx VAMC, 130 Kingsbridge Road, Bronx, NY 10468; Richard C. Mohs, Ph.D., James Schmeidler, Ph.D., Michael Davidson, M.D., Kenneth L. Davis, M.D.

Summary:

Five different approaches were employed to determine the annual rate of cognitive deterioration [ARCD] on the cognitive part of the "Alzheimer Dementia Assessment Scale" [c-ADAS] and the relation between dementia severity and ARCD on this scale. The 121 patients with NINCDS-ADRDA probable AD included in the study were assessed on the ADAS at six month intervals over a period of up to 90 months. Mean (+/− SD) ARCDs in ADAS points per year were 9.8 (8.6) by MIA-12, the potentially most suitable approach; 10.4 (12.6) by MIA-6; 7.7 (7.5) by UTPE; 10.3 (10.2) by RTPE; 10.2 (7.5) by MS. There was a significant quadratic ($p < 0.0002$) but not a linear or cubic association between c-ADAS baseline scores and ARCD across all approaches indicating that patients with lower or higher c-ADAS scores progress at a slower rate than those in the mid-range. In addition significant differences were found between the patterns of progression on the various c-ADAS items (i.e. language, praxis, orientation and memory). These findings have implications on the methodology to be applied in assessing rate and pattern of deterioration on AD scales in general and on the ADAS specifically. Furthermore these results have immediate relevance to the interpretation and design of pharmacological studies, which employ the ADAS.

NR74 Monday May 4, 9:00 a.m.-10:30 a.m.

The Delirium of Trauma

Yasutaka Iwasaki, M.D., Critical Care, Nippon Med. School, 50 East 98st #14F2, New York, NY 10029; Hisashi Kurosawa, M.D., Nobuo Watanabe, M.D.

Summary:

Objectives: The authors studied the incidence and the profile of the delirium patients of trauma patients in a Critical Care Medical Center (CCM). *Method:* Two hundred sixty eight patients were studied at Nippon Medical School Hospital CCM in Japan. One hundred twenty-five trauma and 143 non-trauma, who were consecutively admitted from April 1, 1990-June 30. Exclusions were: 1) Dead on Arrival, 2) Length of stay one day or less, 3) Children age five or younger. Psychiatrists screened the patients, examined the medical charts, and received information from the nursing staff. Psychiatric diagnosis was made according to the criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (third revised edition, American Psychiatric Association). T-test and Chi-square test were performed for continuous and dichotomouse variables, respectively. *Results:* The incidence of delirium in the trauma was 8.8 percent (N = 11). This was not significantly different from the non-trauma (9.8 percent, N = 14). The trauma delirium were significantly younger than the non-trauma delirium (52.7ave ± 18, lsd vs66, 0 ± 11, 7, $t = 2.22$, $p \pm 0.036$). They remained at the CCM as long as the non-trauma delirium (17, 5ave ± 6, 7sd vs 16.1 ± 16.1, $t = -0.284$, $p = 0.779$). The non-trauma delirium (71.4 percent N = 10) experienced more delirium on the first day of the admission than did the trauma delirium (27.3 percent, N = 3). *Conclusion:* This is the first study of the incidence and the profile of delirium of trauma at a CCM in Japan. The incidence was significant (8.8 percent). Trauma delirium patients remained in the CCM as long as the non-trauma patients.

NR75 Monday May 4, 9:00 a.m.-10:30 a.m.

Delirium Presenting With Symptoms Of Depression

Linda M. Nicholas, M.D., Psychiatry, Univ of North Carolina, 522 Colony Woods Drive, Chapel Hill, NC 27514; Byron A. Lindsey, M.D.

Summary:

Objective: This study was designed to determine if symptoms of delirium are mistaken for symptoms of depression in hospitalized patients referred for psychiatric consultation. *Methods:* Records were surveyed for all patients seen by a university hospital psychiatric consultation service during a 38-month period. A computer search identified those patients referred for evaluation of symptoms of depression. Among this group of patients, a further search identified those whose final psychiatric diagnosis was delirium, and the charts for each of the patients were reviewed. *Results:* Of the total 2897 patients., 737 (25 percent) were referred for symptoms of depression. Of these patients, 42 (6 percent) were given a diagnosis of delirium by the consulting psychiatrist. The mean age for all patients referred for depressive symptoms was 53 ± 18.2 years, while the mean age for those whose final diagnosis was delirium was significantly greater (65 ± 12.4 years). *Conclusion:* The present study supports the assumption that symptoms of delirium may be misinterpreted as symptoms of depression in an inpatient hospital setting. Given the prevalence of delirium, especially in the hospitalized elderly, as well as the grave prognostic implications of missed or delayed diagnosis, the physician needs to be aware that its presentation may be disguised as depression.

NR76 Monday May 4, 9:00 a.m.-10:30 a.m.

Psychiatric Diagnoses in Desert Storm Casualties

Charles Perrotta, Jr., M.D., Psychiatry, Eisenhower AMC, DDEAMC, Ft. Gordon, GA 30905; Carolyn D. Randle, M.D.

Summary:

It is generally accepted that among medical and surgical patients evacuated from a combat zone, a percentage will have psychaitric symptoms. However, to our knowledge, there are no available data describing the prevalence of psychiatric diagnoses in this population. The current study was undertaken to determine the prevalence of psychiatric diagnoses in patients medically evacuated from Operation Desert Storm. One hundred and seventy-five patients were evacuated to Dwight David Eisenhower Army Medical Center between February 11, 1991, and May 16, 1991. Representatives of a psychiatric consultation team were able to conduct diagnostic evaluations on 112 soldiers, to include psychiatric history and mental status examination. Diagnoses were determined according to *DSM-III-R* criteria. Sixteen patients were determined to have active Axis I diagnoses in addition to their medical diagnoses. The results of this study, to include the types of diagnoses encountered, patient demographics, and implications for future research will be discussed.

NR77 Monday May 4, 9:00 a.m.-10:30 a.m.

Severity Of Psychosocial Parameters: Young Versus Old

Ibrahim Gunay, M.D., Psychiatry, Univ of Cinn Col of Med, 231 Bethesda Avenue ML559, Cincinnati, OH 45267; Julia Rothe, M.Ed., Eugene Somoza, M.D.

Summary:

As individuals age their subjective feelings of distress in response to psychosocial stressors, as well as the perceived intensity of the stressors themselves change. We studied this by measuring the severity of symptoms and stressors for all geriatric (≥60, N = 331) and younger (N = 1202) walk-in patients to a VA psychiatric emergency room during a two year period. There was a pronounced change in the relative frequency of certain diagnoses; depression being over-represented in the geriatric group while schizophrenia and manic-depressive disorders were underrepresented. There were also substantial changes in the severity of certain symptoms as measured by the BPRS. Somatic concerns and psychomotor retardation were higher in the geriatric group while depressed mood, guilt feelings, paranoia, hallucinations were lower, all were significant at the $p < 0.0005$ level. Older patients were much less (60.2 percent lower) suicidal on arrival than the younger ones as measured by a 0 to 6 point scale ($p < 0.0005$). The severity of stressors, both from the point of view of *DSM-III-R* (i.e., Axis IV) and from the patients' perspective were lower for the older group ($p < 0.0005$ in each case). The effects of race, diagnosis, admission status, household composition, and combat experience will also be discussed.

NR78 Monday May 4, 9:00 a.m.-10:30 a.m.

Silent Myocardial Ischemia, Denial And Locus Of Control

Christine Reynaert, Psychiatry, Univ of Louvain, UCL Mont-Godinne, B-5530 Yvoir 5530, Belgium-Europe; Pascal Janne, Ph.D., Patric De Coster, M.D., Rene Kremer, M.D., Edgard Coche, M.D., Leon Cassiers, M.D.

Summary:

Myocardial ischemia, even when severe, may occur without anginal symptoms (silent myocardial ischemia, SMI). The mechanisms underlying such absence of angina pain remain unclear. Two hypotheses (Denial of Pain, Internal Locus of Control) were tested in a multi-center research trial (London & Louvain) involving 152 consecutive coronary pts. 79 pts met the painful condition and 73 presented various degrees of absence of symptoms (according to Cohn's classification of SMI; four levels). *Methods:* Health Locus of Control (MHLCS, Wallston & al), and Denial (Pennebaker Inventory of Limbic Languidness; PILL) were assesed before exercise stress testing. *Results:* As hypothesized, a significantly ($p = 0.0061$) higher Internal MHLCS was found in type 1 (totally) asymptomatic coronary patients when compared to types 2, 3 and 4 of the Cohn's classification of SMI. Similarly, a higher ($p = 0,0001$) propensity to avoid complaining behaviour (denial, as assessed by the PILL) was found in these patients. *Conclusions:* There is a conceptual overlapping between desire for control and denial. As a result of these two psychological characteristics, undercomplaining behaviour appears to be involved in the absence of pain in the so called "SMI" syndrome. We postulate in this respect that a psychological "Gate Control Effect" could be responsible for the absence of angina pain in painless ischemia.

NR79 Monday May 4, 9:00 a.m.-10:30 a.m.

Patient Controlled Analgesia And Psychiatry

Christine Reynaert, Psychiatry, Univ of Louvain, UCL Mont-Godinne, B-5530 Yvoir 5530, Belgium-Europe; Pascal Janne, Ph.D., Michelle Pirard, Ph.D., Vincent Delire, M.D., Edgard Coche, M.D., Leon Cassiers, M.D.

Summary:

Introduction: It remains unclear whether an "Internal Health Locus of Control orientation" improves (Johnson – al., ***Pain*** 39: 17-22, 1989) the effectiveness of PCA or not (McGrath D. & al., ***Pain*** 37:265-270, 1989). *Patients & Methods:* examined 23 pts before heart surgery and included in a 48hrs follow-up (PCA pump = Abbott Lifecare®). Anesthesia was induced and maintained with propofol and alfentanil. Postsurgical morphine consumption (PSMC), and number of unsatisfied demands were recorded (NID). Assessment of pain was made by means of Visual Analogue Scales, and Locus of Control by the Multidimensional Health Locus of Control (MHLC). *Results:* We observed a reverse and statistically significant correlation coefficient between MHLC and PSMC ($r = 0,5633$, $p = 0,036$): «internally-oriented» patients consumed $0,87 \pm 0,23$ mg/h whereas «externals» requested $1,43 \pm 0,53$ mg/hr, that is, «internals» consumed an average 40 percent less morphine than «externals», as confirmed by mean comparisons ($p = 0,026$). Moreover, «internals» showed less NID than «externals». *Conclusion:* Health Locus of Control, when internal, is associated with a lower consumption of morphine during PCA. This may reflect, either the fact that «internals» like to keep control, and accordingly do not abuse *when they are in control* with analgesia, either the fact that «externals» are more dependent, anxious, and prone to use PCA as an anxiolytic agent, with the corresponding consequence of a higher frequency of unsatisfied demands.

NR80 Monday May 4, 9:00 a.m.-10:30 a.m.

Psychiatric and Psychometric Features In ACNE Excoriee

Michael Bach, M.D., Psychiatry, Univ of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria; Doris Bach, Ph.D.

Summary:

Considering acne excoriée (AE) as a psychiatric disorder still remains questionable. In this pilot study a psychometric assessment (including MMPI, BDI, STAI, FAF) and a psychiatric interview was performed in 12 patients with AE. None of these patients reported pruritic sensations as a possible explanation for the self-inflictive behavior. The presence of three males as well as the age distribution in our sample (18-49 years, mean 21 years) differed from previous reports on predominantly young females. As compared to nonpatients standards, AE patients showed decreased FAF scores of aggression inhibition ($p.<0.01$) and elevated MMPI scores of conversion hysteria ($p<0.01$), psychopathic deviate ($p<0.05$), and schizophrenia ($p<0.05$). Two patients met *DSM-III-R* criteria for dysthymia and two for a personality disorder. In these patients AE might be considered as an associated feature. However, the majority of patients (66.7 percent did not exhibit any affective, anxiety or anxiety or adjustment disorder. Rather, they reported a sense of tension immeidately before and a sense of relief after manipulating their skin. As far as this feature might reflect a particular psychiatric syndrome, as proposed for trichotillomania too, we would suggest to attribute these AE patients to *DSM-III-R* impulse control disorders NOS.

NR81 Monday May 4, 9:00 a.m.-10:30 a.m.

Noncompliance In Adolescent And Young Adult Liver Transplant Recipients

Angela H. Lee, M.D., Psychiatry, CA Pacific Medical Center, 2340 Clays Street Ste. 711, San Francisco, CA 94115; Robert G. Gish, M.D., Waldo Concepcion, M.D., Paul Nakazato, M.D., Carlos O. Esquivel, M.D.

Summary:

A high prevalence of noncompliance has been reported in adolescents and young adults with chronic medical conditions necessitating long-term treatment and follow-up. However, few studies to data have explored noncompliance in organ transplant recipients. This study had two objectives: 1) to assess the prevalence of non-

compliance in adolescent and young adult liver transplant recipients and 2) to identify psychosocial factors that are predictive of noncompliance in this population. *Methods:* We undertook a retrospective chart review of 17 patients aged between 11-23 years who underwent liver transplantation. Demographic, psychiatric and psychosocial variables were analyzed. Noncompliance was assessed in three components: 1) noncompliance with medications; 2) noncompliance with clinic visits and lab work; and 3) delay in seeking medical treatment. A score of 0, 1 and 2 was given for nil, moderate or severe noncompliance in each component. The noncompliance score was a composite of the three component scores. *Results:* The prevalence of noncompliance was 46%, with 35% of patients demonstrating mild or moderate noncompliance and 11 percent, severe noncompliance. Mild or moderate noncompliance was not significantly correlated with any psychosocial or demographic variables. A high noncompliance score was significantly associated ($p<0.05$) with family dysfunction, alcohol and drug abuse, psychiatric diagnoses (especially conduct disorder) and the number of readmissions per year. It was also associated with the only death in this population. *Discussion:* These data confirm that noncompliance is a significant problem in adolescent and young adult liver transplant recipients. Mild or moderate noncompliance does not appear to be necessarily associated with a poor outcome, but severe noncompliance is strongly associated with late post-transplant morbidity and mortality.

NR82 Monday May 4, 9:00 a.m.-10:30 a.m.

Magnesium In Menstrual-Related Mood Disorders

Donald L. Rosenstein, M.D., BPB, NIMH Bldg 10/3N238, 9000 Rockville Pike, Bethesda, MD 20892; Jeanette M. Hosseini, B.S., Ronald J. Elin, M.D., David R. Rubinow, M.D.

Summary:

Deficits in red blood cell (RBC) magnesium (Mg) levels have been reported in the luteal phase in women with menstrual-related mood disorders (MRMD). To address limitations of previous studies (e.g. single samples, single measures) we measured plasma, RBC and mononuclear blood cell (MBC) Mg across the menstrual cycle in 27 women with prospectively confirmed MRMD and in a control group of 19 women. Blood samples were collected at four weekly intervals, and ovulatory phase was determined in relation to subsequent menses. Data were analyzed using ANOVA-R. Significant diagnostic group effects were observed for RBC Mg and MBC Mg content and concentration ($p < .05$ for all). These effects reflected lower values in patients at each sampling time. No significant effects were observed for plasma Mg, nor were there significant time by diagnosis effects for any of the measures. Conclusions: consistent with earlier studies, we found decreased RBC Mg levels in women with MRMD; these decreases were not confined to the luteal phase, however. Further, the group differences for MBC content and concentration were seen only when data were analyzed by menstrual cycle phase (not week number). We suggest that disturbances in intracellular Mg may increase the risk of mood destabilization during the menstrual cycle.

NR83 Monday May 4, 9:00 a.m.-10:30 a.m.

Fluoxetine Versus Placebo In Treatment Of Late Luteal Phase Dysphoric Disorder

David E. Schenk, M.D., Psychiatry, Eisenhower Army Med., Fort Gordon, GA 30905; Charles Perrotta, Jr., M.D., James S. Williford, M.D., Joseph A. Whitfield, M.D., James P. Reed, M.D.

Summary:

Serotonin has been implicated in the control of pain symptoms as well as in the modulation of affective symptoms, irritability, aggression, and violence. Serotonin has also been postulated as a mediator of the many symptoms noted in Late Luteal Phase Dysphoric Disorder (LLPDD). The current study was conducted to examine the potential use of a selective serotonin reuptake inhibitor in the treatment of LLPDD. Women volunteers 18 to 40 years of age were evaluated for LLPDD under *DSM-III-R* criteria. Patients that met the prospective rating criteria were entered into a seven-month, double-blind, placebo-controlled crossover study to evaluate the efficacy of fluoxetine versus a placebo in the treatment of LLPDD. Symptom ratings were conducted on a daily basis and included both prospective and retrospective evaluations. Results of this study was well as implications for further research will be discussed.

NR84 Monday May 4, 9:00 a.m.-10:30 a.m.

Dopamine System in Schizotypal Personality Disorder

Farooq Amin, M.D., Psychiatry, VA Medical Center, 130 W. Kingsbridge Road, Bronx, NY 10468; Larry J. Siever, M.D., Robert Trestman, M.D., Jeremy Silverman, Ph.D., Peter Knott, Ph.D., George Anderson, Ph.D., Kenneth L. Davis, M.D.

Summary:

An involvement of dopamine (DA) system in schizotypal personality disorder (SPD) is hypothesized because of the close relationship of SPD to schizophrenia and the therapeutic response of SPD patients to neuroleptics. This hypothesis is supported by the preliminary findings of increased plasma homovanillic acid (HVA)levels in SPD patients compared to other personality disorders (PD) patients and normal controls, as well as by a positive correlation between plasma HVA and the severity of "psychotic-like" SPD traits (Siever et al, Am J Psychiat, 1991). In an extension of this study, plasma HVA levels continue to positively correlate with the severity of "psychotic-like" SPD traits in the total sample of SPD patients ($n=24$) ($r=40$, $p<.03$). A subsample of the total PD cohort ($n=22$ for CT, $n=13$ for WCST) were also evaluated by CT-scans and WCST (Wisconsin Card Sorting Test) both of which are associated with deficit-related symptoms in this sample. Preliminary data show that plasma HVA is negatively correlated with frontal horn ventricular-brain-ratio ($r=.52$, $p=.007$) and with WCST perseverative errors ($r=.57$, $p<.05$). These data raise the possibility of a bi-directional relationship between DA activity and SPD pathophysiology, with increased DA activity associated with "psychotic-like" SPD traints and reduced DA activity with structural/functional brain impairment.

NR85 Monday May 4, 9:00 a.m.-10:30 a.m.

Biology Of Impulsivity, Suicide And MDD In Axis II

Robert L. Trestman, M.D., Psychiatry, VA Medical Center, 130 W. Kingsbridge Road 116A, Bronx, NY 10468; Emil F. Coccaro, M.D., Susan Weston, M.D., Vivian Mitropoulou, M.A., Felice Ramella, B.A., Steven Gabriel, Ph.D., Larry J. Siever, M.D.

Summary:

On the basis of prior work, we hypothesized that 1) central noradrengeric (NA) dysfunction is associated with irritability or overreactivity to the environment, but not with violence per se, and that 2) central serotonergic (5-HT) dysfunction is associated with motoric impulsivity, assaultiveness and suicidal behavior in personality disorder (PD) patients. 39 patients from two medical centrs with *DSM-III* PD participated in this extension of a previous study (Coccaro et al, AGP 1989). The growth hormone (GH) response to IV clonidine, a measure of central α-$_2$ NA function, correlated with self-rated measures of irritability in all PD patients: (Buss-Durkee Hostility Inventory (BDHI) – Irritability: $r=0.28$, $p<0.07$; BDHI – Verbal Hostility: $r=0.37$, $p<0.03$) but not overt violence (BDHI – Assault: ns) or history of suicidal behavior; and in the male subgroup ($n=18$). Peripheral plasma NE levels also correlated with

these measures in the whole sample of PD patients and in the male subsample. Central 5-HT function was assessed with plasma prolactin response (delta PRL) to fenfluramine (FEN; 60 mg orally), a 5-HT releasing/uptake - inhibiting agent. The delta PRL was inversely correlated in males with several self-rated measures of impulsivity and aggression (n = 32; Barratt Impulsivity Scale (BIS) – Motor Impulsivity: r = −0.34, p<0.03; BDHI – Assault: r = −12 0.56, p<0.001), and both with history of suicide attempts (r = −0.27, p<0.07) and the medical lethality of the attempts (r = −0.33, p<0.03). Present or past history of major depression neither altered nor correlated with any of the above findings. The NA and 5-HT systems may therefore each contribute differentially to aspects of impulsivity and aggression. These findings are discussed in terms of hypothesized dimensions underlying PD diagnoses.

NR86 Monday May 4, 9:00 a.m.-10:30 a.m.

Cognitive Processes In Borderline Personality

Kathleen T. Hamblin, Ph.D., Research Inst., Chestnut Lodge, 500 West Montgomery Avenue, Rockville, MD 20850;

Summary:

To discover more bout the cognitive processes associated with splitting and borderline psychopathology, measures of simultaneous and successive information processing Disorder (BPD), and to 17 "normal" control females.

Each subject received a battery of simultaneous and successive processing tests. Measures of simultaneous processing were the Raven Advanced Progressive Matrices, Block Design, Visual Motor Integration, and Street Gestalt Test; measures of successive processing were the Digit Span, Serial Recall, Visual Short-Term Memory, and Visual Memory Span.

The performance of subjects with BPD and of control subjects was compared using a paired *t*-test and two 2-group MANOVAs.

Compared to controls, individuals with BPD performed significantly worse on measures of simultaenous (*p* .04), but not successive processing. Individuals with BPD did significantly worse overall on the simultaneous measures than they did on the successive measures (*p* .04).

Results suggest that individuals with BPD rely predominantly on a successive information processing style and, as a group, demonstrate impairment in simultaneous processing. These data suggest that therapeutic approaches, such as Linehan's, that emphasize assisting patients in sequentially ordering confusing interpersonal experiences may be of particular value to these patients.

NR87 Monday May 4, 9:00 a.m.-10:30 a.m.

Diagnosis Of BPD By Three Scales

Reed Goldstein, Ph.D., D. Garroway Lab., Inst of Penn Hospital, 111 N. 49th Street, Philadelphia, PA 19139; William G. Herron, Ph.D., Alan M. Gruenberg, M.D.

Summary:

Thirty inpatients and 30 outpatients provisionally diagnosed as having borderline personality disorder (BPD) by the Structured Clinical Interview for *DSM-III-R* Personality Disorders were then administered three additional diagnostic scales in order to determine the degree of concordance for the three most popular and psychometrically sound diagnostic instruments for BPD: (1) The Personality Diagnostic Questionnaire-Revised (PDQ-R), (2) The Personality Disorder Examination (Version:1985; PDE), and (3) The Diagnostic Interview for Borderlines (Revised: 1983; DIB). *Results:* Agreement above chance was found only for the PDE and PDQ-R for inpatients (Kappa = .52, *p*<.05) and for the PDE and DIB for outpatients (kappa = .29, *p*<.05). According to the DIB, 43 percent of inaptients and 46.7 percent of outpatients were diagnosed as borderline. The PDB and PDQ-R diagnosed 83.3 percent of inpatients and 76.7 percent of outpatients as borderline. *Discussion:* The borderline diagnosis is difficult to operationalize as demonstrated by the low rates of agreement between scales. Item construction of the different scales contributes to the understanding of differential rates of agreement of BPD diagnostic systems. The diagnosis of BPD as made by alternative semistructured interviews varies. BPD remains an idiosyncratic construct, difficult to define and measure, even if operational criteria exist.

NR88 Monday May 4, 9:00 a.m.-10:30 a.m.

BPD At three Sites

James J. Hudziak, M.D., Psychiatry, Washington Univ, 4940 Audubon Avenue, St. Louis, MO 63110; Todd J. Boeffeli, M.D., Samuel B. Guze, M.D., Jerold Kreisman, M.D., Marco M. Battaglia, M.D.

Summary:

patients assessed by their primary psychiatrist as meeting five of eight *DSM-III-R* criteria for borderline personality disorder were recruited from three different sites; the Washington University Adult Psychiatry Outpatient Clinic (N = 38), the Inpatient Borderline Treatment Unit at St. John's Hospital in St. Louis (N = 30) and the University of Milan in Milan, Italy (N = 12). Eighty-one of 83 patients referred met the more rigorous diagnostic interview for borderline-revised (DIB-R) and were included in the study. Comorbid Axis I diagnoses were assessed using *DSM-III-R* checklist interview and total diagnoses per patient were tabulated (average 5.1, 4.9, 3.8, respectively). Similarities between rates of panic disorder (55 percent, 47 percent, 50 percent), major depression (92 percent, 90 percent, 83 percent), somatization disorder (31 percent, 40 percent, 25 percent), alcohol abuse (45 percent, 47 percent, 50 percent), and other substance use disorders (20 percent, 27 percent, 33 percent) were found. Rates of the 17 other Axis I diagnosis will also be presented. Clinical histories were documented including sexual abuse (68 percent, 70 percent, 8 percent), physical abuse (52 percent, 33 percent, 0 percent), and family history of alcoholism (59 percent, 53 percent, 33 percent). Beck Depression Inventory Scores (25,28,25) and Perley-Guze hysteria criteria checklist items (22,22,20) were also obtained. Tridimensional Personality questionnaire results were: novelty seeking (18,16,19; norms = 13), harm avoidance (25,26,21; norms = 12.9), and reward dependence (19,20,19; norms = 21). Discussion of relationships between life events, diagnosis, important symptoms and personality profiles between the three sites will be presented.

NR89 Monday May 4, 9:00 a.m.-10:30 a.m.

Personality Disorders In Atypical Depression

Ron G. Goldman, M.D., Psychiatry, Columbia University, Box 35 722 West 168th Street, New York, NY 10032; Patrick J. McGrath, M.D., Deberah S. Goldman, Ph.D., Jonathan W. Stewart, M.D., Frederic M. Quitkin, M.D.

Summary:

Patients with major depression were assessed with the Structured Interview for *DSM-III-R* Personality Disorders (SCID-II) and the Tridimensional Personality Questionnaire (TPQ) at baseline, and a modified TPQ before and after treatment with open-label fluoxetine. Of 72 patients interviewed, personality disorders occurred in 31 (43 percent): a single diagnosis in 17 (24 percent), two disorders in 8 (11 percent), and three in 6 (8 percent). The most common diagnoses on Axis II were Avoidant PD, Borderline PD, Obsessive PD, and Dependent PD.

Sixty-five (90 percent) of the patients interviewed had atypical features, while 44 (61 percent) met criteria for atypical depression.

Axis II disorders occurred in 26 (59 percent) of the patients with definite atypical depression and were significantly more prevalent in this group compared to other categories (Chi square = 13.08, $p<.01$).

In 53 patients who completed a 10-12 week trial of open-label fluoxetine 20mg QD, comorbid personality disorder had no significant effect on response. Fluoxetine responders showed a significant decrease in harm avoidance, but no change in other personality dimensions assessed by the TPQ. Relationships between symptoms of atypical depression, Axis II disorders and personality dimensions will be presented.

NR90 Monday May 4, 9:00 a.m.-10:30 a.m.

Personality And Perceptual Asymmetry In Depression

Ron G. Goldman, M.D., Psychiatry, Columbia University, Box 35 722 West 168th Street, New York, NY 10032; Gerard E. Bruder, Ph.D., Jonathan W. Stewart, M.D., Patrick J. McGrath, M.D., Deberah S. Goldman, Ph.D., Frederic M. Quitkin, M.D.

Summary:

Fifty-five patients with *DSM-III-R* major depression completed the Tridimensional Personality Questionnaire (TPQ) and underwent assessment of perceptual asymmetry by dichotic listening with fused word, fused syllable, and complex tone tests. Based on published studies of emotion and hemispheric arousal, we predicted that novelty seeking would be positively correlated with right ear advantage (REA) for verbal tasks, reflecting greater left hemisphere activation. In contrast, harm avoidance would be negatively correlated with REA. The results were consistent with these predictions: Novelty seeking was positively correlated with REA for dichotic words ($r=.32$, $p<.01$) and harm avoidance was inversely correlated with REA for fused syllables ($r=-.23$, $p<.05$). Also, 27 depressed patients were assessed with the Structured Interview for *DSM-III-R* Personality Disorders (SCID II). The number of Paranoid ($r=-.66$, $p<.001$), Narcissistic ($r=-.51$, $p<.01$), Dependent ($r=-.48$, $r<.02$), Obsessive ($r=-.48$, $p<.02$), and total Cluster C traits ($r=-.51$, $p<.01$) was associated with less left ear advantage (LEA) for complex tones, reflecting diminished right hemisphere superiority. In contrast, the number of Schizoid traits ($r=.54$, $p<.01$) was associated with greater LEA. This latter result is consistent with findings in schizophrenia.

NR91 Monday May 4, 9:00 a.m.-10:30 a.m.

Severity Of Sleep Apnea And Degree Of Psychopathology

Rocco L. Manfredi, M.D., Psychiatry, Penn. State Univ., 500 University Drive, Hershey, PA 17033; Anthony Kales, M.D., Alexandros N. Vgontzas, M.D., Edward O. Bixler, Ph.D., David Myers, B.A.

Summary:

Secondary psychopathology is frequently present in patients with severe sleep apnea. In order to explore the underlying etiological factors of this psychopathology, this study examined the relationship between psychopathology and severity of apnea at baseline and following treatment in 25 patients who had obstructive sleep apnea of severity sufficient to warrant recommendation for tracheostomy. Measurements included the MMPI immediately before and six months after tracheostomy. At baseline compared to controls, five scales were significantly elevated for the apneics, with the three highest scales being Hypochondriasis, Depression, and Hysteria. Severity of apnea as measured by the total number of apnea-hypopnea events and maximum oxygen desaturation was negatively correlated with degree of psychopathology, indicating that less severe apnea was associated with higher degree of reported psychopathology. It may be that patients with severe sleep apnea report less psychopathology because of their higher degree of cognitive impairments. Following treatment, there was a significant improvement in the mean scores of three of the elevated scales and marked improvement in the other two. The most improvement was seen among the less severe apneics, while the more severe subgroup showed minimal change. The findings indicate that the relationship between severity of apnea and psychopathology appears to be an inverted U-shape.

NR92 Monday May 4, 9:00 a.m.-10:30 a.m.

Sleep Apnea: Cognitive Deficits Are Not Mood Related

Alexandros N. Vgontzas, M.D., Psychiatry, Penn. State Univ., 500 University Drive, Hershey, PA 17033; Ralph A.W. Lehman, M.D., Rocco L. Manfredi, M.D., Edward O. Bixler, Ph.D., Lynne Curran, B.A.

Summary:

Psychopathology, which is frequently a result of sleep apnea, may adversely affect patient performance in neuropsychological testing. In a previous report we showed that severe sleep apnea is linked to irreversible verbal/cognitive deficits significantly correlated to the severity of apena. In this study, the potential role of psychopathology on these cognitive deficits was evaluated. Twenty-five patients who had obstructive sleep apnea of severity sufficient to warrant recommendation for tracheostomy were assessed for severity of apnea, neuropsychological function and associated psychopathology immediately before and approximately six months after tracheostomy. At baseline there was significant psychopathology; the three highest elevated MMPI scales were, in descending order, 1 (Hypochondriasis), 2 (Depression), and 3 (Conversion Hysteria). However, there was no significant correlation between these three highest MMPI scales and deficits on the WAIS-R scales of Verbal IQ (VIQ), Performance IQ (PIQ) and Full Scale IQ (FSIQ). Further, there was no significant correlation between pre- to post-treatment changes in MMPI and WAIS-R scores. These findings indicate that secondary psychopathology associated with sleep apnea is not a significant causative factor of verbal/cognitive deficits in these subjects. Further, our current results confirm and expand our previous findings and conclusions that hypoxia is the primary causative factor of the cognitive deficits associated with severe sleep apnea.

NR93 Monday May 4, 9:00 a.m.-10:30 a.m.

Sleep Disturbances In Chronic Fatigue Syndrome

Jon K. Zubieta, M.D., University of Michigan, 1500 East Medical Center Drive, Ann Arbor, MI 48109; Mark A. Demitrack, M.D., Dean Krahan, M.D., N. Cary Engleberg, M.D., James E. Shipley, M.D., Alan B. Douglass, M.D.

Summary:

Chronic fatigue syndrome (CFS) is an idiopathic disorder characterized by persistent, relapsing fatigue, feverishness, diffuse pains, and other constitutional complaints. Sleep disturbances are frequently reported by these patients and comprise one of the operationalized criteria for its diagnosis. Characterization of sleep phenomenology in CFS patients may help in: 1) clarifying its relationship to other known clinical syndromes, and 2) targeting specific therapeutic interventions.

We have previously shown that the Sleep Disorders Questionnaire (SDQ), a 175-item, self-report questionnaire, reliably differentiates among sleep disturbances due to either primary dyssomnias or psychiatric illnesses. In this study, we compared SDQ scores in a consecutive series of 37 patients presenting with a chief complaint of chronic (>6 months), idiopathic fatigue, with

those of a comparison sample of patients diagnosed with narcolepsy (n = 73), sleep apnea (n = 158), nocturnal myoclonus (n = 96), or major depressive episode (n = 108), and a group of healthy individuals (n = 94). The fatigued subjects consisted of 27 individuals who met the Centers for Disease Control (CDC) criteria for CFS, and ten with sybsyndromal CFS. Notably, the response patterns of fully syndromal or subsyndromal fatigue subjects did not differ on any of the SDQ scales, lending further support to the idea that the CDC definition does not readily discriminate a group of patients distinct from the larger population of individuals with idiopathic fatigue. As a group, fatigued patients reported a pattern of sleep interruption, non-restorative sleep, a nocturnal excess of physical movements, and a chronic anhedonia. These disturbances are significantly less than those reported by either depressed patients or patients with nocturnal myoclonus. On the other hand, they are significantly worse than those seen in normal individuals.

NR94 Monday May 4, 9:00 a.m.-10:30 a.m.

Residents' Attitudes Toward Suicidal Patients

Helen M. Biren, M.D., Psychiatry, UCLA, 760 Westwood Plaza, Los Angeles, CA 90024; William C. Wirshing, M.D., Joel Yager, M.D.

Summary:

The acutely suicidal individual is among the most emotion-provoking of emergency room (ER) patients seen by psychiatrists in residency training. The dispositional decisions made about these patients (e.g., involuntary admission, outpatient referral, pragmatic crisis intervention) are probably determined by a constellation of factors including individual resident characteristics, professional experience, and the training institution's attitude. To assess the impact of residency training on this decision-making process, 122 residents were surveyed with a questionnaire designed to quantify the respondents' tendency to admit a variety of hypothetical ER patients. A total of 57 residents returned the survey. Gender, year in residency, experience with patients who attempted or completed suicide, and therapeutic orientation (on a self-rated biologic-to-pyschotherapeutic continuum) demonstrated no relationship to residents' tendency to admit. The total experience with patients who had threatened suicide was positively related to tendency to admit (i.e., greater experience correlated with an increased tendency to admit; $r = 0.44$, $p = 0.038$). Little variability across the group, though, was accounted for by threatened suicide experience and other unsurveyed, nontraining-based factors (e.g., preconceived attitudes) are probably of greater importance.

NR95 Monday May 4, 9:00 a.m.-10:30 a.m.

Suicide In 336 Acute Patients: A Five-Year Follow-Up

Anelise Muhiebach, Ph.D., Psychiatry, University of Geneva, Rue Des Vollandes 69, Geneva, GE 1207, Switzerland; Antonio V. Andreoli, M.D., Gabriel Bittar, Ph.D.

Summary:

Significance: In order to test the hypothesis of increased suicide risk in acute psychiatric patients, particularly in males and during the first two years of follow-up, we carried out a five-year follow-up study. *Methods:* 336 consecutive patients (187 females, 149 males), age range 18-65, referred for psychiatric hospitalization/outpatient crisis intervention during one year (1985) in a catchment area were studied. The causes of death were determined using the Swiss Register of deaths. Observed suicide rates were compared with expected suicide rates in general population (Standardized Mortality Ratio, SMR). *Results:* 16 patients (4.8 percent) had died by suicide at five-years follow-up, giving a ratio (SMR) 51 times higher than in general population. Another 81 percent of suicides occured during the two first follow-up years. Male sex was not associated with increased suicide rates ($p = 0.13$) at follow-up. Furthermore, suicide ratios in both sexes were increased in the same proportion compared with population norms (Males SMR = 31. (Females SMR = 34.2). Females had increased SMR (68.3) within the first year and decreased SMR (34.4) after the second follow-up year, compared to males (SMR = 40.9; SMR = 53.9) who present more constant suicide rates during the five years. *Comment:* Our results suggest that being a psychiatric patient seems to be in itself a factor increasing suicide rates, independently of sex. However, our results showed that the periode of greatest risk is different in males and in females. Further research should determine whether this difference results from specific characteristics of these subjects and their disorders.

NR96 Monday May 4, 9:00 a.m.-10:30 a.m.

Assaults On An Inpatient Ward

Martha L. Crowner, M.D., Research, Manhattan Psych. Center, Ward's Island, New York, NY 10035; Brian Anderson, M.D., Menahem Krakowski, M.D., Jan Volavka, M.D.

Summary:

We have installed a closed-circuit television camera system on a specialized ward for the treatment of violent patients in a state psychiatric hospital in order to record and analyze assaults between patients. Cameras are mounted in a large dayroom where they record during daytime hours. Patients themselves and the ward environment have also been studied. We hypothesize that assaults can be better predicted when patient and environmental characteristics and patients' behavioral cues are taken into account. In 23 months of videotaping we have studied 102 patients and 133 assaults. Of the patients 72 percent were male and 70 percent were Black. The mean age was 42. A total of 40 percent were schizophrenic, 32 perent had affective illness, and 24 percent had organic disorders.

There were detectable cues or patient behaviors occuring before assaults significantly more often than before time periods not involving assaults. A total of 34 percent of cues occured within 15 seconds of the assault. The BPRS activation factor was higher in patients involved in assaults compared to those not involved, while the total score and other factors for the same time period before assault did not differ. Patient/staff ratio was not significantly related to assault.

These data and others and their implications for the prediction and management of inpatient assaultiveness will be discussed.

NR97 Monday May 4, 1:00 p.m.-2:30 p.m.

Blood Pressure Change and Memory Deficit in ECT

Ioannis M. Zervas, M.D., Psychiatry, Suny at Stony Brook, HSC T10 Suny at Stony Brook, Stony Brook, NY 11794; Lina Jandorf, M.A., Max Fink, M.D.

Summary:

Twenty-three psychiatric inpatients, mean age 52.7 years, 60.9% female, were treated with electroconvulsive therapy for major depressive disorder. Memory measures were obtained at baseline and during the subacute period of memory disturbance after the course of ECT. Serial blood pressures were recorded during the ECT course, and the mean arterial blood pressure change was calculated. Correlation analysis indicated that mean arterial blood pressure changes significantly correlated with ($r : 0.53$, $p<0.01$), and in fact predicted ($F = 12.05$, $p<0.01$) the ECT-specific anterograde memory deficit. We argue that this may represent a valuable peripheral index of cerebral processes rather than being the cause of the amnestic effects.

NR98 Monday May 4, 1:00 p.m.-2:30 p.m.

High-Dose of Glycine in the Treatment of Schizophrenia

Ilana Z. Nussenzveig, M.D., Psychiatry, Albert E. College of Med., 1300 Morris Park Ave F-111, Bronx, NY 10461; Daniel C. Javitt, M.D., Gail S. Silipo, M.A., U. Heresco-Levy, M.D., Jean-Pierre Lindenmayer, M.D., Stephen R. Zukin, M.D.,

Summary:

Phencyclidine (PCP) induces a psychotomimetic state that closely resembles schizophrenia. Compared with other drug-induced model psychosis, PCP-induced psychosis uniquely reproduces the degree of negative symptomatology and cognitive dysfunction in schizophrenia by binding to a specific brain PCP receptor at which it antagonizes excitatory *N*-methyl-D-aspartate (NMDA) receptor-mediated neurotransmission. Glycine stimulates NMDA receptor functioning and, in animals, may ameliorate PCP-induced behavioral effects. Our study investigates whether glycine, added adjunctively to neuroleptics, ameliorates negative symptomatology and cognitive dysfunction in schizophrenia. Schizophrenic subjects with moderate-severe symptomatology despite neuroleptic treatment were stabilized on their medications and randomly assigned to receive adjunctive therapy with glycine (0.4 g/kg/day) or placebo for eight weeks. At the conclusion of the double blind, subjects were treated with open-label glycine (0.4 g/kg/day) for eight weeks. Glycine promoted a significant improvement in negative symptomatology as measured by the Positive and Negative Syndrome Scale, compared to both prestudy (mean = 16.7%, ste = 5.2%, n = 9, $p<0.02$) and pre-open-label (mean = 16.3%, ste = 3.4%, n = 9, $p<0.002$) levels. A trend towards improvement in cognitive symptoms occurred as well. WCST performance improved in five of seven subjects studied. These findings suggest that interventions at NMDA receptor may provide novel approaches for treatment of schizophrenia.

NR99 Monday May 4, 1:00 p..-2:30 p.m.

One Hundred Years of Schizophrenia

James D. Hegarty, M.D., Psychiatry, Harvard Medical, McLean Hosp 115 Mill Street, Belmont, MA 02178; Mauricio Tohen, M.D., Ross J. Baldessarini, M.D.

Summary:

A meta-analysis of the schizophrenia outcome literature was performed by searching Index Medicus (1895-1965) and Medline© (1966-1992). Inclusion required a diagnosis of schizophrenia or dementia praecox, mean follow-up of ≥1 year, <33% loss to follow-up, ≥15 patients followed and information on proportions of subjects with defined clinical, social or vocational outcome. In all, 817 studies were identified; 260 were excluded because of inadequate duration, size or follow-up, and 557 were reviewed in detail, of which all criteria were met by N = 359. The meta-analysis examined outcome as a function of diagnostic system, treatment, duration and era. There was considerable improvement in mean outcome between 1930 and 1970 ($p<0.01$). This has been attributed to new treatments, particularly convulsive therapy (1936) and neuroleptics (since 1952), as well as an increased emphasis on family and community supports (1960s). However, between 1970 and 1992 outcomes have worsened such that there was no significant difference found between outcomes before 1930 and after 1970. We conclude that changes in the criteria for the diagnosis of schizophrenia, more than new treatments or improved social supports, account for both the apparent improvement in outcomes between 1930 and 1970, and the less favorable outcomes since 1970.

NR100 Monday May 4, 1:00 p.m.-2:30 p.m.

Cocaine-Ethanol and Cocaethylene: Clinical Effects

Elinore F. McCance-Katz, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Lawrence H. Price, M.D., Christopher J. McDougle, M.D., Jed E. Black, M.D., Thomas R. Kosten, M.D., Peter I. Jatlow, M.D.

Summary:

Simultaneous abuse of cocaine and ethanol is a common occurrence. Cocaethylene (EC), the ethyl ester of benzoylecgonine, has been detected in the urine of patients reporting concurrent use of cocaine and ethanol, and high levels have been found in the blood of victims of fatal drug overdose. This study prospectively evaluated the interaction of cocaine and ethanol in humans. METHOD: Four double-blind, placebo-controlled, intranasal cocaine (2 mg/kg) oral ethanol (1 g/kg) challenges were administered to subjects (n = 6). Physiological and subjective measures, plasma cocaine, EC, and ethanol levels were assessed. Results showed that EC was found in the plasma only following administration of both cocaine and ethanol. Peak plasma EC concentration was about ⅕ that of cocaine. The apparent elimination half-life of EC was 148 ± 15 minutes, about twice that observed for cocaine. Cocaine levels following cocaine/ethanol administration were significantly higher than during cocaine alone ($p<0.001$). Euphorigenic effects were both more intense and prolonged, and heart rate was significantly increased, following cocaine/ethanol administration as compared with administration of cocaine or ethanol alone. This study confirms that EC is formed in humans following coadministration of cocaine and ethanol and may contribute to physiological and behavioral effects.

NR101 Monday May 4, 1:00 p.m.-2:30 p.m.

Carbamazepine Use in Geropsychiatric Patients

Stephen M. Aronson, M.D., Psychiatry, Univ of Michigan, 1500 E. Medical Center Dr 0704, Ann Arbor, MI 48109-0704; Alan M. Mellow, M.D.

Summary:

The efficacy and safety of carbamazepine (CBZ) in elderly psychiatric patients have not been adequately studied, despite the increasing frequency of its use in bipolar disorder and in the treatment of behavioral symptoms in dementia. We reviewed the records of inpatients over 60 years of age at a chronic-care VA hospital who had received CBZ for at least four consecutive weeks during 1989-1991. We assessed severity of illness and measured improvement using the Clinical Global Impressions Scale (CGI). Sixty-three patients (mean age: 67.3 ± 5.3 yrs) were identified: 33% of patients had a mood or psychotic disorder; 50% had dementia of various clauses. The remaining 12 patients had other neuropsychiatric diagnoses. A total of 79% (50/63) derived benefit from CBZ, with 50% (32/63) showing moderate to marked improvement by CGI scores; 21% (13/63) had no change in severity of symptoms. Mean CBZ level was 7.2 μg/ml; mean CBZ dose was 738 mg/day. CBZ was well tolerated; side effects required discontinuation of the medication in only one patient. Our findings suggest that CBZ is an effective therapeutic agent in several neuropsychiatric disorders in the elderly. We will discuss demographic and clinical correlates of response, including subtype of dementia, CBZ blood levels, and concomitant psychotropic medications. Anticonvulsants such as CBZ are increasingly important psychopharmacologic interventions in the elderly, due to the limited efficacy of neuroleptic agents in the treatment of behavioral symptoms in dementia, as well as demographic changes that have resulted in larger numbers of patients with cyclical mood disorders surviving into old age.

NR102 Monday May 4, 1:00 p.m.-2:30 p.m.

Treatment of Older Depressives in a Geropsychiatry Versus General Psychiatry Clinic: A Comparison Study

Nusrath Hasan, M.D., Psychiatry, Hillside Hospital, P.O. Box 38 Lowenstein Res Bld, Glen Oaks, NY 11004; Elisse Kramer-Ginsberg, Ph.D., Blaine S. Greenwald, M.D., Jorge Ramos-Lorenzi, M.D., Peter Aupperle, M.D., Neil Kremen, M.D.

Summary:

Geriatric psychiatry has achieved increasing subspecialty recognition; however, few empirical studies actually document more informed treatment of elderly patients in focused geropsychiatric programs. To evaluate whether psychopharmacologic treatment of elderly depressives differs in a specialized geropsychiatry clinic, psychotropic prescription practices were compared between 65+ year olds with unipolar major depression in a general adult psychiatry clinic ($n=21$) and a geropsychiatry clinic ($n=26$) at the same institution. Mean age, number of medical illnesses, and number of past depressive episodes were similar between general and geropsychiatry patients. Use of agents associated with greater risk of adverse effects in the elderly, but not greater efficacy, were examined. No geropsychiatry patients, but 40% of general patients received a tertiary tricyclic antidepressant ($p<.05$). Among benzodiazepine prescriptions, 20% of geropsychiatry patients vs. 67% of general patients received a long-acting drug. use of newer antidepressants and adjunctive psychotropics were similar between clinics. Cognitive ratings were conducted in 58% of geropsychiatry and 0% of general patients ($p<.0001$). Postural blood pressure monitoring was documented in 39% of geropsychiatry patients vs. 0% of general patients ($p<.01$). Data suggest significant clinical benefits are associated with specialized geropsychiatry care and that clinicians in nongeriatric treatment settings may require refreshers in cognitive assessment, geriatric psychopharmacology, and side-effect monitoring. Prospective comparisons of geriatric and nongeriatric mental health treatment settings to evaluate outcome and cost effectiveness are indicated.

NR103 Monday May 4, 1:00 p.m.-2:30 p.m.

Fluoxetine and Bupropion in Old-Old Depressives

Barry Mildener, M.D., Psychiatry, Hillside Hospital, P.O. Box 38 Lowenstein Res Bld, Glen Oaks, NY 11004; Elisse Kramer-Ginsberg, Ph.D., Blaine Greenwald, M.D., Neil Kremen, M.D., Peter Aupperle, M.D., Rosanne Leipzig, M.D.

Summary:

Almost no data are available on fluoxetine and bupropion in "old-old" patients. An extensive chart review investigation was conducted on 67 psychiatric inpatients over age 75 who met *DSM-III-R* criteria for major depression and were prescribed fluoxetine or bupropion during the past three years. Mean ages of fluoxetine ($n=40$) and bupropion ($n=27$) patients were 81 ± 4 and 82 ± 5 years, respectively. Tricyclics (79%), MAOIs (3%), and ECT (62%) had previously been prescribed. Forty-six percent of bupropion patients had received fluoxetine, while only 8% of fluoxetine patients had received bupropion. Cardiac conduction disturbances and prior antidepressant intolerance or lack of efficacy were largely the reasons for newer antidepressant prescription. Mean dosages of fluoxetine and bupropion were 25 ± 13 mg and 241 ± 106 mg, respectively. Both drugs achieved remission after five to six weeks in 50-60% of patients. Anxiety/agitation (80% fluoxetine; 50% wellbutrin), insomnia (20% fluoxetine; 50% wellbutrin), and psychosis (0% fluoxetine; 17% wellbutrin) were common side effects. No fluoxetine patients developed suicidality. At discharge, antianxiety medications were adjunctively prescribed in 86% of fluoxetine and 69% of wellbutrin patients. Conclusions include: (1) fluoxetine and bupropion are reasonably tolerated alternative antidepressants in octogenerians; (2) anxiety was a remarkably frequent adverse effect, especially with fluoxetine; (3) possibly as a consequence, adjunctive anxiolytics were regularly prescribed, further exposing this population to psychotropic polypharmacy; (4) fluoxetine appears to be more readily prescribed than wellbutrin; (5) MAOIs are probably underutilized in "old-old" depressives; (6) prospective, double-blind studies of wellbutrin and fluoxetine are needed in this population.

NR104 Monday May 4, 3:00 p.m.-5:00 p.m.

Effects of Depression and ECT on Subjective Memory

Eliza A. Coleman, B.A., Psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; Harold A. Sackeim, Ph.D., Joan Prudic, M.D., D.P. Devanand, M.D.

Summary:

Patient self-evaluation of memory functioning is a critical domain in assessing effects of electroconvulsive therapy (ECT). Sixty-one patients were randomized to either low-intensity (near threshold) or high-intensity(150% above threshold) treatment and to either right-unilateral or bilateral ECT. The Squire Memory Self-Rating Questionnaire (SMRQ) was administered, using traditional scoring and a new method to quantify explicit memory complaints. Depressed patients reported markedly improved memory functioning both a few days and two months following ECT, relative to pre ECT. Change in clinical state, as assessed by the Hamilton Rating Scale for Depression, was a potent predictor of change in SMRQ scores. Effects of type of ECT were observed only after statistical control for changes in depressive symptomatology. Patients who received high-intensity treatment reported less SMRQ improvement. There were no effects attributable to electrode placement (unilateral vs. bilateral). These findings suggest that: (1) the vast majority of depressed patients report improved memory functioning shortly following ECT; (2) the extent of this improvement covaries strongly with the reduction of depressive symptoms; (3) effects of ECT treatment technique are manifest only after control for clinical change, and high-intensity stimulation may result in less improvement in subjective memory reports.

NR105 Monday May 4, 3:00 p.m.-5:00 p.m.

Psychodynamic Defenses in Dysthymia

Amy L. Bloch, M.D., Psychiatry, Payne Whitney Clinic, 525 East 68th Street, New York, NY 10021; John M. Markowitz, M.D., M. Katherine Shear, M.D., Andrew C. Leon, Ph.D., Elizabeth Winkelman, Frederick Busch, M.D.

Summary:

Introduction: The psychodynamic approach to dysthymia has rarely been empirically tested. Using the Defense Mechanism Rating Scale (DMRS), a new tool for assessing defensive functioning, we compared defenses of dysthymic(D) and panic disorder(P) subjects to test two psychodynamic hypotheses: (1) As D and P are neurotic illnesses, both will favor immature defense mechanisms; (2) As the symptoms of D and P differ, D subjects will endorse a distinct pattern of defense mechanisms.

Methods: Twenty D and 20 P subjects, diagnosed using DSM-III-R by SCID interview, underwent videotaped psychodynamic interviews. Two of six trained raters, blind to hypotheses, developed consensus ratings for each subject, achieving acceptable interrater reliability. DMRS generates a Defense Maturity Score (1 = low, 7 = high) from 28 operationalized defense mechanisms that cluster into eight maturity levels (mature, obsessional neurotic, narcissistic, disavowal, fantasy, borderline, and action). Chi square and T tests compared findings between groups.

Results: There was no significant difference ($t=.11$, $p=.92$) in mean overall maturity scores for D ($\bar{x}=2.44$, $SD=.57$) and P ($\bar{x}=2.45$, $SD=.61$). However, dysthymics scored significantly

higher in the narcissistic ($t=2.62$, $p=.01$), borderline ($t=2.48$, $p=.02$), and action ($t=2.92$, $p<.01$) levels. Significantly greater proportions of dysthymics endorsed the defenses of devaluation (75% vs. 25%; $x^2=8.1$, $p<.01$), projection (35% vs. 0%; $x^2=6.2$, $p=.01$), and hypochondriasis (45% vs. 5%; $x^2=6.5$, $p=.01$).

Discussion: Findings supported both hypotheses. Both groups had similarly low maturity scores. Dysthymics preferentially used specific defense mechanisms compared with P subjects. If further studies confirm these results, therapists could anticipate defensive styles in preparing treatment strategies.

NR106 Monday May 4, 3:00 p.m.-5:00 p.m.

Defining Remission in Major Depression

Markus Peter Fickinger, M.D., Psychiatry, Univ of Mainz, Untere Zahlbacher Strasse 8, Neinz 6500, Germany; Michael H.M. Philipp, M.D.

Summary:

Keller and Shapiro (1981) proposed a clinically based definition of remission in major depression. Frank et al. (1991) have recently stressed the importance of empirically validating this and other episode-related definitions. We have analyzed the follow-up data on 66 patients with non-bipolar major depression and used the DSM-III-R definition for comparing five possible syndrome cut-offs (0/1 to 4/5) to define remission. We could show that the episode length relies heavily on the cut-off definition: defining remission as disappearance of the last item-defining symptom (cut-off 0/1) results in a median length of 48 weeks; defining remission by the drop of the syndrome score below 5 (cut-off 4/5) leads to a much shorter median of four weeks. A comparative validation was done using two criteria: a) optimizing the distinction between episode and residual state, and b) maximizing the difference between the length of single and recurrent episodes. For both criteria, the syndrome cut-off ¾was highest in validity. We suggest using this cut-off in follow-up studies of major depression, because it is the first definition that is founded on an empirical data base.

NR107 Monday May 4, 3:00 p.m.-5:00 p.m.

Elevated Platelet Membrane Phosphatidylinositol-2 in Bipolar Mania

Alan S. Brown, M.D., 329 Windsor Road, Englewood, NJ 07631; Alan G. Mallinger, M.D.

Summary:

The phosphoinositide cycle is emerging as a major second messenger signal transduction system that may play an important role in the biologic mechanisms underlying psychiatric illnesses. The purpose of our study was to determine whether bipolar manic patients had an elevated relative quantity of platelet membrane phosphatidylinositol-4,5-bisphosphate (PIP-2), a phospholipid (PL) that mediates the action of several neurotransmitters. We employed a novel method of quantitating nanomolar amounts of membrane PL's utilizing extraction with methanol : chloroform : HC1, separation by two-dimensional high performance thin layer chromatography, and quantitation by scanning laser densitometry. Nine membrane PL's were measured in platelets of six medication-free patients in the manic phase of bipolar affective disorder (mean age 38.7 ± 11.4; two men, four women) and six healthy controls (mean age 30.2 ± 71; three men, three women). The bipolar manic subjects had a significantly increased relative percentage of PIP-2 (0.53 ± 0.21) then the controls (0.19 ± 0.12) ($p<.01$); no significant differences were found with respect to the remaining eight PL's. Given numerous similarities between platelets and neurons, these results are consistent with increased neuronal responsiveness in bipolar mania, which may produce enhanced neurotransmitter release after 5-hydroxytryptamine (5HT-2) receptor stimulation, since the resulting hydrolysis of excessive PIP-2 after G protein activation leads to intraneuronal calcium release, followed by secretion of neurotransmitters.

NR108 Monday May 4, 3:00 p.m.-5:00 p.m.

Clomipramine Augmentation in Resistant Depression

Martin H. Rosenzweig, M.D., Psychiatry, Depression Research, 36th Spruce St. 1-Gibson HUP, Philadelphia, PA 19104; Jay D. Amsterdam, M.D.

Summary:

As many as 30% of depressed patients fail to respond to treatment with a tricyclic antidepressant (TCA). The substitution of clomipramine or a monoamine oxidase (MAO) inhibitor is often beneficial. Moreover, the combination of a MAO inhibitor with a TCA has also been shown to be of value in treatment resistant depression.

We examined the outcome of clomipramine augmentation in 20 patients (six men and 14 women) with a mean ± SD age of 42 ± 12 years who failed to respond to either fluoxetine or MAO inhibitor treatment for at least eight weeks duration. Results demonstrated that two out of nine (22%) patients on a MAO inhibitor and four of 11 (36%) patient on fluoxetine had improvement with clomipramine augmentation ($X^2=3.117$, $p=0.077$). Serious side effects with the clomipramine/MAO inhibitor combination were not uncommon and were characterized by symptoms of the serotonin syndrome, including restlessness, myoclonus, diaphoresis and tremor. These data indicate that clomipramine augmentation of a failed MAO inhibitor trial should be used with extreme caution due to a high likelihood of significant side effects.

NR109 Monday May 4, 3:00 p.m.-5:00 p.m.

MDD State Dependent Cortisol Response to Clonidine

Julia Temple, M.D., Psychiatry, Mt. Sinai Medical School, One Gustave L. Levy Pl Bx1230, New York, NY 10029; Robert L. Trestman, M.D., Emil Coccaro, M.D., Vivian Mitropoulou, M.A., Felice Ramella, B.A., Steven Gabriel, Ph.D., Larry J. Siever, M.D.

Summary:

In an attempt to understand the relationship between the hypothalamo-pituitary-adrenal (HPA) axis and the noradrenergic system in patients with major depression, 26 normal controls (age 47 ± 16), 32 acutely depressed patients (53 ± 11) and 21 patients with remitted depression (53 ± 11), all male, were studied, Subjects were administered intravenous clonidine, a centrally acting α-2 adrenergic agonist (2 ≒g/kg) or placebo. Plasma cortisol was measured at baseline and at 15-minute intervals for one hour. All subjects were drug-free for two weeks, were on a low monoamine diet for three days, and fasted overnight prior to testing. Cortisol was measured by RIA. Acutely depressed patients had a significantly greater average decrease in plasma cortisol in response to clonidine than to placebo whether measured by absolute decrease ($t=2.5$, $p<0.02$) or by percentage decrease ($t=2.5$, $p<0.02$) or by percentage decrease ($t=2.5$, $p<0.02$) with or without covariation for age. Neither the normal controls nor the remitted depressed patients had a significant difference in plasma cortisol response following clonidine challenge as compared to placebo. There were no significant group differences in baseline or time by group interactions by ANOVA. These results provide conditional support for a state-dependent noradrenergic-HPA axis regulatory disturbance in depressed patients, replicating previous studies suggesting that clonidine inhibits plasma cortisol in depressed patients but not in normal controls and extending them to suggest that this phenomenon is state dependent.

NR110 Monday May 4, 3:00 p.m.-5:00 p.m.

Measures of Serotonin Function After Sleep Deprivation

Ronald M. Salomon, M.D., Psychiatry, Yale School of Medicine, 950 Campbell Avenue, West Haven, CT 06516; Pedro L. Delgado, M.D., Helen L. Miller, Julio Licinio, M.D., Dennis S. Charney, M.D., George R. Heninger, M.D.

Summary:

Sleep deprivation (SD) improves mood in depressed patients by unknown neurobiological mechanisms. Most antidepressant medications enhance brain serotonin (5HT) function. This study assesses 5HT function during SD in depression. *Method:* Five drug-free depressed patients received, in a rater-blind protocol, intravenous *l*-tryptophan (L-TRP) (100 mg/kg) after a night of undisturbed sleep (US) and again after a night of SD. Repeated ratings of mood (Hamilton Depression Scale (HAM-D)) and blood for prolactin (PRL), cortisol, and growth hormone were collected at baseline prior to the L-TRP infusion and at 30, 60, 90, 120, 150, and 180 minutes after the infusion. *Results:* SD resulted in an improvement of mood ($\geq$10 pt decrease in total HAM-D) in three of five of these drug-free depressed patients. The mean decrease in total Ham-D score for the five patients was 13 after SD but only three after US. Hormone data is available for four of the five patients. PRL response to L-TRP infusion was greater after SD than after US in three of four subjects. Their mean ΔPRL (peak minus baseline) was 2.7 ng/ml after US and 9.6 ng/ml after SD. *Implications:* SD improved mood in 60% of these depressed patients, consistent with previous literature. Preliminary data suggest that as with other AD treatments, SD causes an enhanced response to L-TRP infusion. Data on the relationship between ΔPRL response to L-TRP infusion and the improvement of mood are currently being obtained.

NR111 Monday May 4, 3:00 p.m.-5:00 p.m.

Idazoxan: Effects on Catechols and Depression

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Summary:

Measurement of norepinephrine (NE) function and output in depression consistently points to some degree of abnormality. Both unipolar (UP) and bipolar (BP) patients have an elevated excretion of NE and normetanephrine (NMN) relative to total catecholamines and an exaggerated rise in plasma NE with orthostatic challenge. A possible mechanism for these changes is subsensitivity of α_2 autoreceptors, a hypothesis supported by studies on platelet α_2 receptors in depressed patients. We therefore initiated a study of a selective α_2 antagonist, idazoxan (IDX), for its effects on catecholamine parameters and as a possible antidepressant. We gave IDX for six to eight weeks under double-blind conditions at 80-120 mg/day either alone or in combination with lithium to 13 depressed patients with UP, BPI or BPII mood disorder. Baseline NE measures were obtained after four weeks drug free and were compared to those after four to six weeks of IDX. Out of six patients who responded (a 3 point or more reduction in the average daily Bunney-Hamburg rating), only one of seven UP responded compared to give of six BP patients. Urinary MHPG (a measure of total turnover) decreased ($p<.07$), while the (NE + NMN)/MHPG + VMA ratio (an index of extraneuronal NE) increased ($p<.001$). CSF MHPG decreased. Basal and post-orthostatic challenge plasma NE increased. The differential changes in plasma NE, turnover measures, and the ratio are consistent with an increase in extraneuronal NE and a centrally mediated reduction in sympathetic outflow (indexed by MHPG), mediated through central and peripheral α_2 blockade. In spite of some common abnormalities of NE in UP and BP depression, our clinical and biochemical data suggest that α_2 regulation may have a unique role in the pathophysiology or treatment of the bipolar form.

NR112 Monday May 4, 3:00 p.m.-5:00 p.m.

Fluoxetine Reduces CSF, CRH and Arginine Vasopressin in Depression

Michael D. De Bellis, M.D., CNE Branch, NIMH Bldg 10 RM 3S231, 9000 Rockville Pike, Bethesda, MD 20892; Thomas D. Geracioti, Jr., M.D., Samuel J. Listwak, M.A., William T. Gallucci, M.S., David Michelson, M.D., Philip W. Gold, M.D., Mitchel A. Kling, M.D.

Summary:

Neuroendocrine abnormalities such as sustained hypercortisolism and reduced arginine vasopressin (AVP) function, as well as altered function of central serotonin (5-HT) systems that may influence these endocrine axes, have been implicated in the pathophysiology of major depression. Fluoxetine (FLX) is a highly selective 5-HT uptake blocker that is now widely used in the treatment of major depression. However, relatively little is known regarding its effects on central neurohormones in such patients. We report here a study in which we measured cerebrospinal fluid (CSF) levels of the neuropeptides corticotropin-releasing hormone (CRH), corticotropin (ACTH), oxytocin (OT) and AVP in eight outpatients with DSM-III-R and RDC major depression (mean age 42.7 $\pm$ (s.e.) 4.1; 4 male) both while medication free and following at least six weeks (mean, 89 $\pm$ 14 days) of FLX treatment at 20 mg/d, and in 20 healthy volunteers (mean age 42.2 $\pm$ 2.6; 10 male). Lumbar punctures (LPs) were done at 9:30 a.m. following an overnight fast and at least three hours of bed rest. Blood was drawn (in all subjects) before LP. The mean HAM-D and Beck scores were 24.3 $\pm$ 2.2 and 21.9 $\pm$ 4.2 off, and 18 $\pm$ 1.8 and 14.1 $\pm$ 1.3 on FLX, respectively. Mean plasma FLX and norfluoxetine levels were 77.9 $\pm$ 15.3 and 125.6 $\pm$ 15.5 ng/ml, respectively. ACTH, CRH, OT, and AVP were measured by RIA following Sep-Pak C-18 extraction. CSF, ACTH, CRH, OT, and AVP levels in medication-free patients did not differ from controls. However, CSF CRH and AVP decreased significantly (from 34.9 $\pm$ 4.5 to 28.2 $\pm$ 4.8 pg/m., $p<0.05$; and 1.05 $\pm$ 0.10 to 0.84 $\pm$ 0.11 pg/ml, $p<0.01$, respectively, by paired 2-tailed t-tests) during FLX treatment. These results suggest that FLX reduces centrally directed CRH and AVP while having little effect on ACTH and OT under these conditions. This reduction of CSF CRH levels is of interest in the light of recent data showing that chronic FLX treatment decreases CRH mRNA levels in rat hypothalamus. Whether these reductions represent a direct consequence of sustained 5-HT uptake antagonism or a secondary effect remains to be elucidated.

NR113 Monday May 4, 3:00 p.m.-5:00 p.m.

MRI Basal Ganglia Volumes in Bipolars

Joy Roberts, M.D., Psychiatry, Johns Hopkins University, 600 N Wolfe St. Meyer 3-166, Baltimore, MD 21205; Elizabeth Aylward, Ph.D., Carol E. Peyser, M.D., Godfrey D. Pearlson, M.D.

Summary:

Neurodegenerative conditions involving the basal ganglia (BG) are often associated with pathologic mood changes. PET studies in affective disorders show altered metabolism in BG, and preliminary MRI studies in depression reveal regional structural change (e.g., Husain et al, *Ann. Neurol,* in press). Thirty young DSM-III-R bipolar patients were individually matched to 30 screened normal controls on age, sex, race, and parental SES. Five-mm axial proton- and T2-weighted MRI's were acquired parallel to the AC-PC line and blindly rated using the method described by Harris.

No significant differences in caudate, putamen, or globus pallidus volume were detected on paired t-tests. No finding became significant following reanalysis expressing BG volumes as a ratio of total intracranial volume. These findings suggest that although functional basal ganglia pathology may exist in bipolar disorder, structural abnormalities are not present.

NR114 Monday May 4, 3:00 p.m.-5:00 p.m.

Mixed and Dysphoric States in Bipolar Patients

Gianni L. Faedda, M.D., Psychiatry, Albert Einstein, 1300 Morris Park Avenue, Bronx, NY 10461; Stephen M. Strakowski, M.D., Mauricio Tohen, M.D., Trisha Suppes, M.D., Andrew L. Stoll, M.D., Pierre V. Mayer, M.D., Daniel C. Goodwin, Meredith L. Kolbrener, Ross J. Baldessarini, M.D.

Summary:

Patients (N = 54) with DSM-III-R bipolar disorder, manic or mixed, were evaluated prospectively at first hospitalization. Demographic variables, SCID diagnoses, weekly BPRS and CGI scores, length of hospitalization, and recovery rate were assessed. The BPRS dysphoria score was used to separate patients with mania and dysphoria (DM), from manic patients without dysphoria (M).

Eleven patients (21%) met criteria for bipolar disorder, mixed (Mx). Compared with manic patients, Mx patients had a higher age at first hospitalization; higher rate of comorbid substance abuse and anxiety; and higher ratings of depression, guilt and suicidal ideation. In contrast, DM patients were younger, had low comorbidity, but had higher BPRS and CGI admission scores, and stayed longer in the hospital. No differences were found in short-term recovery measures. These preliminary results seem to support a possible heterogeneity between mania with dysphoria (DM), and mania with depression (Mx).

NR115 Monday May 4, 3:00 p.m.-5:00 p.m.

Personality Disorders in Patients with Depression

Bonnie L. Stewart, Ph.D., Garroway Lab., Inst of Penn Hospital, 111 N. 49th Street, Philadelphia, PA 19139; Alan M. Gruenberg, M.D., Reed Goldstein, M.D., Gary S. Bruss, Ph.D.

Summary:

We examined the comorbidity of personality disorder in a sample of 28 depressed inpatients and outpatients. Patients were diagnosed using structured interviews according to DSM-III-R criteria. Axis II disorders were assessed using the Personality Disorder Examination. *Results:* Forty-three percent of the sample were diagnosed with major depression, recurrent; 15% had bipolar disorder, depressed; and 32% had dysthymia with superimposed major depression. Fifty percent of the patients were diagnosed with a comorbid personality disorder. The most commonly diagnosed personality was borderline (18%) with avoidant and histrionic comprising the next most common groups (11% and 7%, respectively). Patients with major depression superimposed on dysthymia were most likely to receive a comorbid personality disorder diagnosis (78%). *Discussion:* The comorbidity of personality disorder in patients with depression may impact the time to remission, ultimate response to treatment, and prognosis. In a naturalistic treatment environment, the implications of comorbidity suggest that further prospective and longitudinal assessment is needed.

NR116 Monday May 4, 3:00 p.m.-5:00 p.m.

Mood Disorder in Families with Marfan Syndrome

Francis J. McMahon, M.D., Psychiatry, Johns Hopkins University, Meyer 3-181 600 N Wolfe Street, Baltimore, MD 21205; Reed E. Pyeritz, M.D., Colleen M. Dougherty, M.S., J. Raymond DePaulo, Jr., M.D.

Summary:

Objective: Several case reports have documented the co-occurrence of severe psychiatric symptoms and Marfan syndrome, an inherited disorder of connective tissue recently mapped to the fibrillin gene on chromosome 15q21. We describe three families with several members suffering from both Marfan syndrome and major affective disorder.

Method: Families were ascertained through a proband with bipolar I or II (BPI or BPII) disorder and Marfan syndrome diagnosed at the Johns Hopkins Medical Genetics Clinic. Marfan syndrome diagnoses conform to the criteria of Pyeritz and McKusick. Psychiatric diagnoses were made by direct interview with the SADS-L (47%) or via the Family History Method (52%), and conform to RDC. Affected psychiatric phenotypes include BPI, BPII and recurrent unipolar depression.

Results: Nineteen individuals have been evaluated to date. Of these, two have only Marfan syndrome, three have only major affective disorder, eight have both and six have neither disorders ($\chi^2 = 4.23$, $p < 0.04$).

Conclusions: Although psychiatric diagnoses were not usually assigned blind to the Marfan status, these data suggest the possibility of an association between Marfan syndrome and affective disorder in certain families, and implicate 15q21 as a candidate region for linkage analysis. Future work will aim at evaluating more families for a formal linkage study using DNA markers flanking the fibrillin gene.

NR117 Monday May 4, 3:00 p.m.-5:00 p.m.

Expressed Emotion and Siblings: Compounded Stress?

Solange Marchildon, Ph.D., Psychosocial, Child Research Center, 6875 Blvd LaSalle, Verdun QC H4H 1R3, Canada; Suzanne King, Ph.D., Teeya Blatt, M.A.

Summary:

The relationship between high expressed emotion (EE) and relapse in schizophrenics has been replicated repeatedly. The implication is that high EE is "bad" while low EE is "good." Most EE research, however, oversimplifies a complex family situation.

Our study goes beyond relapse as outcome variable, uses EE scales independently and in raw, not dichotomized, state, and takes advantage of differences among family members.

Seventy-four schizophrenics were interviewed with the BPRS and the Social Adjustment scale. One-hundred-sixteen of their family members were interviewed with the Camberwell Family Interview (CFI) for EE levels. To date, 35 CFI's for mothers have been coded, 20 for fathers and 13 for siblings.

Preliminary results suggest that the relationship between EE and patient outcome differs for mothers and siblings depending upon the CFI scale considered and the outcome variable of interest. For example, higher Critical Comments scores for siblings are associated with *better* social adjustment in patients but also with *more* positive symptoms. High Emotional Overinvolvement scores for siblings are associated with *worse* social adjustment and *more* negative symptoms but *fewer* positive symptoms. Almost all of these correlations are reversed for mothers. More results, for the complete data set, and implications for EE research and family interventions, will be presented.

NR118 Monday May 4, 3:00 p.m.-5:00 p.m.

DST in Drug-Free Patients

Isil Vahip, M.D., Psychiatry, EGE University, TIP Fakultesi Bornova, Izmir 35100, Turkey; Simavi Vahip, M.D., Levent Mete, M.D., Figen Toprak, M.D.

Summary:

Specificity, sensitivity, and diagnostic confidence of DST for major depression were determined in patients with schizophrenia and major depression according to DSM-III-R criteria. Patients who did not take psychotropic medication during the previous two months were included. DST was (+) in 12 of 28 schizophrenic (42.9%) and 21 of 45 depressive (46.7%) patients. For major depression, we found the sensitivity of DST 46.7%, the specificity of DST 57.1%, and the diagnostic confidence of DST 63.6%.

NR119 Monday May 4, 3:00 p.m.-5:00 p.m.

Depression and Lyme Disease: A Controlled Survey

Brian A. Fallon, M.D., Psychiatry, Columbia Univ NYS Psych, 722 West 168th Street Box 13, New York City, NY 10032; Jenifer A. Nields, M.D., Donato DelBene, B.A., Jay Saoud, M.S., Kenneth Wilson, M.D., Michael R. Liebowitz, M.D.

Summary:

Case reports suggest that depressive symptoms can be a prominent feature of Lyme disease. No controlled studies have yet been published that specifically investigate DSM-III-R depression during Lyme disease.

Methods. A questionnaire was sent to patients who attend Lyme disease support groups. Only data from seropositive patients were analyzed. To obtain a comparison sample, the questionnaire was sent to patients with non-Lyme arthritis who attend arthritis support groups.

Results. Among the 51 patients with seropositive Lyme disease, the mean age was 45 years old with a predominance of women (82%). The median number of years symptomatic was five. Sixty-six percent of the 51 patients reported having had a major depression during Lyme disease, most (90%) for the first time. Only 23% of the 30 patients with non-Lyme arthritides reported having had a major depression during their illness, even though the patients with non-Lyme arthritides had been ill three times longer (14 years) and were older (65 years). The difference in these frequencies of depression was statistically significant (66% vs. 23%, $p < .001$).

Conclusion. Major depression was three times more common among patients with Lyme disease than among patients with chronic non-Lyme arthritides. Mental health professionals need to include Lyme disease in the differential diagnosis of depression.

NR120 Monday May 4, 3:00 p.m.-5:00 p.m.

Longitudinal Study of Women with Breast Cancer and Major Depressive Disorder

Mary L. DeFlorio, M.D., Psychiatry, Memorial Hospital, 1275 York Room 767C, New York, NY 10021; Jimmie C. Holland, M.D., Lynna Lesko, M.D., Alice Kornblith, Ph.D., Diane Baiano, R.N.

Summary:

The objectives of this study are to follow the natural course of depressive symptomatology and psychological distress in those patients with advanced (Stage III, IV) breast cancer referred for psychiatric evaluation, and to identify sociodemographic and medical/treatment characteristics in this population that are predictive of developing Major Depressive Disorder (MDD). We also hope to ascertain whether this population of medically ill with depressive symptoms, but not meeting DSM-III-R criteria of MDD, follow the DSM-III-R parameters of Adjustment Disorder (AD). Of particular interest are the parameters of time and severity, and whether this parallels illness or psychosocial stressors. The study plans to address the hypothesis that a majority of the severely medically ill with AD will have a protracted course that extends beyond the six-month period of DSM-III-R criteria, yet do not meet criteria of MDD. It is expected that the course of psychiatric illness and severity, as reflected by the Hamilton Depression and Anxiety Scales (HAM-D, HAM-A), will be correlated with illness parameters, pain level, as estimated by the Memorial Pain Assessment Card (MPAC), and psychosocial stressors as reflected in quality of life, Functional Living Index-Cancer (FLIC), and life event measures. The study plans to test the hypothesis that increased severity of illness, increased pain, and increased psychosocial stressors will be predictive factors in developing MDD.

Patients will be women, aged 18-70, English speaking, with a current diagnosis of Stage III or IV breast cancer, who have been referred to the psychiatry service for depression or psychological distress. DSM-III-R criteria will be used in the psychiatric diagnostic interview. Patients with AD and MDD will be followed for the study. Patients with other diagnoses will receive appropriate psychiatric referral and follow-up.

Eligible patients will be followed for a three month period: T1, T2, T3. At T1, initial interview, T2, four weeks +/− 10 days, and T3, 12 weeks +/− 10 days, the patient will be interviewed and assessed on the following inventories: a demographic inventory (T1), HAM-D, HAM-A, FLIC, and MPAC. In addition the patients will be asked about any life stressors and changes.

Analysis of variance with repeated measures will be done with time as the independent variable, and the following as dependent variables: HAM-D, HAM-A, FLIC, and MPAC. Multivariate analysis will be used to examine the influence of sociodemographic, medical/treatment and physical functioning characteristic in predicting whether a patient develops MDD. These predictors include: age, occupational status, income, education, marital status, prior and current cancer treatments, pain medication, comorbid conditions, MPAC Pain Intensity, and the Physical Well-Being and Ability Subscale of the FLIC.

NR121 Monday May 4, 3:00 p.m.-5:00 p.m.

Fluoxetine versus Desipramine in Women with Breast Cancer and Major Depressive Disorder

Mary L. DeFlorio, M.D., Psychiatry, Memorial Hospital, 1275 York Room 767C, New York, NY 10021; Jimmie C. Holland, M.D., Lynna Lesko, M.D., Alice Kornblith, Ph.D., Diane Baiano, R.N.

Summary:

The objective of this study is to compare the efficacy and side-effect profile of fluoxetine vs. desipramine in a depressed population of women, ages 18-70 with Stage III and IV breast cancer. This trial has been designed as a double-blind, randomized, parallel study with approximately 124 patients divided among six investigator sites, Memorial Sloan Kettering Cancer Center (MSKCC), M.D. Anderson, Dana Farber, Massachusetts General, University of California at Los Angeles, and the University of Tennessee at Memphis. MSKCC hopes to accrue 50 patients to the study over an approximately 12-month period. The following abstract is a summary of the study in progress at MSKCC.

Patients will be accrued from a referral base of patients, either inpatient or outpatient at MSKCC, who have been identified by a member of their treatment team as having psychological distress consistent with major depressive disorder (MDD). Patients will be interviewed and rated on a Hamilton Depression Rating Scale (HAM-D). Patients scoring above 14 on the HAM-D and clinically meeting DSM-III-R criteria of Major Depressive Disorder (MDD) will be asked to participate in the study provided they are not medically or psychiatrically excluded (history of thyroid abnormality, cardiac abnormality preventing antidepressant use, pregnancy, seizure disorder, glaucoma, urinary retention, organic mental syndromes, substance abuse within the past year, psychotic disorders, and regular use of psychotropic drugs). Patients will be randomly assigned to a regime of either fluoxetine or desipramine for a six-week, double-blind period.

During the study interval patients will be followed weekly to assess mental status and any medication side effects. The following

will be administered: HAM-D, Hamilton Anxiety Scale (HAM-A), Functional Living Index-Cancer (FLIC), Quality of Life (QOL), Memorial Pain Assessment Card (MPAC), and the Clinical and Patient Global Impression Scales (CGI), (PGI).

Analysis of the independent variable treatment group, upon clinical outcome will be done using the dependent measures of the HAM-D, HAM-A, QOL, FLIC, CGI, and PGI. The analysis will yield information about therapeutic exposure and its effect on the patient's clinical course including response vs. non-response and remission vs. non-remission of MDD. Remission will be assessed clinically according to DSM-III-R criteria, and a score of less than 14 on the HAM-D.

Thus far, 26 patients have been referred to the study. Of these, 14 had MDD, eight had an adjustment disorder, and four had comorbidity of MDD with an anxiety disorder. All but three of the patients with MDD refused antidepressants. Two of the three patients completed the study, one with clinical remission, one without.

NR122 Monday May 4, 3:00 p.m.-5:00 p.m.

Hypochondriasis and Medical Illness in Depressives

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Summary:

Hypochondriasis is a recognized concomitant of major depression in many patients. Popular perception holds that older people are more hypochondriacal, despite the increased prevalence of medical illnesses in late life. Studies have been mixed regarding whether depressed patients demonstrate more hypochondriasis with increasing age; the assessment of physical illness in these studies has been limited.

We hypothesized that, with older age, "hypochondriasis" in depressives represents actual level of medical burden as well as degree of depression. We prospectively studied 133 psychiatric inpatients with a unipolar major depressive syndrome (as determined by the Structured Clinical Interview for DSM-III-R), ages 21-89. Variables of interest included age, sex, education, depressive severity (Hamilton Rating Scale for Depression [Ham-D]), objective organ system pathology (Cumulative Illness Rating Scale [CIRS]), physical functional level (Karnofsky Performance Status Scale [KPSS]), and psychiatric functional level (Global Assessment of Function). Hypochondriasis was measured by the hypochondriasis item from the Ham-D and the somatic concern item from the Brief Psychiatric Rating Scale. Preliminary multiple regression analysis showed that age and Ham-D significantly predicted hypochondriasis, but the CIRS and KPSS did not. We will present results of further analyses, including the effects of age on the association between medical illness and hypochondriasis.

NR123 Monday May 4, 3:00 p.m.-5:00 p.m.

Psychopathology in Ill Children: Discrepancies Between Parent and Child Reports

Emily S. Harris, M.D., Child Psychiatry, Stanford University, 725 Welch Road, Palo Alto, CA 94340; Suzanne B. Hanser, Ed.D., Kathryn A. Shade, B.A.

Summary:

Mental disorders affect 18% to 20% of children in primary care and often remain unrecognized by care providers. In our study of chronically ill children, we address the discrepancies between parent and child reports of their psychiatric disorders.

Eighty-three subjects, ages 9-18 (mean = 12.6), recruited from specialty care clinics had the following diagnoses; cystic fibrosis (n = 14), diabetes mellitus (n = 20), inflammatory bowel disease (n = 11) and cancer (n = 38). Subjects and one parent were interviewed separately, using the revised Diagnostic Interview Schedule for Children (DISC-2.1R). Psychiatric diagnoses were established using computer algorithms based on information from parent only, child only, or a combination of their reports.

Forty-one (49%) subjects reached threshold criteria for a psychiatric diagnosis using the combined algorithm. Only 22 (54%) were identified by the child and 28 (68%) by parent alone. Thus, reliance on one informant resulted in missing one third to one half of those cases identified using both parent and child sources. Physicians correctly identified 41% with disorder by combined algorithm.

The outcome of clinical or research evaluations of children with chronic illness, and the identification of children with mental health problems may depend largely on the choice of informant.

NR124 Monday May 4, 3:00 p.m.-5:00 p.m.

Epileptoid Features in Mood Disorders

Nutan Atre-Vaidya, M.D., Psychiatry, Chicago Medical School, 3333 Green Bay Road, North Chicago, IL 60064; Michael A. Taylor, M.D., V. Chowdary Jampala, M.D., Harriett Stein, R.N.

Summary:

Epileptoid features (psychosensory/psychomotor and interictal behavioral) are observed in psychiatric (bipolar mood disorders) and neurologic (complex partial seizures) disorders. The exact pathophysiology of epileptoid features is not known, although they are thought to be of temporolimbic origin. Epileptoid features may predict the nature and the course of an illness. To further characterize epileptoid features and to determine their prevalence in mood disorders, two investigators independently assessed affectively ill outpatients for the presence of (1) epileptoid features, using a scale of known reliability (POPS), and (2) psychopathology using the SANS (Schedule for Assessment of Negative Symptoms), the SAPS (Schedule for Assessment of Positive Symptoms, and an emotional blunting scale (EBS). Epileptoid features included: perceptual, emotional, neurological and interictal behavioral. We have so far evaluated 35 patients (by DSM-III-R criteria: 22 bipolar, five unipolar and eight schizoaffective). Their mean index age was 52.55 (S.D. 14.0), and their illness onset was 31.93 (S.D. 14.35). Eleven patients had a positive family history of major psychoses, and 12 patients had co-occurring drug or alcohol abuse. In addition, 35.9% reported a lifetime prevalence of four or more epileptoid features; 34.3% reported four or more current epileptoid features; while 55.8% reported four or more past epileptoid features. Less than 3% reported four or more current features in each perceptual, emotional and interictal behavioral group. Less than 1% of the patients reported current neurological epileptoid features. Past perceptual features correlated with recent ($r = .51$, $P = .001$) and past ($r = .55$, $P = 000$) emotional epileptoid features, while recent perceptual features tended to be associated with recent emotional features ($r = .25$, $P = .07$), but had no correlation with past emotional features. Past emotional features showed a trend towards recent ($r = .27$, $P = .050$) and past ($r = .27$, $P = .053$) interictal behavioral features. Perceptual features had no correlation with behavioral features. Significance of these findings will be discussed.

NR125 Monday May 4, 3:00 p.m.-5:00 p.m.

Intravenous Haloperidol for Treatment-Resistant Mania

Atul Mahableshwarkar, M.D., Psychiatry, Chicago Medical School, 3333 Green Bay Road, North Chicago, IL 60064; Chandra Vedak, M.D., V. Chowdary Jampala, M.D., J.S.R. Van, M.D.

Summary:

Lithium and other antimanic agents are sometimes not effective in treating manic symptomatology. Neuroleptics are used either orally or intramuscularly in these patients. Even then, a significant minority remain treatment unresponsive. We report on a series of five patients who had very little or no response to antimanic agents (lithium, carbamezapine and valproic acid) at therapeutic levels coadministered with oral/intramuscular neuroleptic agents (haloperidol dosage range from 10 to 80 mgs. per day). The patients subsequently showed significant response to one to three doses of 10 mgs. to 20 mgs. of intravenous haloperidol. Retrospective application of the Brief Psychiatric Rating Scale (BPRS) showed 85.14% drop in post-treatment scores. All patients tolerated intravenous haloperidol without any side effects. The clinical improvement was subsequently maintained with conventional antimanic agents. The case histories of these five patients will be presented. Intravenous haloperidol, which has been used safely and effectively in medically ill, delirious patients, may also be used effectively in treatment of resistant manics.

NR126 Monday May 4, 3:00 p.m.-5:00 p.m.

Social Zeitgeber Disruption in Major Depression

Martin P. Szuba, M.D., Psychiatry, UCLA-NPI, 760 Westwood Plaza Room 27-384, Los Angeles, CA 90024; Alison Yager, Barry H. Guze, M.D., Eva M. Allen, B.A., Lewis R. Baxter, Jr., M.D.

Summary:

Dysregulation of physiological circadian rhythms are common in depression and may mediate depressive episodes. Recently the role of social circadian rhythms in the pathogenesis of depression has been a focus of interest. The Social Rhythm Metric (SRM), designed to provide an account of the regularity of a human's social circadian rhythms, was used in this study to compare depressed patients with controls and to determine the relationship between SRM scores and depression severity. Nineteen patients with major depression and 19 age- and sex-matched, medication-free, healthy controls completed the Social Rhythm Metric. Subjects were rated with the Hamilton Depression Scale and the Profile of Mood States.

The SRM scores were significantly lower in patients (3.5 ± 0.49) versus normals (3.9 ± 0.49) ($t = 2.2$, $p = 0.03$, d.f. $= 36$). However, the Activity Level Index (ALI), a subscale of the SRM that reflects overall activity, scores were not significantly different (43.8 ± 10 for patients; 47.1 ± 5.7 for normals) ($t = 1.2$, $p = .23$, d.f. $= 36$).

The SRM scores showed a significant negative correlation with the Hamilton rating scale ($r = -.32$, $p = .05$). There were also trends for negative correlations between SRM scores and various POMS subscales ($p = 0.1$).

The results of this study support the hypothesis that social rhythms are disrupted in major depression.

NR127 Monday May 4, 3:00 p.m.-5:00 p.m.

Diurnal Mood Variation in Seasonal Affective Disorder

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Summary:

Objective: The "reverse" pattern of diurnal mood variation described in patients with seasonal affective disorder (SAD) has been suggested as evidence in support of phase-delayed circadian rhythms in SAD. The purpose of this study was to determine whether consistent daily mood patterns are present in this subgroup of depressed patients.

Method: Depressed SAD patients ($N = 43$), diagnosed with DSM-III-R criteria, completed daily mood ratings at 08:00, 12:00, 16:00, and 20:00 during a baseline week prior to treatment, using a modified visual analog scale. Multivariate statistical analyses were used to determine whether there were significant differences between mood ratings at different times of the day. A cluster analysis was done to determine whether patients could be grouped according to diurnal patterns.

Results: Preliminary results indicate that there was a significant difference in self-rated mood at different times of the day, with mood ratings worst at 08:00 and 16:00 ($p < 0.004$). Cluster analysis separated the patients into two distinct groups; one with an "afternoon dip" in mood at 16:00 ($N = 19$), and the second with worsening of mood at 08:00 and improvement through the day ($N = 24$).

Conclusions: Although many patients have the "afternoon dip" in mood described in SAD, a similar number show a "typical" depressive pattern of early morning mood worsening. These results suggest that patients with SAD represent a heterogeneous group with different patterns of daily subjective mood fluctuation.

NR128 Monday May 4, 3:00 p.m.-5:00 p.m.

The Brief Quality of Life Rating Scale

Ariane Rogue, M.D., Ch.H.S., BP304, Hoerdt 07728, France; Patrick Rogue, M.D.

Summary:

Quality of life (QL) as it relates to mental health is an essential component of patient care, and rating scales for its objective measure in psychiatric patients have been developed. The limitations of currently available instruments will be discussed. The BQLS, a novel QL rating scale for use by physicians, will be presented. It is an easily administered instrument designed for assessing the QL associated with psychiatric disorders, with unambiguous, easy to understand items. It is short yet comprehensive, covering several areas: psychosocial functioning, subjective perception of well-being, and psychopathology and medical illness. The rationale for its design and scoring will be outlined. The patient is the primary informant, but the rater may use other sources of information. In view of use in transcultural settings, both French and English versions have been developed. Additional data on its reliability (inter-rater and test-retest) and validity will be presented.

NR129 Monday May 4, 3:00 p.m.-5:00 p.m.

Prospective Long-Term Follow-Up of Seasonal Affective Disorder Patients

Georg K. Leonhardt, M.D., Psychiatry, Psych Universitaetsklinik, Wilhelm Klein-Strasse 27, Basel 4025, Switzerland; Hans J. Haug, M.D., Peter R. Graw, Ph.D., Dorothee Wunder, Anna Wirz-Justice, Ph.D.

Summary:

Seasonal Affective Disorder (SAD) was first defined by Rosenthal in 1984 (1), and rather stringent criteria for the diagnosis were incorporated in DSM-III-R. In the DSM-IV Options Book (2) it has been proposed that the criteria for SAD be broadened. Prospective data on the course of SAD are rare. We have been documenting SAD course since 1984, using a validated and reliable tool for documenting depressive state, the von Zerssen self-rating scale (vZ). In our studies we have administered this self-rating scale weekly to all SAD patients who had taken part in clinical light therapy trials, together with questionnaires on medication, body weight, illness, menstrual cycle, and external events. This prospective analysis concerns 25 SAD patients (18 women, seven men), with major depression according to DSM-III, who prospectively carried out these ratings for a period of two to seven years. Of these, one patient was found to have major depressive phases

in summer, and three others had depression in both winter and summer. The onset of a depressive phase was defined as a vZ score $\tau 10$ for more than two consecutive weeks, the offset ≤ 10 for at least two weeks in 11 patients where this could be reliably measured, the onset of depression from year to year varied from being within six days to 144 days (mean 64 days) and the offset varied from being within nine days to 120 days (mean 63). With respect to the depth of successive depressive phases, 10 SAD patients showed no clear depressive phases in the years following a light therapy trial. In seven, the depressive phases remained unchanged form year to year, and in eight the depth of depression appeared to have diminished. These prospective data support the proposal to delete the 60-day window for SAD diagnostic criteria.

NR130 Monday May 4, 3:00 p.m.-5:00 p.m.

Psychoneuroendocrine Effects of Physostigmine

Susan G. Silva, Psychiatry, UNC-Chapel Hill, CB 7160 Medical School Wing B, Chapel Hill, NC 27599-7160; Robert A. Stern, Ph.D., Robert N. Golden, M.D., Elizabeth J. Davidson, Ph.D., George A. Mason, Ph.D., David S. Janowsky, M.D.

Summary:

The cholinergic-aminergic imbalance hypothesis of mood disorders postulates that depression is associated with the predominance of central cholinergic to aminergic neurotransmission in brain areas that regulate affect. The extent to which central cholinergic dysfunction accounts for the various components of depression symptomatology, however, is unknown. The cognitive, mood, and endocrine effects of intravenous administration of physostigmine, a central cholinesterase inhibitor, were studied in nine normal males. Each subject attended three study days, with a single dose of either 0.022 mg/kg physostigmine, 0.011 mg/kg neostigmine (a non-central cholinesterase inhibitor), or saline administered on each day. A double-blind, within-subjects design was employed, counterbalancing for drug-order effects. Cognitive, mood, psychomotor, and endocrine measures were gathered during the predrug and postdrug sessions on each day. When compared with neostigmine and saline, physostigmine produced behavioral inhibition ($p = .0001$), but did not induce dysphoria or significantly alter neurocognitive functioning. Stress hormones were significantly elevated following the physostigmine challenge ($p < .001$). Previous studies have consistently demonstrated that depressives experience a pronounced inhibitory-dysphoric reaction to cholinomimetic drugs, while normals exhibit behavioral inhibition only. Additionally, the present study found that physostigmine exerts behavioral inhibition without mood or cognitive impairments. Past and present findings suggest group differences in cholinergic functioning in brain areas that regulate mood and cognition.

NR131 Monday May 4, 3:00 p.m.-5:00 p.m.

Neuroleptic Exposure in Lithium-Treated Mania

Michael J. Sernyak, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Robin Johnson, M.D., Ruth Griffin, R.N., H. Rowland Pearsall, M.D., Scott W. Woods, M.D.

Summary:

Neuroleptics are frequently employed as adjuncts to lithium in the inpatient treatment of acute mania and are often continued past discharge. This study was undertaken to define the extent of neuroleptic exposure in this population subsequent to discharge. *Method:* Charts were reviewed using a structured instrument for all 51 patients discharged on lithium with a diagnosis of bipolar disorder between 2/1/89 and 6/1/91 from the Connecticut Mental Health Center Inpatient Division. *Results:* Follow-up information was obtained on 47 of 51 patients (92%). Forty-two of these patients (89%) were discharged on neuroleptic in addition to lithium. At six-months follow-up, only two of these 42 (5%) were completely off neuroleptic. Twenty-two (52%) were on a reduced dosage, nine (21%) were on the discharge dosage, and another nine (21%) were on an increased dosage. *Discussion:* The subsequent outpatient neuroleptic exposure in this bipolar population discharged on lithium is substantial. This finding underscores the need to investigate non-neuroleptic adjuncts to lithium in the inpatient treatment of bipolar illness. Additional data will be presented in an attempt to characterize subgroups, including those patients with bipolar disorder who require long-term neuroleptic maintenance.

NR132 Monday May 4, 3:00 p.m.-5:00 p.m.

Research versus Clinical Diagnosis of Mood Disorders

Leah Gniwesch, B.A., Psychiatry, Cornell Univ Med. College, 525 East 68th Street, New York, NY 10021; James Kocsis, M.D.

Summary:

Background: While conducting structured clinical interviews as a part of the DSM-IV Field Trial on Mood Disorders, we developed the anecdotal impression that many inpatients having mood disorders were misdiagnosed by staff psychiatrists. Therefore, we conducted a review to compare hospital chart diagnoses with those obtained by a SCID interview. *Method:* Patients given a diagnosis of non-bipolar, non-psychotic mood disorder by the admitting service of the Payne Whitney Clinic were given SCID interviews as a part of the field trial. Hospital diagnoses were those given by the treating psychiatrist at the time of admission. *Results:* Forty-six patients (30 female, 16 male) were included in the study. In 27 cases (59%) the research diagnosis based on the SCID agreed with the hospital chart diagnosis for mood disorders. Disagreement occurred in 19 cases (45%), of which the SCID interview diagnosed 10 cases of antecedent dysthymia ("double depression"), eight cases of bipolar disorder (prior mania or hypomania), and one case of "pure" dysthymia. *Conclusion:* These findings suggest the utility of a structured clinical assessment of psychiatric inpatients having mood disorders. It appeared that clinicians in inpatient settings underdiagnosed prior episodes of dysthymia, mania, and hypomania when using free-form diagnostic assessment.

NR133 Monday May 4, 3:00 p.m.-5:00 p.m.

Serum Chloride Levels in Agitated Depression

Cheng-Jen Chen, M.D., Psychiatry, Cornell University, 525 East 68th Street RM PW277, New York, NY 10021; Elisha M. Tarlow, B.A., Herminia Ombid, B.A., Peter E. Stokes, M.D.

Summary:

We have reported that patients with major depression ($n = 81$) had significantly lower serum chloride levels than psychiatric controls ($n = 82$), and that serum chloride levels alter thyroid hormone serum protein binding (*J Affective Disorders* 20: 159-163, 1990). Chloride ion concentration also affects the resting potential across the neuronal membrane, which subsequently alters the excitability of neurons. These changes may be important in the pathogenesis of disturbed mood in depression. We report here, in a second retrospective inpatient chart study, the relationship of these serum chloride and thyroid indices to clinical subdivisions (agitated and retarded) of depressed patients. We hypothesized that the serum chloride in agitated depression is lower than that of the comparison group. Patients on antidiuretics and those with serious medical problems, eating disorders, and histories of substance abuse were excluded. Fasting serum electrolytes, BUN and creatinine levels were compared between the two groups. The results showed chloride levels in agitated depression ($Cl = 106.1 \pm 4$, $n = 59$) to be significantly lower than those of the psychiatric comparison group ($Cl = 107.3 \pm 3.4$, $n = 46$) ($t = 1.71$, $0.01 < p < 0.05$, one-sided com-

parison). Chloride levels in retarded depressed patients tended to be higher (107.8 ± 3.7, n = 8) than the other groups. The physiological meaning of these findings and the potential clinical applications will be discussed.

NR134 Monday May 4, 3:00 p.m.-5:00 p.m.

Comparison of Primary and Secondary Panic Disorder

Vladan Starcevic, M.D., Psychiatry, Univ of New Mexico, 2400 Tucker NE, Albuquerque, NM 87131; Eberhard H. Uhlenhuth, M.D., Robert Kellner, M.D., Dorothy Pathak, Ph.D.

Summary:

We compared the onsets of comorbid psychiatric disorders relative to the onset of panic disorder (PD) in 54 patients with PD, diagnosed by the means of a Structured Clinical Interview for DSM-III-R disorders (SCID). In 42 patients, PD was preceded by another psychiatric disorder (secondary PD group), while in 12 patients, PD occurred first or was the only diagnosed mental disorder (primary PD group). The most common primary conditions in secondary PD patients were simple phobia and social phobia.

Patients with primary and secondary PD did not differ with respect to demographic variables, including sex, age, ethnic origin, educational level, and employment status. In addition, there were no significant differences in the proportions of the PD subtypes, and no differences in the duration of PD and in the mean ages of onset of PD. Except for the anger and sleep scales of the HOpkins Symptom Checklist 90, primary PD patients had significantly less self-rated psychopathology, and had lower rates of current, SCID-diagnosed psychiatric comorbidity; both of the latter findings were maintained at the one-year follow-up.

The results of this pilot study suggest that in a substantial proportion of patients, PD is preceded by another psychiatric disorder. This finding is not particularly relevant to the conceptualization of the PD psychopathology in terms of the primary/secondary dichotomy, since the chronological appearance of PD does not seem to account even for the relatively minor differences between patients with primary and secondary PD.

NR135 Monday May 4, 3:00 p.m.-5:00 p.m.

Effects of Desipramine on Resting Metabolic Rate in Panic Disorder

Naresh P. Emmanuel, M.D., Psychiatry, Medical University of SC, 171 Ashley Avenue, Charleston, SC 29425; Robert B. Lydiard, M.D., Alex W. Morton, Pharm.D., Michele T. Laraia, M.S.N., Joseph J. Zealberg, M.D., Gail W. Stuart, R.N., James C. Ballenger, M.D.

Summary:

Weight gain is a common side effect of tricyclic antidepressants. This study attempts to study the relationship between desipramine and body weight. In a double-blind study, 28 nondepressed patients with the primary diagnosis of panic disorder with or without agoraphobia were evaluated for resting metabolic rate and weight changes in response to treatment with desipramine or placebo. The resting metabolic rate (RMR) was measure using a Sensormedic Horizon 4400 Metabolic Cart. In addition the thyroid functions and various rating scales including the HAM-A and the HAM-D were assessed. The tests were repeated eight weeks later.

Results: Thirteen of the 28 patients were receiving desipramine. Fifteen patients were in the placebo group, 13 of whom were women. All 13 in the desipramine group were women. There was no statistical difference in the biological variables between the two groups. The two groups were not different at baseline. The group on desipramine lost an average of 4.1 lb. over this period, which was significant ($P<0.0066$); there was no significant difference in RMR. Differences in T3, T4 and TSH were not significant. The practical and theoretical implication of these findings will be discussed.

NR136 Monday May 4, 3:00 p.m.-5:00 p.m.

CSF, CCK and Beta-Endorphin in Panic Disorder

Richard Payeur, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; Robert B. Lydiard, M.D., Kathleen Brady, Ph.D., Joseph J. Zealberg, M.D., James C. Ballenger, M.D.

Summary:

Cholecystokinin is an excitatory neurotransmitter that under its tetrapeptide form was found to be a potent panicogenic agent. We recently reported that CSF CCK-8S was significantly lower in panic disorder patients compared with normals. In the same population, we also reported that CSF B-endorphin was not significantly different between the two groups, but a positive correlation between B-endorphin and the Hamilton Anxiety Ratings was found in the control group only. CCK-8S in particular has been shown to antagonize opioid-mediated analgesia, maternal behavior, hyperactivity, feeding and thermoregulation. We therefore examined the correlation between CCK-8S and B-endorphin in a population of panic disorder patients. A strong correlation was found between CSF concentration of CCK-8S in control ($r=0.85$, $p<0.005$, $N=12$) but this correlation is lost in the panic disorder population ($r=0.12$, $p<0.61$, $N=20$). Also, in the control group only, CCK-8S was correlated with the Hamilton Anxiety Score ($r=0.55$, $p<0.05$, $N=13$). These results suggest that there may be a dysregulation in the interaction of B-endorphin and CCK-8S in patients with panic disorder. Theoretical implications will be discussed.

NR137 Monday May 4, 3:00 p.m.-5:00 p.m.

CSF and Beta-Endorphin in Panic Disorder and Social Phobia

Michael P. Johnson, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; Robert B. Lydiard, M.D., James C. Ballenger, M.D., Michele T. Laraia, M.S.N., Mark D. Fossey, M.D., Joseph J. Zealberg, M.D.

Summary:

Despite the growing body of research in the area of social phobia, there have been few studies demonstrating biological abnormalities in this disorder. As part of a project examining the biology of panic disorder, we compared cerebrospinal fluid levels of β-endorphin of panic patients with comorbid social phobia ($N=5$) with CSF β-endorphin levels in panic patients without social phobia ($N=7$) and a set of normal controls ($N=16$). The lowest levels of CSF β-endorphin were found in the social phobia group (mean = 83.6 ± 15.1), and the highest levels were found in the group of patients without social phobia (mean = 121.0 ± 24.8). The normal control patients had levels of β-endorphin that were intermediate (mean = 97.4 ± 24.0). One-way ANOVA demonstrated that there were significant between-group differences ($F=4.25$, $p=.026$), and group comparisons using T-tests demonstrated significant differences between the patient groups ($t=2.97$, $p=.014$) and between the non-social-phobic patients and normal controls ($t=2.14$, $p=.044$). The difference between the social phobic patients and the normal controls did not reach significance ($t=11.20$, $p=24$). These findings suggest that there may be an association between social phobia and CSF β-endorphin levels. Implications of this finding will be discussed.

NR138 Monday May 4, 3:00 p.m.-5:00 p.m.

Lack of Effect of Flumazenil on CCK-4-Panic

Anne Couetoux-Dutertre, M.D., Psychiatry, St. Mary's Hospital, 3830 Lacombe Avenue, Montreal PQ H3T1M5, Canada; Jacques Bradwejn, M.D., Diana Koszycki, M.A., Michel Paradis, M.D., Michel Bourin, M.D.

Summary:

Cholecystokinin (CCK) is a neurotransmitter found in high quantities in mammalian brain. Considering that benzodiazepine (BZD) receptor agonists antagonize CCK-induced excitation of rat hippocampal neurons, and that CCK_4 is panicogenic in panic disorder patients and in healthy volunteers, this study determined whether CCK_4 might act as an inverse agonist of BZD receptors. Healthy volunteers (20M; 10F) were pretreated with flumazenil (2 mg i.v.), the BZD receptor antagonist, or placebo (0.9% NaCl i.v.) 15 minutes before CCK_4 challenge (50 μg i.v.), in a randomized, double-blind, crossover design. Responses were evaluated with the Panic Symptom Scale; DSM-III-R criteria, including moderate to severe anxiety were used to judge the occurrence of a panic attack. The panic rate following CCK_4 was similar for flumazenil (13/30) and placebo (14/30). Treatment effects and treatment by injection period interactions were not statistically significant for the number, sum intensity and duration of symptoms. Mean (±SD) scores for flumazenil and placebo respectively were 10.57±3.3 and 10.87±3.3 for the number of symptoms ($P<.50$), 24.03±11.6 and 23.80±11.9 for the sum intensity of symptoms ($P<.87$), and 111.57±37.7 and 123.23±47.5 seconds for the duration of symptoms. These findings do not support the hypothesis that CCK_4 acts as a BZD receptor inverse agonist in inducing panic attacks in healthy volunteers.

NR139 Monday May 4, 3:00 p.m.-5:00 p.m.

PTSD and Hypertension

Olga Brawman-Mintzer, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; Thomas A. Mellman, M.D., Nelson D. Hernandez, M.D., S. George Hanna, M.D., Ramon A. Boza, M.D.

Summary:

Studies suggest an association of stress and possibly anxiety with hypertension (HTN). Post-traumatic stress disorder (PTSD) is an anxiety disorder linked to severe stressors. Increased noradrenergic activity and sympathetic arousal have also been implicated in PTSD and HTN.

We conducted a preliminary investigation of HTN and PTSD. The study population was recruited from the psychiatric outpatient clinic of the Miami VAMC. The study groups included veterans of military combat and/or captivity from Vietnam, Korea, or WWII, with PTSD symptoms ($n=49$); and a control group with primary complaints of anxiety and/or depression without PTSD ($n=49$). The groups were comparable with regard to age, race and other cardiovascular risk factors. A diagnosis of HTN required use of antihypertensive medication or consecutive blood pressure readings exceeding 140/90.

Fifty-three percent (26/49) of the PTSD group versus 31% (15/49) of the control group met the study criteria for HTN ($x^2=5.0$, $p<.03$). Other categories of medical illness did not differ between the two groups.

HTN was increased in the PTSD group. In both groups HTN was more prevalent among older-age veterans. PTSD may, therefore, be a risk factor for the subsequent development of HTN. If replicated, this finding has implications for preventive measures and the pathophysiology of PTSD.

NR140 Monday May 4, 3:00 p.m.-5:00 p.m.

Clomipramine, Fluoxetine and Glucose Control

Lawrence Katz, M.D., Psychiatry, SUNY at Stony Brook, University Hosp HSC T10-020, Stony Brook, NY 11794; Laura J. Fochtmann, M.D., Michele T. Pato, M.D.

Summary:

The impetus for this study of the effects of clomipramine and fluoxetine on glucose control in rats arose from observations in three clinical cases (Katz LM, Fochtmann LJ, Pato MT. Clomipramine, fluoxetine, and glucose control. *Annals of Clinical Psychiatry,* 3:271-274 1991) in which the use of antidepressants appeared to further destabilize glucose control in adult-onset diabetic patients with affective disorders or obsessive compulsive disorder. The destabilization appeared to be a product of changes in central and peripheral neuronal activities of 5-HT, NE, EPI, and ACh. We present the results of having administered serotonergic and noradrenergic antidepressants to alloxan-induced diabetic Sprague-Dawley rats, following the course of serum glucose levels over four weeks, and then data corresponding to discontinuation of the drugs and serum glucose concentrations. Hypotheses include that initiation of clomipramine might be related to hyperglycemia in patients and rats with diabetes, while discontinuation of fluoxetine might also be related to hyperglycemia in those patients and rats. Further, acute and chronic use of fluoxetine in those subjects might be linked to improved control of glucose. Finally, the hypothalamic-pituitary-adrenocortical axis might be involved along with the noradrenergic neurons of the raphe nuclei.

NR141 Monday May 4, 3:00 p.m.-5:00 p.m.

Acute Tryptophan Depletion in Drug-Remitted OCD

Linda C. Barr, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Lawrence H. Price, M.D., Christopher J. McDougle, M.D., Pedro L. Delgado, M.D., Wayne K. Goodman, M.D.

Summary:

The majority of depressed patients remitted on serotonin reuptake inhibitors (SRIs) demonstrate reemergence of depression following acute tryptophan depletion (ATD), which is thought to lower brain serotonin. This study examined the effects of ATD in drug-remitted obsessive compulsive disorder (OCD) patients with and without a history of major depression. *Methods:* Nine OCD patients remitted on SRIs (five female, four male; four with a lifetime history of major depression) participated in two test sessions: (1) ATD (24 hr. 160 mg/day, low tryptophan diet followed the next AM by a 16-amino acid drink without tryptophan) and (2) sham depletion (both diet and drink supplemented with L-tryptophan) in random order. Blind ratings of depression and obsessive compulsive (OC) symptoms were obtained. *Results:* ANOVA revealed significantly ($p = .04$) increased mean depression ratings on the ATD compared to the sham test day. Four of four patients with a history of depression showed an exacerbation of depressive symptoms during ATD relative to sham, compared with two of five patients without such history. ATD had no significant effect on mean OC ratings: only one of nine patients showed an exacerbation on OC symptoms with ATD. Data on additional subjects will be presented. *Conclusions:* This study replicates preliminary findings from a smaller non-overlapping sample that ATD increases depressive, but not OC, symptoms in OCD patients remitted on SRIs. This suggests that maintainence of SRI-induced remission of OC symptoms, unlike remission of depressive symptoms, may not depend entirely upon ongoing availability of serotonin.

NR142 Monday May 4, 3:00 p.m.-5:00 p.m.

Specificity of Anger Response to M-CPP

Mark Germine, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Andrew W. Goddard, M.D., Diane E. Sholomskas, Ph.D., George R. Heninger, M.D., Dennis S. Charney, M.D., Scott W. Woods, M.D.

Summary:

In a recent study we reported increased anger in GAD patients relative to healthy subjects after IV administration of MCPP, a serotonergic agent. In order to determine if this finding is specific to GAD, we examined unpublished self-rated anger data from MCPP challenges in unmedicated patients. Based on a visual analog scale (0-100 mm) and infusion of MCPP 0.1 mg/kg IV, the following mean baseline anger ratings and peak MCPP/placebo differences were noted; GAD (n = 10), 3 mm, +22 mm ($p < 0.005$); healthy (n = 19), 1 mm, +4 mm (NS); panic disorder (n = 23), 7 mm, +10 mm (NS); obsessive-compulsive disorder (n = 9), 9 mm, +9 mm (NS); and schizophrenia (n = 12), 20 mm, +1 mm (NS). ANOVAs comparing patients and healthy subjects showed a significant drug × diagnosis × time interaction for GAD ($p = 0.0005$), but not for any of the other diagnoses. In major depression (n = 39), mean baseline anger rating and peak MCPP/placebo difference after MCPP 0.075 mg/kg IV were 7 mm, +2 mm (NS). In post-traumatic stress disorder (PTSD) patients (n = 14), anger was compared to healthy subjects (n = 10) after MCPP 0.1 mg/kg IV using a scale of 1 (none) to 5 (most ever), with the following mean baseline and peak MCPP/placebo differences: PTSD, 1.48, −0.06 (NS); healthy, 1.00, +0.10 (NS). Drug × diagnosis × time interaction on ANOVA was not significant. These data suggest that anger response to MCPP is relatively specific to GAD. This specificity suggests a link between the serotonin system, aggression, and GAD, and supports the validity of GAD as a clinical entity.

NR143 Monday May 4, 3:00 p.m.-5:00 p.m.

Serotonin-3 Receptor Blockade on MCPP Response in OCD Patients

Andreas Broocks, M.D., LCS, NIMH Bldg 10 Rm 3D41, 9000 Rockville Pike, Bethesda, MD 20892; Teresa A. Pigott, M.D., Dennis L. Murphy, M.D., Stephanie Canter, B.A., Tana A. Grady, M.D., Francine L'Heureux, M.D.

Summary:

The 5-HT agonist, m-chlorophenylpiperazine (m-CPP), has been associated with an exacerbation of OCD and behavioral symptoms in patients with OCD in comparison to controls. In order to investigate 5-HT_3 function in OCD and potentially localize the 5-HT receptor site(s) affected by m-CPP, we intravenously administered m-CPP (0.08 mg/kg.) and the potent 5-HT_3 antagonist, ondansetron (0.15 mg/kg), to OCD patients and controls. All of the subjects received four separate challenges (m-CPP after pretreatment with ondansetron or placebo; ondansetron with placebo and placebo alone). This was performed under double-blind conditions using standardized rating scales; serial blood samples and vital signs were obtained throughout the three-hour procedure. Physical symptoms were recorded for a total of 10 hours. In controls, ondansetron or placebo administration did not produce any behavioral effects or sedation. In contrast, m-CPP administration was associated with significant behavioral effects, particularly anxiety, activation, and functional impairment. Interestingly, m-CPP's acute behavioral effects (0-15 min.) after pretreatment with ondansetron were not significantly different from m-CPP administration alone, but later behavioral ratings (≥45 min. after m-CPP administration) revealed significant reductions in some of the behavioral responses after pretreatment with ondansetron. We observed an increase of norepinephrine levels 30 min. after the administration of m-CPP. This response was not affected by pretreatment with ondansetron. Comparative behavioral effects between the OCD patients and the controls, as well as further neuroendocrine data, will be presented.

NR144 Monday May 4, 3:00 p.m.-5:00 p.m.

A Controlled Trial of Clonazepam Augmentation in OCD Patients Treated with Clomipramine or Fluoxetine

Teresa A. Pigott, M.D., LCS/SCN, NIMH Bldg 10 Rm 3D41, 9000 Rockville Pike, Bethesda, MD 20892; Francine L'Heureux, M.D., Cheryl S. Rubenstein, M.A., James L. Hill, Ph.D., Dennis L. Murphy, M.D.

Summary:

Psychotropic medications that are selective for serotonin (5-HT) reuptake-inhibition, including clomipramine (CMI) and fluoxetine, (FLX) appear to be particularly effective in the treatment of obsessive compulsive disorder (OCD). Unfortunately, effective treatment is associated with only partial reduction in OCD symptoms. There have been several case reports of the successful use of the benzodiazepine, clonazepam (CNZ), which has some 5-HT1a receptor effects, as an adjuvant agent in the treatment of OCD. Eighteen patients who met DSM-III-R criteria for OCD and who had been receiving a stable dose of CMI (mean dose ± SEM, 195 ± 12 mg/day, n = 10) or FLX (mean dose ± SEM, 80 ± 0 mg.day, n = 8) for at least 10 weeks with at least partial OCD symptom reduction (mean YBOCS ± SEM, 18.4 ± 0.8) were enrolled in a 10-week, double-blind, crossover trial of four weeks each of adjuvant CNZ and placebo (PBO). Patients were serially rated with standardized rating scales (YBOCS, NIMH-OC, Ham-D, Global Anxiety). Analyses of the data by repeated measures ANOVA revealed a significant drug difference between adjuvant CNZ and PBO treatment on two scales (Global Anxiety and OC Scale). Adjuvant CNZ was associated with a significant reduction in anxiety symptoms; OCD symptoms were significantly reduced on the Global OC Scale, but not on the YBOCS or NIMH-OC Scales. These results, in contrast to previous controlled adjuvant medication trials (buspirone, lithium, and thyroid) in OCD patients, suggest that adjuvant CNZ treatment may be associated with additional antianxiety, and possible antiobsessive, effects when combined with CMI or FLX.

NR145 Monday May 4, 3:00 p.m.-5:00 p.m.

Dissociative Experiences Scale Scores in Patients with OCD

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Summary:

Obsessive compulsive disorder (OCD) is currently classified as an anxiety disorder in DSM-III-R and is generally associated with intrusive thoughts and/or perseverative, stereotypical behaviors. The Dissociative Experiences Scale (DES) has been shown to be a reliable and valid measure of dissociative experiences in a variety of psychiatric disorders, and DES scores of 30 or greater have been reported to reflect significant levels of dissociative psychopathology. Patients with post-traumatic stress disorder (which is often associated with intrusive thoughts or images) have relatively high DES scores (mean ± SEM, 30.0 ± 1.5). Since some investigators have hypothesized that OCD, like PTSD, is associated with increased levels of dissociation, we administered the DES to 38 patients (mean age ± SEM, 37.7 ± 1.7 yr., 20 females, 18 males) meeting DSM-III-R criteria for OCD. The total DES score for the OCD patients (mean ± SEM, 8.8 ± 1.7) was similar to DES scores previously reported in control groups. Only one OCD patient (2.6%)

had a DES score greater than 30 (total, 59.8). The OCD patients scored higher on the DES subscales of absorption/involvement (mean ± SEM, 13.3 ± 2.1) in comparison to the subscales of amnestic experiences (mean ± SEM, 3.3 ± 1.4) or derealization/depersonalization (mean ± SEM, 3.4 ± 1.3), but the subscale scores were similar to those reported for control populations. These results suggest that OCD is not characterized by substantial levels of dissociative symptomology, at least as measured by the DES.

NR146 Monday May 4, 3:00 p.m.-5:00 p.m.

Neuropsychological Testing in OCD

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Summary:

There is some evidence from brain-imaging studies that basal ganglia dysfunction may be associated with obsessive compulsive disorder (OCD); moreover, certain basal ganglia lesions may be associated with the development of OCD symptoms. In order to further evaluate basal ganglia dysfunction in patients with OCD as well as the potentially related disorder of trichotillomania, we administered a series of neuropsychological tests to a group of patients meeting DSM-III-R criteria for OCD (n = 19) or trichotillomania (n = 11) and compared them to age- and sex-matched normal volunteers (n = 16). Based on previous studies of patients with Huntington's disease (HD), the neuropsychological test battery included measures of attention, information processing speed, spatial orientation, retrieval processes, memory, and motor-skill learning. Contrary to expectation, overall analyses of the data failed to demonstrate any statistically significant differences between patients with OCD or trichotillomania and the normal volunteers. These results do not support the presence of HD-like basal ganglia dysfunction in patients with OCD or trichotillomania, and also raise the question of other brain area involvement besides the basal ganglia in OCD and trichotillomania.

NR147 Monday May 4, 3:00 p.m.-5:00 p.m.

Body Dysmorphic Disorder: 50 Cases of Imagined Ugliness

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Summary:

Problem: Body dysmorphic disorder (BDD), a preoccupation with an imagined defect in appearance, is included in DSM but has received little empirical study. *Method:* We assessed in 50 patients BDD's demographics, phenomenology, course, associated features, treatment history and response, and comorbid DSM-III-R disorders, using the SCID and a semistructured interview. Family history was obtained by a blinded investigator. *Results:* The 28 men and 22 women studied reported a lifetime average of four bodily preoccupations, most commonly "defects" of the hair, nose, and skin. BDD's average age of onset was 16 (range 6-42 years), and it had an average duration of 17 years. A total of 76% reported associated ideas or delusions of reference; 78% excessive mirror checking; and 78% attempts to camouflage the "deformity." As a result of their BDD, 94% had experienced significant impairment in social, school, or occupational functioning; 26% had been housebound; 24% had been psychiatrically hospitalized; and 26% had made suicide attempts. Also, 92% had an associated lifetime diagnosis of major mood disorder; 28% a psychotic disorder; and 72% an anxiety disorder. Patients generally responded poorly to surgical, dermatologic, and dental treatments and to most psychotropic medications, with the exception of fluoxetine and clomipramine (61% of trails led to a 30%-100% improvement vs. 5% with all other medications). *Conclusion:* BDD is an often secret, chronic disorder that can cause significant distress and impairment and that may respond to serotonergic antidepressants.

NR148 Monday May 4, 3:00 p.m.-5:00 p.m.

Serotonin Responses to D-Fenfluramine and Buspirone in OCD

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Summary:

Cortisol and prolactin responses to D-Fenfluramine (D-Fen) were measured in 10 drug-free normothymic patients with a DSM-III-R diagnosis of obsessive compulsive disorder. Animal work suggests the prolactin (PRL) responses to D-Fen are mediated by 5HT-2 receptor subtype. The endocrine responses in OCD were significantly attenuated when compared with 10 matched, healthy controls. However, this attenuation was not specific to OCD as 10 matched DSM-III-R major depressives were similarly blunted. Buspirone (BUSP) is a 5HT agonist with activity at the 5HT-IA receptor. The BUSP induced PRL response was examined in 10 additional patients with a DSM-III-R diagnosis of OCD. The responses were compared with the PRL responses to BUSP challenge in 10 matched, healthy controls. These results indicate that the 5HT-IA receptor functions normally in OCD. Taken together the evidence suggests that in OCD a complex interaction of 5HT receptor subtypes may be occurring, possibly with dysfunction primarily of the 5HT-2 subtype.

NR149 Monday May 4, 3:00 p.m.-5:00 p.m.

Caffeine Use in Generalized Anxiety Disorder

Jeffrey N. Billett, M.D., Psychiatry, Univ Calif. Davis Med Ctr, 4430 V. Street, Sacramento, CA 95817; Richard J. Maddock, M.D., Cameron S. Carter, M.D.

Summary:

In light of published data about increased sensitivity to caffeine and decreased caffeine use in patients with panic disorder, we have investigated caffeine consumption and subjective sensitivity to caffeine in patients with generalized anxiety disorder (GAD). Using the Structured Clinical Interview for DSM-III-R, patients with GAD are being identified and their caffeine histories obtained. In the same so far, N = 20, mean daily caffeine consumption of 290.1 mg (sd = 417 mg) compares with published norms for caffeine consumption in the general population as well as nonpsychiatric control groups (means ranging 200 to 385). This contrasts with earlier studies of panic disorder patients that showed means for daily caffeine consumption ranging from 120 mg to 150 mg. We have identified a comparison group of 51 panic disorder patients, also using SCID criteria; the mean daily caffeine consumption in the panic group is significantly lower than in our GAD group (mean = 138.4, sd = 165.8, T = 2.21, d = 69, p = 0.03). These preliminary results suggest that GAD patients differ from PD patients in that they do not exhibit a heightened sensitivity to or a decreased consumption of caffeine. Final results on 40 patients with GAD will be presented along with clinical correlations.

NR150 Monday May 4, 3:00 p.m.-5:00 p.m.

Soft Signs and Familial Transmission of OCD

Bonnie Aronowitz, M.A., psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; Eric Hollander, M.D.,

Salvatore Mannuzza, Ph.D., Jodee Davis, M.A., Tim Chapman, M.S., Abby J. Fyer, M.D.

Summary:

We previously found that a subgroup of obsessive compulsive disorder (OCD) patients have neurological soft signs, a measure of neuropsychiatric impairment. Family psychiatric disorder history is contrasted in first-degree relatives (N = 104) of DSM-III-R-diagnosed OCD probands with high (5 or greater) vs. low (1 or 0) neurological soft signs. Relatives of high soft sign probands had a significantly greater rate of OCD (30%) and broadly defined OCD, (both DSM-III-R OCD and obsessions and compulsions that did not meet disorder impairment criterion) (40%), in comparison with low soft sign probands (10% and 13% respectively) (chi square = 7.03; $p<0.00$ and chi square = 9.64; $p<0.002$, respectively). In contrast, low soft sign probands' relatives had elevated rates of Generalized Anxiety Disorder (GAD), (44%) in comparison with high soft sign probands' relatives (23%) (chi square = 4.86; $p<0.028$). There were no significant differences between relatives' rates of all non-OCD anxiety disorders in the low (64%) and high (53%) groups. Findings suggest heterogeneous OCD subgroups, one of which is characterized by neurological deficits and high familial aggregation of OCD/OC symptoms and the other by a lack of neurological findings and high familial aggregation of gAD. Analysis of direct interview data on these families will be presented.

NR151 Monday May 4, 3:00 p.m.-5:00 p.m.

Symptom Progressions in OCD

David C. Rettew, B.A., Child Psychiatry, NIMH Bldg 10 Rm 6N240, 9000 Rockville Pike, Besthesda, MD 20892; Susan E. Swedo, M.D., Henrietta L. Leonard, M.D., Marge C. Lenane, M.S.W., Judith H.L. Rapoport, M.D.

Summary:

Specific symptoms from onset to follow-up of 79 children and adolescents with severe primary obsessive compulsive disorder (OCD) were recorded from chart review and grouped into categories according to the Yale-Brown Symptom Checklist. No significant age-related trends were found with any type of symptom. Across the study period, patients reported symptoms from many different symptom categories, with 47% displaying both washing and checking compulsions among others. No patients maintained the same constellation of symptoms from onset to follow-up. These data support the concept of OCD as an illness with a common underlying deficit and varied clinical manifestations.

NR152 Monday May 4, 3:00 p.m.-5:00 p.m.

A Descriptive Study of Compulsive Shoppers

Gary A. Christenson, M.D., Psychiatry, University of Minn, Box 393 420 Delaware St. SE, Minneapolis, MN 55455; Ronald J. Faber, Ph.D., Martina De Zwaan, M.D., Nancy C. Raymond, M.D., Sheila M. Specker, M.D., James E. Mitchell, M.D.

Summary:

Compulsive shopping has been suggested as a possible variant of obsessive compulsive disorder. To better characterize the compulsive shopping population, we compared 24 compulsive shoppers (CS) with 24 age- and sex-matched normal spenders (NS) who were differentiated using a diagnostic scale with prior demonstrated utility for this purpose. Subjects were evaluated with multiple instruments including a semi-structured interview inquiring about shopping behaviors and the Structured Clinical Interview for DSM-III-R (SCID). The typical CS was a 37-year-old married female with a household income of $65,000 who developed compulsive shopping at 18 years of age. She spent $110 during each compulsive shopping episode, usually buying clothes, shoes, and/or makeup. Purchases frequently went unused, and a debt of $5,000 had resulted solely from this behavior. Depression often preceded compulsive shopping, while feelings of elation, power, and loss of control were more typical during shopping. Subgroups of CSs may be characterized by impulsivity and compulsivity (especially hoarding). Compared with NSs, CSs were more likely to have generalized anxiety disorder (20.8% vs. 0%, $p = .018$), a lifetime history of alcohol abuse/dependence (47.8% vs. 12.5%, $p = .008$) and a lifetime history of a proposed DSM-IV eating disorder diagnosis (17.4% vs. 0%, $p = .033$). This study suggests that compulsive shopping is a definable syndrome worthy of further psychiatric study.

NR153 Monday May 4, 3:00 p.m.-5:00 p.m.

Psychological Symptoms in Mitral Valve Prolapse: A Control Study

Larry V. Amsel, M.D., Psychiatry, Payne Whitney Clinic, 525 East 68th Street, New York, NY 10021; Katherine M. Shear, M.D., Richard Devereux, M.D., Randi Kramer-Fox, M.S.

Summary:

Purpose: The relationship between mitral valve prolapse (MVP) and anxiety disorders has seen a decade of extensive and somewhat contradictory research findings. It has been suggested that ascertainment bias may account for much of the variation in research findings on MVP. The patients' help-seeking behavior patterns might select for different populations depending on the clinical setting.

Methods: In order to simultaneously control for this ascertainment bias and MVP status, we examined 121 patients presenting to a cardiology clinic for evaluation and 144 primary relations who did not seek medical or psychiatric attention. All subjects were given cardiac evaluations for MVP and completed SCL-90 questionnaires. A two-way ANOVA was conducted to test for effects of help-seeking status and MVP status on SCL-90 variables.

Results: The help-seeking group had significantly higher scores on SCL-90 total, and on somatization, anxiety, obsessive compulsive, and depressive subscales. We also found that subjects who did not have MVP had significantly higher scores on SCL-90 totals, and on all subscales except somatization and phobia.

Conclusions: Subjects who present for cardiac evaluation who do *not* have MVP have higher scores on SCL-90 than similar subjects who do have MVP and also score higher than on-help seeking relatives with or without MVP. We found no evidence of an association between any SCL-90 subscales and MVP. These findings fail to support an association between MVP and anxiety, somatization, or other neurotic symptoms. Instead, they support a significant relationship between help seeking and psychological symptoms.

NR154 Monday May 4, 3:00 p.m.-5:00 p.m.

Descriptive Characteristics of Various Somatoform Disorders

Michael Bach, M.D., Psychiatry, Univ of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria; Detlev O. Nutzinger, M.D., Martina De Zwaan, M.D., Lydia Hartl, M.D.

Summary:

The diagnostic utility of different types of somatoform disorders as proposed by DSM-III-R still remains to be investigated. We determined the lifetime prevalence of DSM-III-R diagnoses among 122 patients with an anxiety disorder using a structured clinical interview (SCID). Seventy-six patients (62%) met criteria for a somatoform disorder with two-thirds reporting hypochondriasis. We did not find a significant difference in the lifetime prevalence of depression between patients with or without somatoform disorders

(57% vs. 48%). With regard to different types of somatization, undifferentiated somatoform disorder (USD) was found more often to be the primary disorder ($p < 0.01$) as compared with somatization disorder (SD) and hypochondriasis (HYP). Patients with an USD exhibited an earlier disease onset with respect to any Axis I diagnosis (13.4a vs. 15.4a in SD and 19.7a in HYP, respectively) as well as to the somatoform disorder (16.9a vs. 23.2a in SD and 28.3a in HYP, respectively). In addition, a chronic course of illness was more common in USD (83.3%) as compared with SD (77.8%) and HYP (71.4%). These findings underline the clinical utility of USD as a distinct diagnostic entity in addition to SD and HYP, as suggested in DSM-III-R.

NR155 Monday May 4, 3:00 p.m.-5:00 p.m.

Decreased Hippocampal Volume iN PTSD

J. Douglas Bremner, M.D., Psychiatry, Yale Univ. West Haven, 116A West Haven VAMC, West Haven, CT 06516; John P. Seibyl, M.D., Tammy N. Scott, B.S., Steven M. Southwick, M.D., Dennis S. Charney, M.D., Robert B. Innis, M.D.

Summary:

Objective: Studies in nonhuman primates suggest that high levels of cortisol may have neurotoxic effects on the hippocampus. The purpose of this study was to measure hippocampal volume in patients with post-traumatic stress disorder (PTSD) and matched controls. *Methods:* Magnetic resonance imaging (MRI) with T1-weighted images was used to perform volumetric assessments of hippocampal volume. Vietnam combat veterans with PTSD ($N = 22$) and comparison subjects ($N = 20$) were matched for age, sex, height, weight, years of education, handedness, and alcohol use. *Results:* PTSD patients had decreased mean hippocampal volume when compared with comparison subjects: 1591 ± 229 v. 1798 ± 3418 ($t = 2.24$; $df = 39$; $p = 0.026$). There was no difference in a control organ, the corpus callosum (158.8 ± 28.9 v. 155.5 ± 22.9). *Conclusions:* We conclude that decreased hippocampal volume may be associated with combat-related post-traumatic stress disorder, possibly through glucocorticoid-mediated neurotoxicity.

NR156 Monday May 4, 3:00 p.m.-5:00 p.m.

Deficits in Short-Term Memory in PTSD

J. Douglas Bremner, M.D., Psychiatry, Yale Univ. West Haven, 116A West Haven VAMC, West Haven, CT 06516; Tammy N. Scott, B.S., Richard Delaney, Ph.D., Steven M. Southwick, M.D., David R. Johnson, Ph.D., Dennis S. Charney, M.D.

Summary:

Objective: Studies in nonhuman primates suggest that cortisol may have neurotoxic effects on the hippocampus. This study compared memory function in patients with combat-related post-traumatic stress disorder (PTSD) to matched controls. *Method:* The Wechsler Memory Scale (WMS), Selective Reminding Test (SRT), and Wechsler Adult Intelligence Scale-Revised (WAIS-R) were administered to PTSD patients ($N = 22$) and controls matched for age, sex, alcohol abuse, education, and handedness. *Results:* PTSD patients scored lower on the Logical Memory component of the WMS for immediate recall (11.2 ± 2.9 v. 23.5 ± 17.0; $p = 0.01$), delayed recall (7.7 ± 3.4 v. 16.8 ± 5.5; $p = 0.0001$), and percent retention (68% v. 81%; $p = 0.06$), as well as on all components of the SRT, including Verbal Recall (89 ± 21.8 v. 112 ± 13.1; $p = 0.0005$) and Visual Recall (114 ± 16 v. 132 ± 6.5; $p = 0.0001$), while there was no difference in Full Scale IQ (100.2 ± 20.2 v. 104.3 ± 17.7). *Conclusions:* Patients with post-traumatic stress disorder may have deficits in attention and short-term memory.

NR157 Monday May 4, 3:00 p.m.-5:00 p.m.

The Clinician Administered Dissociative States Scale

J. Douglas Bremner, M.D., Psychiatry, Yale Univ. West Haven, 116A West Haven VAMC, West Haven, CT 06516; Frank W. Putnam, M.D., Steven M. Southwick, M.D., Cathryn Hansen, M.S., Glenna King, B.A., Dennis S. Charney, M.D.

Summary:

Objective: The Clinician Administered Dissociative States Scale (CADSS) is a 27-item scale (range 0-128) developed to measure dissociative states at baseline and following pharmacological challenges. *Method:* We used the CADSS for the measurement of dissociative states following infusion of the alpha-2 noradrenergic antagonist, yohimbine, in PTSD patients and comparison groups. *Results:* The CADSS was found to have acceptable validity when administered with the DES ($r = 0.51$; $p < 0.01$) and to discriminate patients ($N = 68$) with PTSD from other psychiatric disorders. PTSD patients had higher scores on the CADSS during yohimbine infusion (22.4 ± 22.9) than Vietnam veterans without PTSD (3.0 ± 3.2) and normal controls (5.9 ± 7.2) ($p < 0.05$). *Conclusion: The CADSS appears to be a valid and useful instrument for the measurement of dissociative states following pharmacological challenge.*

NR158 Monday May 4, 3:00 p.m.-5:00 p.m.

Noradrenaline: Serotonin Function in Insecure Primates

Jeremy D. Coplan, M.D., Psychiatry, Columbia Univ/NYSPI, 722 West 168th Street, New York, NY 10032; Leonard A. Rosenblum, Ph.D., Steven Friedman, Ph.D., Trina B. Bassoff, M.A., Jack M. Gorman, M.D.

Summary:

It has been proposed that the acute anxiety attacks evident in human panic disorder may involve malfunctions of the noradrenergic and/or serotonergic systems, and that disturbed early attachment experiences may provide a significant antecedent condition. In this study of nonhuman primates, early environments that produced variations in the relative security of infant attachment to mother resulted in differences in adult response to two putative anxiety-provoking agents: the noradrenergic probe yohimbine, and the serotonergic probe, mCPP. For instance, enervation, a form of behavioral withdrawal, was increased by yohimbine only in the insecurely reared subjects, and not in the normally reared subjects; in contrast, mCPP increased enervation in the normally reared but not abnormally reared animals (group X drug interaction; $p < 0.006$). These differences in response suggest that both neuronal systems can be permanently altered by disturbances in this aspect of development. The study supports the view that insecurity of early rearing experiences may adversely affect systems relevant to panic states.

NR159 Monday May 4, 3:00 p.m.-5:00 p.m.

Noradrenaline: Serotonin Interaction in Panic

Jeremy D. Coplan, M.D., Psychiatry, Columbia Univ/NYSPI, 722 West 168th Street, New York, NY 10032; Laszlo A. Papp, M.D., Jose Martinez, M.D., Leonard A. Rosenblum, Ph.D., Jack M. Gorman, M.D.

Summary:

In order to explore the interaction of noradrenergic and serotonergic systems in panic, oral clonidine challenges were performed before and during 12 weeks of treatment with fluoxetine, a serotonin reuptake blocking drug. We report on four sets of blood samples; 1) before treatment prior to the first clonidine challenge (BT1), 2)

before treatment during the first clonidine challenge (BT2), 3) after treatment prior to the second clonidine challenge (AT1), and 4) after treatment during the second clonidine challenge (AT2). Controls were also challenged twice with clonidine, but did not receive treatment between challenges. BT1 MHPG levels were higher in patients ($n=17$) vs controls ($n=5$) ($p<0.5$). MHPG levels fell in patients ($n=13$) from BT1 vs AT1 ($p=0.007$). All subjects ($n=17$) showed MHPG reductions in BT2 and AT2 ($p<0.001$). For neuroendocrine data, a group-by-time interaction ($p<0.001$) indicated that patients ($n=9$) showed blunted GH responses compared to controls ($n=3$). Of note, blunted GH responses persisted in the patients during AT2 despite fluoxetine treatment. These preliminary data support an interaction of noradrenergic and serotonergic systems in panic response—normalization of MHPG levels occurs during chronic serotonin reuptake blockade. GH response remains unaffected by treatment as reflected by persistent blunting despite noradrenergic normalization.

NR160 Monday May 4, 3:00 p.m.-5:00 p.m.

Biogenic Amines in HIV Infection Patients

Donatella Marazziti, M.D., Psychiatry, University, Via Roma 67, Pisa 56100, Italy; Pasquale Perretta, M.D., Letizia Galli, M.D., Cristiana Nisita, M.D., Antonio Scasso, M.D., Giovanni B. Cassano, M.D.

Summary:

We investigated the possible existence of a correlation between some urinary and cerebrospinal fluid (CSF) metabolites of biogenic amines and psychopathological disorders in HIV infection patients.

Thirty patients who were psychotropic drug-free and at different stages of HIV infection were included. The measurement of serotonin (5HT), noradrenaline (NA), and of dopamine (DA) metabolites was performed by means of a high-performance liquid chromatography (HPLC). The clinical status of all patients was assessed by the following rating scales: HRSD, HAMA, and SCL-90; diagnoses were made according to DSM-III-R criteria.

Our results seem to suggest that HIV infection decreases the 5HT synthesis, as shown by the reduced concentration of the 5-hydroxyindol-acetic acid (5HIAA) in both urines and CSF, and that the concomitant presence of depressive symptoms provokes a further decrease in HIAA levels.

NR161 Monday May 4, 3:00 p.m.-5:00 p.m.

Psychiatric Morbidity and Grief in HIV Infected Men

Jacquelyn Summers, M.S.W., Psychiatry, Summers, 2760 5th Avenue, San Diego, CA 92103; J. Hampton Atkinson, M.D., Sidney Zisook, M.D., Wesley W. Whitehall, M.A., J. Chandler, M.D., I. Grant, M.D.

Summary:

Objective: Unresolved grief is thought to be associated with subsequent psychiatric morbidity, but few data are available vigorously identifying the premorbid psychiatric histories and current findings of unresolved grief following loss. We examined psychiatric correlates in a sample at high risk for bereavement (men at high risk for human immunodeficiency virus infection).

Methods: Ambulatory men ($n=284$; CDC IV = 80, CDC II-III = 144, HIV− = 60) in a longitudinal cohort study were examined using the Structured Clinical Interview for DSM-III-R (SCID I) and Texas Revised Inventory of Grief (TRIG). Bereavement was measured for losses within the preceding 12 months. Resolution of grief was determined on a 0-4 Likert scale evaluating: (1) experience of grief for the deceased, (2) adjustment to the loss, and (3) capacity to discuss the loss without discomfort. Men categorized with "unresolved grief" exceeded standard cutoff scores of $\chi \geq 6$. Chi square was used to determine group differences. *Results:* 56% of the men reported a loss, 42.1% indicated a multiple loss. Of the 159 men reporting any loss, 13.8% ($n=22$) exceeded standard cutoff scores for unresolved grief. Grief was not associated with stage of illness. Chi-square analysis suggested a trend ($p \leq .06$) for men with unresolved grief to meet criteria for current major depression (18.2%) when compared with men with unresolved grief (5.1%) and men with no loss (5.6%). Premorbid lifetime histories of major depression, alcohol use disorder, substance use disorder, and generalized anxiety disorder were not associated with unresolved grief. Current assessment of mood symptomatology by use of ANOVA showed.

	I. Unresolved N = 22	II. Resolved n = 137	III. No Loss n = 125	p	Group Differences
Hamilton Depression (SD)	9.1 (8.4)	5.2 (5.4)	5.9 (6.7)	.03	1 & 2
Hamilton Anxiety (SD)	6.1 (4.9)	3.6 (4.0)	3.8 (4.3)	.04	1 & 2

Conclusion: Men with unresolved grief may be at risk for current major depression. Conversely, premorbid psychopathology did not appear to increase the risk of difficulties with grief resolution.

NR162 Monday May 4, 3:00 p.m.-5:00 p.m.

Health Education for HIV Subjects in Clinical Setting: An Evaluation

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Summary:

Eighty-five HIV seropositive subjects among consecutive new registrants in the STD department were given health education directed at avoiding high-risk behaviours and other events with a high potential for transmission of infection. The emphasis was on the use of condoms and discontinuing risky sex behaviours. The Health Education Programme was delivered individually to each subject over two or three sessions, each lasting for 30 to 45 minutes. At the time of follow up (one to 30 months), 42% of subjects had become nonpromiscuous. There was a good compliance on advice against marriage and pregnancy. Seven infants born during the follow-up period were seronegative. The use of condoms was not found to be acceptable. The prostitutes comprised the most resistant group to education. Among the factors that influenced the behaviour change favourably was the absence of earlier STD or a short duration of the current STD. Literacy, marital status, and awareness of AIDS did not influence the outcome of education. The study demonstrated the feasibility of health education at the individual level in the clinical setting. A follow-up study will evaluate the sustainability of behaviour change.

NR163 Monday May 4, 3:00 p.m.-5:00 p.m.

Comparison of Hemophiliacs and Gay Men with HIV

Snezana Cvejin, M.D., Psychiatry, Univ of North Carolina, Campus Box #7160, Chapel Hill, NC 27599; Jane Leserman, Ph.D., Diana O. Perkins, M.D., Carol Murphy, R.N., Kimberly Thompson, B.A., Dwight L. Evans, M.D.

Summary:

Although much has been written about depressed mood and social support among HIV seropositive homosexuals, little is known about these factors in seropositive hemophiliacs. Among men who are HIV seropositive, we compared hemophiliacs and homosexuals on dysphoria and social support. The sample included 130 HIV seropositive men (77% asymptomatic): 21 hemophiliacs, and 109 homosexuals. Hemophiliacs and homosexuals did not differ on disease progression ($p=.23$); however, the hemophiliacs were older ($p=.0004$) and less educated ($p=.03$). These groups did not significantly differ on current dysphoria (e.g. Carroll Rating Scale (CRS), Hamilton Depression (HAM-D), Profile

of Mood States (POMS) depression, tension and anger), but both had moderate dysphoria (CRS, x = 9.9, SD = 7.5; HAM-D, x = 5.5, SD = 5.1). The two groups did not differ on current major depression (modified SCID), although three (14%) of the hemophiliacs and 12 (11%) of the gay men presently had a major depression. The gay men tended (p = .06) to have more lifetime major depression (41%) than the hemophiliacs (19%). The groups also differed on some indicators of social support. Hemophiliacs participated in fewer AIDS-related groups (p = .0001) and sought less emotional support when coping with the threat of AIDS (p = .006). Hemophiliacs, however, reported less conflict in relationships (p = .03), and were more likely to disclose HIV status to their parents (p = .01) and receive parental support (p = .0004). These differences held when controlling for age, education, and disease progression. The two groups did not differ on overall satisfaction with social support (p = .64). To conclude, both groups had similar levels of dysphoric mood, however, hemophiliacs tend to use family supports, while homosexuals rely more on community support networks.

NR164 Monday May 4, 3:00 p.m.-5:00 p.m.

Social Conflict, Depression and AIDS

Martha E. Leatherman, M.D., Psychiatry, Univ of North Carolina, Campus Box #7160, Chapel Hill, NC 27599; Jane Leserman, Ph.D., Diana O. Perkins, M.D., Carol Murphy, R.N., John Boucvalt, B.S., Dwight L. Evans, M.D.

Summary:

Research suggests that social support influences the outcome of medical and psychiatric illnesses, but few studies have examined how social conflict may affect these conditions. As part of the Coping in Health and Illness Project (CHIP), we studied the relationship among dysphoric mood, social conflict, and social support measures. The sample included 69 asymptomatic HIV seropositive homosexual men with negative history of drug or alcohol abuse. Dysphoria was measured using self-report scales (POMS, Carroll Rating Scale) and interview methods (HAM-D, HAM-A). Diagnosis of RDC major depression was determined by review of a structured diagnostic interview (modified SCID) at a diagnostic conference. Social support was measured using self-report instruments; social conflict was measured with the Multicenter AIDS Cohort Study scale (Cronbach's alpha = .87). We found a consistent positive relationship between social conflict and all depression measures: 1) POMS depression (r = .47, p = .0001), 2) POMS tension (r = .40, p = .0006), 3) POMS anger (r = .42, p = .00024), 4) Carroll (r = .47, p = .0001), 5) HAM-17D (r = .37, p = .002), 6) HAM-A (r = .36, p = .003), 7) RDC major depression (r = .39, p = .0008). These relationships remained constant even after controlling for age, education, income, and length of time knowing HIV status. Instruments assessing positive aspects of social support were not significantly related to depression or dysphoria when controlling for social conflict. Our data suggest that clinicians should assess social support and social conflict in their HIV positive patients, since patients with substantial social conflict may be at high risk for depressive symptoms and major depression.

NR165 Monday May 4, 3:00 p.m.-5:00 p.m.

Prevalence of Unsafe Sexual Behaviors Among Psychiatric Inpatients

Strikumar Menon, M.D., Psychiatry, Loch Raven VAMC, 3900 Loch Raven Blvd., Baltimore, MD 21218; Sherry Pomerantz, Ph.D., Ernest Peacock, M.A., Corinthia Cohen, R.N., Sarahlee Horowitz, Psy.D.

Summary:

Persons with chronic mental illness are at high risk of acquiring HIV infection because they may have poor judgement, be impulsive and exhibit hypersexual behavior. These characteristics could lead to unsafe sexual behaviors such as having unprotected sex with multiple partners and exchanging sexual favors for drugs. We conducted a study to determine the prevalence and sociodemographic distribution of unsafe sexual behaviors among psychiatric inpatients (excluding those admitted only for drug and alcohol problems) and to investigate an association between crack-cocaine use and these behaviors. Two hundred and thirty-nine patients admitted to three psychiatric inpatient units in two Philadelphia hospitals during a 12-month period were interviewed to obtain a detailed sexual history, substance abuse history, knowledge about AIDS prevention and attitudes toward condom use. Having sex with three or more partners during the previous six months was reported by 27.3% of male patients and by 8.6% of female patients. A history of receptive anal intercourse at least once in the previous six months was reported by 3.7% of males and 26.7% of females. Statistically significant associations ($p < .05$) were observed between crack-cocaine use and unsafe sexual behaviors. This study draws attention to the role of crack-cocaine in the transmission of HIV infection and the need for intensive AIDS prevention programs directed at this population.

NR166 Monday May 4, 3:00 p.m.-5:00 p.m.

Suicidality, Psychiatric Morbidity and HIV Infection

John S. McDaniel, M.D., Psychiatry, Emory University/Clinic, 1365 Clifton Road, Atlanta, GA 30322; Elisabeth Fowlie, B.S., Obo Addy, M.D., Steven A. Cohen-Cole, M.D.

Summary:

This retrospective chart review was conducted to examine the extent of suicidality and psychiatric morbidity in HIV-related psychiatric consults in a large inner-city teaching hospital. Eighty-four percent of HIV-related consult records for the 24-month period (1/1/89 to 12/31/90) were reviewed. The chi-square test was used for data analysis. Records for first-time consults for 81 males and 19 females, ages 20-57, were included. No demographic differences were found.

Patients with a current diagnosis of substance abuse were more likely to have made a recent suicide attempt (p .05); four out of the five recent attempts had been made by patients with a diagnosis of substance abuse. According to their past psychiatric history, patients were categorized in one of the following groups; Group I—none (n = 35); Group II—psychiatric history without substance abuse (n = 11); Group III—substance abuse alone, including alcohol abuse (n = 39); Group IV—substance abuse and psychiatric co-morbidity (n = 12). The lifetime prevalence of suicide attempts increased from 0% in Group I, to 18% in Group II, to 23% in Group III, to 58% in Group IV (p = .00010). The lifetime prevalence of suicidal ideation rose from 3% in Group I, to 18% in group II, to 28% in Group III, to 67% in Group IV (p = .00009). These findings suggest that HIV-seropositive patients with a history of substance abuse alone or with other psychiatric comorbidity present a significant risk of suicidality.

NR167 Monday May 4, 3:00 p.m.-5:00 p.m.

A Prospective Study of HIV-Associated Psychosis

Daniel D. Sewell, M.D., Psychiatry, Univ of California, 9500 Gilman Drive 0603V, San Diego, CA 92093; Dilip V. Jeste, M.D., J. Hampton Atkinson, M.D., James L. Chandler, M.D., Igor Grant, M.D., and the HNRC Group

Summary:

New-onset psychosis in individuals infected with HIV is a poorly studied entity. *Methods:* 20 subjects developing psychosis after infection with HIV were studied. Exclusion criteria included history of functional psychosis before HIV infection or presence of delirium or drug-induced organic disorder. Subjects received an extensive

evaluation including structured psychiatric interview, cerebral spinal fluid (CSF) analysis, and comprehensive neuropsychological assessment. HIV seropositive controls (N = 20) were matched to index subjects one-to-one according to age, race, education, and CDC Stage. *Results:* Mean values for the entire sample were: age = 35 years, educational level = 14 years, and absolute T4 cell count = 320 cells/cc. Subjects were diagnosed as CDC Stages (N) II (2), III (6) and IV (12). CSF analysis revealed that psychotic subjects had a lower mean protein level, (30.9 ± 8.5 for subjects and 41.8 ± 10.2 for controls; $p = 0.029$, two-tailed t-test). Subjects also showed a trend toward lower mean CSF white blood cell count (3.3 ± 4.5 cells/cc for subjects and 9.7 ± 9.0 for controls; $p = 0.10$, two-tailed t-test). Two different global ratings of neuropsychological function revealed that subjects had significantly more neuropsychological impairment than controls. The mean values (SD) for subjects and controls on the Average Impairment Index were 1.41 (0.54) and 0.99 (0.46), respectively ($p < 0.05$, one-tailed t-test), and the mean values for subjects and controls for the Halstead Impairment Index were 0.47 (0.27) and 0.29 (0.23) respectively ($p < 0.05$, one-tailed t-test). *Summary:* Despite similar age, gender, education level, and CDC stage, psychotic subjects, compared with controls, appeared to have less evidence of an immunologic response in CSF and more neuropsychological impairment. Clinicians should be alert to the potential for HIV-associated cognitive disorders in HIV patients with new-onset psychosis.

NR168 Monday May 4, 3:00 p.m.-5:00 p.m.

Psychological Distress of IV Drug Users with HIV Disease

Vasu Putcha, M.D., Psychiatry, East Orange VAMC, 30 Bergen St. #1501, Newark, NJ 07107; Maureen Kahn, M.D., Edward Latimer, M.D., Carol L. Alter, M.D., James Maher, M.D., Haftan Eckholdt, Ph.D., Thomas M. Sprague, D.O.

Summary:

Intravenous drug users (IVDU) comprise the largest group of patients currently with HIV disease, yet the majority of studies examining psychosocial disorders in patients with HIV disease have focused on homosexual males. The present cross-sectional study of 75 IVDU's 1) assessed levels of self-reported psychological distress ("distress"); 2) screened for neuropsychological dysfunction; 3) examined how the degree of HIV disease, current level of substance use and AIDS-related concern impacts on the level of distress. All subjects underwent a battery of psychosocial assessments, including the Brief Symptom Inventory (BSI), Halstead-Reitan Trails A & B, Addiction Severity Index (ASI), and the Impact of Events Scale (IES). Of the subjects, 25 were HIV positive asymptomatic, 15 patients had CDC class III, IVA and IVC2 (ARC) disease, 15 patients had CDC-defined AIDS, and 20 were HIV-negative IVDU's. Patients with HIV disease, regardless of degree of illness, scored significantly worse on the Trails A ($t = -2.17$, $p < .05$), Trails B ($t = -2.56$, $p < .02$) and had greater levels of distress (BSI) ($r = .29$, $p < .05$). Severity of drug use (ASI) was also significantly related to level of distress (BSI) ($r = .31$, $p < .02$). Multiple regression analyses revealed that distress (BSI) was predicted by drug use and AIDS-related distress (IES) ($f = 5.96$, $p < .001$).

NR169 Monday May 4, 3:00 p.m.-5:00 p.m.

Psychiatric Symptoms and Stress in HIV Positive Women

Cheryl Ann Kennedy, M.D., Psychiatry, UMDNJ-NJ Medical School, 185 South Orange Avenue, Newark, NJ 07103; Patricia Kloser, M.D.

Summary:

Psychological factors may influence the course of HIV illness and adversely affect compliance with treatment and educational directives to reduce high-risk behaviors for HIV transmission. Little is known about psychological symptomatology in HIV+ women. We are assessing psychological symptoms, perceived stress and intrusion/avoidance symptoms in HIV+ women attending an inner-city university hospital infectious disease clinic. Among 14 HIV+ women in this ongoing study (median age 40, range 27-53), 12 were African-American; nine were asymptomatic, four had AIDS. Self-report measures included the Brief Symptom Inventory (BSI), Impact of Events Scale (IES) and Perceived Stress Scale (PSS).

The mean PSS was 28.3 ± 11.1, contrasted with population norms of 21 for women of comparable age and ethnicity. Fifty-seven percent of subjects were >1 s.d. above the population mean. PSS scores appeared higher among the four women with AIDS (30.5 ± 5.9) than among asymptomatic women (27.4 ± 12.8), although not statistically significant. Three women, *all* with AIDS, fulfilled the BSI "case definition" for psychiatric disorder; three women (21%), two with AIDS, warranted intervention because of suicidal ideation, and four, two with AIDS, showed clinical paranoid features.

HIV+ women show high levels of distress and, especially for symptomatic patients, appear at risk for psychiatric morbidity. The findings, to be extended by additional subjects, underscore the need for psychiatric assessment and intervention in this population.

NR170 Monday May 4, 3:00 p.m.-5:00 p.m.

Psychiatric Morbidity in Women Infected with HIV

Steven L. Prenzlauer, M.D., Psychiatry, Beth Israel Med Center, First Avenue at 16th Street, New York, NY 10003; Elizabeth Getter, M.D., Philip A. Bialer, M.D., Joel J. Wallack, M.D.

Summary:

Objective: To determine the level of psychological distress and the prevalence of psychiatric disorders in HIV+ women attending an AIDS outpatient clinic in New York City. *Method:* We randomly recruited 45 women registered for clinic appointments and administered three self-report questionnaires: the Millon Clinical Multiaxial Inventory-II (MCMI-II), the Beck Depression Inventory (BDI), and the Spielberger State-Trait Anxiety Inventory (STAI). In addition, demographic data and stage of HIV illness according to the CDC Classification System were obtained. All test scores and data were anonymous. *Results:* Demographically, the majority of our subjects were Hispanic (60%) and Black (24%), and of child-bearing age (20-30: 18%, 31-40: 67%). Marital status revealed 38% married, 40% single, 11% divorced, and 9% widowed, with 77% of the women having children. Reported risk factors included IV drug use (76%), sexual contact with an IVDU (13%), and "other" (11%). The STAI revealed high levels of anxiety in the majority of the patients with scores greater than one standard deviation above the norm. The BDI showed scores consistent with no or mild depression in 46% of our sample and moderate or severe depression in 44%. The MCMI-II profiles also demonstrated high scores on anxiety scales but showed little evidence of depression. A high prevalence of character pathology in the Histrionic/Narcissistic/Antisocial cluster was also noted. *conclusion:* Our study demonstrates high levels of anxiety in HIV+ women, a group that has so far received inadequate attention regarding psychiatric morbidity. Additional research is required to identify the special needs of HIV+ women, as compared with the cohorts of gay white men studied extensively, in order to develop more specific interventions and programs.

NR171 Monday May 4, 3:00 p.m.-5:00 p.m.

Personality Disorders in HIV

Stephen J. Brown, M.D., Psychiatry, Univ of Calif San Diego, 2760 5th Avenue, San Diego, CA 92103; Jacquelyn Summers, M.S.W., J. Hampton Atkinson, M.D., Wesley W. Whitehall, M.A., James L. Chandler, M.D., Igor Grant, M.D.

Summary:

Objective: To examine the prevalence of Axis II disorders in a population at risk for HIV infection. Previously, we have observed with others, elevated lifetime prevalences of Axis I diagnoses often preceeding the AIDS epidemic. We wanted to examine the relationship between lifetime Axis I diagnoses and Axis II diagnoses.

Method: Subjects were ambulatory HIV+ and HIV− men (N = 188) participating in a longitudinal cohort study, who were examined using the Structured Clinical Interview for DSM-III-R Axis 1 and Axis II diagnoses (SCID I & II). Subjects were excluded for lifetime presence of IV drug use. Men were classified as seronegative (n = 47), CDC II-III (n = 92), and CDC IV (n = 47). Mean age was 32.1 years; mean education, 14.3 years.

Results: The prevalence of Axis II diagnoses was 9.6% characterized as follows:

Cluster A (n = 7)	Cluster B (n = 4)	Cluster C (n = 7)
Paranoid = 4	Borderline = 1	Avoidant = 1
Schizotypal = 3	Narcissistic = 1	Obsessive compulsive = 3
Schizoid = 0	Personality NOS = 2	Passive-Aggressive = 3
	Histrionic = 0	Dependent = 0
	Antisocial = 0	

There was no significant association between serostatus or CDC class and the presence of an AXIS II diagnosis. There was no association between lifetime diagnoses of major depression, generalized anxiety disorder, nor any substance use disorder and an Axis II diagnosis. There was no association between the presence of "any" lifetime Axis I diagnosis, nor the number of lifetime Axis I diagnoses and the presence of an Axis II disorder.

Conclusion: Previous reports of high rates of Axis II disorders in HIV samples may reflect inclusion of IV drug abusing subjects. Assumptions about subpopulations at risk for HIV may need to be re-examined. Furthermore, studies of personality disorders in psychiatric samples may not be applicable to the general population.

NR172 Monday May 4, 3:00 p.m.-5:00 p.m.

Personality Disorder in HIV

David F. Naftolowitz, M.D., Psychiatry, Univ of North Carolina, Campus Box 7160, Chapel Hill, NC 27599; Diana O. Perkins, M.D., Robert A. Stern, Ph.D., Jane Leserman, Ph.D., Michael A. Senger, M.A., Dwight L. Evans, M.D.

Summary:

We recently reported a high prevalence of DSM-III-R personality disorder (PD) in HIV-infected persons. To evaluate for possible organic PD and for PD effects on psychosocial functioning, we now examine: 1) PD prevalence in a larger sample (n = 144) of asymptomatic HIV-seropositive (n = 81) and seronegative (n = 63) gay men; 2) relationships between PD and neuropsychologic and immune function; and, 3) the influence of PD on illness coping and mood state. As part of the Coping in Health and Illness Project, subjects underwent psychiatric (using SCID and SCID-II; diagnoses by consensus) and neuropsychologic evaluation as well as questionnaire measures of coping behavior and affect. In seropositives, despite evidence of mild neuropsychologic impairment, there was no correlation between PD and neuropsychologic function (in a subsample without confounding histories of moderate-severe substance abuse; n = 69). Measures of illness severity, such as helper/suppressor ratio, also were not correlated with PD. Among seropositives, PD subjects showed more denial (p = .0031), helplessness (p = .0103), conflict (p = .0172), hopelessness (p = .0044), anxiety (p = .0008), depression (Hamilton, p = .0001; Carroll, p = .003), and POMS depression (p = .0037), tension (p = .0042), and total mood disturbance (p = .0101) than non-PD subjects. As previously reported, seropositives tended to have more PD diagnoses (31%) than seronegatives (17%) (p = .065), perhaps due to greater sexual risk-taking and less education among PD subjects before becoming infected. Overall, the results of this study suggest PD does not have an HIV-related organic basis in this sample. PD patients also appear to have exaggerated difficulties coping effectively with their illness and treatment.

NR173 Monday May 4, 3:00 p.m.-5:00 p.m.

Psychiatric Referral for Substance Disorders

Iqbal Q. Sheikh, M.D., Psychiatry, Nassau County Med. Ctr., 2201 Hempstead Turnpike J Bldg, East Meadow, NY 11554; Maria L. Tiamson, M.D., Ronald C. Golinger, M.D., Ethan Kass, D.O.

Summary:

Studies of low referral rates of patients with psychoactive substance use disorders (P-SUDs) have not differentiated clearly between actual recognition of the disorders and subsequent referral patterns.[1,2] This prospective study attempted to do so in a general hospital. Of 337 recent consecutive referrals for psychiatric consultation, 88 were for inpatients who had P-SUDs diagnosed by the psychiatrists. Of all the referrals, 8.6% specifically were for evaluation of P-SUDs, 99.4% for other psychiatric reasons and 8.1% for both categories of reasons. Prior to revealing their diagnoses, the consultants asked the referring physicians whether they believed the patients had major problems with psychoactive substances. The physicians did so believe for 81.8% (72/88) of patients with P-SUDs and for only 4.0% (10/249) of patients without those disorders (chi-square = 209.6, p<.00005), which suggests a high degree of recognition of the presence of the disorders. However, suspicion of P-SUDs had been mentioned at the time of initial referral for only 33.0% (29/88) of patients with P-SUDs, and for only 40.3% (29/72) of such patients regarding whom the physicians subsequently indicated that they believed psychoactive substance use was a major problem. There is a discrepancy between recognition of P-SUDs and explicit mention of this at the time of referral. We discuss some possible explanations for this referral behavior.

NR174 Monday May 4, 3:00 p.m.-5:00 p.m.

Neuropsychology of Polysubstance Abuse in Dual Diagnosis: A Jacksonian Model

Godehard Oepen, M.D. Affective Disorders, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Michael Levy, Ph.D., Anne Harrington, Ph.D., Meredith Handren, R.N., Linda Pinnone, Lic.SW, Ruth Saemann, PsyD.

Summary:

In psychiatric patients with both a major psychiatric illness and substance abuse ("dual diagnosis") two major problem areas seem to be overlooked: (1) the frequent presence of additional neuropsychological dysfunctions, both in the patient's history and in current clinical presentation; (2) the fact that most dual diagnosis patients do not restrict their abuse to one substance only, but usually abuse many substances, either at the same time or sequentially. We suggest a nonaccidental link between the frequent presence of neuropsychological dysfunction and frequent polysubstance abuse. We screened for the co-occurrence of a range of neuropsychological disorders in the chart documentation of 50 dual diagnosis patients and compared the results with 36 long-term psychiatric control inpatients. The significantly higher pattern of organic comorbidity in the dual diagnosis patients led us to suggest that a heterogeneous predisposing pattern of neuropsy-

chological dysfunction (neurodevelopmental, affective, impulsive, attentional) plays a causal role in the ultimate capitulation to dual diagnosis (psychiatric illness and polymorphous addictive behavior). It is suggested that failure to address "extra" neuropsychological conditions is a major cause of the treatment resistance and relapse in dual diagnosis patients.

NR175 Monday May 4, 3:00 p.m.-5:00 p.m.

Carbamazepine as an Aid to Smoking Cessation

Roger R. Laroche, M.D., Psychiatry, Mayo Clinic, 1903 22nd Street NW, Rochester, MN 55901; Teresa A. Rummans, M.D., Richard D. Hurt, M.D., Gary G. Lauger, M.S., Kenneth P. Offord, M.S., Barbara K. Bruce, Ph.D.

Summary:

Nicotine dependence is the leading preventable cause of death in the United States and constitutes the largest national public health problem. Yet no intervention to date provides uniform help with nicotine withdrawal and prolonged abstinence. Carbamazepine has been used to treat cocaine, alcohol, and benzodiazepine withdrawal (possibly secondary to its ability to suppress kindling-induced CNS excitability), but has never been studied for nicotine withdrawal. Carbamazepine also has mood stabilizing and antidepressant actions, which are particularly relevant regarding the coexisting mood disorder symptoms associated with nicotine abuse. We have investigated carbamazepine's impact on nicotine withdrawal and short-term abstinence through a randomized, double-blind, placebo-controlled study lasting eight weeks. Nine men and 11 women were divided into either a group administered carbamazepine 400 mg or a placebo group. Various parameters including change in smoking pattern, intensity of withdrawal symptoms, and change in mood, anxiety, and somatic symptoms were analyzed to determine the impact of carbamazepine on smoking cessation.

NR176 Monday May 4, 3:00 p.m.-5:00 p.m.

Alcohol Use and Psychotropic Compliance of Elders

Daniel P. Chapman, Ph.D., Preventive Medicine, University of Iowa, 2800 Steindler Building, Iowa City, IA 52242; Robert B. Wallace, M.D.

Summary:

Alcohol abuse and dependence are frequently comorbid with a variety of psychiatric disorders. The identification of heavy drinking in older adults has proven particularly problematic as alcohol abuse may exacerbate psychiatric symptoms, such as depression, slowed mentation, memory retrieval impairment, and agitation. Since cognitive status has been identified as an important predictor of medication compliance of older adults, this investigation examines the effect of alcohol use on compliance with psychotropic medications among older adults living in the community. History of alcohol use and psychotropic medication compliance were assessed during in-person interviews of 1,155 men and 1,942 women respondents in the Iowa 65+ Rural Health Study. Psychotropic noncompliance was associated with a self-reported history of ever drinking heavily over a period of time among women—but not men—although neither former nor current drinking status individually predicted psychotropic compliance. These results support the importance of assessing lifetime alcohol use history in the psychiatric evaluation of older women and suggest that current sobriety is not a reliable predictor of psychotropic compliance.

NR177 Monday May 4, 3:00 p.m.-5:00 p.m.

Buprenorphine and Laudanum for Opiate Maintenance

Marc Auriacombe, M.D., Psychiatry, Univ of Pennsylvania, 3900 Chestnut Street, Philadelphia, PA 19104; Denis Grabot, M.A., Jean P. Daulouede, M.D., Jean P. Vergnole, M.D., Charles P. O'Brien, M.D., Jean Tignol, M.D.

Summary:

The purpose of this study is to evaluate the impact of opiate maintenance pharmacotherapy (OMP) on the biopsychosocial status of opiate addicts in a cultural environment (France) that is not favorable to OMP and where methadone is not available. Buprenorphine, which has been shown in some studies to be potentially as useful as methadone, and laudanum (opium tincture) which, to our knowledge, has not been reported previously in the scientific literature for OMP, are used in this study of a group of 18 DSM-III-R opioid-dependant subjects. At time of initiation of OMP mean age was 33 years, sex ratio male/female 14/4, average duration of drug use 11.2 years. Six patients received laudanum p.o., 15 g daily; 12 patients received buprenorphine sublingual 2 to 4 mg daily. This group of patients was selected because of persistent relapse and impairment after an average of 5.7 drug-free oriented treatments. Initial evaluation and follow-up were made by way of a 150-minute semistructured interview using the Lifetime Retrospective Evaluation Score Table (Grabot et al) and the Addiction Severity Index (McLellan et al). Both instruments allow for a quantitative evaluation of addicted patients. Results show that body weight [Kg] and scores [scale 0 (extremely bad) to 6 (excellent)] for physical and psychological health, socioprofessional status and family relationships go respectively from 55;2.1;2;2.5;2.4 before OMP to 61;3.7;3.7;3.3;3.6 after 14 months of OMP. These increases in scores are statistically different (except socioprofessional status) with both parametric (Student t test $p<0.01$) and nonparametric tests (Wilcoxon t test $p<0.01$). These results show that highly impaired opiate addicts doing poorly in drug-free treatment can respond to OMP even though methadone is not available and the idea of OMP is not favored.

NR178 Monday May 4, 3:00 p.m.-5:00 p.m.

Assault, Substance Abuse and Axis II Comorbidity

Lorraine R. Dustan, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; Kathleen T. Brady, M.D., Dorothy E. Grice, M.D., Robert Malcolm, M.D., Dean G. Kilpatrick, Ph.D.

Summary:

Studies have indicated a high co-occurrence of substance abuse disorders, Axis II psychopathology, and assault. The overlap between these areas has not been well explored. The present study was undertaken to further clarify the relationship between substance abuse, assault, and Axis II disorders. Fifty-seven randomly selected inpatients (29 women, 28 men) being treated for substance abuse disorders were evaluated for a history of assault (sexual assault/molestation, attempted sexual assault/molestation, or aggravated assault) using a physician-administered screening instrument for victimization (Kilpatrick et al, 1990) and for the presence of an Axis II disorder using the structured clinical interview for DSM-III-R part II (SCID II). The SCID was administered after at least 14 days of abstinence. Mean age at the time of interview was $31.2 +/- 10.6$ years. There were no significant age differences between men and women, or victims and nonvictims. Seventy percent of the population were Caucasian. Substance abusers with a history of assault were significantly more likely to have an Axis II diagnosis than substance abusers without a history of assault ($F = 11.12$, $p<.05$). Substance abusers with a history of assault were more likely to have evidence of severe character pathology

(as defined by two or more Axis II diagnoses) when compared to substance abusers without a history of assault ($X^2 = 10.37$, $p<.005$). There were no significant gender differences noted. The most common Axis II diagnoses among those subjects with a history of assault were paranoid, borderline and antisocial personality disorders. The most common disorders in the ETOH-abusing group were avoidant, dependent and borderline personality disorders. The most common disorders in the cocaine-abusing group were paranoid, histrionic and antisocial personality disorders. There were significantly more cluster C personality disorders (avoidant/dependent/passive-aggressive) in the ETOH-abusing group when compared with the cocaine-abusing group ($X^2 = 4.6$, $p<=.05$). In this study, substance abuse patients with a history of assault were at substantially greater risk for Axis II disorders. Delineation of subsets within substance abuse patient populations may be helpful in developing more effective treatment strategies and more accurately predicting treatment outcome for individuals.

NR179 Monday May 4, 3:00 p.m.-5:00 p.m.

Assault, Substance Abuse and Axis I Comorbidity

Dorothy E. Grice, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; Lorraine R. Dustan, M.D., Kathleen T. Brady, M.D., Robert Malcolm, M.D., Dean G. Kilpatrick, Ph.D.

Summary:

Studies have indicated that both comorbid psychiatric diagnoses and a history of assault place individuals at risk for substance abuse disorders. This study presents data exploring the relationship between types of assault, psychiatric comorbidity, and substance abuse disorders. Fifty-seven randomly selected patients (28 men and 29 women) entering inpatient substance abuse treatment were surveyed using a structured standardized interview to determine lifetime histories of completed sexual assault, attempted sexual assault, or physical assault. The Structured Clinical Interview for DSM-III-R was administered to subjects after at least 14 days of abstinence in order to determine Axis I diagnoses. There were no significant differences in age between men and women or assault victims and non-victims at the time of interview. Seventy percent of the subjects were white and 30% were nonwhite although nonwhite individuals were twice as likely to have assault histories compared to white individuals ($\chi^2 = 3.78$, $p<.10$). Thirty-eight patients (66%) had experienced at least one type of assault. Men and women had the same risk for both a lifetime experience of assault (completed sexual, attempted sexual or physical) and for childhood assault (sexual and physical). Women had a significantly higher prevalence of lifetime sexual assault compared to men ($\chi^2 = 4.2$, $p<.05$). There was a trend for cocaine abusers ($n = 20$) to be at significantly higher risk for a lifetime prevalence of any type of assault when compared to other substance abuse classes ($n = 37$) ($\chi^2 = 3.26$, $p<.10$). There was a significantly higher prevalence of post-traumatic stress disorder in substance abusers with a history of assault ($\chi^2 = 7.39$, $p<.05$), even when controlling for the presence of other traumatic life events ($\chi^2 = 5.31$, $p<.05$). Substance abusers with a history of assault had a significantly higher lifetime prevalence of mood disorders ($\chi^2 = 6.6$, $p<.05$) and a trend for a higher lifetime prevalence of anxiety disorders ($\chi^2 = 3.2$, $p<.10$).In the present study of a substance abusing population, the majority had assault histories. Those individuals with a history of assault were more likely to have Axis I psychopathology. This study emphasizes the need to obtain both a detailed history of assault as well as a clinical history to determine the presence of psychiatric comorbidity in order to adequately assess and treat the substance abusing patient.

NR180 Monday May 4, 3:00 p.m.-5:00 p.m.

Compulsive Behaviors and Cocaine

Jed E. Black, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Wayne K. Goodman, M.D., Beth K. Boyarsky, M.S.N., Lawrence H. Price, M.D.

Summary:

CNS stimulant agents such as cocaine and amphetamines induce repetitive stereotypic behaviors in animals. Brain dopamine (DA) systems are thought to play a critical role in this effect. Serotonin (5HT) has also been implicated. Recently, cocaine has been reported to intensify symptoms in obsessive compulsive disorder (OCD) and elicit compulsive behavior in non-OCD primary cocaine abusers. We undertook to explore the possible relationship between cocaine and compulsive or stereotypic behavior in two populations of cocaine users. *Methods:* 14 OCD patients form our clinic who had used cocaine (group 1) and 26 age-, and sex-matched primary cocaine abusers from a substance abuse clinic (group 2) were administered a structured interview by a research psychiatrist. *Results:* Eleven (79%) of the group 1 (OCD) patients experienced symptom intensification during cocaine use. Of these three reported continued exacerbation during the six to 12 months following cessation of cocaine use, and one experienced the new onset of OCD following cocaine exposure. Twenty (77%) of the group 2 (primary cocaine abusers) subjects regularly experienced repetitive, stereotyped behaviors during cocaine use. Of these, nine experienced compulsive behaviors; nine experienced purposeful, repetitive behaviors that were not ego-dystonic, but which were excessive; and two experienced aimless repetitive behavior. *Conclusions:* The association of cocaine (a monoamine reuptake blocker) with repetitive, stereotyped behavior in the majority of subjects in both groups suggests a role for altered DA activity in OCD and is compatible with a probably regulatory role of 5HT systems. Also, the potential for long-term OCD exacerbation following cocaine use is suggested. The relationship between compulsive and non-compulsive repetitive stereotyped behavior will be discussed.

NR181 Monday May 4, 3:00 p.m.-5:00 p.m.

Movement Disorders in Schizophrenic Alcoholics

Robin M. Johnson, M.D., Psychiatry, Yale University, 950 Campbell Ave, West Haven, CT 06516; Thomas R. Kosten, M.D., Douglas M. Ziedonis, Boris Meandzija, M.D., William M. Glazer, M.D.

Summary:

Schizophrenic alcoholics may be predisposed to develop acute movement disorders when treated with antipsychotic medications, because chronic alcohol abuse may induce dopamine receptor supersensitivity (1). To assess this question we interviewed 398 schizophrenic patients treated with neuroleptics for one to 20 years and asked them about acute responses to neuroleptics and examined them using the Webster Parkinsonism exam. The rate of alcohol abuse was 23% ($n = 93$) with 17 subjects also being drug abusers. While the Webster showed no difference in alcoholics vs nonalcoholics, the alcoholics were more likely to report drooling as an acute neuroleptic response (25% vs 13%; $X2 = 6.7$; $p<0.01$), particularly if they had had delirium tremens (DT) (47% vs 15%; $X2 = 9.5$; $P<0.002$). Alcoholics with tremors after stopping alcohol more often reported stiffness after neuroleptics (53% vs 24%; $X2 = 8.2$; $P<0.005$), and alcoholics with hallucinations after stopping alcohol less often reported tremors after neuroleptics (6% vs 33%; $X2 = 5.6$; $P<0.02$). These associations were not due to age or duration of treatment, but neuroleptic dosage was related to both drooling and DTs. Thus, alcoholism may lead to noncompliance with neuroleptics due to increased acute side effects in schizophrenics.

NR182 Monday May 4, 3:00 p.m.-5:00 p.m.

Mazindol Augmentation of Neuroleptics in Cocaine Abusers

Robin M. Johnson, M.D., Psychiatry, Yale University, W. Haven VA Hosp Campbell Ave, West Haven, CT 06516; J. Seibyl, M.D., J. Erdos, M.D., D. Miles, R.N., D. Charney, M.D., George R. Heninger, M.D., J. Krystal, M.D.

Summary:

Despite the high prevalence and significant morbidity associated with cocaine abuse in schizophrenic patients, there has been little study of pharmacotherapies targeted to this group. The purpose of the present study is to evaluate the efficacy of the dopamine reuptake blocker, mazindol, in the treatment of cocaine-abusing schizophrenics. Mazindol binds to the dopamine transporter with greater affinity than cocaine. In an ongoing study, patients (n = 5) meeting DSM-III-R (SCID) criteria for cocaine abuse and schizophrenia participated in a 12-week study involving a four-week baseline evaluation period while receiving their usual dose of neuroleptic prior to an eight-week double-blind placebo-controlled trial of mazindol 2 mg/d, p.o. Outcome measures include the PANSS, AIMS, Webster Scale for Extrapyramidal Symptoms, Cocaine Craving Scale, reported amount of cocaine use, and twice weekly urine toxicology screens. Blood was also sampled for prolactin and HVA determinations. Preliminary findings suggest that mazindol may produce delayed beneficial effects on cocaine craving, cocaine abuse, and symptoms of schizophrenia in this population. Further analyses from this ongoing study will be presented. Also the clinical implications of mazindol augmentation of neuroleptic will be reviewed.

NR183 Monday May 4, 3:00 p.m.-5:00 p.m.

Serotonin Drugs Slow Brain Noradrenergic Cells in Opiate Withdrawal

Gary Aston-Jones, Ph.D., Mental Health, Hahnmann University, Broad & Vine MS 403, Philadelphia, PA 19102; Hideo Akaoka, Ph.D.

Summary:

Noradrenergic (NA) neurons of the nucleus locus coeruleus (LC) in morphine-dependent rats are strongly activated during opiate withdrawal (OW). We have recently shown that such activation of LC neurons is largely mediated by direct excitatory amino acid (EAA) input to LC (Akaoka and Aston-Jones, 1991). We have also shown that EAA-induced excitation of LC neurons is strongly attenuated by 5HT (Aston-Jones et al., J. Neurosci. 1991). Here, we examined the effects of systemically administered 5HT drugs on the OW-induced activation of LC neurons in halothane anesthetized, morphine-dependent rats. The 5HT releaser, d-fenfluramine (2 mg/kg, i.v.), substantially decreased the LC hyperactivity induced by naloxone-precipitated OW, from 3.9 ± 0.4 to 2.2 ± 0.3 Hz (n = 14 and 12). Fluoxetine, a 5HT reuptake blocker (4 mg/kg IV), yielded similar results (2.3 ± 0.2Hz post NLX + fluoxetine, n = 6). Sertraline, another 5HT reuptake-blocker (3 mg/kg + 100 mg/kg 5HTP, IV), also attenuated the LC hyperactivity (to 2.2 ± 0.3 Hz, n = 5). These results suggest that such 5HT drugs may be useful in treating opiate dependency. Supported by USPHS grant DA 06214.

NR184 Monday May 4, 3:00 p.m.-5:00 p.m.

Rational Recovery as an Alternative to Alcoholics Anonymous

Ceane Willis, Ph.D., Addiction Service, Mass General Hospital, MGH-ACC 812, Boston, MA 02114; David R. Gastfriend, M.D., Stephanie E. Meyer, B.A.

Summary:

Rational Recovery is a growing self-help organization for chemical dependence. We analyzed 165 responses to a questionnaire included in the R.R. treatise, "The Small Book." Most of the respondents were men with a mean age of 45 years (17-76) and dependence on alcohol, primarily. Over 90% reported currently being sober (mean duration 27 months). Almost 90% had attended Alcoholics Anonymous meetings, but of these, 72% discontinued. Nearly half left A.A. over conflicts with the principle of spirituality. Other reasons included disagreement with powerlessness and chemical dependence as a lifelong disease, difficulty relating to the A.A. program, feeling mistreated, or having outgrown the process.

One-fourth reported believing in God, while similar proportions described their personal philosophy as agnostic, atheist or humanist/other. The single most frequently attributed method for achieving sobriety was personal strength or willpower, followed by R.R. or Rational Emotive Therapy, and individual professional treatment.

These responses, notwithstanding methodologic limitations on generalizability and reliability, suggest that a substantial number of chemically dependent persons may be attracted to Rational Recovery from Alcoholics Anonymous because of philosophical and conceptual differences. Results suggest that these differences should be studied for their usefulness in clinical assessment, referral and treatment.

NR185 Monday May 4, 3:00 p.m.-5:00 p.m.

Desipramine in Crack Cocaine Treatment

Elisa G. Triffleman, M.D., Psychiatry, San Francisco VAMC, 650 42nd Avenue, San Francisco, CA 94121; Kevin Delucchi, Ph.D., Sharon Hall, Ph.D., Sandra Tunis, Ph.D., Peter Banys, M.D.

Summary:

This poster reports preliminary findings from a randomized, double-blind, placebo-controlled study of desipramine (DMI) treatment in crack cocaine dependence in male veterans. Of 71 subjects (Ss), 86% are African-American, 28% are homeless and 75% are unemployed. Abuse of other substances was not an exclusion criterion. Thus, this population is unique from previous study populations in the literature. Ss were started on DMI or placebo while inpatients and followed in the outpatient clinic. Thirty-five Ss were titrated to a maximum dose of 200 mg/day of DMI. Mean DMI blood level was 127 ± 104 ng/ml at wk. 2; 116 ± 101, at week 3. No differences have been found between the DMI or placebo conditions in measures of craving; cocaine withdrawal symptoms; POMS subscores; urine tox. results; or entry into outpatient phase. DMI blood levels also showed no correlation with these variables. Data from other measures of retention, abstinence, additional substance use, and the relationship with DMI blood levels will be presented.

NR186 Monday May 4, 3:00 p.m.-5:00 p.m.

The Use of Fluvoxamine in Detoxified Alcoholics

Lucien Barrelet, Psychiatrie, Hopital Cantonal, Perreux CH 2018, Switzerland; Claude Uehlinger

Summary:

Alcoholic patients shift between five main behaviors: stable abstinence, unstable abstinence with controlled or uncontrolled drinking, stable controlled drinking, stable uncontrolled drinking. They don't reach a stable abstinence. Controlled drinking is also a fair outcome category. It is reasonable to look for drugs that favor either abstinence or controlled drinking. Fluvoxamine, a selective serotonin reuptake inhibitor (SSRI), has been claimed to be useful in reducing alcohol intake and craving. In a double-blind clinical trial, 18 men and six women alcohol abusers recently detoxified were randomly assigned to receive daily doses of fluvoxamine (max.

300 mg) or placebo for 52 weeks. At follow-up visits on week 2, 4, 6, 7, 12, 16, 24, 32, 40, 52, information is collected about alcohol intake and intensity of alcohol crawing. Preliminary results have shown four drop-outs because of adverse experiences, loss of efficacy, or desire to be treated with other medication. We saw that moderately dependent drinkers decreased their alcohol consumption. Relapse rates of uncontrolled drinking were 33% during the 16 first weeks and will be calculated at a later date. Rehospitalizations were 66% during the first 16 weeks.

NR187 Monday May 4, 3:00 p.m.-5:00 p.m.

Benzodiazepine Treatment in Psychotic Disorders and Alcohol/Substance Dependence

Mohamed Toutoungi, M.D., Psychiatry, University of Geneva, CH Du Petit Bel Air 2, Geneva GE 1225, Switzerland; Anelise Muhlebach, Ph.D., Veronique Bahler, M.D., Antonio V. Andreoli, M.D.

Summary:

Significance: Benzodiazepines (BZ) may represent a valuable treatment in psychiatric patients with DSM-III-R psychotic disorders and alcohol/substance dependence, but received little attention within these clinical conditions. *Methods:* To explore BZ treatment and response in patients with both psychotic disorders and substance dependence, we developed a prospective pilot study of psychiatric patients referred for inpatient care. Inclusion criteria were age range 18-65 and multiple severe psychotic symptoms. Exclusion criteria were bipolar disorder, organic disorder other than alcohol/BZ withdrawal syndrome, mental retardation and multiple hospitalizations. Each subject was assessed with a battery of instruments (SCID-I, GAS, SAS, BPRS) and was carefully evaluated by an independent psychiatrist who assessed the clinical status at intake and discharge. *Results:* A total of 47 patients were studied; 10 patients met criteria for both brief reactional psychosis or atypical psychotic disorder and alcohol/BZ dependence (21.2%; alcohol : 6, 12.7%; BZ : 4, 8.5%). Those subjects who first received neuroleptic treatment were not clinically improved and developed dyskinetic side effects. *Comment:* We found high rates of acute psychotic disorders associated with alcohol/Bz drug dependence. The reported effects of BZ in these patients may be related to high prevalence of withdrawal syndrome. Further research should be directed to confirming the nosographic autonomy of these clinical conditions that are suggested to respond better to BZ than neuroleptic medication.

NR188 Monday May 4, 3:00 p.m.-5:00 p.m.

Liver Transplantation: Effects on Psychosocial Function and Psychological Symptoms

Ondria C. Gleason, B.S., Psychiatry, Univ of NE Med Center, 600 South 42nd Street, Omaha, NE 68198; William H. Roccaforte, M.D., William J. Burke, M.D., Barbara L. Bayer, M.S.N., Carl B. Greiner, M.D.

Summary:

The present study assessed the effect of liver transplantation (LT) on psychosocial function and psychological symptoms. Forty subjects being evaluated for LT as outpatients were studied prospectively using the Psychosocial Adjustment to Illness Scale (PAIS) and Brief Symptom Inventory (BSI).

At initial evaluation the two groups were comparable in age, gender, type of liver disease, cognitive function, PAIS and BSI scores. Twenty-three subjects received LT and 17 remained on the waiting list. Evaluations were repeated an average of 10.3 months later for those waiting and 11.6 months after LT for transplanted subjects.

BSI and PAIS scores did not change significantly over time within the waiting group. For those transplanted, significant improvement was seen for the social environment subscale and total PAIS scores, and for the BSI depression subscales at follow-up.

Comparing the two groups at follow-up, transplanted subjects scored significantly better in total PAIS score and in the categories of health care orientation and psychological distress. Global BSI scales 1 and 2 and the anxiety, depression, hostility and somatic subscales were also better in those transplanted.

These results indicate that subjects receiving liver transplants have better psychosocial functioning and less emotional burden when compared to a control group awaiting transplantation.

NR189 Monday May 4, 3:00 p.m.-5:00 p.m.

Eating Pathology in Diabetic Children

Ann C. Childress, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; Timothy D. Brewerton, M.D., Christina Rock, B.S.

Summary:

Some, but not all, studies have reported a high frequency of anorexia nervosa (AN) and bulimia nervosa (BN) in adolescent and young adult females with insulin dependent diabetes mellitus (IDDM). However, the prevalence of eating disorders in diabetic children has yet to be investigated. In the present study, 38 (N = 21 females, N = 17 males) diabetic middle school students in grades 5-8 (age range 10-14, $\bar{x} = 11.5 \pm 1.2$) completed the newly developed Kids' Eating Disorders Survey (KEDS) and were matched by grade, age, gender, race, and body mass index (BMI) to subjects randomly selected from 3,175 students who completed the KEDS six months earlier. More than 47% of diabetic respondents reported feeling fat. The following frequencies of weight control measures were reported also by diabetic children: dieting 18.4%, fasting 5.3%, vomiting 5.3%, diet pill use 2.6%, diuretic was 2.6%. No statistically significant differences were found between diabetics and controls for individual items, factor stores, and total scores on the KEDS. To achieve conclusive results on the possible increased risk for eating disorders in diabetics, prospective studies must be performed on diabetic children beginning with their initial diagnosis through early adulthood. In addition, data regarding glycemic control should be collected throughout, as some investigators have found a higher prevalence of eating disorders in older diabetics with poor glycemic control.

NR190 Withdrawn

NR191 Monday May 4, 3:00 p.m.-5:00 p.m.

Lifetime Prevalence of Eating Disorders in OCD

Cheryl Rubenstein, M.A., SCN LCS, NIMH Bldg 10 RM 3D41, 9000 Rockville Pike, Bethesda, MD 20892; Teresa A. Pigott, M.D., Francine L'Heureux, M.D., James L. Hill, Ph.D., Dennis L. Murphy, M.D.

Summary:

While obsessive compulsive disorder (OCD) is classified as an anxiety disorder, it appears to have some clinical and neurobiological overlap with the eating disorders. In order to assess in a controlled fashion the lifetime prevalence of the eating disorders in patients with OCD, we administered portions of the Structured Clinical Interview for DSM-III-R (SCID-P) to 31 males and 31 females with a primary DSM-III-R diagnosis of OCD. Among the OCD patients, the lifetime prevalence of anorexia nervosa and/or bulimia nervosa was 12.9%; an additional 19.7% met subthreshold criteria for either anorexia or bulimia nervosa. Interestingly unlike

multiple epidemiological studies that have reported a substantial female preponderance among patients diagnosed with anorexia or bulimia nervosa, there was no significant gender difference in the lifetime prevalence of eating disorders among the patients with OCD. Almost 13% of the males and 6.5% of the females with OCD met criteria for a lifetime diagnosis of anorexia nervosa, and 3.2% of the males and 6.5% of the females with OCD met criteria at some time in their lives for bulimia nervosa. Subthreshold criteria for anorexia nervosa or bulimia nervosa were met by an additional 12.9% of the males and 25.8% of the females. These data suggest that OCD patients, regardless of gender, have a substantial lifetime prevalence of anorexia and bulimia nervosa.

NR192 Monday May 4, 3:00 p.m.-5:00 p.m.

Eating Attitudes in Seasonal Affective Disorder and Bulimia Nervosa

Kevin G. Berman, M.D., Psychiatry, University of B.C., 2255 Wesbrook Mall, Vancouver BC V6T 2A1, Canada; Raymond W. Lam, M.D., Elliot M. Goldner, M.D.

Summary:

Objective: Seasonal affective disorder (SAD) is associated with atypical depressive symptoms including hypersomnia, hyperphagia, carbohydrate craving, and weight gain. The appetite disturbances seen in SAD also occur in other disorders such as bulimia nervosa. We decided to determine if the dysfunctional eating attitudes found in bulimia nervosa were also present in SAD.

Method: Depressed female SAD patients (N = 29), diagnosed using DSM-III-R criteria, completed the Eating Disorders Inventory (EDI), a standardized, self-rating questionnaire that assesses abnormal eating attitudes and eating behaviors. EDI subscale scores of SAD patients were compared to those of patients with bulimia nervosa (N = 21) and a matched nonclinical control group (N = 30).

Results: Preliminary results indicate that SAD patients have significantly elevated scores on some EDI subscales compared with controls. On EDI subscales considered to be specific to the psychopathology of eating disorders, the bulimia patients had significantly higher scores than the SAD patients on the Drive for Thinness and Bulimia subscales ($p<0.0005$), but not on the Body Dissatisfaction subscale ($p<0.70$). Some SAD patients (N = 5, 17%), however, had EDI profiles very similar to that of bulimic patients.

Conclusions: These results suggest that SAD patients have abnormal eating attitudes compared with a nonclinical sample. Although these dysfunctional eating attitudes are less severe than those in bulimia, there is heterogeneity in abnormal eating attitudes in SAD.

NR193 Monday May 4, 3:00 p.m.-5:00 p.m.

Cytogenetic Study of Autism in Taiwan

Luke Y. Tsai, M.D., Psychiatry, National Cheng-Kung Univ., 138 Sheng-Li Road, Tianan 70428, Taiwan R.O.C.; Joseph Y.C. Chen, M.D., Shuan-Yow Li, Ph.D., Chen-Chin Hsu, M.D.

Summary:

This is the first report on the cytogenetic study of autism in Taiwan. The authors conducted a community-based survey to ascertain the number of autistic children in the city of Tainan with a population of 700,000 between September 1990 and August 1991. Sixty-three children, age ranged from 3 to 18 with a mean age of 10.5 ± 3.6 years, who met the DSM-III criteria for autistic disorder were referred for cytogenetic analyses. Standard fra(X) technique with 96 hours culture was applied, and trimethoprim was added at the final 24 hours of culture to enhance the appearance of the fra(X) at band Xq27.3. A minimum of 100 G-banded metaphase-stage cells from each subject were examined. Fourteen individuals (22.2%) showed some forms of chromosomal abnormalities: one with mosaic Down syndrome (46,XY/47,XY, + 21), eight males and three females with fragile X syndrome (17.5%), one with balanced translocation (46,XY,t[5;6][q13☎3]), and one having pericentric inversion of Y chromosome (46,X,inv[Y][P11▽1]) combined with 1% Fragile X cell. The result suggests that the fragile X syndrome is strongly correlated with infantile autism. Multiple fragile sites on different chromosomes were also observed in several cases, the significance of this finding warrants further investigation.

NR194 Monday May 4, 3:00 p.m.-5:00 p.m.

Self-Image, Delinquency and Psychiatric Symptomatology in Normal Male and Female Adolescents

Susan K. Williams, M.D., Psychiatry, Northwestern University, 923 Washington Street #2, Evanston, IL 60202; Daniel Offer, M.D., Kenneth I. Howard, Ph.D., Kimberly Schonert-Reichl, Ph.D.

Summary:

Previous research has shown that gender may have an influence on emotional disturbance in adolescents. The purpose of this study was to better understand the relationship between adolescent self-image, psychiatric symptomatology, and delinquent behavior with respect to gender.

Students from 16 to 18 years of age were randomly selected from three midwestern high schools, chosen to reflect contrasting demographic statuses. Participants (n = 497) completed modified versions of the Offer Self-Image Questionnaire, the Delinquency Checklist, and the Symptom Checklist-90. Three OSIQ scales (Emotional Tone, Family Relationships, and Emotional Health), which best differentiated normal from disturbed adolescents in previous studies, were correlated with factors derived from the DCL and SCL. Poor self-image, as measured by the three OSIQ scales, correlated strongly with psychiatric symptoms in both males and females. Poor family relationships in particular, however, were associated with multiple delinquent behaviors, the type of which was variable with gender. The findings of the present study show important relationships between self-image, delinquency, and psychiatric symptomatology with respect to gender. Implications for planning interventions for disturbed adolescents and their families are discussed.

NR195 Monday May 4, 3:00 p.m.-5:00 p.m.

Child Psychiatry Diagnoses by Pictorial Instrument

Monique Ernst, M.D., Psychiatry, NYU Medical, 550 First Avenue, New York, NY 10016; Raul R. Silva, M.D., Jana Signe, B.A., Joan Welkowitz, Ph.D.

Summary:

DSM-III-R diagnoses based on self-reports using a pictorial instrument were compared with clinical discharge diagnoses in 50 psychiatrically hospitalized children (78% male), 6 to 15 years old, (median = 9). The self-report instrument included 136 pictures representing symptom criteria for anxiety, mood, psychosis, and disruptive disorders. The subjects rated each picture on a 6-point scale within one week of admission. By self-report, 37 children (74%) met criteria for at least one anxiety disorder; simple phobia was found in 33 children (66%), irrespective of the clinical diagnoses. The instrument generated an average of 2.9 diagnoses per child, including 24 diagnoses of psychosis, 17 of conduct disorder, and seven of mood disorder. The clinical discharge diagnoses included psychosis (N = 22), conduct disorder (N = 21) and mood disorder (N = 7). Five children had a secondary diagnosis of anxiety disorder. Concordance rates between instrument and clinical diagnoses were 86% for psychosis, 43% for conduct disorder, and 29% for mood disorder. Issues to be discussed will be the value of

self-report for diagnostic decisions in children, comorbidity, and overlap of symptoms among disorders.

NR196 Monday May 4, 3:00 p.m.-5:00 p.m.

Stimulant Treatment of Pediatric Tourette's Syndrome and ADHD

F. Xavier Castellanos, M.D., Child Psychiatry, NIMH Bldg 10 RM 6N240, 9000 Rockville Pike, Bethesda, MD 20892; Josephine Elia, M.D., Charles S. Gulotta, Judith H.L. Rapoport, M.D.

Summary:

Because of the striking clinical association between attention deficit hyperactivity disorder (ADHD) and Tourette's syndrome (TS), the need for concurrent treatment is not unusual. For many patients, drugs that benefit tics do not sufficiently control hyperactivity, while stimulants that control the ADHD have been reported to worsen tics. However, a single-blind trial of increasing doses of methylphenidate (MPH) with four boys with TS and ADHD suggested that increasing doses of MPH may actually decrease tic severity over time (Sverd, et al, 1989).

As part of an ongoing comparison of dextroamphetamine and MPH treatment, boys aged 6-12 with concurrent diagnoses of TS and ADHD undergo a nine-week, double-blind, crossover comparison of the two stimulants and placebo, each given for three weeks in increasing doses. Data from the first five patients suggest that after initial worsening of tics, continued treatment and/or increased drug dose produces a return toward baseline level of tic severity, or in some cases further amelioration. Two additional patients are under study.

The continued beneficial effects of stimulants on hyperactivity contrasts with the change in effect over time on motor tics. The implications of this contrast in terms of differential chronic effects of stimulants on different brain systems and tolerance and/or sensitization will be discussed.

NR197 Monday May 4, 3:00 p.m.-5:00 p.m.

Effect of Quiet Room Design on Children

Carol A. Glod, M.S.N., McLean Hospital, 115 Mill Street, Belmont, MA 02178; Martin H. Teicher, M.D., Martha Butler, M.S.N., Eleanor Magnus, B.S., David Harper, B.S., Kambiz Pahlavan, M.D.

Summary:

Over the years, a variety of techniques have been used by psychiatric staff to decrease agitation and control assaultive behavior. There are no published reports on optimal quiet room (QR) design. Thus, we sought to modify QR design (pastel paint, picturesque mural, carpeting) to see if we could produce a more rapid calming effect. To date data are available on 10 inpatients (8m,2f) ages 5-16 who were randomly assigned and assessed in both a modified QR and at least one of four standard QRs. *Results:* Data were analyzed using a within subject design (ANOVA, ANCOVA), so that each subject served as their own control. Overall subjects had an average of two placements in each QR. Use of prn medications appeared to differ based on QR placement. In the standard QR six patients required prn medications, while in the modified QR only two patients did ($p = .052$; one-tail). Also two patients in the standard QR required restraint, while this was unnecessary in the modified QR. There was also a trend for patients in the standard QR to take 48% longer to calm ($p < .12$) and to require 47% more time in the QR before release ($p < .12$). Rater-based assessment of motor activity and verbal aggression revealed significant effects of the QR. Modified QR exerted stronger calming effects, producing greater overall reduction in motor activity ($F(1,9) = 14.6$, $p < .004$). Maximal effect occurred at 15 min., when patients in the standard QR were 5.6-fold more active ($p < .005$). QR design also exerted a significant time-dependent effect on aggression which was also maximal at 15 min. (e.g., verbal aggression 6.1-fold greater in standard QR; $p < .04$). And thus modifying QR design may lead to more rapid calming and decrease the need for prn medication and additional protective measures (restraint).

NR198 Monday May 4, 3:00 p.m.-5:00 p.m.

Defense Mechanisms in Latency Age Children

Marshal Blatt, M.D., Child Psychiatry, Stanford University, 725 Welch Road, Palo Alto, CA 94304; Shirley Feldman, Ph.D., Afsaneh Nasserbakht, M.S., Hans Steiner, M.D.

Summary:

There are no empirical studies examining the development of defenses prior to adulthood, although Vaillant has demonstrated that defense mechanisms (DM) correlate strongly with adaptation and psychopathology. In this study, building on our previous adaptation of Bond's Defense Style Questionnaire (DSQ), we report results from another extension of Vaillant's work—the modification of the DSQ for school-age children. The 78-item questionnaire was modified in a three-step process, and given to 50 elementary school children (mean age 10.1; SD 0.53; males = 26, females = 24). Scores were derived using Bond's factors for adults and our factors for adolescents. There were significant age effects when school-age children were compared with adolescents: school-age children used immature and mature defenses less frequently than adolescents, favoring the use of reaction formation, withdrawal and humor. There were some gender effects: school-age boys scored lower than girls in the neurotic style and comparably in other styles. These results suggest a nonlinear progression in the development of defense styles from school age through adolescence and adulthood. Adolescents expand their defensive repertoire, using more immature and more mature defenses than younger children. Adults further increase the use of mature defenses while reducing use of immature defenses. These findings conform to psychodynamic theories of development.

NR199 Monday May 4, 3:00 p.m.-5:00 p.m.

The Longitudinal Outcomes of Regulatory Disordered Infants

Georgia A. Degangi, Ph.D., Lourie Center, 11710 Hunters Lane, Rockville, MD 20852; Stephen Porges, Ph.D., Ruth Sickel, Ph.D., Stanley Greenspan, M.D.

Summary:

This follow-up study examined the stability of the processes that contribute to regulatory disorders in children, and the long-term developmental outcomes of infants with regulatory disorders. It was hypothesized that a sample of untreated regulatory disordered infants with early symptoms of irritability, poor behavioral organization, and sleep and feeding problems would be at high risk for developmental, learning and emotional problems in the preschool years. The performance of samples of untreated regulatory disordered ($n = 9$) and normal ($n = 13$) children were compared at eight to 11 months and at four years. Three levels of analyses were conducted to examine group and individual differences and prediction of group classification status. eight of the nine regulatory disordered children exhibited developmental, sensorimotor, and/or emotional and behavioral deficits at four years. Group differences were found in general behaviors of attention and activity level, emotional maturity, motor coordination, and tactile sensitivity using a Sensorimotor History Questionnaire at four years. When examining individual differences, infants with sensory hypersensitivities on the Test of Sensory Functions in Infants scored lower on perceptual, verbal, motor and general cognitive functioning as measured by the McCarthy Scales of Children's Abilities and displayed problems

in bilateral motor integration, reflex integration and overall sensory integrative functions as measured by the DeGangi-B Test of Sensory Integration.

NR200 Monday May 4, 3:00 p.m.-5:00 p.m.

OCD Symptoms in Adults with Autistic Disorder

Susan T. Naylor, M.S.N., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Christopher J. McDougle, M.D., Fred R. Volkmar, M.D., Wayne K. Goodman, M.D., Donald J. Cohen, M.D., Keith A. Hawkins, Psy.D., Lawrence H. Price, M.D.

Summary:

Autistic disorder (AD) is a complex neuropsychiatric syndrome characterized by a core disturbance in social relatedness. Stereotyped, ritualistic behavior is also an integral part of the current diagnostic formulation of AD. This study examined the occurrence and types of obsessive compulsive (OC) symptoms in adults with AD. *Methods:* 50 consecutive adult patients admitted to the Yale Adult Pervasive Developmental Disorders (Autism) Clinic with a principal diagnosis of AD (DSM-III-R) were assessed using the symptom checklist (SCL) of the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), a clinician-rated inventory of 72 types of obsessions and compulsions. Global severity of autistic symptoms and I.Q. were determined by the Autism Behavior Checklist (ABC) and WAIS-R, respectively. *Results:* Preliminary analyses of these data indicate that most adults with AD demonstrate some OC symptoms as measured by the Y-BOCS SCL. In those patients who are mute or whose cognitive capacity is limited, it is often not possible to determine the presence or absence of obsessions. The observed compulsive behaviors are, in some instances, similar to those performed by patients with obsessive compulsive disorder (OCD). Data regarding the specific types of OC symptoms, as well as the relationships between OC symptoms and severity of autistic symptoms and I.Q., will be presented. *Conclusions:* Consistent with Kanner's original observations, most adults with AD demonstrate OC symptoms. Based on the clear efficacy of serotonin reuptake inhibitors in the treatment of OCD, and preliminary data suggesting a preferential response with these medications for particular interfering symptoms of AD, additional investigations of the clinical, neuroanatomical, and neurochemical parallels between AD and OCD seem warranted.

NR201 Monday May 4, 3:00 p.m.-5:00 p.m.

The Prevalence of Autism in Taiwan

Yung-Cheng J. Chen, M.D., Psychiatry, National Cheng-Kung Univ., 138 Sheng-Li Road, Tianan 70428, Taiwan R.O.C.; Der-Jen Lai, M.D., Chen-Chin Hsu, M.D., luke Y. Tsai, M.D.

Summary:

The epidemiological surveys conducted in North America, Europe, and Japan estimated the prevalence of autism to be between 2 and 21 per 10,000 in the general population. This is the first report on the prevalence of autism in Taiwan. The authors conducted a two-stage screening study to ascertain all autistic children in the School District of Tainan City with a student population of 122,000, ages between 6 and 15. First, teachers filled out the Chinese version of Clancy's Behavior Scale for Autism (CBSA) for students as the initial screening procedure. Children with CBSA scores equal to or greater than 10 would enter the second phase of the study to receive semistructured clinical interviews administered by two child psychiatrists who did not know their scores of CBSA. The UCLA Modified Behavior Observation Scale for Autism was adopted to score the historical and present symptoms of autistic disorders. The DSM-III and DSM-III-R criteria for autistic disorders were applied. There were 52 children (4.26 per 10,000) who met the DSM-III criteria for autistic disorders, and 59 children (4.84 per 10,000) met the DSM-III-R criteria for autistic disorders. The finding of higher prevalence rate of autism from DSM-III-R criteria is consistent with that of Volkar.

NR202 Monday May 4, 3:00 p.m.-5:00 p.m.

Auditory N100 in Conduct Disordered Adolescents

Lyndee P. Oberwetter, M.D., Psychiatry, Univ of Colo Hlth Sci Ctr, 4200 E. 9th Avenue Box C-268, Denver, CO 80262; Martin L. Reite, M.D., Thomas J. Crowley, M.D.

Summary:

Conduct disorder (CD) is frequently comorbid with substance abuse in adolescents. Little is known of the biological correlates of CD. This study recorded auditory evoked potentials (EP) (N = 128, 20 msec duration 1 KHz tones), and scores on a standardized neurological soft sign examination in 35 substance-abusing CD males aged 14-19 (mean 16.3y). Severity of CD was estimated by number of CD symptoms (range 0-9) on the Diagnostic Interview Schedule for Children. N100 latency was significantly correlated with the number of CD symptoms present ($r = .576$, $p < .01$). N100 amplitude was significantly correlated with total number of soft signs ($r = .486$, $p < .05$) (greater negativity = fewer soft sign). Number of CD symptoms was not significantly correlated with number of soft signs; and the amplitude and latency of the N100 peak varied independently. These findings suggest that CD severity is not indexed by neurological soft signs per se, but may covary with auditory EP measures, suggesting that the latter may reflect altered CNS function related to CD. Of note, there was no dose effect of alcohol in the last year (range 0-17, 088 drinks in the last year, mean = 2054 drinks) on any of the neurologic or EP parameters measured, except the number of CD symptoms. This suggests that the findings reported here are not a function of the amount of alcohol used, but may reflect a CNS alteration that predates substance abuse. (Supported by USPHS DA06941, USPHS MH15442, and USPHS MH46335.)

NR203 Monday May 4, 3:00 p.m.-5:00 p.m.

Treatment of Children with Language and Behavior Disorders

Sue Batth, M.D., Pre-School, Royal Ottawa Hospital, 1145 Carling Avenue, Ottawa Ontario K1K 7K4, Canada; Gary Tait, M.A., Marjorie Button, M.Sc.

Summary:

In the preschool outpatient psychiatric service of the Royal Ottawa Hospital, 80% to 90% of referred children have emotional/behavioral problems. Of this group, 30% to 35% present with speech and language communication disorders. The co-existence and causal relationship between these two problems is well discussed in the literature. Treatment of children with this combination of disorders is a challenging task. Without treatment, these children are increasingly at risk as they grow older for further developmental delays, learning disabilities, social isolation, and poor self-esteem. Individual treatment of the child in isolation from the family does not allow generalization of skills learned by children in the natural context of their environment. In this paper, the authors describe the process of clinical assessment, evaluation of family-child interactions and the formulation of an individualized treatment plan that establishes goals for the child and parents. This family-centered approach combines principles of behaviour modification and McDonald's ecological communication intervention program (1989). Clinical vignettes describe the application of the treatment process.

NR204 Monday May 4, 3:00 p.m.-5:00 p.m.

Dissociation in a Mental Health Center Population

Howard C. Wetsman, m.D., Psychiatry, LSU Medical School, 1542 Tulane Avenue, New Orleans, LA 70112; Elizabeth David, M.D., Edward Morse, Ph.D.

Summary:

Recent studies have associated dissociative symptoms, as measured by the Dissociative Experiences Scale (DES), with a history of childhood physical and/or sexual abuse. To date, this relationship has not been studied in a lower socioeconomic population. Data for this study come from 41 adult admissions to an inner-city community mental health center (CMHC), of whom 32 (78%) consented to take the DES, though 38% of subjects scored above 30 on the DES, 24% reported childhood physical abuse, and 20% reported sexual abuse as a child, no association was found between DES score and abuse history. History of physical/sexual abuse was found to correlate with age of onset of first psychiatric symptoms and the number of past hospitalizations. The authors discuss the implications of findings for future research and clinical practices serving lower socioeconomic populations.

NR205 Monday May 4, 3:00 p.m.-5:00 p.m.

Dissociation in Medically Indigent Inpatients

Howard C. Wetsman, M.D., Psychiatry, LSU Medical School, 1542 Tulane Avenue, New Orleans, LA 70112; Elizabeth David, M.D., Deborah Tosh, M.D., Edward Morse, Ph.D.

Summary:

Studies have shown a correlation between histories of childhood physical and/or sexual abuse and their scores on the DES. These studies implicitly assumed no correlation between socioeconomic status and DES score. No studies to date have been done using clinical data drawn primarily from a lower socioeconomic population. Data for this study come from 100 admissions to a general psychiatry ward of a large inner-city hospital serving an 80% indigent population. One-third of the subjects were given the DDIS. Thirty-seven percent of the subjects scored over 30 on the DES. While 36% reported sexual abuse as a child, and 42% reported physical abuse, there were no statistically significant correlations between DES score and histories of these abuses. However, DES score did correlate with clinical diagnosis of MPD, chronic complex dissociative disorders, and any dissociate disorder. This replicates the authors' earlier findings in a sample of outpatients from a community mental health clinic. The findings suggest that the relationship between physical and/or sexual abuse and DES score may not be universal across socioeconomic classes, and that other factors in low SES environments can lead to dissociation. This is important because patients with dissociative disorders in this population can be easily misdiagnosed as schizophrenic.

NR206 Monday May 4, 3:00 p.m.-5:00 p.m.

A Survey of the Errors in 100 Civil Commitments

Howard C. Wetsman, M.D., Psychiatry, LSU Medical School, 1542 Tulane Avenue, New Orleans, LA 70112; Guillermo Urrutia, M.D., Margo Hammond, J.D.

Summary:

A properly executed emergency certificate is the primary route by which psychiatric patients enter the hospital against their will. While protecting patients' rights, emergency certificates allow mental health care workers an opportunity to overcome dangerous situations. Improperly executed emergency certificates violate patients' rights, open the hospital to liability, and potentially dilute the resources of the emergency mental health system. One hundred consecutive involuntary admissions to the psychiatric inpatient service of a metropolitan general hospital were reviewed. Forty-five percent were found to have invalidating errors and 37% of valid certificates were considered flawed. Rates of errors inversely correlated with the clinical experience of the examining psychiatrist, suggesting the need for continuing education in legal requirements for emergency certificates. The authors propose such a course of education and a method of follow-up.

NR207 Monday May 4, 3:00 p.m.-5:00 p.m.

Dissociation and Abuse in First-Episode Psychosis

Stephen M. Strakowski, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Susan C. Batson, Ph.D., Mauricio Tohen, M.D., Shelly F. Greenfield, M.D., Meridith L. Kolbrenner, B.A.

Summary:

We studied dissociative symptoms, childhood abuse, and initial outcome in first-episode psychosis. Thirty-eight of 71 (53.5%) consecutively admitted inpatients with first episode psychosis completed the Questionnaire of Experiences of Dissociation (QED) and a self-report regarding childhood abuse. Outcome measures were length of hospitalization and operationalized recovery criteria. The clinical records of the 33 nonresponders were carefully reviewed for selection basis. Twenty (52.6%) subjects had histories of childhood abuse (nine with physical abuse only, three with sexual abuse only, and eight with both). Sexual abuse was more common in women (p 0.02). QED scores did not differ by type of abuse, although elevated QED scores were noted in those with combined compared to no abuse (13.1 vs. 6.7; $Z = 2.76$, $p = 0.006$). Twelve subjects (31.6% of total) reported abuse by one or both parents. QED scores were elevated in subjects with abuse by a parent ($n = 12$) compared with those by a nonparent ($n = 8$) or not abused ($n = 18$) ($p = 0.01$). Seven of eight (87.5%) subjects with combined abuse were abused by a parent, a significant association ($chi^2 = 7.1$, $df = 2$, $p = 0.03$). There were no differences in outcome measures between abused and nonabused subgroups. No male nonresponders reported childhood abuse clinically (0/17; 0%) compared with 10 of 19 (52.6%) responders reporting by self-report ($p = 0.004$); this same pattern was not observed in the women subjects. These results suggest childhood abuse may be underrecognized in male patients and is related to dissociative symptoms in this cohort.

NR208 Monday May 4, 3:00 p.m.-5:00 p.m.

Dissociation and Self-Destructive Behavior

Glenn N. Saxe, M.D., Psychiatry, Trauma Clin/EL MHC, 25 Staniford Street, Boston, MA 02114; Bessel A. van der Kolk, M.D.

Summary:

This study attempts to investigate the relationship between dissociation and self-destructive behavior. Fourteen psychiatric inpatients with DSM-III-R diagnosed dissociative disorders were matched for age and gender with a control group of inpatients who report few dissociative experiences (Dissociative Experiences Scale (DES) score <5). All subjects were then blindly interviewed to determine history of self-destructive behavior. Significant differences between the dissociation group and the control group were found for the average number of suicide attempts (4.7 vs. 0.5), and average number of different types of suicide attempts (2.6 vs. 0.5), and age at first suicide attempt (13.9 vs. 24.8). A significant correlation ($r = 0.47$) was found between the number of attempts and degree of dissociation (DES Score) in the dissociation group ($p < .001$). These results are discussed in terms of the function of self destructiveness in the lives of patients with dissociative disorders.

NR209 Monday May 4, 3:00 p.m.-5:00 p.m.

Somatization in Patients with Dissociation

Glenn N. Saxe, M.D., Psychiatry, Trauma Clin/EL MHC, 25 Staniford Street, Boston, MA 02114; Gary Chinman, M.D., Bessel A. van der Kolk, M.D.

Summary:

This study attempts to determine the relationship between dissociation and somatic symptoms. Fourteen patients with DSM-III-R dissociate disorders were matched for age and gender with a control group of inpatients who reported few dissociative experiences (Dissociative Experiences Scale (DES) score<5). All subjects were blindly interviewed, and chart reviews were completed to determine somatic symptoms and medical history. Sixty-four percent of patients with dissociative disorders met DSM-III-R criteria for somatization disorder and reported an average of 12.4 somatic symptoms. None of the control patients met criteria ($p<.0005$), and these patients reported an average of 3.1 somatic symptoms ($p<.0001$). Significant differences were also found in the number of medical hospitalizations and interventions. A significant correlation was found between degree of dissociation (DES score) and number of somatic symptoms in patients in the dissociative group ($r=0.404$, $p < .01$). These results are discussed in terms of the psychological and biological relationship between dissociation and somatization.

NR210 Monday May 4, 3:00 p.m.-5:00 p.m.

Adolescent Bereavement with Peer Death

Sherry Schachter, B.S.N., Cancer, Memorial Sloan Kettering, 1275 York Avenue, New York, NY 10021

Summary:

The frequency with which today's teenagers have had to confront the death of a peer is understated. A convenience sample of 249 adolescents responded to a 22-question survey instrument addressing their experiences with peer death. Subjects included high school and undergraduate college students, from both rural and urban communities. One hundred fifty-five adolescents had experienced peer death and were included in this descriptive, exploratory study: 67% reported one experience with peer death, and 32.9% reported more than one. Participants were predominantly female (68%) and Catholic (60.6%). The mean age was 17 years. Variables such as social supports, gender, and the circumstances surrounding a death have been previously identified in bereavement literature as influencing grief reactions and resolution. The purpose of this study was to: (1) describe adolescent experiences following the death of a peer and (2) describe the effects of these variables on adolescent grief reactions. Themes that surfaced repeatedly included the adolescent's need for seeking more information and knowledge about the peer's death, and an affirmation of their beliefs and identification of intense, closer relationships with their friends.

NR211 Monday May 4, 3:00 p.m.-5:00 p.m.

Spinal Cord Injury and Depression

Andres Vasquez, M.D., University of Miami, 1611 NW 12th Avenue, Miami, FL 33133; Paul J. Goodnick, M.D.

Summary:

The majority of diagnostic studies done on patients with spinal cord injuries (SCI) have worked under the assumption that reactive depression is a natural sequela to traumatic SCI (Howell et al, 1981). The incidence of depression in patients with SCI has been found to be higher than in the general population (Fullerton et al, 1981). Other studies in this area have focused on medication management, adaptive mechanisms, and the maximization of patient strengths and support systems (Gallagher et al 1982, Stewart 1988). This study examines the psychiatric status of patients with traumatic SCI and the effectiveness of brief supportive psychotherapy with patients having recently sustained SCI during inpatient rehabilitation, with special attention to those showing signs of depression.

In this eight-week study, SADS-L was used as a baseline diagnostic aid. Instruments for assessment included Hamilton Depression Rating Scale (HDRS), Beck Depression Inventory (BDI) and General Behavioral Inventory (GBI). Both randomly assigned groups were assessed as follows: HDRS (baseline, 4 & 8 weeks), BDI (baseline, 4 & 8 weeks), GBI (baseline & 8 weeks). The experimental group received brief supportive psychotherapy sessions twice a week for eight weeks. The control group was only seen for the administration of the diagnostic assessments. Data analysis is in progress and will be presented in context of results of previous studies.

NR212 Monday May 4, 3:00 p.m.-5:00 p.m.

The Firestone Voice Scale for Self-Destructive Behavior

Lisa Firestone, Ph.D., Glendon Association, 2049 Century Park East, Suite 3000, Los Angeles, CA 90067

Summary:

The Firestone Voice Scale for Self-Destructive Behavior (FVSSDB) assesses the frequency of "voice" attacks or negative thoughts about oneself stated in the second person. It has been shown that when self-critical thoughts are stated in this format, the patient is able to separate them from rational thoughts of self-interest.

The voice attacks (items) on the FVSSDB were obtained directly from clinical material gathered over a 15-year period from patients and subjects in individual and group sessions. A total of 507 respondents (all currently receiving psychotherapy) were recruited for the main study, primarily from outpatient clinical settings throughout the United States and western Canada. Respondents also completed a battery of nine other assessment scales including the Beck Hopelessness Scale and the Suicide Probability Scale.

To evaluate the criterion-related validity, the FVSSDB scores were compared with previous suicide attempts. FVSSDB scores correlated higher than the Beck Hopelessness Scale with previous suicide attempts as reported by subjects and their therapists. Statistical analysis of a shortened version, designed as a brief measure to assess suicide potential proved significant as well, indicating it could be a valuable tool for assessing risk in time-limited situations such as crisis evaluations.

NR213 Monday May 4, 3:00 p.m.-5:00 p.m.

On the Usefulness of DSM-III, Axis III

Ihsan M. Salloum, M.D., Psychiatry, Univ of Pitts., 3811 O'Hara Street, Pittsburgh, PA 15213; Juan E. Mezzich, M.D., Javier E. Saavedra, M.D.

Summary:

Few studies have examined the impact of DSM-III Axis III on the identification of physical disorders. This study evaluates the usefulness of Axis III by examining the extent of its use and its ability to enhance clinical description.

Two hundred inpatient charts randomly selected over two timeframes, before and after the implementation of DSM-III (1975-1979 & 1981-1985), were reviewed. Frequency and types of psychiatric and physical diagnoses made at admission and discharge evaluations were comparatively analyzed.

The results showed striking differences in the frequency of physical diagnoses made at admission and at discharge before and after DSM-III. Before DSM-III, 9% of the patients received a positive physical diagnosis, while 53% received such diagnoses after DSM-III was implemented. In terms of number of physical diagnoses, only 11 were recorded for the group before DSM-III vs. 96 recorded physical diagnoses for the group after DSM-III. On discharge evaluation the number of physical disorders diagnoses was 52 and 100 in the pre- and post-DSM-III, respectively.

The results indicated that Axis III significantly enhanced the recording of physical diagnoses in psychiatric patients. The multiaxial format appears to be highly useful for the identification of clinically relevant problems.

NR214 Monday May 4, 3:00 p.m.-5:00 p.m.

Changing Office Site Lowers Therapy Compliance

Kelly L. Dunn, M.D., Psychiatry, Hershey Medical Center, 500 University Drive, Hershey, PA 17033; Paul A. Kettl, M.D.

Summary:

Subjectively, therapists have been aware of factors that influence a patient's compliance with outpatient psychotherapy. This study objectively examines the effect of changing a resident's office site on patient compliance in outpatient psychotherapy with the resident. To test the hypothesis that a change in outpatient site was correlated with a decrease in outpatient attendance in psychotherapy, outpatient hours for eight residents who changed office sites were compared with outpatient hours for eight residents who remained at the same site seeing their patients. The number of outpatient hours one and two weeks before and after the office site change for each group, over a one-year study period, was obtained. At one week, residents who changed offices had 6.45 fewer psychotherapy hours per week than did residents who did not change offices ($p = 0.350$). For the two weeks after the change, the effect was greater, but did not quite reach statistical significance. At two weeks, residents who changed offices had 17.7 fewer psychotherapy hours per week than did the control residents ($p = 0.107$). This decreased compliance interferes with the therapeutic process and resident education and decreases revenue for the department. Residents should, therefore, maintain the same psychotherapy office for as long as possible.

NR215 Monday May 4, 3:00 p.m.-5:00 p.m.

Sitters: Substitutes for Psychiatric Consultation

Raymond R. Remmel, M.D., Psychiatry, Univ of Ark. Med Sci, 4301 W. Markham Slot 554, Little Rock, AR 72205; Francis J. Kane, M.D.

Summary:

We are reporting a retrospective chart study of all patients who were assigned sitters by the nursing service of the University of Arkansas University Hospital.

All charts for a three-month period ($N = 55$) were scrutinized for 1) presence of psychiatric disorder; 2) therapy of same; 3) use of psychiatric consultation.

To date 55 consecutive charts have been reviewed. Only three patients were assessed as not needing psychiatric consultation. Twenty-four patients had consultation (mostly suicide attempts) 28 patients were seen to need consultation (15 deliria, 8 DT's, 1 dementia and 1 suicide attempt). Postoperative delirium was often unrecognized and poorly treated when recognized. Patients who suffered from seizures and DT's were discharged in a few days without mental status evaluation despite evidence of cognitive impairment. Delirious and demented patients who were not competent to give informed consent were asked to sign permits for operations, discharges AMA, etc. One suicidal patient was discharged without consultation. Beer "therapy" and IV alcohol were used for patients with alcohol withdrawal, and benzodiazepines used almost exclusively for nonalcoholic deleria. The findings underscore the need for increased teaching of psychiatric topics in medical and surgical teaching programs. Increased use of psychiatric consultation will also result in financial savings to the nursing service because of improved treatment.

NR216 Monday May 4, 3:00 p.m.-5:00 p.m.

Personality Dysfunction and Outcomes in the Homeless Mentally Ill

Gavin E. Rose, M.D., Psychiatry, Univ. of Maryland, 645 W. Redwood Street, Baltimore, MD 21201; Lisa Dixon, M.D., James Thompson, M.D., Marcela V. Somoza-Lennon, M.D., Bruce Warr, M.S., Anthony Lehman, M.D.

Summary:

Recent research has suggested that Axis I/Axis II comorbid symptomatology is a significant barrier to treatment in the homeless mentally ill (HMI). Personality dysfunction was evaluated in HMI patients treated by an experimental assertive community treatment team. *Methods:* 20 affective or schizophrenic patients received the SCID-II interview and concurrent BPRS when clinically stable. The number of threshold symptoms rather than diagnoses were recorded by specific personality cluster. We hypothesized that patients with greater personality symptoms would have poorer outcome. *Results:* The mean number of symptoms for each patient was: A (8.65 ± 2.83); B (10.8 ± 6.0); and C (15.5 ± 6.4). A, B and C clusters were not intercorrelated or correlated with BPRS total (mean = 26.8 ± 4.4) or psychotic symptom subscale scores (mean 5.3 ± 1.7). Men ($n = 12$) had significantly more total ($p < .01$) and B symptoms ($p < .02$) than women. There was a trend for affective patients to have more B symptoms than schizophrenics ($p = .07$). Active substance abusers ($n = 10$) also had more B symptoms ($p < .02$) and total symptoms ($p < .02$) than non-abusers. Medication compliers had more total ($p < .01$) and C symptoms ($p < .001$) than noncompliers. Patients who spent nights on the street after referral had significantly more B symptoms than patients who remained in shelter ($p < .02$). *Conclusions:* The total number of personality symptoms as well as specific clusters predicted outcomes in homelessness and medication compliance. Individuals who spent time on the street had more B symptoms and were perhaps more likely to be male, affective substance abusers. Medication compliers had more C symptoms and were possibly female, nonsubstance abusers. Effective service of this population requires attention to the severity of personality dysfunction.

NR217 Monday May 4, 3:00 p.m.-5:00 p.m.

Sheltering the Homeless: Housing Patterns

Lisa Dixon, M.D., Psychiatry, Univ of Maryland, 1222 W. Baltimore Street, Baltimore, MD 21223; Nancy Friedman, M.S.W.,

Summary:

Little is known about the housing patterns and problems associated with moving the chronically homeless mentally ill (HMI) into stable housing. Shelter patterns of HMI patients receiving psychiatric/case management services from an experimental assertive community treatment (ACT) program were evaluated. *Methods:* Patients' nightly housing and reasons for changes were recorded ($n = 34$). Shelter types consisted of streets/missions (*SM*), Institutions (*I*), transitional (*T*), and permanent (*P*). All patients were homeless prior to referral, and 26 (71%) on the street more than a year. *Results:* Number of treatment days was 160 ± 91, housing changes was 5.0 ± 5.7 with 42 ± 31 days per placement. Patients had 17 ± 47 *SM* days (median = 0), 39 ± 51 *I* days, 58 ± 55 *T* days, and 44 ± 61 *P* days. Of 165 shelter changes, 90 (55%) were toward

independent housing. Psychiatric relapse (20%), preference for the streets (19%), and drug/alcohol use (16%) were most common reasons for loss of shelter. Patients referred from hospital (n = 14) had more *P* days ($p<.05$), and less *I* days ($p<.05$) than from the street. Patients with SSI or SSDI spent more days housed than those without public assistance ($p<.05$). Affective patients had more *T* days than schizophrenics ($p<.01$). *T* shelter days were negatively correlated with three-month BPRS scores ($p<.05$) and positively correlated with compliance with recommendations for daily structure ($p<.05$) and ADL's ($p<.02$). *Conclusions:* Most HMI in this program were successfully moved off the streets. However, this did not imply stability; most patients had multiple subsequent moves. Hospitalization conferred an advantage in gaining subsequent shelter. Days in transitional shelter seemed most influenced by patient factors and may represent the critical point in moving homeless patients off the streets.

NR218 Monday May 4, 3:00 p.m.-5:00 p.m.

Compliance Among the Homeless Mentally Ill

Lisa Dixon, M.D., Psychiatry, Univ of Maryland, 1222 W. Baltimore Street, Baltimore, MD 21223; Marcela V. Somoza-Lennon, M.D., Gavin E. Rose, M.D., Kerry Petrucci, Ph.D., Bruce Warr, M.S., Anthony Lehman, M.D.

Summary:

Poor compliance with standard services is a problem in the treatment of the homeless mentally ill (HMI). Compliance patterns with psychiatric/case management services were evaluated after three months of an experimental assertive community treatment (ACT) program. *Methods:* The domains of housing (*H*), finance (*F*), daily structure (*DS*), substance abuse (*SA*), medical (*M*), *ADL*'s and general patient compliance (n = 26) were rated using a 4-point scale (1 = substantively compliant—4 = substantively noncompliant). Psychiatrists rated medication compliance. *Results:* Mean compliance ratings were: *ADL*'s (1.81), *F* (1.86), *H* (1.96), *M* (2.08), general (2.15), *SA* (2.17), and *DS* (2.96). Over 50% received scores of 1 or 2 (at least moderate compliance) on all items except *SA* and *DS*. *SA* and general compliance were significantly positively correlated with all other items except *ADL* and *F*. Surprisingly, no other intercorrelations were found. Schizophrenics were less compliant than affectives on *M* ($p<.05$) and *ADL*'s ($p<.05$). Active substance abusers were less compliant on *SA* ($p<.01$). Increased BPRS scores correlated with worse medication ($p<.01$) and *ADL compliance* ($p=.005$). *H* noncompliance was significantly correlated with increased housing changes ($p<.02$). *Conclusions:* Though many HMI complied overall with an ACT outreach approach, compliance seemed largely domain-specific. Patients most resisted daily structure and substance abuse recommendations, compliance with which are frequent housing program requirements. The intercorrelation of SA noncompliance with other noncompliance ratings underlines the importance of innovative approaches to substance abuse in this population. Higher compliance in specific domains was often specifically associated with better outcome in that domain.

NR219 Monday May 4, 3:00 p.m.-5:00 p.m.

Medication Compliance Among Homeless Mentally Ill

Marcela V. Somoza-Lennon, M.D., Psychiatry, University of Maryland, 22 South Greene Street, Baltimore, MD 21201; Lisa Dixon, M.D., Peter J. Weiden, M.D., Kerry Petrucci, Ph.D., Gavin E. Rose, M.D., Anthony Lehman, M.D.

Summary:

Medication noncompliance is prevalent in the chronically mentally ill, though unstudied among the homeless mentally ill (HMI). Experience in side effects and illness and health beliefs were assessed in patients served by an experimental treatment program for the HMI. *Methods:* 21 patients received independent interviews on health beliefs, influences on compliance patterns, and side-effects. The treating physician rated baseline (BL) and 3-month medication compliance. *Results:* More BL noncompliers (*NC*)) (n = 11) than compliers (*C*) (n = 10) were influenced to *not* take medication by denial of mental illness (75% to 33%). Although there was a trend toward *C* reporting more distress from neuroleptics ($p=.08$), and they also reported more distress from lithium, they were less likely than *NC* to consider side effects as a strong influence toward noncompliance (33% to 71%), 43% of all patients believed they had a mental illness, and this did not differ between *NC* and *C*. However, more *C* endorsed beliefs consistent with the stress-vulnerability model: biology (70% to 27%) and lite stress (70% to 46%). 80% of BL *NC* became compliers by month 3. Though older patients were overrepresented in the BL *NC* group, they were as likely as younger patients to become compliers. *Conclusions:* These preliminary results show that medication compliance in the HMI is amenable to an assertive treatment program. They also indicate that health beliefs are an important and potentially changeable factor in noncompliance and that those with a better understanding of their illness tend to have better compliance. In this population, the degree of side effects did not predict the importance of side-effects as an influence on medication-taking behavior. The validity of these findings will be further tested with more patients and a non-homeless control group.

NR220 Monday May 4, 3:00 p.m.-5:00 p.m.

Suicidality and Final Exit

Michael Lavin, M.D., Psychiatry, Hillside Hospital, 193-41 McLaughlin Avenue, Holliswood, NY 11423; Glenn Martin, M.D., Alex Roy, M.B.

Summary:

Derek Humphry's *Final Exit* has generated much debate in the medical community. The popularity of this best seller "how to" suicide manual gives testimony to the growing interest of society in the role of physicians in euthanasia and assisted suicide. While the book is directed at those suffering from terminal illness, much concern has been expressed about potential misuse. Many feel that patients with depression will follow instructions in this book which will lead to more lethal or frequent suicide attempts. In this presentation we report a series of cases in which patients presented to the psychiatric emergency room after reading *Final Exit*. Two individuals actually made suicide attempts, while another expressed suicidal ideation. In each case the patient remarked on the immediate and influential effect of having read the book. Yet, on closer inspection it becomes difficult to conclude that their intent or plans were actually influenced. Previous history with other such manuals and the role of the media in fostering possible "copycat" or clustering of suicide outbreaks will also be reviewed. Although such a book raises concerns about potential misuse, our experience suggests the need to not be quick to jump to conclusions.

NR221 Monday May 4, 3:00 p.m.-5:00 p.m.

The Clinical Impact of Benzodiazepine Regulation

Donna M. Flansaas, M.D., Psychiatry, Beth Israel Medical Ctr., 1st Avenue at 16th Street, New York, NY 10003; David J. Hellerstein, M.D., Lynda D. Zweben-Howland, M.S.W., Lisa W. Samstag, M.A.

Summary:

In January 1989, New York became the first state to require triplicate prescriptions for benzodiazepines (BZDs). We screened all patients applying to an urban psychiatric clinic after this regulation went into effect, and identified 41 patients who were seeking

follow-up because their physicians no longer prescribed BZDs. The identified patients were 90.2% female, 92.7% Hispanic, and of low socioeconomic status (100% unemployed). Mean age ± standard deviation (s.d.) was 47.1 ± 9.1 years. Though 22 (53.7%) had discontinued BZDs prior to intake, only eight reported mild and none reported serious withdrawal symptoms. The study patients reported taking BZDs for 8.2 ± 4.6 years at an average daily dose of 11.9 mg. of diazepam (± 10.9 mg.). On evaluation, most common diagnoses included depression (46.3%), anxiety disorders (43.9%), and personality disorders (22%). Current alcohol abuse or dependence was noted in 17%, and previous abuse in 9.8%; 7% had a history of drug abuse.

At follow-up six months to three years later, 39% were still in treatment. Fourteen had been prescribed benzodiazepines, 85% with adequate compliance. Seventeen were prescribed antidepressants, 70.6% with adequate compliance. Though 28 were assigned to group or individual therapy, only 10 (35.7%) complied with this recommendation.

Thus, in our population, the benzodiazepine regulations affected a cohort of impoverished minority women, diagnosed primarily with anxiety and mood disorders. Most were not drug or alcohol abusers. Despite their multiple psychosocial problems, they had poor compliance with psychotherapy interventions. Modest doses of benzodiazepines were apparently useful for symptomatic relief.

NR222 Monday May 4, 3:00 p.m.-5:00 p.m.

Family Problems Among Southeast Asian Refugee Patients

Hung D. Tran, M.D., Psychiatry, OHSU, 3181 SW Sam Jackson Park Road, Portland, OR 97201; James K. Boehnlein, M.D.,

Summary:

Objective: There have been anecdotal reports of increasing family dysfunction among Southeast Asian refugees, but this has not been studied objectively. This project aimed to 1) determine the extent of family problems among S.E. Asian psychiatric patients, 2) evaluate the associations between family problems and psychiatric symptoms, and 3) compare and contrast the Vietnamese and Cambodian patients. *Method:* All of the adult Vietnamese (N = 50) and Cambodian (N = 47) patients in the Indochinese Psychiatric Program of the Oregon health Sciences University who had teenage children were interviewed. The interview was structured by a culturally sensitive family questionnaire that elicited a wide range of family problems. *Results:* Twenty-seven (54%) Vietnamese and 12 (26%) Cambodian patients reported having problems with their children. Thirty (60%) Vietnamese and 22 (47%) Cambodian patients described psychiatric symptoms as a direct result of these problems. On average, Vietnamese patients had two times the number of complaints about their children (3.0 vs. 1.5) and 2.8 times the number of symptoms (2.8 vs. 1.0) as Cambodian patients. *Conclusions:* The high prevalence of family problems in S.E. Asian psychiatric patients influenced their psychiatric illness and affected more Vietnamese than Cambodian patients. Consequently, a family intervention program may be clinically helpful.

NR223 Monday May 4, 3:00 p.m.-5:00 p.m.

Psychotropics and Hispanic Nursing Home Residents

Mary Vince, M.D., Psychiatry, Hillside Hospital, P.O. Box 38 Lowenstein Res Bld, Glen Oaks, NY 11004; Blaine S. Greenwald, M.D., Elisse Kramer-Ginsberg, Ph.D., Arthur Lennon, M.D., Robert Corcoran, M.S.

Summary:

Little is known about mental health delivery to Hispanic nursing home residents. Cultural and language differences have been suggested as discriminating against Hispanics, hence accounting for both Hispanic underrepresentation in nursing homes, and interference with effective mental health care. However, data to support or refute these claims are wanting. This exploratory study identified all Hispanic residents (n = 65) of a large NYC nursing home (541 beds) and investigated differences in psychotropic prescription between Hispanic and age- and sex-matched non-Hispanic (n = 65) residents of the same facility. Duration in nursing home, number of psychotropic medications, mean chlorpromazine-equivalent neuroleptic dose, and mean Valium-equivalent benzodiazepine dose were compared between Hispanic and non-Hispanic groups. No differences were found. Mean age of Hispanics was significantly lower than non-Hispanic nursing home residents (81.2 +/− 8.69 vs. 85.29 +/− 7.68, $p < .0001$). Furthermore, amongst Hispanics, proportion of men was significantly greater than in non-Hispanic counterparts (42% vs. 20%; $p < .0001$). Breakdown of Hispanics by original country were as follows: Puerto Rico (40%); Cuba (25%); Dominican Republic (21%); other Central/South America (12%); Spain (2%). These preliminary data do not support the notion that Hispanic nursing home residents are either under- or over-medicated with psychotropics as compared with non-Hispanic controls. Treatments appeared similar between groups. Implications of the unexpected and interesting findings that men are overrepresented amongst Hispanics in nursing homes; and that Hispanics may be younger than typical nursing home residents will be discussed.

NR224 Monday May 4, 3:00 p.m.-5:00 p.m.

Monitoring Resident Supervision in Times of Change

Louis J. Kraus, M.D., Psychiatry, North Western University, 303 East Superior St. Rm 583, Chicago, IL 60611; Philip K. McCullough, M.D., John S.Lyons, Ph.D.

Summary:

Objectives—This study explores training directors' view of the supervisory process at a time of change resulting in a shift away from a primary dynamic psychotherapy model to new paradigms, both psychotherapeutic and biologic. Problems in supervision and mechanisms for dealing with this are discussed.

Method—A questionnaire was designed and sent to residency directors of all U.S. general psychiatry programs and results calculated.

Results—We received a 50.5% response, higher than anticipated. Of responding directors, 97.2% acknowledged that supervision problems exist; 63.9% felt that supervisors were the source of the problem 50% or more of the time; 63% of the time adherence to outdated treatment paradigms was problematic. Other primary areas of difficulty include: 1) maintainence of a cordial, safe environment; 2) fund of knowledge; 3) countertransference reaction to the resident. When difficulties center around the supervisor, no action was taken approximately 18.5% of the time; interventions that were made varied.

Conclusions—There appears to be no universal pattern of overseeing supervision. With the changing curriculum in residency programs, there is a need to re-examine supervision and address the sensitive issue of monitoring the supervisory process.

NR225 Monday May 4, 3:00 p.m.-5:00 p.m.

Predictors of Psychiatric Inpatient Length of Stay

Irvin P. Brock III, M.D., Psychiatry, Wilford Hall Med, 8430 Dorsetshire, San Antonio, TX 78250; George R. Brown, M.D., Cliff Butson, Ph.D.

Summary:

We respectively examined 21 demographic and clinical variables for their contribution to length of stay (LO(S) during 1040 consecutive admissions to an inpatient psychiatric unit in the Air Force's

largest teaching hospital over a two-year period. The median LOS was nine days (mean 13 days, SD 13.06; range 1-94d), less than the ten-day median LOS seen nationally in civilian inpatient psychiatric units in general hospitals. Our inpatient population consisted of active duty military (70%) and their dependents (17%) and civilian retirees (13%). Presentation with paranoia ($P<.05$), violence during treatment ($P<0.001$), the need for restraint ($P < 0.001$) and being active duty military ($P<0.001$) were independent predictors of longer LOS. DSM-III-R discharge diagnoses of bipolar disorder, major depression, psychotic disorders, and any personality disorder were also independent predictors ($P<0.001$). However, these variables accounted for only 31% of the variance in LOS. Discharge diagnoses were also helpful in separating a short stay (8-11d) group: adjustment disorders, drug and alcohol disorders, and V codes, from a long stay (22-24d; $P<0.001$) group: bipolar, major depressive disorder, and psychotic disorders. We also compared our LOS for each of the psychiatric DRGs to those suggested by the HCFA and found that except for substance abuse/dependence, they consistently underestimated LOS in our population. These results support previous observations that hospital type and severity of illness (as measured by paranoia, violence, and the need for restraint) are significant predictors of psychiatric LOS, and confirm previous reports that albeit helpful, demographic and clinical variables, including discharge diagnoses still leave much of the variance in LOS unaccounted for.

NR226 Monday May 4, 3:00 p.m.-5:00 p.m.

No Correlation Between Psychiatric Resident In-Training Examination (PRITE) and Clinical Skills

Errol M. Aksu, M.D., Psychiatry, Hershey Medical Center, Hershey P.O. Box 850, Hershey, PA 17033; Edward O. Bixler, Ph.D.

Summary:

The Psychiatric Resident In-Training Examination (PRITE) is given each year as a means to measure an individual resident's psychiatric knowledge. According to the American College of Psychiatrists, it may be used by training programs "as one factor among many for assessing the competency of a resident." This study examined if there is a relationship between PRITE scores and clinical performance evaluations. In our program, a resident is evaluated at the end of each rotation by the attending physician on seven subscales covering a broad range of skills. These include psychiatric and general neurologic and medical knowledge, patient care, and interpersonal skills. For each resident, scores on the 1990 PRITE and clinical evaluations for the preceding year were compared. Using a Pearson correlation, a higher PRITE standard score (PSS) was significantly correlated with more years of training ($r=.63$). After correcting for this finding, no clinical subscale was significantly correlated with PSS. The results of this study indicate that a resident's performance on the PRITE is independent of his/her clinical skills as measured by faculty evaluation.

NR227 Monday May 4, 3:00 p.m.-5:00 p.m.

Characteristics of a Forcibly Medicated Population

Safwat Attia, M.D., Psychiatry, Bergenpines Hospital, East Ridgewood Avenue, Paramus, NJ 07652; William M. Greenberg, M.D., Nighat Mirza, M.D.

Summary:

Nonemergent forcible medication of psychiatric patients is a controversial process, which in New Jersey adheres to the "Rennie" clinical review procedure. Despite national legal controversy, this forcibly medicated patient population has received relatively little systematic clinical study. We reviewed the cases of the 43 acute nonforensic adult inpatients who were forcibly medicated using the Rennie process in a large county hospital in 1990, comparing them with a control group matched for time of admission. We found no significant differences in age, ethnicity, marital status, discharge disposition, or principal diagnosis. Rennie patients were less likely to have an Axis II diagnosis ($p=.03$), had much longer hospitalizations (65 vs. 24 days, $p<.001$) not principally accounted for by time refusing medication (mean of 15 days), and, surprisingly, were more likely to be female ($p=.03$). Rennie patients were more likely to have a known history of assaultive or threatening behavior or property damage ($p=.001$, "alloplasty"), but *less* likely than controls to have a known history of suicidal behavior ($p=.04$, "autoplasty"). Possible explanations for the latter findings include: staff concerns in selecting Rennie patients, compliance of "autoplastic" patients, and perceived inadequacy of available injectable antidepressants.

NR228 Tuesday May 5, 9:00 a.m.-10:30 a.m.

The McLean First-Episode Psychosis Projects

Mauricio Tohen, M.D., McLean Hospital, 115 Mill Street, Belmont, MA 02178; Andrew L. Stoll, M.D., Stephen M. Strakowski, M.D., Gianni L. Faedda, M.D., Pierre V. Mayer, M.D., Daniel C. Goodwin

Educational Objectives:

To learn about risk factors of short term outcome in first-episode psychosis.

Summary:

The McLean First-Episode Psychosis Project was started in 1989. The authors describe recovery and relapse data on the first 102 recruited subjects. Fifty-nine percent of the subjects had a diagnosis of psychotic mania, fifteen percent had psychotic depression, 10 percent schizophrenic spectrum (schizophrenia & schizophreniform), 9 percent delusional disorder, and 8 percent other psychosis. By six months, 80 percent had recovered syndromically, but only 55 percent had recovered functionally (Odds Ratio [OR] = 4.5, 95 percent Confidence Interval [C.I.] = 1.3-15.9, P = 0.01), and only 50 percent had recovered both functionally and syndromically. Nonwhite (OR = 9.8, 95 percent C.I. = 1.6-61.4, P = 0.01) and male patients (OR = 8.2, 95 percent C.I. = 1.5-61.4, P = 0.02) were more likely to have a recurrence after adjusting for age. Men (OR = 2.3, 95 percent C.I. = 6.9-5.9, P = 0.07) were less likely and manic patients were more likely to recover functionally (OR = 4.0, 95 percent C.I. = 1.4-11.1, P = 0.008). Among manic patients, psychiatric comorbidity was associated with risk of inability to recover syndromically at the time of discharge (OR = 3.8, 95 percent C.I. = 1.2-12.3, P = 0.02). The McLean First-Episode Psychosis Project with ongoing evaluations at six-month intervals will provide valuable information regarding long-term clinical course and also stability of diagnosis, especially in individuals who initially present with an affective or acute psychosis. In addition, it will provide an opportunity to test the validity of concepts such as recovery, relapse, and recurrence.

References:

1. Beiser, M.; Iacono, W.; and Erickson, D. Temporal Stability in the Major Mental Disorders. In: The Validity of Psychiatric Diagnosis, Robins L and Barrett J (eds), Raven Press, New York, pages 77-98, 1989.

2. Rabiner, C.J.; Wegner, J.T.; and Kane, J.M. Outcome Study of Just-Episode Psychosis I: Relapse Rates After 1 year. *Am J Psychiatry* 143:1155-1158, 1986.

NR229 Tuesday May 5, 9:00 a.m.-10:30 a.m.

Neuroleptic Metabolism and Response in the Elderly

Carolyn M. Mazure, Ph.D., Psychiatry, Yale Univ Sch of Med, Yale New Haven Hosp MU-10-5, New Haven, CT 06504; J. Craig

Nelson, M.D., Janet S. Cellar, M.S.N., Peter I. Jatlow, M.D., Malcolm B. Bowers, Jr., M.D.

Educational Objectives:

To provide data on serum drug levels and clinical effects of low dose neuroleptics in the treatment of acute psychosis in the elderly.

Summary:

Low doses of neuroleptics have been the standard in treating acute psychosis in elderly patients due to concern about increased sensitivity to drug treatment. One explanation for this sensitivity is that drug metabolism is slower in the elderly, leading to higher parent drug or metabolite concentrations. However, it remains unclear whether low doses provide adequate levels or whether low dose treatment is effective. The current work examined mean steady state drug levels, acute response, and the relationship of levels to response in ten patients ($\bar{X}$) age = 75, range = 69-82 yrs) without dementia given fixed low dose perphenazine (PPZ) (0.15 mg/kg/day) for ten days. *DSM-III-R* diagnoses: schizophrenia (N = 3), manic psychosis (N = 2), psychotic depression (N = 4), delusional disorder (N = 1). BPRS ratings at pretreatment and at ten days were blind to blood level. PPZ levels were determined by HPLC. Findings: (1) PPZ levels were low (median = 0.65 ng/mL, range = .01-1.5). Seven of ten patients had steady state levels below the 0.8 ng/mL reported therapeutic threshold for PPZ. The ratio of drug level (ng/mL) to dose (mg/kg) was not significantly higher in the elderly than in 66 younger patients given 0.5 mg/kg of PPZ (median : 4.0 vs 2.8), and the ratio of metabolite level to parent was significantly lower in the elderly (median : 1.1 vs 1.5) (Mann-Whitney U = .02). (2) Only two of ten patients met response criteria. (3) Neither BPRS total or symptom change scores correlated with PPZ level. These preliminary findings suggest that low doses result in low levels which may be ineffective in acute psychosis.

References:

Cohen BM & Sommer BR. Metabolism of thioridazine in the elderly. *J Clin Psychopharmacology, 8* (5): 336-339, 1988.

Mazure CM, Nelson JC, Jatlow PI, Kincare P, Bowers MB, Jr. The relationship between blood perphenazine levels, early resolution of psychotic symptoms, and side effects. *J Clin Psychiatry, 51* (8): 330-334, 1990.

NR230 Tuesday May 5, 9:00 a.m.-10:30 a.m.

Mazindol in Negative Symptom Schizophrenia

John P. Seibyl, M.D., Psychiatry, Yale University, 950 Campbell Avenue, West Haven, CT 06516; John H. Krystal, M.D., Joseph Erdos, M.D., Laurence Karper, M.D., Robin Johnson, M.D., Louise Brenner, R.N.

Educational Objectives:

To describe an investigational pharmacological treatment of negative schizophrenic symptoms with the dopamine reuptake agent, mazindol. Secondary objectives include the discussion of relevant pathophysiological models of positive/negative symptom clusters in schizophrenia.

Summary:

Mesofrontal dopamine (DA) deficits have been implicated in negative schizophrenic symptoms, including affective flattening, withdrawal, and alogia. Consistent with this, most schizophrenics experience minimal negative symptom improvement or even worsening with standard neuroleptic treatment. Mazindol is a long-acting agent that blocks DA reuptake at the dopamine transporter site. We tested the responses of positive and negative symptoms to mazindol augmentation of neuroleptic in partially-refractory, stable outpatient schizophrenics. *Methods:* In an ongoing study, outpatients stabilized on neuroleptic medication were enrolled in a double-blind, placebo controlled trial of mazindol (2 mg/day) augmentation of typical neuroleptic agents. Weekly Brief Psychiatric Rating Scale (BPRS), Positive and Negative Symptom Scale (PANSS), AIMS, Webster EPS ratings, and fasting prolactin and HVA were obtained for four weeks prior to mazindol/placebo augmentation and for six-eight weeks after randomization. *Results:* Nine patients receiving active mazindol demonstrated a 30-40 percent reduction of BPRS and PANSS negative symptom ratings compared to placebo mazindol patients (N = 8). Increases in positive symptoms were noted in one patient who received a pilot dose of mazindol 8 mg/day. No other increases in positive symptoms were seen in patients treated with mazindol 2 mg/day. There was a modest reduction of extrapyramidal side effects and 1/9 patients showed worsening of tardive dyskinesia and mazindol. Subjectively, 7/9 patients experienced increased mood, energy, and affective reactivity and correctly guessed the identity of the randomized medication. *Conclusions:* Preliminary data from this double-blind trial suggest mazindol may be a useful adjunct to standard neuroleptic medication for treating refractory negative symptoms in otherwise stable outpatient schizophrenics.

References:

1) Krumholz and White, *Curr. Ther. Res.*, 12:609-610, 1970.

2) Seibyl, Krystal, Johnson, et al. *Soc. Neurosci. Res.*, 148.6, 1991.

NR231 Tuesday May 5, 9:00 a.m.-10:30 a.m.

The Impact of Drug Abuse on Psychotic Outpatients

Douglas M. Ziedonis, M.D., Psychiatry, Yale University, 904 Howard Avenue, New Haven, CT 06519; Thomas R. Kosten, M.D., William M. Glazer, M.D.,

Educational Objectives:

This presentation will teach participants about the relationship of drug abuse and psychiatric symptomatology in psychotic outpatients. In addition, the impact of drug abuse on the development of neuroleptic induced movement disorders (parkinsonism and tardive dyskinesia) will be reviewed.

Summary:

Drug abuse impacts the course of psychotic disorders. This study of 398 chronic psychotic outpatients on neuroleptics compared the rate of movement disorder symptoms (parkinsonism and tardive dyskinesia) and negative symptoms (using the Scale for the Assessment of Negative Symptoms, SANS) in those with and without drug abuse. Using Research Diagnostic Criteria, 75 percent of the patients were schizophrenic and 24 percent were drug abusers. The 95 dually diagnosed patients (24 percent) were younger (31 years vs 45 years, $p < 0.0001$) and more often male (70% vs 41%). In the dually diagnosed patient group, there were less negative symptoms as measured by the SANS (19 vs 27, $p < 0.0001$). Specific psychiatric symptoms will be discussed. The Webster rating scale was used to assess parkinsonism. Drug abuse correlated with decreased rates of parkinsonism symptoms of bradykinesia (4 percent vs 22 percent, $p < 0.001$), masked facies (3 percent vs 22 percent, $p < 0.0001$), rigidity (12 percent vs 31 percent, $P < 0.001$), and reduced arm swing (2 percent vs 14 percent, $p < 0.004$). Also, drug abuse correlated with increased rates of dyskinesia symptoms of dystonia (30 percent vs 13 percent, $p < 0.0001$), tremor (40 percent vs 24 percent, $p < 0.008$), and akathesia (48 percent vs 18 percent, $p < 0.0001$). Because of the age differences, we examined those under 50 years old, and all associations remained significant. Supported by NIDA P50-DA04060 and R18-DA06190.

References:

Olivera AA, Kiefer MW, and Manley NK. Tardive Dyskinesia in Psychiatric Patients with Substance Use Disorders. *Am. J. Drug Alcohol Abuse*. 16: 57-66, 1990.

Dixon L, Hass G, Weiden PJ, Sweeney J, and Frances AJ. Drug Abuse in Schizophrenic Patients: Clinical Correlates and Reasons for Use. *Am J Psychiatry.* 148: 224-230, 1991.

NR232 Tuesday May 5, 9:00 a.m.-10:30 a.m.

Multisite Evaluation of VA Intensive Case Management

Robert Rosenheck, M.D., NEPEC 182, VA Medical Center, 950 Campbell Avenue, West Haven, CT 06516; Michael Neale, M.S., Philip Leaf, Ph.D.

Educational Objectives:

Following the presentation, the attendee should be able: (1) to describe the implementation of intensive case management within the VA system; (2) to contract VA medical center types: and (3) to summarize preliminary results with respect to health services utilization and costs.

Summary:

This study reports on the experimental design evaluation of an intensive case management (ICM) initiative implemented at nine Department of Veterans Affairs (VA) Medical Centers in 1987. In this evaluation, high hospital users (N = 873) were randomly assigned to either ICM (N = 454) or standard VA care (N = 419) at two different types of VA medical center: former neuropsychiatric hospitals (NP sites) (N = 345), and acute general medical and surgical hospitals (GM&S sites) (N = 528). National computerized workload data were used to track all VA health services use for 24 months following program entry. The cost of these services was estimated using patient specific cost data from each hospital. Among IPCC patients at NP sites, days of psychiatric inpatient hospitalization were 36 percent less than among STD-VA patients. No differences were apparent between the groups at the GM&S Sites. Average VA health care costs per patient (including the cost of IPCC treatment and all inpatient and outpatient medical, surgical, and psychiatric care for two years) were $20,573 *less* for IPCC patients at NP sites, as compared to STD-VA patients, and $7,605 *more* for IPCC patients as compared to STD-VA patients at GM&S sites. These findings suggest that site and patient characteristics, rather than differences in specific clinical program design, may be largely responsible for variation in the cost-effectiveness of intensive case management initiatives.

References:

Olfson M. Assertive community treatment: An evaluation of the experimental evidence. *H&CP,* 4+, 634-641, 1990.

Weisbrod B, Test MA, Stein LI. Assertive community treatment: II. Economic cost benefit analysis. *Arch Gen Psychiatry,* 37, 400-405, 1990.

NR233 Tuesday May 5, 9:00 a.m.-10:30 a.m.

A New Screening Instrument for DSM-IV Dissociative Disorders

Marlene Steinberg, M.D., Psychiatry, Yale University, 100 Whitney Avenue, New Haven, CT 06510; Bruce J. Rounsaville, M.D., Domenic Cicchetti, Ph.D.

Educational Objectives:

1. To present data on the reliability, sensitivity, and specificity of a new screening instrument for patients with the dissociative disorders. 2. To summarize the clinical and research utility of the Mini-Structured Clinical Interview for *DSM-IV* Dissociative Disorders (Mini-SCID-D).

Summary:

Numerous investigations suggest that standard criteria and structured clinical interviews can bring necessary rigor to the diagnosis and study of psychiatric disorders. As the dissociative disorders are difficult to detect, a brief screening interview is needed to rapidly and efficiently identify patients who require additional evaluation. The Mini-SCID-D is the first instrument that can quickly screen for the presence of the dissociative disorders on the basis of *DSM-III-R* and proposed *DSM-IV* criteria. Forty-three subjects were screened for the dissociative disorders using the Mini-SCID-D. They were then evaluated for the presence of a dissociative disorder, using the Structured Clinical Interview for *DSM-III-R* Dissociative Disorders (SCID-D), a comprehensive diagnostic tool. Screening interviews were scored independently by two co-raters blind to diagnosis. Results indicate that the Mini-SCID-D has excellent interrater reliability (94 percent overall agreement) and good to excellent sensitivity and specificity as a screening inventory. The Mini-SCID-D can be used to identify cases who should receive further assessment, whether an in-depth clinical follow-up or the administration of a comprehensive diagnostic instrument.

References:

1. Steinberg, M, Rounsaville, B, Cicchetti, D: The Structured Clinical Interview for DSM-III-R Dissociative Disorders (SCID-D): Preliminary Report on a New Diagnostic Instrument. *Am J Psychiatry* 147:76-82; 1990

2. Kluft R: The dissociative disorders, in The American Psychiatric Press Textbook of Psychiatry. Edited by Talbott JA, Hales RE, Yudofsky SC. Washington, DC, American Psychiatric Press, 1988

NR234 Tuesday May 5, 9:00 a.m.-10:30 a.m.

Comorbid Panic Disorder and Outcome in Depression

J. Craig Nelson, M.D., Psychiatry, Yale University, 20 York Street, New Haven, CT 06504; Carolyn M. Mazure, Ph.D., Peter I. Jatlow, M.D., Malcolm B. Bowers, Jr., M.D.

Educational Objectives:

To inform about the prevalence of comorbid panic disorder in major depression and its effects on outcome.

Summary:

Previous work suggests an association between major depression (MDD) and panic disorder (PD). However, to our knowledge, the effect of comorbid panic on treatment outcome in MDD has not been examined. We determined the prevalence of PD using *DSM-III* criteria in inpatients with nonpsychotic unipolar MDD using the Yale Depression Inventory (which includes panic items) and determined the effect of PD on response to one week of hospitalization without antidepressants and a four-week desipramine (DMI) trial with dose adjusted to reach a target drug level. Of 68 consecutive admissions with MDD, 20 also met criteria for PD. In ten, the onset of PD pre-dated the MDD by one to 29 years (mean = 6 yrs). In the other ten, panic attacks were confined to the depressive episode. MDD patients with PD tended to be younger (mean age 42.0 vs 48.1, p = .15) and female (90 percent vs 71%, p = .17). Patients with or without PD had similar initial HAM-D totals and global severity scores. MDD patients with PD were significantly less likely to respond to one week of hospitalization (0 percent vs 37 percent, p = .04) and thus they required drug treatment. Response to DMI was identical (75 percent) in MDD patients without PD and those with panic attacks confined to the depressive episode. Response tended to be lower in those with preexisting panic (44 percent, p = .15) and HAM-D percent change was significantly less in those with preexisting panic disorder than in all others (31 percent vs 52 percent, p = .02). Panic disorder during a major depressive epi-

sode is common, but does not affect outcome unless antecedent to the depression.

References:

1) Leckman, et al. Panic disorder and major depression. *Arch Gen Psychiatry* 40:1055-1060, 1983.

2)Coryell W., et al. Depression and panic attacks: the significance of overlap as reflected in follow-up and family study data. *Am J Psychiatry* 145:293-300, 1988.

NR235 Tuesday May 5, 9:00 a.m.-10:30 a.m.

Maintenance/Discontinuation of Imipramine in Panic/ Agoraphobia

Matig R. Mavissakalian, M.D., Psychiatry, The Ohio State University, 473 West 12th Avenue, Columbus, OH 43210; James M. Perel, Ph.D.

Educational Objectives:

To present systematic data on the importance of imipramine maintenance in the long-term management of panic/agoraphobia patients, and to provide empirically based guidelines for a successful low-dose imipramine maintenance regimen.

Summary:

Several issues remain to be ascertained beyond the acute response to imipramine in panic disorder. Two interlocking studies were done in two consecutive and comparable samples of panic disorder with agoraphobia patients who had shown good and stable response to six months of acute treatment with imipramine. In Study I, the dose received during acute imipramine treatment (2.18 ± 0.36 mg./kg./day) was systematically reduced by half (1.1 ± 0.1 mg./kg./day) in 19 patients who were prospectively followed with scheduled assessments every two months for a year. In Study II, the subsequent sample of 16 patients (imipramine, 2.04 ± 0.23 mg./kg./day) was randomly assigned to double-blind discontinuation or continuation conditions for a three-month period with scheduled monthly assessments and a three-month, drug-free follow-up period. The same assessment battery and operationalized criteria for response and relapse were used in the two studies, and the integrity of drug conditions was verified by plasma level determinations. In contrast to the approximately 75 percent cumulative six-month relapse rate following discontinuation of acute treatment, none of the patients relapsed or had sustained worsening in panic or phobia measures during the Half-Dose Maintenance Study. The results underscore the importance of pharmacologic prophylaxis and provide empirical guidelines for a successful low dose maintenance regimen for panic disorder and agoraphobic patients who respond markedly to imipramine.

References:

1. Noyes R, Garvey MJ, Cook BL, Samuelson L: Problems with tricyclic antidepressant use in patients with panic disorder or agoraphbia: Results of a naturalistic follow-up study. *J Clin Psychiatry* 50 (5):163-169, 1989.

2. Mavissakalian M, Michelson L: Two-year follow-up of exposure and imipramine treatment of agoraphobia. *Am J Psychiatry* 143 (9):1106-1112, 1986.

NR236 Tuesday May 5, 9:00 a.m.-10:30 a.m.

A Multicenter Trial of Fluvoxamine in OCD

Steven A. Rasmussen, M.D., Psychiatry, Brown University, Butler Hosp 345 Blackstone, Providence, RI 02906; John H. Greist, M.D., Michael A. Jenike, M.D., Delbert G. Robinson, M.D.

Educational Objectives:

To present results on efficacy and adverse events of multicenter parallel design double-blind placebo controlled trial of fluvoxamine in obsessive compulsive disorder.

Summary:

One hundred and sixty patients who met *DSM-II-R* criteria for obsessive compulsive disorder participated in a multicenter double-blind, placebo controlled trial of the potent serotonin reuptake inhibitor fluvoxamine. One hundred and forty subjects completed the two-week, single-blind, placebo washout period, followed by ten weeks of random double-blind assignment to either fluvoxamine or placebo. The mean dose of fluvoxamine at week 10 was 250 mgs. Analysis of the intent to treat sample revealed significant differences in efficacy between fluvoxamine and placebo treated groups at weeks 6, 8, 10, and endpoint (final visit) as measured by the Yale Brown Obsessive Compulsive Scale and the NIMH Global OC scale. Clinical global improvement scores were also significantly higher for fluvoxamine compared to placebo beginning at week 4. At week 10, 28 or 42.4 percent of patients treated with fluvoxamine rated themselves as much or very much improved compared to 13.3 percent of patients taking placebo. The most frequently reported side effects were insomnia, nausea, headache, asthenia, and somnolence. The incidence of premature discontinuation of treatment in the fluvoxamine group due to adverse side effects was 11.3 percent. A total of 65.4 percent of the patients who received fluvoxamine had previously failed an adequate trial of alternate drug treatment. This study supports previous double-blind studies that have demonstrated fluvoxamine's efficacy and safety in the treatment of obsessive compulsive disorder.

References:

1. Goodman WK, Price LH, Rasmussen SA et al (1989) Efficacy of fluvoxamine in obsessive compulsive disorder a double-blind comparison with placebo. *Arch Gen Psychiatry* 46:36-44.

2. Perse TL, Greist JH, Jefferson JW et al (1987) Fluvoxamine treatment of obsessive compulsive disorder. *Am J Psychiatry* 144:1543-1548.

NR237 Tuesday May 5, 9:00 a.m.-10:30 a.m.

Effect of Yohimbine and Placebo in PTSD

Mark B. Hamner, M.D., Psychiatry, VAMC, 109 Bee Street, Charleston, SC 29403; Bruce I. Diamond, Ph.D.

Educational Objectives:

To teach the audience about the potential role of the noradrenergic system in PTSD. The results of a pilot study will be presented investigating the effects of the alpha-2 adrenergic antagonist yohimbine and placebo in patients with PTSD.

Summary:

To further investigate noradrenergic function in post-traumatic stress disorder (PTSD), we administered the alpha-2 adrenergic receptor antagonist yohimbine (16.2 mg oral dose) to ten Vietnam veterans meeting *DSM-III-R* criteria for PTSD and to five healthy controls in a double-blind, placebo-controlled study. Subjects completed various rating instruments to assess anxiety symptoms. Blood samples were obtained at baseline and at intervals post-drug for assay of plasma norepinephrine, 3-methoxy-4-hydroxyphenylglycol (MHPG), dopamine (DA), homovanillic acid (HVA), and epinephrine by HPLC-EC. All controls experienced a mild increase in anxiety and/or other autonomic arousal symptoms with yohimbine. Two of the ten PTSD patients endorsed increased anxiety, autonomic arousal, and/or reexperiencing symptoms with yohimbine. Plasma catecholamines, including MHPG, did not change significantly with yohimbine or placebo challenge in either group. Interestingly, resting plasma DA levels were elevated in PTSD pa-

tients (89.3 ± 12 ng/ml versus 41.6 ± 5.4 ng/ml in controls, df = 13, t = 2.52, p < 0.025) and remained higher post-drug challenge. Plasma HVA levels were comparable between groups. These pilot data suggest that PTSD patients may be relatively hyporeactive at this dose of yohimbine compared with controls and that higher doses may be required to elicit significant psychophysiologic changes as recently reported by others. These data suggest a peripheral DA hyperactivity in PTSD that appears independent of either noradrenergic changes or the psychometrics employed in this study. Supported in part by VA.

References:

1. Kosten TR, Mason JW, Giller EL, et al: Sustained urinary norepinephrine elevation in post-traumatic stress disorder. *Psychoneuroendocrinology,* 12: 13-30, 1987.

2. Krystal JH, Southwick, SM, Charney DS: Yohimbine effects in PTSD patients. *CME Syllabus and Proceedings Summary,* 143rd Annual Meeting of the American Psychiatric Association, New York, New York, 1990.

NR238 Tuesday May 5, 9:00 a.m.-10:30 a.m.

The Relationship of Dieting Severity and Alcohol Use

Dean Krahn, M.D, Psychiatry, University of Michigan, 1500 E. Medical Ctr Drive, Ann Arbor, MI 48109; Candace Kurth, M.P.H., Mark A. Demitrack, M.D., Edith Gomberg, Ph.D., Adam Drewnowski, Ph.D.

Educational Objectives:

To highlight the fact that the increased alcohol abuse observed in eating disordered patients is related to a more general association of increasing dieting severity with increasing prevalence of alcohol use, abuse, and dependence.

Summary:

Food deprivation increases drug self-administration in animals. We hypothesized that if this also occurred in humans, then increased alcohol use would be related in a continuous, graded manner to dieting severity. We recently reported this type of relationship between dieting severity and alcohol use in a sample of 1796 freshmen college women (1990) based on self-report survey data (Soc. of Biol. Psych., 1991). We now report a replication and important extension of these findings. We used a survey to classify 1420 college freshmen into the following dieting groups: bulimic (B, 2 percent of population), at risk (AR, 20 percent), severe (S. 21 percent), intense (I, 23 percent), casual (C, 26 percent) and non-dieters (ND, 8 percent). Subsequently, we conducted SCID interviews on 305 women randomly selected within dieting groups. Interviewers were blind to survey and had >95 percent interrater agreement for SCID diagnoses. The dieting severity classification correlated well with SCID eating disorder diagnoses. Dieting severity was related to frequency of alcohol consumption (gamma = .16, p < .001). Limiting the analyses to drinkers, dieting severity was also related to frequency of altered mental status due to drinking (gamma = .20, p < .001) and to number of negative consequences of alcohol use (gamma = .23, P < .001). For example, the percentages reporting alcohol-related blackouts in each group were: 27 percent B, 22 percent AR, 20 percent S, 11 percent I, 8 percent C, and 7 percent ND. The percentages reporting unintended sexual activity due to alcohol use in each group were: 35 percent B, 18 percent AR, 13 percent S, 15 percent I, 8 percent C, and 9 percent ND. Dieting severity was also positively related to scores on the CAGE alcoholism screening tool (gamma = .21, p < .001). The prevalences of subjects answering yes to two or more CAGE questions (a cut-off for diagnosis of alcoholism) were elevated for the AR and B groups (17 percent and 37 percent, respectively). Past and/or present alcohol abuse or dependence was diagnosed using SCID interviews. The prevalences of alcohol diagnoses by group were: 26 percent B, 12 percent AR, 7 percent S, 8 percent I, 5 percent C, and 6 percent ND. Thus, dieting severity was related not only to frequency and intensity of alcohol use, but also to the CAGE score, number of negative consequences, and SCID diagnosis. Dieting in young women is associated with increased alcohol use, abuse, and dependence.

References:

(1) Krahn, D.S.,. The Relationship of Eating Disorders and Substance Abuse, *J Substance Abuse,* 3, 239-253, 1991.

(2) Mitchell, J.E., Hatsukami D., Eckert E.D., Pyle R.L., Characteristics of 275 patients with bulimia, *Am J Psychiatry,* 142, 482-485.

NR239 Tuesday May 5, 9:00 a.m.-10:30 a.m.

Bulimic's Eating Behavior in a Feeding Laboratory

L. K. George Hsu, M.D., Psychiatry, WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213; Theodore Weltzin, M.D., Walter H. Kaye, M.D.

Educational Objectives:

At the end of the program the learner should be able to know the methodology of a human feeding laboratory, the 24-hour feeding pattern of normal controls, the 24-hour feeding pattern of bulimics, and how it changed with treatment.

Summary:

Fifty-three female bulimic patients were evaluated in a human feeding laboratory (HFL) for a 24-hour period before and after 14 weeks of outpatient treatment: nutritional counseling (N = 7), cognitive therapy (N = 17), combined nutritional and cognitive treatment (N = 18), and attendance at support group (N = 11). In the HFL subjects may self-select from two vending machines any of the 38 food or drink items, the selections (items, calories, macronutrients, and time selected) are recorded automatically on a computer. Unconsumed food or drink items are removed periodically, but no attempt is made to observe the subject's eating behavior. Medication (e.g., laxatives) are not allowed. There is an attached bathroom, but vomiting is not encouraged or discouraged. Findings: (1) Total caloric intake pre- vs. post-treatment was significantly lower in the cognitive (7779 ± 6133 vs. 3015 kcal ± 1761, paired t = 3.25, df = 16, p = 0.005) and the combined (4934 ± 3260 vs. 3093 ± 2512, paired t = 2.94, df = 17, p = 0.009), but not in the nutritional or support group condition. (2) At pre-treatment, 62 percent of patients ate significantly more than a group of normal controls in the HFL, 26 percent ate normally, and 12 percent underate. The proportion of macronutrients (i.e., carbohydrate, protein, fat) in the meals did not differ between patients and normals. (3) At pre-treatment, 21 percent of the meals consumed by the patients exceeded 1000 kcal. Controls did not eat any meal larger than 1000 kcal. (4) At post-treatment, the abstainers (AB; i.e., no longer binge or vomit at week 14) improved more than the nonabstainers (NAB): 72 percent AB ate normally (vs. 56 percent NAB), 22 percent overate (vs. 32 percent NAB), and 6 percent underate (vs. 12 percent NAB). We believe that studying the eating behavior of bulimic patients in an HFL significantly increases our understanding of the disorder, and that self-report of abstinence is not always correlated with normal eating behavior in the HFL.

References:

1. Weltzin, TE, Hsu, LKG, Pollice, C, Kaye, WH. Feeding patterns in bulimia nervosa. *Biol Psychiatry,* 30:1093, 1991.

2. Hsu, LKG, Santhouse, R, Chesler, BE. Individual cognitive behavioral therapy for bulimia nervosa. *International J Eating Disorders,* 10, 273-283, 1991.

NR240 Tuesday May 5, 12:00 noon-2:00 p.m.

Gender Related PET Differences in Normal Controls

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Summary:

PET studies have not consistently matched controls and subjects on gender. PET data have correlated increasing symptoms of depression with decreasing left anterolateral prefrontal cortical (LAPFC) glucose utilization (CMRglu) and increases in the number of violent episodes with decreases in orbital frontal (OF) CMRglu. Adults with ADHD have lower global CMRglu than adult normal volunteers.

As we are studying patients with the above symptoms, we evaluated gender differences in regional CMRglu in healthy, normal volunteers (n = 21 males and 21 females) with particular interest in the global, OF, and LAPFC CMRglu. Results indicate that the samples were not atypical because global CMRglu was greater in females than in males ($p = 0.03$*). In addition, regional CMRglu was lower in men than in women in the OF area ($M < F$, absolute CMRglu differences $p = 0.006$*; normalized CMRglu differences $p = 0.04$*). There were no gender differences in normalized CMRglu values in the LAPFC regions; however, absolute values showed LAPFC regions to be higher in women than men ($p = 0.03$*).

Based on these data, we suggest consideration be given to gender matching in PET studies, particularly when studying disorders that are disproportionately represented among the sexes.

*Two tailed *t*-test.

NR241 Tuesday May 5, 12:00 noon-2:00 p.m.

Dopaminergic Innervation in Human Brain

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Summary:

We have reported that PET and SPECT images with [^{125}I](S)-N-[(1-ethyl-2-pyrrolidinyl)-methyl]-2,3-dimethoxy-5-iodobenzamide (epidepride) and its [^{18}F] 5-(3-fluoropropyl) analog, respectively, indicate significant levels of extrastriatal dopamine D2 receptors and have presented *in vitro* kinetic analysis of D2 receptors in specific thalamic nuclei in man using [^{12}§I]epidepride (J Nucl Med 32, 961, 1991). Additional PET studies using (S)-N-[(1-ethyl-2-pyrrolidinyl)-methyl]-2,3-dimethoxy-5-(3-fluoropropyl)-6-hydroxybenzamide, which due to its pharmacokinetic properties and lack of lipophilic metabolites make it a superior PET ligand, also identified D2 receptors in extrastriatal areas. *In vitro* kinetic analysis of [^{125}I]epidepride binding in additional human brain regions revealed D2 receptor densities (pM/g tissue) in substantia inominata (1.00), amygdala (0.87), inferior temporal cortex (0.41), anterior hippocampus (0.39), anterior perforated substance (0.27), anterior cingulate (0.26), medial frontal lobe (0.26), orbito frontal cortex (0.22), and medial frontal gyrus (0.17). Concurrent measures of dopamine (DA), DOPAC, HVA, 5-HIAA and 5-HT were also made in these regions. D2 receptor density was correlated with DA, HVA and DOPAC levels in motor and limbic areas ($p < .001$), but was not correlated with any dopaminergic parameter in cortical or thalamic areas. DA turnover, as assessed by calculating HVA/DA ratios, was correlated with D2 receptor density in limbic areas ($p > .001$), was not correlated in thalamic and cortical areas and was negatively correlated in motor areas ($p < .001$). Also, D2 density was significantly correlated with serotonergic parameters in limbic, thalamic and cortical areas ($p > .01$). These studies further confirm the presence of levels of D2 receptors in extrastriatal brain regions in man that are quantifiable by PET and suggest that these receptors may be associated with serotonergic function in certain brain regions.

NR242 Tuesday May 5, 12:00 noon-2:00 p.m.

Cortical Perfusion in Frontal Lobe Type Dementia

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Summary:

To examine the pathophysiology of frontal lobe type dementia (FLD), we measured regional cerebral blood flow (rCBF) by 133-xenon inhalation in six patients (ages 54-73), referred with a diagnosis of FLD, who had documented ratings of dementia severity and illness duration. This FLD sample was compared to a group of probable Alzheimer's disease (AD; n = 6) and elderly normal (n = 6) subjects on cortical perfusion (ISI) and relative gray matter weight (wg) with rCBF. All three groups were closely matched on age, gender, and education, and the two patient groups were additionally matched on dementia severity and duration.All FLD patients showed a marked hypofrontal perfusion pattern on rCBF. Both dementia groups had lower global mean flows than the normals ($p < .02$), and the AD patients showed relative flow reductions in the parietotemporal region compared to the FLD and normal groups. The FLD patients had lower flows in the frontal cortex compared to the AD patients and normals ($p < .0003$); and also showed lower global mean wg values than the AD and normal groups ($p < .002$).

These findings support the use of rCBF in distinguishing FLD from typical AD and normal aging. Further, our finding of lower wg values in the FLD group suggests that for the same level of dementia severity and duration, cortical cell loss may be a more prominent feature of FLD compared to AD.

NR243 Tuesday May 5, 12:00 noon-2:00 p.m.

Temporal Lobe Abnormalities in Schizophrenia: An MRI Study

Martha E. Shenton, Ph.D., Psychiatry, Harvard Medical, 116A 940 Belmont, Brockton, MA 02401; Ron Kikinis, M.D., Ferenc A. Jolesz, M.D., Seth Pollak, M.A., M. LeMay, M.D. R.W. McCarley, M.D.

Summary:

Data from post-mortem, CT, MRI, and event-related potential studies suggest left temporal lobe pathology in schizophrenia. To localize and to delineate these abnormalities further, we conducted an MRI study to derive volumetric measurements and 3D surface renderings of temporal lobe structures in 15 male, right-handed, chronic, thought disordered, medicated schizophrenics (SZs), and 15 normal controls matched for sex, age (NCLs; mean = 38 years), handedness, social class of origin, and verbal I.Q. MR data from entire brain were acquired axially (TE = 30/80-msec, TR = 3000-ms, slice thickness = 3-mm) and coronally (3DFT SPGR, TE = 5-msec, TR = 35-msec, one repetition, 45° nutation, 1.5-mm slices). Semi-automated segmentation procedures were then used to segment brain into specific tissue classes and specific regions of interest. Comparisons between SZs and NCLs were statistically significant and revealed: 1) 19 percent decrease in left anterior hippocampus/amygdala; 2) 13 percent decrease in volume in left parahippocampal gyrus (vs. 8 percent on the right); and 3) 15 percent decrease in volume in left superior temporal gyrus (STG), with decreases in the posterior portion correlating $4 = -0.81$ with amount of thought disorder. None of these decreases in regional volume was accounted for by decreases in overall brain or temporal lobe volume. These findings confirm left-lateralized reductions in

grey matter volume in temporal lobe structures in schizophrenia. Moreover, a new and potentially important clinicopathological correlation was observed between thought disorder and left posterior STG.

NR244 Tuesday May 5, 12:00 noon-2:00 p.m.

Cerebral SPECT Abnormalities in Depression

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Summary:

Single photon emission computed tomography (SPECT) studies have demonstrated reductions in cerebral blood flow (rCBF), e.g., hypoperfusion of the frontal lobes, in depressed patients. This presentation will report data from an ongoing study of rCBF in patients with major depressive disorders during depressed episodes and, in some cases, following ECT. SPECT scans using Technetium 99-m labelled HMPAO (Ceratec) are performed on a dedicated brain SPECT system with reconstructive resolution of approximately 7 mm. Preliminary results from the first ten patients studied (mean ± SD Hamilton Depression Rating Scale score = 26 ± 7) showed perfusion defects including areas of hypoperfusion bilaterally in the frontal lobes in nine patients on clinical reading; two patients also had temporoparietal or occipital hypoperfusion. In a preliminary quantitative analysis, mean frontal lobe/whole brain ratio of radioactivity was significantly lower ($p < .05$, one tailed t-test) in four depressed patients (1.05 ± .05) than in four controls (1.13 ± .03). SPECT studies on additional depressed patients are currently in progress. For this presentation, data analysis will be extended to include comparisons of mean frontal lobe/whole brain and frontal lobe/cerebellum ratios in depressed patients and age-matched normative controls, as well as in depressed patients before and after ECT. Data will be examined to determine whether changes in rCBF following ECT are related to changes in clinical state.

NR245 Tuesday May 5, 12:00 noon-2:00 p.m.

SPECT Brain Imaging of Benzodiazepine Receptors

John P. Seibyl, M.D., Psychiatry, Yale University, 950 Campbell Avenue, West Haven, CT 06516; Betka Sybirska, Ph.D., Andrew Goddard, M.D., Douglas Bremner, M.D., Scott W. Woods, M.D., Robert Innis, M.D.

Summary:

Benzodiazepine (BZ) receptor function has been implicated in a number of neuropsychiatric conditions, including anxiety disorders, alcohol withdrawal, and hepatic encephalopathy. ^{123}I Iomazenil is a superior benzodiazepine receptor ligand we have utilized in human and nonhuman primate studies with single photon emission computed tomography (SPECT). The present study investigated the effects of administering the BZ receptor agonist lorazepam during dynamic brain SPECT scanning with ^{123}I iomazenil. *Methods:* Twelve healthy human subjects received 5 mCi ^{123}I iomazenil i.v. for a single SPECT scan. Six subjects received lorazepam (0.03 mg/kg i.v.) and six received placebo (saline) 90 min after ^{123}I iomazenil injection. In parallel experiments in baboons, animals received increasing doses of lorazepam (up to 0.5 mg/kg i.v.) after ^{123}I iomazenil injection. Regions of interest were drawn in cortical and subcortical brain areas and a linear curve fit to the time-activity data from each region. Rates of radioactivity washout were calculated for the pre- and post-lorazepam periods. *Results:* In humans, radioactivity distributed in regions of high BZ receptor density. Washout of activity from cortical areas was not increased by injection of lorazepam, despite significant pharmacological effects at the 0.03 mg/kg dose. Baboons showed a dose-response effect of lorazepam on cortical washout, with minimal effect on washout for low dose (0.03 mg/kg) consistent with the humans, but increased washout for high doses (0.5 mg/kg) of the BZ agonist. The *in vivo* ED50 of lorazepam was calculated to be 0.17-0.26 mg/kg i.v. *Conclusions:* Pharmacologically-active doses of lorazepam have minimal effect on washout rates of cortical radioactivity during ^{123}I iomazenil SPECT scanning. These data can be interpreted to indicate that the pharmacological effects of lorazepam are achieved at low percentage occupancy of BZ receptors.

NR246 Tuesday May 5, 12:00 noon-2:00 p.m.

MRI Perfusion Imaging of Brain Activity

Jeffrey R. Zigun, M.D., CBDB, NIMH, 2700 M.L. King Jr. Ave SE, Washington, DC 20032; Fernando A. Barrios, Ph.D., Douglas W. Jones, Ph.D., Daniel Z. Press, B.S., Joseph A. Frank, M.D., Daniel R. Weinberger, M.D.

Summary:

Belliveau et al used an echo planar MRI technique to study cerebral perfusion during visual activation. We describe a replication of these findings using a more readily available MRI protocol.

Three normal subjects were studied during visual stimulation (Grass SV20 goggles flashing at 7.8 Hz) and darkness (goggles turned off) MRI scans were performed on a GE-SIGNA 1.5T machine using a Warp GRASS pulse sequence (TR = 16 msec, TE = 12 msec, Flip angle = 10°; FOV = 24 cm [128 × 256 matrix] slice thickness = 10 mm) and a 3" surface coil. During each study an IV bolus of gadolinium DTPA was administered and 60, 2.048 sec acquisitions were obtained.

Image analysis involved drawing anatomical ROIs of primary visual cortex on a registered high resolution scan and transferring to concentration maps. These maps were created from the original images using a logarithmic transformation. Activation was assessed by comparing the peak height of the concentration time curves for the two conditions. We found and average of 11.7 percent (range 5.7-17.4 percent) increased blood volume during visual stimulation.

MRI based studies have several advantages over PET and SPECT techniques including superior spatial and temporal resolution, ability to repeat frequently, and lack of ionizing radiation.

NR247 Tuesday May 5, 12:00 noon-2:00 p.m.

High-Resolution 18 Fluorine Deoxyglucose PET Studies in Late-Life Depression

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Summary:

The purpose of this study was to examine cerebral glucose metabolism (CMRglc) in late-life depression and to compare CRMglc in this group to healthy age-matched controls. Eight subjects (2M, 6W, mean age ± SD = 72 ± 5.8) who met *DSM-III-R* criteria for major depressive disorder (mean Hamilton Rating Scale Score for Depression = 22 ± 6) and eight healthy age-matched controls (2M, 6W, mean age ± SD = 65 ± 4.6) were scanned using the PENN PET (pin plane and axial resolution = 6 mm). All subjects were scanned in the resting state with eyes open, ears unoccluded, and room noise minimized. 2 mm slices were obtained parallel to the canthomeatal line and a lumped constant of 0.52 was used to calculate CMRglc. Whole Brain CMRglc (mg/100 gm/min.) in the depressed group was 3.3 ± 0.5, while the mean Whole Brain CMRglc in the control group was 5.0 ± 1.0 ($p < 0.01$, Robust Rank Order Test), The metabolic decline in the depressed group was generalized and involved all major neocortical and subcortical structures without any focal pattern of hypometabolism. These pre-

liminary data suggest that late-life depression in the absence of complicating medical illness presents with a significant decline in cerebral glucose metabolism when compared to healthy controls.

NR248 Tuesday May 5, 12:00 noon-2:00 p.m.

Acute Effects of ECT on Memory

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Summary:

Forty-two patients, undergoing a major depressive episode and treated with bilateral moderately suprathreshold titrated ECT, were assessed for memory functioning one hour after eight of their treatments. Twenty-three patients were assessed acutely, four times after simulated ECT and four times after real ECT (the twice weekly real-ECT group, mean number of treatments: 7.69). Nineteen patients received real ECT treatments (M = 10.79 treatments). Twenty-seven of these patients were also assessed for subjective symptoms (such as headaches, tiredness, and having dry mouth) after their memory assessments. Patients and examiner were blind to the type of treatment (real or simulated) that the patient received. The results showed that there were no acute measurable effects on memory after simulated treatments; in contrast to previous findings with low-dose ECT, the decrements in acute memory after ECT accumulated over treatments; the acute effect of the first ECT was disproportionally more dramatic than the rest. Seizure duration predicted acute memory deficits. The acute subjective symptoms were greater after real than simulated ECT; they decreased as a function of the number of treatments in the series. This definitive characterization of acute effects is discussed in relation to former speculations and findings. (Supported by NIMH Grant #40734)

NR249 Tuesday May 5, 12:00 noon-2:00 p.m.

SPECT in Psychopathology Secondary to Head Injury

Zafar A. Sharif, M.D., Psychiatry, Columbia University, 722 West 168th Street Box 72, New York, NY 10032; Gene E. Alexander, Ph.D., Isak Prohovnik, Ph.D., Jonathan M. Silver, M.D.

Summary:

Traumatic brain injury (TBI) may result in significant neuropsychiatric disability without evidence of physical handicap or morphological abnormality on MRI. We used SPECT to investigate the pathophysiology of prominent behavioral disturbance presumably resulting from TBI. To date we have analyzed four patients (age 24-32) with TBI and loss of consciousness of ten minutes to two weeks. All patients ceased gainful employment secondary to symptoms ranging from decreased attention and memory to rage attacks, assaultive behavior, and psychosis. MRI (4-54 months post-injury) was normal in three patients and showed possible increased signal in the region of injury in one patient. SPECT scans were performed 12-54 months post-injury using Tc-99m.HMPAO to visualize cerebral blood flow. Focal asymmetries greater than 15 percent were considered abnormal. Three patients who had prominent psychotic symptoms, rage attacks, and a normal MRI demonstrated significant flow asymmetries in the anterior temporal lobe. The one patient with an abnormal MRI showed a flow deficit extending well beyond the structural lesion.

Thus, functional imaging of remote TBI demonstrated perfusion abnormalities in regions with no significant structural abnormalities. Further, all patients that exhibited psychotic and aggressive behavior had temporal lobe perfusion abnormalities. This suggests a role for temporal lobe dysfunction in the pathogenesis of these symptoms.

NR250 Tuesday May 5, 12:00 noon-2:00 p.m.

Normal Caudate Nucleus in OCD Using MRI and SPECT

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Summary:

Some neuroimaging studies suggest abnormal caudate nucleus in obsessive-compulsive disorder (OCD). Reports implying abnormal OCD caudate structure and function have not been replicated by other groups.

We examined caudate structure by measuring volumes and bicaudate ratios on magnetic resonance images (MRI) in 24 *DSM-III-R* OCD patients and 21 matched controls. Volumes were calculated by outlining manually head of caudate on all axial slices on which it appeared, then multiplying the sum of these areas by slice thickness. We also examined caudate blood flow with single photon emission computed tomography (SPECT) using the radiotracer [Tc-99m]-hexamethylpropyleneamine oxime (HMPAO) in ten OCD patients and 8 matched controls. Caudate SPECT values were normalized to mean cortical value and to mean cerebellum. All regions were defined blind to diagnosis.

All structural and functional measures in our population failed to exhibit differences between obsessive-compulsive patients and matched controls. Both SPECT normalization values produced similar results.

Although Luxenberg *et al.* (1988) report reduced CT caudate volume in OCD, Kellner *et al.* (1991) found no difference in MRI caudate area, nor did we for MRI caudate volume. Functionally, Baxter *et al.* (1987; 1988) found increased PET caudate metabolism in the presence of global OCD hypermetabolism, while Martinot *et al.* (1989) found decreased PET caudate metabolism with global OCD hypometabolism. Swedo *et al.* (1989) and Nordahl *et al.* (1989) both found normal PET caudate metabolic rate in OCD. Neither our SPECT study nor any PET report has found abnormal caudate function after normalizing for global values.

NR251 Tuesday May 5, 12:00 noon-2:00 p.m.

Cerebral Metabolism by PET in Patients with Generalized Resistance to Thyroid Hormone

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Summary:

Generalized resistance to thyroid hormone (GRTH) is a disease with a primarily autosomal dominant inheritance, characterized by reduced responsiveness of pituitary and peripheral tissues to the action of thyroid hormone. Following the linkage of GRTH to the human beta thyroid receptor (hTRB) gene, a number of different mutations in the ligand-binding domain of the receptor have been reported. To date, we have identified 13 distinct mutations located in exons 9 and 10 of the hTRB gene in 13 of 18 unrelated kindreds with GRTH. Symptoms of hyperactivity are among the various somatic and neuropsychiatric manifestations of GRTH that have been observed, and a recent systematic study of ADHD in our 18 kindreds with GRTH found that over 60 percent of affected patients met diagnostic criteria for ADHD. PET scan studies have found decreased cerebral metabolism in areas subserving sustained attention in ADHD patients compared to normal controls. The purpose of this study was to determine whether patients with GRTH have an altered cerebral metabolism. The study population consisted of nine adult patients with GRTH and nine age- and sex-

matched normal controls. Positron emission tomography (PET) brain scans were obtained with a Scanditronix scanner using [^{18}F] fluoro-2-deoxy-D-glucose while subjects performed an auditory continuous-performance task (CPT) designed to activate areas of the brain necessary for sustained attention. Our results demonstrate that the auditory CPT 'hits' score (the number of correct responses) was significantly lower in patients with GRTH than the age- and sex-matched controls (mean score; 148 vs 187, $p < 0.03$). Of the sixty regions of interest (ROI) measured, normalized glucose metabolic rates of GRTH patients were significantly decreased in the superior right parietal ROI ($p < 0.05$) and increased in the mid-occipital ROI ($p < 0.01$) and the right thalamus ($p < 0.05$). These data suggest that GRTH affects the ability to perform attentional tasks. Also, GRTH may be associated with decreased metabolism in an area of the brain (right parietal lobe) that subserves sustained attention.

NR252 Tuesday May 5, 12:00 noon-2:00 p.m.

High-Resolution PET-FDG in Schizophrenia

Thomas E. Nordahl, M.D., Research Med., Lawrence Berkeley, 1 Cyclotron Road ML 55-121, Berkeley, CA 94720; Thomas Budinger, M.D., Anne Cummings, Shariar Salamet, M.D., Tasha Kusubov, B.S., William Jaqust, M.D.

Summary:

Eleven medication-free outpatients with chronic schizophrenia who were enrolled in a Merck study of remoxipride were compared using 2.6 mm resolution PET and FDG with ten normal controls. The two groups of subjects did not differ in terms of age, sex, or handedness, or in whole brain metabolism. Significant regional metabolic differences were noted in the left thalamus, posterior midtemporal gyi bilaterally, and the left posterior parietal region. No significant differences were noted for hippocampal or superior temporal gyral region rCMRglc. Positive symptoms elicited from the BPRS positively correlated with the rCMRglc of the right superior temporal gyrus, left superior temporal gyrus (trend), left anterior hippocampus, right anterior hippocampus and the left thalamus. Positive symptoms negatively correlated with the rCMRglc of the left posterior parietal region. Discussion of the significance of the above findings will be presented.

NR253 Tuesday May 5, 12:00 noon-2:00 p.m.

Psychoeducational Testing and SPECT in Adolescents

Gregory T. Slomka, M.D., Psychiatry, Allegheny General Hosp., Allegheny Neuropsych Inst., Oakdale, PA 15071; H. Jordan Garber, M.D., Mustafa H. Adatepe, M.D.

Summary:

Associations between psychoeducational (IQ and academic achievement tests) and neurodiagnostic data remain poorly defined in adolescent psychiatric patients. Relationships between results of SPECT, MRI, EEG, and scores on WISC-R and WRAT-R were explored in 17 consecutive admissions to an adolescent neuropsychiatric unit (ages 11-16, mean[sd] = 13.7[1.4]; 14 male/3 female) who met *DSM-III-R* criteria for affective (n = 13, 9 with organic factors), disruptive behavior (n = 2) or anxiety (n = 2) disorders, without PDD, substance use, MR (FSIQ range 66-105, mean[sd] = 84.4[12.7]) or degenerative disorders. T-tests between groups with and without frontal SPECT abnormalities had lower scaled scores on the WISC-R Object Assembly subtest (abnormal n = 6, mean[sd] = 6.8[1.5]; normal n = 11, mean[sd] = 9.5[2.5]; df = 15, t = 2.365, $p < .03$) but not on other subtests, nor by age, FSIQ, PIQ, VIQ or WRAT-R scores (Reading, Spelling Arithmetic). No differences were found between groups based on normal and abnormal SPECT in parietal (abnormal n = 8), temporal (abnormal n = 4) or subcortical areas (abnormal n = 6), nor did patients with abnormal EEG (n = 7) and normal EEG (n = 10) differ on any measure. Subtest variability did not accurately predict the presence of SPECT, MRI, or EEG abnormalities. Impaired Object Assembly may reflect deficient motor organization and planning associated with frontal lobe dysfunction. The lack of differences between groups on most WISC-R subtests in relation to SPECT abnormalities suggests routine psychoeducational assessment is insensitive to brain dysfunction, often detected by formal neuropsychological testing.

NR254 Tuesday May 5, 12:00 noon-2:00 p.m.

Basal Sympathoadrenal Function in PTSD

M. Michele Murburg, M.D., Psychiatry, Univ of Washington, 116A VAMC 1660 Columbian Way, Seattle, WA 98108; Miles E. McFall, Ph.D., Nancy Lewis, R.N., Eric Petrie, M.D., Richard C. Veith, M.D.

Summary:

Findings of elevated resting blood pressure (BP) and heart rate (HR) in patients with post-traumatic stress disorder (PTSD) suggest that basal sympathetic nervous system (SNS) activity may be increased in this disorder. We have measured epinephrine (EPI) and norepinephrine (NE) in arterialized venous plasma (Study #1) and assessed plasma norepinephrine kinetics in arterialized plasma using a radioisotope dilution technique (Study #2) in order to investigate basal SNS function in male Vietnam combat veterans with PTSD compared with age-matched normal male controls. In the first study, 11 veterans with PTSD diagnosed using the SCID were compared with 11 controls. PTSD patients did not exhibit statistically significant differences from controls in HR (62 ± 7 vs 62 ± 10), systolic (124 ± 11 vs. 120 ± 7) or diastolic BP (79 ± 8 vs. 76 ± 7) or in resting plasma levels of NE (237 ± 52 vs. 232 ± 70 ng/dl) or EPI (67 ± 33 vs. 81 ± 36 ng/dl). In the second study, nine veterans with PTSD diagnosed by the SCID and six controls have been compared to date. Neither the rate of appearance of NE into plasma (0.216 ± 0.979 vs 0.365 ± 0.220 mg/min/m^2), nor the rate of clearance of NE from plasma (1.25 ± 0.25 vs 1.36 ± 0.42 L/min/m^2) differed significantly between the PTSD patients and controls. these results do not support the hypothesis that SNS activity is tonically increased in patients with PTSD.

NR255 Tuesday May 5, 12:00 noon-2:00 p.m.

SPECT in Chronic Schizophrenia: Preliminary Findings

Robert W. Baker, M.D., Psychiatry, Univ of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213; Nina R. Schooler, Ph.D., Ajit N. Shah, M.D., Joyce B. Delaney, G.N., James W. Baird, Ph.D.

Summary:

We are evaluating the relationship of cerebral blood flow measured by SPECT, multiple clinical parameters, and treatment outcome in schizophrenia indexed by both length of hospital stay and improvement in psychopathology. Consenting patients newly transferred to the state hospital were assessed with a battery of clinical and neuropsychological ratings and underwent SPECT utilizing technetium Tc99m exametazime. Subjects received standard but uncontrolled antipsychotic chemotherapy and milieu therapy. Clinical measures were repeated after three months or at discharge if that occurred earlier. Preliminary results are reported for the first 19 of 40 subjects. Subjects included 12 males and seven females, 58 percent white with a mean age of 36.3. At admission they were rated between mildly and moderately ill (mean CGI = 3.84). Scans were mapped as 5 regions/hemisphere or transaxial slices at the level of the basal ganglia. Left frontal/left occipital ratio showed a trend indicating lower activity with increasing age ($r = -.417$, $p =$

.075), as did left/right frontal ratio (r = −.447, p = .063). A higher left/right frontal ratio was associated with BPRS anergia (r = .433, p = .073). These preliminary findings suggest that abnormalities in left frontal blood flow are related to clinical factors in schizophrenia.

NR256 Tuesday May 5, 12:00 noon-2:00 p.m.

EEG and Electrophysiological Mapping as a Tool in Psychiatry

Remy Luthringer, Psychiatry, C.H. Specialise, Forenap 27 Rue Du 4 R.S.M., Rouffach 68250, France; Jean-Paul Macher, M.D., Richard Minot, M.D., Michel Toussaint, Ph.D., Koudou Dago Toussaint, Ph.D., Laurent Soufflet, Ph.D.

Summary:

EEG and EPs mapping is used in psychopharmacology and psychopathology. The former allows the assessment of psychotropic drug effects on the CNS, whereas the latter permits the determination of functional disturbances. To show the utility of this technique, this study presents, in 30 patients (major depressive episode (*DSM-III-R* criteria)), first the functional modifications, and second the therapeutic effects, of a new antidepressant. EEG and EPs (P300, CNV) mapping data were collected before drug administration, after one week and one month of treatment. The statistical analysis consisted in comparisons of the depressives versus age matched controls. In wash-out, an alpha shift towards more anterior areas exists. Theta activities are increased, unlike beta activities which are decreased. Concerning the EPs, amplitudes are decreased and P300 latency is increased. No specific topographic localization are identified. After one week of treatment, some predictive EEG effects (alpha normalization) are described, whereas after one month of treatment a complete normalization of the EEG and EPs criteria is present in the responder group, unlike the non-responder group. These results seem to be due to decreased electrocerebral vigilance and decreased selective attention capacities. Interestingly, these functional disturbances are only normalized, by the treatment, in the responder group.

NR257 Tuesday May 5, 12:00 noon-2:00 p.m.

CT Prediction of Decline in Alzheimer's Disease

Elizabeth Aylward, Ph.D., Psychiatry, Johns Hopkins University, 600 N. Wolfe Street 3-166, Baltimore, MD 21205; Lisa Raimundo, Marshal Folstein, M.D., Godfrey Pearlson, M.D., Gary Chase, Ph.D., Kathryn Carson

Summary:

Previous studies reveal significant relationships between quantitative CT measures and level of cognitive functioning in patients with Alzheimer disease (AD). This study was designed to determine if measurements from CT scans of AD patients can predict the *rate* of decline in cognitive function.

Subjects were 16 males and 22 females diagnosed as probable or possible AD, based on NINCDS-ADRDA Diagnostic Criteria (mean age = 71.1; mean score on the Mini-Mental State Exam (MMSE) = 14.7, range = 0-22). CT measures included bifrontal ratio, bicaudate ratio, and areas of lateral ventricles, third ventricle, and suprasellar cistern (SSC). Measures of cognitive and adaptive functioning were obtained at the time of the scan and on follow-up. Of the CT measures, the SSCR (SSC corrected for brain size) was most highly correlated with MMSE (p = .01) and other cognitive measures at time of scan. Follow-up data were obtained for those individuals who were mildly to moderately demented at time of the scan (MMSE > 10). The mean interval between the time of scan and follow-up for these 29 patients was 53.9 months. Rate of change per month was calculated for each neuropsychological measure. The SSCR significantly correlated with rate of change measures for MMSE (p = .003) as well as other measures of cognitive and adaptive functioning.

NR258 Tuesday May 5, 12:00 noon-2:00 p.m.

SPECT and MRI in Multiple Sclerosis with Depression

H. Jordan Garber, M.D., Psychiatry, Allegheny General Hosp., Allegheny Neuropsych Inst., Oakdale, PA 15071; Thomas Scott, M.D., Christopher Starratt, Ph.D., Mustafa H. Adatepe, M.D., Ziad Deeb, M.D., Gilbert H. Isaacs, M.D.

Summary:

Although depression has been associated with "hypofrontality" on PET and SPECT, multiple sclerosis (MS) patients with psychiatric symptoms have been reported to more frequently evidence MRI abnormalities in the temporal lobes. Results from SPECT (Tc-99m-HmPAO or 1-123-IMP) imaging and high-field MRI were studied in nine consecutive MS patients (ages 25-69, mean [s.d.] = 49 [14.7]; six females, three males) with *DSM-III-R* major depression (organic affective disorder). Nuclear medicine and neuroradiologic evaluations were provided by specialists unaware of the nature of this research. SPECT studies were abnormal in 8/9 patients: tracer uptake was decreased bilaterally in the frontal lobes in all eight (right worse than left in 5/8), with abnormalities in the temporal lobes in 2/8 patients and in posterior parietal cortex in 5/8. All nine depressed MS patients had frontal lobe abnormalities on MRI: frontal white matter lesions were present in 8/9 (7/8 with abnormal SPECT); frontal and generalized atrophy was prominent in 7/9 (7/8 with abnormal SPECT); periventricular hyperintensity involving frontal horns was apparent in 3/9 (3/8 with abnormal SPECT). Temporal lobe involvement by white matter abnormalities was noted in 5/9 patients, and parietal lobe involvement in 8/9. These pilot findings suggest that frontal lobe structural involvement may underlie frontal lobe dysfunction and be related to depression in MS patients. Future studies with SPECT and MRI in nondepressed MS patients and in depressed patients without MS are needed, as well as studies of MS patients before and after treatment for depression.

NR259 Tuesday May 5, 12:00 noon-2:00 p.m.

Wisconsin Card Sorting Test and Frontal Lobe Findings by MRI and SPECT

Christopher Starratt, Ph.D., Psychiatry, Allegheny General Hosp., Allegheny Neuropsych Inst., Oakdale, PA 15071; H. Jordan Garber, M.D., Gerene K. Starratt, Mustafa H. Adatepe, M.D., Gilbert H. Isaacs, M.D.

Summary:

The Wisconsin Card Sorting Test (WCST) is used as a sensitive and specific indicator of frontal lobe function in rCBF and PET studies, but a recent study of WCST and MRI lesion analysis did not support this association. We studied consecutive admissions (n = 25, ages 20-66, mean[sd] = 43[12], 12 males, 13 females) to a neuropsychiatric hospital with organic mood (n = 21) or personality (n = 4) disorder, who underwent SPECT and MRI (n = 18) or CT (n = 7) and WCST. Patients had normal IQ, and stable, chronic neurologic deficits, without developmental disorders, delirium, dementia, or active psychosis. Radiologic interpretations were provided by specialists unaware of study purposes. There were no differences in WCST performance between groups with frontal lesions by MRI/CT (n = 11) or without frontal lesions (n = 14). For pts. with MRI/CT abnormalities (n = 22), impaired WSCT performance did not accurately predict frontal MRI/CT findings (true positives n = 8 [36 percent], false positives n = 7 [30 percent], true negatives n = 4 [18 percent], false negatives n = 3 [13 percent]). Pts. with frontal abnormalities on SPECT (n = 17) had impaired WCST performance compared to pts. with no frontal SPECT in-

volvement (n = 8) on 5/6 scoring dimensions (all $p < .05$). In pts. with SPECT abnormalities (n = 19), impaired WCST performance more accurately predicted frontal involvement (true positives n = 12 [63 percent], false positives n = 0, true negatives n = 2 [10 percent], false negatives n = 5 [26 percent]). Results suggest that WCST impairment is less specific and sensitive for frontal lobe structural damage than for "functional" deficits evidenced by SPECT, and may require involvement of other areas in addition to frontal regions.

NR260 **Withdrawn**

NR261 **Withdrawn**

NR262 **Tuesday May 5, 12:00 noon-2:00 p.m.**

Blockade of Nicotinic Receptors Impairs Cognition

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Summary:

As central nicotinic receptors decline substantially in Alzheimer's (AD) and Parkinson's disease (PD) and with normal aging, the nicotinic cholinergic system may be relevant to the cognitive pathology of AD and PD. We have studied the effects of a temporary blockade of central nicotinic receptors with mecamylamine, which blocks the effects of nicotine on learning in monkeys, and produces cognitive deficits in animals. Twelve young (23.9 ± 5.0) and 12 elderly (62.7 ± 5.2) volunteers were administered oral mecamylamine at doses of 5, 10, and 20 mg and placebo in a double-blind, constrained random order on different study days. At baseline, 60, and 120 minutes post drug administration, subjects performed a cognitive battery consisting of measures of acquisition of new and retrieval of previously learned information, recall and recognition memory, attention, reaction time, and spatial processing. In addition, behavioral ratings made by subject and blind observer measured mood, anxiety, physical side effects, and psychopathology. Results for the young normals showed that mecamylamine produced a significant ($p < .04$) dose-related impairment in the acquisition of new information, while not effecting the recall of previously learned information, as well as an increase ($p < .05$) in false alarms. Further, there was a significant ($p < .02$) dose-related slowing of reaction time on several cognitive tasks. Behavioral ratings showed no significant psychopathological or physical symptom changes. Physiological measures showed significant dose-related changes in pulse ($p < .0001$) and blood pressure ($p < .02$) consistent with ganglionic blockade. Elderly normals show a similar slowing of reaction time but there was more dose-related variability on performance measures. Age-related changes remain under investigation. Blockade of central nicotinic function may produce cognitive impairments similar in general character to some deficits seen in AD and PD. Supported by NIMH R29-46625 and GCRC M01-00109.

NR263 **Tuesday May 5, 12:00 noon-2:00 p.m.**

Mood Changes and Subarachnoid 5-HIAA Levels in Temporal Lobe Epilepsy

Candace S. Brown, Pharm. D., Psychiatry, Univ of Tennessee, 200 Wagner Place #202, Memphis, TN 38103; Dietrich Blumer, M.D., Allen R. Wyler, M.D.

Summary:

The objective of this pilot study was to determine whether dysfunction of the serotonergic system affected mood change in 12 patients with intractable temporal lobe epilepsy (TLE). Serotonergic function was measured by subarachnoid 5-hydroxyindoleacetic acid (5-HIAA) concentrations obtained during temporal lobectomy and assayed by high performance liquid chromatography with electrochemical detection (HPLC-EC). The Beck Depression Inventory (BDI) and the Spielberger Anger Expression Inventory (STAXI) were completed by medication-free patients within 24 hours of neurosurgery. Subjects with trait anger scores above the 75th percentile had significantly higher subarachnoid 5-HIAA concentrations (mean ± SD, 68.33 ± 18.04 ng/ml) than those with normal anger scores (mean ± SD, 36.44 ± 18.37 ng/ml) ($p < 0.05$) whereas subjects with at least mild depression (BDI ≥ 10) had lower 5-HIAA concentrations (mean ± SD, 30.50 ± 20.50 ng/ml) than those with depression scores within the normal range (mean ± SD, 51.38 ± 21.43 ng/ml) ($p > 10.0$). Subjects demonstrating trait anger and no depression had significantly higher subarachnoid 5-HIAA concentrations (mean ± SD, 77.00 ± 14.14 ng/ml) compared to those with depressive symptoms and no trait anger (mean ± SD, 23.67 ± 18.72 ng/ml) ($p < 0.05$). These findings suggest that mood changes in TLE may be related to serotonergic dysfunction, with anger most likely reflecting increased, and depression decreased, 5-HT turnover rate.

NR264 **Tuesday May 5, 12:00 noon-2:00 p.m.**

Physical Performance of Medicated Psychiatric Patients

Dante Robert Brebbia, Ph.D., Psychiatry, Nathan S. Kline Inst., Building 37, Orangeburg, NY 10962; Anne F. Brebbia, M.S., James M. Watson, B.S., Evelyn T. Pyne, R.N., Martha L. Heatley, B.A.

Summary:

Information pertaining to the effects of psychotropic medication on physical performance of psychiatric patients is virtually nonexistent. This study assessed physical performance by evaluating cardiopulmonary responses of nine hospitalized, medicated schizophrenic patients (P) and six nonhospitalized, nonmedicated controls (C), during submaximal (SME) and maximal (ME) exercise. Continuous recordings were made of oxygen consumption (VO_2) by indirect calorimetry, and heart rate (HR) by electrocardiography. Both groups exhibited: increased HR and VO_2 with work load; comparable HR with increasing submaximal loads; similar declines in VO_2max with age; comparable VO_2 during SME and recovery. Patients exhibited: a steeper decline in mean maximal heart rate (HRmax) with age; similar absolute HR for homologous SME and ME loads; higher HR during SME; and significantly greater energy expenditure during submaximal exercise. In contrast, controls exhibited higher values for HRmax ($p < .02$), mean maximal oxygen uptake ($= VO_2$max) ($p < .001$), and recovery HR ($p < .02$). Results indicate appropriate directional cardiopulmonary responses to exercise, but greater physiological strain for patients during submaximal and maximal efforts. It is concluded that diminished aerobic capacity and fitness, combined with an inhibitory effect of psychotropic medication on cardiovascular and anaerobic/aerobic processes, curtailed physical performance even during mild exercise stress in these patients.

NR265 **Tuesday May 5, 12:00 noon-2:00 p.m.**

CSF 5-HIAA, Behavior and Tryptophan Hydroxylase Genotype

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Goldman, M.D., Longina Akhtar, Matti Virkkunen, M.D., Robert Rawlings, Ph.D., Markku Linnoila, M.D.

Summary:

Tryptophan hydroxylase is the rate-limiting enzyme in the biosynthesis of serotonin. Decreased turnover of brain serotonin has been associated with impulsivity, aggression, disruption of circadian rhythms, and suicidal tendencies. To assess whether tryptophan hydroxylase plays a role in controlling serotonergic behavior, a polymorphism in the tryptophan hydroxylase gene was identified and correlated to serotonergic function and behaviors.

A PCR amplified, single-strand conformational polymorphism was detected in the human tryptophan hydroxylase gene. In 69 Caucasians, two alleles were detected with frequencies of 0.41 and 0.59. By genetic linkage analysis, this polymorphic tryptophan hydroxylase site was mapped to its location on chromosome 11. This chromosomal region, to which tyrosine hydroxylase and indulin genes previously have been mapped, is also of interest in the genetics of schizophrenia and bipolar phenotypes including suicide attempts, psychopathologic conditions and information on CSF monoamine metabolites and circadian rhythms, were assessed in a population of more than 60 Finnish violent offenders and controls. Analyses indicate significant relationships exist between tryptophan hydroxylase genotype and serotonin turnover as well as specific behavior associated with serotonin function.

NR266 Tuesday May 5, 12:00 noon-2:00 p.m.

Serotonergic Correlates of Aggressive Behavior

Avraham Molcho, M.D., Psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; Barbara Stanley, Ph.D., Ronald Winchel, M.D., Jeannine Guido, M.A., Michael Stanley, Ph.D.

Summary:

Studies that have examined the relationship between aggression and serotonergic dysfunction have typically included patients who have a history of suicide behavior in addition to aggressive behavior[1]. Because both behaviors have been shown to be associated with serotonergic measures[2], it has remained undetermined whether aggression is related to serotonergic dysfunction independent of suicidal behavior. The present study examined a diagnostically heterogeneous group of 64 psychiatric inpatients with no history of suicide attempts. Patients were divided into high and low aggression score groups by the median score on an aggression history scale, administered as a semi-structured interview. The two groups did not differ in diagnostic distribution or psychopathological measures of depression or psychosis. Individuals with high aggression scores had significantly lower CSF 5-HIAA levels ($5 = 3.07$, $df = 62$, $p < 0.05$). This relationship remained significant after factors that affect CSF 5-HIAA levels, such as gender or height, were accounted for. Platelet imipramine binding (Bmax) did not differ between groups ($t = .04$, $df = 47$, $p < 1.0$). The present study suggests that: 1. outwardly directed aggression is associated with serotonergic dysfunction and 2. this association does not depend on the presence of suicidal behavior.

NR267 Tuesday May 5, 12:00 noon-2:00 p.m.

Suicidal Ideation in AIDS: Roles of Pain and Mood

William Breitbart, M.D., Psychiatry, Memorial Hospital, 1275 York Avenue Box 421, New York, NY 10021; Steven D. Passik, Ph.D., Kent Eller, M.D., Antonio F. Sison, M.D.

Summary:

Aims: Factors related to suicidal ideation (SI) in HIV infected patients are not well understood. To assess the relationship between pain, mood, and SI, we surveyed 103 HIV seropositive patients receiving ambulatory care. *Methods:* Assessment included: 1) Memorial Pain Assessment Card (MPAC): consists of visual analog scales for pain intensity (VASPI), pain relief (VASPR), and mood (VASM). 2) Beck Depression Inventory (BDI), total score was used to rate depression, item #9 to rate SI. 3) Profile of Mood States (POMS), brief version. 4) Karnofsky Performance Rating Scale (KPRS). 5) CD4 lymphocyte counts. *Patient Characteristics:* Age: Mean 38.4; Gender: 86.4 percent males, 13.6 percent females; Race: 60.2 percent Caucasian, 17.5 percent black, 20.4 percent Hispanic, 1.9 percent other; HIV risk factor: 89.3 percent sexual contact, 9.7 percent IVDU, 1 percent transfusion; KPRS: Mean 80; HIV stage: 31.1 percent HIV + asymptomatic ($n = 32$), 4.9 percent ARC ($n = 5$), 64.1 percent AIDS ($n = 66$); CD4 Count: Mean 179; Pain: 38 percent with pain ($n = 39$), 62 percent without pain ($n = 64$); Pain Intensity (VASPI): Mean 49mm, range 5-100mm. *Results:* 28 percent had SI, mostly without intent. A total of 29 percent of those with pain had SI, while 19 percent without pain had SI. Patients reporting SI were more likely to have pain (Chi square = 4.20, $df = 1$, $p < 0.04$). Patients with SI had significantly more depression (BDI, 20.9-vs-10.5, $t = -3.62$, $p < 0.001$). SI was not significantly correlated with pain intensity (VASPI, $r = 0.08$, $p < 0.31$), pain relief (VASPR, $r = 0.00$, $P < 0.48$). There were no differences between patients with and without SI as to age, Karnofsky, POMS, CD4 counts, AIDS stage, HIV risk factors, race, or gender. *Conclusion:* Suicidal Ideation in ambulatory HIV infected patients is highly correlated with the presence of pain and depressed mood.

NR268 Tuesday May 5, 12:00 noon-2:00 p.m.

No Evidence of Psychophysiological Differences Between HIV-1 Infected and Noninfected Methadone Maintenance Patients

Norbert Loimer, M.D., Psychiatry, University of Vienna, Waehringerquertel 18-20, Vienna A 1090, Austria; Betinna Rauch, Ph.D., Josef Grunberger, Ph.D., Georg Pakesch, M.D.

Summary:

In order to assess the influence of methadone maintenance treatment and HIV-1 infection on the extent of psychophysiological deficits, 30 long-term, methadone treated HIV-1 infected patients were examined and compared to a group of 54 long-term, seronegative methadone patients as well as to a group of healthy test persons ($n = 67$), using a psychophysiological test battery. Autonomous activation was measured by means of static and light evoked dynamic pupillometry, vegetative excitement by means of skin conductance level and skin conductance response; cognitive performance like attention and concentration were evaluated by Pauli test and Alphabetic Reaction test (ARG). Short-term memory was measured by the numerical memory test, visual retention by the Benton test. These procedures allow to assess psychophysiological and thymopsychic parameters. HIV-1 infected methadone patients did not differ from HIV-1 negative methadone patients in the extent and incidence of deficits. Both groups, however, differed from the normal population group. This study indicates that drug abuse contributes to the psychophysiological and cognitive deficits of HIV-1 patients, while methadone treatment stabilizes deficits of already infected drug users.

NR269 Tuesday May 5, 12:00 noon-2:00 p.m.

Sex Risk Predicted by Past Sexually Transmitted Disease

Haftan M. Eckholdt, M.A., MSB E 561, UMDNJ Psychiatry, 185 South Orange Avenue, Newark, NJ 07103; Jacqueline Bartlett, M.D., Jeanine Dasilva, B.A., Steve Schleifer, M.D., Steve Keller, Ph.D.

Summary:

AIDS knowledge has not been found to predict AIDS sex risk behaviors. However, people who experience a consequence of their sexual behavior (i.e. pregnancy, STD) may personalize HIV information and these factors may predict risky sex behaviors.

A total of 209 sexually active adolescent women from a local public high school in an AIDS epicenter (age 16 ± 1.7, years, range 12-22), 77 percent (229) African American, and 23 percent Hispanic were studied. Data were gathered on sex behaviors, experiences with STD's and pregnancy, and AIDS knowledge and attitudes.

Analyses controlling for age, race, and age at onset of sexual activity revealed that a ratio of safe/unsafe sex practices (i.e., percent condom use) in the past month and the past six months was not predicted by AIDS knowledge or attitude. STD history predicted a lower safe sex ratio for the past month ($F = 3.25$, $df = 1,84$, $p < .08$) as well as the past 6 months ($F = 2.88$, $df = 1,158$, $p < .1$). Pregnancy and abortion did not predict safe sex ratio.

These data show that experiences with consequences of sexual activity are no better than AIDS knowledge and attitudes in predicting safe sex practices. In fact, those who had experienced a consequence (STD) in the past had more unsafe sex. STD's may increase AIDS risk by behavioral as well as biological mechanisms.

NR270 Tuesday May 5, 12:00 noon-2:00 p.m.

Cognitive Tests and HIV: The Sinai AIDS Center Cohort

David Dorfman, Ph.D., Psychiatry, Mt. Sinai Med. Center, 1 Gustave Levy Pl. Box 1230, New York, NY 10029; Norbert Baer, Charlene Bang, B.A., Leonard Handelsman, M.D., David Rose, M.D.

Summary:

Studies of male homosexuals such as the MACS (multicenter AIDS Cohort Studies) have shown that neuropsychological tests, especially timed tests with an attentional and/or motoric component, are sensitive early indicators of HIV associated cognitive impairment, particularly ADC (AIDS Dementia Complex). However, it is unclear the extent to which these findings generalize to other risk groups, or require modification given the increasing effectiveness of medical interventions. Data from the neuropsychological testing program at the AIDS Center Program at the Mt. Sinai Medical Center can address these questions since the major risk groups are well represented. In this preliminary report we present results form a battery (similar to the MACS) from 79 outpatients, (32 females, 47 males) with the following risk factors: homosexual males (17), IVDUs (28), females with HIV+ sexual partners (18), and other or multiple risk factors (16). Generally, the data from each risk group show the same pattern that emerged from the MACS and similar studies: namely, that ADC is unlikely to emerge prior to substantial immunosuppression. Our results indicate that batteries emphasizing timed tests with attentional and/or motoric components are of continuing utility in characterizing HIV associated cognitive impairments.

NR271 Tuesday May 5, 12:00 noon-2:00 p.m.

Cognitive Testing by Reaction Time of HIV Positive IV Drug USers

David Dorfman, Ph.D., Psychiatry, Mt. Sinai Med Ctr, One Gustave Levy Pl Bx 1230, New York, NY 10029; Charlene Bang, B.A., Leonard Handelsman, M.D., Paul J. Rinaldi, M.A., Norbert Baer, Mary M. Schroeder, Ph.D.

Summary:

Neuropsychological tests are sensitive indicators of the early signs of ADC (AIDS Dementia Complex). Recent evidence from populations of gay males shows that reaction time (RT) tests are equivalently sensitive and may also yield information not available by more conventional tests. Since RT tests are brief, simple to administer, and free of cultural bias, they would appear ideal for administration to other risk groups, particularly IVDUs. To assess the feasibility of using this technology for the cognitive testing of IVDUs, 34 male veterans with IVDU histories stratified by CDC staging (13 HIV-controls, 13 HIV+ non-AIDS, six with AIDS) received a battery of three RT tests (simple RT, choice RT, Sternberg task). There were significant differences on all tests: simple RT [$F(2,30) = 4.17$, $p < .03$, for dominant hand], choice RT [$F(2,30) = 11.08$, $p < .01$, for yes responses; $F(2,30) = 8.99$, $p < .01$, for no responses], and Sternberg intercept [$F(2,29) = 4.02$, $p < .03$], while simple RT, nondominant hand was marginally significant [$F(2,30) = 3.15$, $p < .06$]. These results support the conclusion that, as in other risk groups, cognitive impairment as a direct result of HIV infection is unlikely before the onset of full-blown AIDS. These results parallel those obtained using more conventional tests and suggest that RT tests are a feasible alternative to more conventional technologies.

NR272 Tuesday May 5, 12:00 noon-2:00 p.m.

Psychiatric Morbidity in HIV Infection

Diana O. Perkins, M.D., Psychiatry, Univ of North Carolina, Campus Box 7160, Chapel Hill, NC 27599; Carol Murphy, R.N., David Naftolowitz, M.D., Robert A. STern, Ph.D., Jane Leserman, Ph.D., Dwight L. Evans, M.D.

Summary:

HIV infected men may be at high risk for psychiatric morbidity, particularly development of major depression. In this study we compare the lifetime, current, and six month prevalence of *DSM-III-R* Axes I and II disorders in 81 asymptomatic, HIV positive, and 63 negative gay men, recruited from an AIDS low prevalence area. Consensus psychiatric diagnoses were determined by review of a structured diagnostic interview (modified SCID, the SCID-RDC) at a diagnostic conference. The proportion of HIV positive and HIV negative men, respectively, with lifetime history of psychiatric illnesses, were as follows: 1) major depression (38 percent, 38 percent); 2) anxiety disorder (4 percent, 6 percent); 3) drug dependence (14 percent, 14 percent); 4) alcohol dependence (21 percent, 27 percent); and 5) personality disorder (31 percent, 17 percent; $p = .06$). At the time of initial study evaluation 10 percent of the HIV positive and 3 percent of the HIV negative subjects were diagnosed with a current major depression. Six month follow-up of the initial 38 of the HIV positive and 46 of the HIV negative subjects revealed that 13 percent of the positive and 11 percent of the negative subjects met criteria for major depression during the follow-up period. Lifetime history of major depression predicted development of a major depression during the follow-up period. lifetime history of major depression predicted development of a major depression during the follow-up period ($p = .05$). Our findings suggest that gay men are at high risk for development of major depression, with past history of major depression a significant risk factor. Furthermore, personality disorder is common in HIV infected men, possibly due to behaviors associated with personality disturbance that resulted in increased risk for HIV exposure. Comprehensive care of the HIV infected patient should thus include careful evaluation of psychiatric illness, particularly major depression and personality disorder.

NR273 Tuesday May 5, 12:00 noon-2:00 p.m.

Computerized Screening for AIDS Dementia Complex

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Summary:

AIDS dementia complex (ADC) is a common neurologic disorder of HIV-1 infection. Its early detection is critical, since potentially therapeutic neuroprotective agents are being identified and evaluated. To determine the effectiveness of reaction time (RT) measures as a screening test for early ADC, 16 patients with mild-moderate ADC and 18 healthy HIV-1 seronegative subjects (mean age = 40.9 and 32.8 ≥an yrs. education = 14.4 and 16.8, respectively) took a computer-administered battery of four measures: simple RT, choice RT, and two types of sequential RT (1 & 2). Group mean performances on the four measures were analyzed by ANCOVA, using age and education as covariates. The ADC group differed significantly from the control group on Sequential RT1 ($p < 0.05$) and Sequential RT2 ($p < 0.001$). Bayesian analyses were conducted on these two measures, using z scores (0.5, 1.0, 1.5, 2.0) to represent deviation from the control group's mean. Sequential RT2 was found to be the best discriminator: sensitivity 0.69-0.81; specificity 0.61-0.94; and correct classification rates 0.71-0.85. Receiver operating characteristic analyses, based on z scores, indicated that the recommended cut-off z score of 2.0 may be overly conservative. Optimal cut-off z scores in the current study ranged from 1.0 to 1.5. These preliminary findings suggest that computerized RT, using these two measures of sequential RT, may provide a sensitive and specific method of detecting early ADC.

NR274 Tuesday May 5, 12:00 noon-2:00 p.m.

Risk Factors for Needle Sharing in HIV Positive and Negative Intravenous Drug Abusers

David W. Brook, M.D., Psychiatry, New York Medical College, Valhalla, NY 10595; Josephine Roberto, M.S.W., Joseph R. Masci, M.D., Jacques De Catalogne, M.d., Frances Amundsen, M.P.S., Judith S. Brook, Ed.D.

Summary:

This study explores the relationship between psychosocial risk factors and needle sharing HIV transmission behavior among HIV+ and HIV− intravenous drug abusers. Interviews were conducted with a sample of 225 inner city male IVDAs who attended a methadone treatment program or an AIDS clinic. The interviews included psychosocial measures from four domains: personality, family, friendship networks, and acculturation/cultural factors. The findings indicated that variables in the personality domain related to needle sharing reflected aspects of unconventionality, e.g. more sensation-seeking and greater impulsivity. Needle sharing subjects were found to have higher levels of psychiatric symptoms (e.g. low ego integration, depression, and psychotic-like symptoms). Moreover, needle sharing was related to lower levels of self-esteem. Within the family domain, a close father-son attachment characterized by warmth, identification, and a conflict-free relationship, insulated the individual from needle sharing behavior. While supportive marital relations were significantly associated with decreased needle sharing behavior, supportive relationships with friends were not. Acculturation/cultural measures were not related to needle sharing behavior. Findings were obtained for those who were HIV+ and for those who were HIV−. Implications of the findings for prevention and treatment, future research, and public policy are discussed.

NR275 Tuesday May 5, 12:00 noon-2:00 p.m.

Risk of HIV Infection in the Menttally Ill

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Summary:

There have been few controlled studies that precisely identify those behavioral factors that place psychiatric patients at risk for HIV infection. In this study, 61 consecutively-admitted psychiatric patients were compared to a normal control group (n = 32) and to a "high risk" control group of 29 IV drug abusers. The three groups were compared for differences in sexual practices, AIDS knowledge, and for differences on the various dimensions of the Health Belief Model (e.g. perceived health risk, benefits of risk reduction). Data indicate no differences between the three groups in frequency of sexual behavior. Psychiatric patients engaged in more homosexual activity ($p < .08$) than the two control groups, and they abused IV drugs more frequently than normal controls ($< .0003$). Psychiatric patients also differed from controls on several dimensions of the Health Belief Model. Patients with different psychiatric diagnoses differed significantly on a number of HIV risk factors and patient diagnosis had to be taken into account in order to predict high-risk behavior. These data indicate that the mentally ill engage in behaviors that place them at high risk for HIV infection and they suggest that the mentally ill require interventions that address their unique social and cognitive deficits.

NR276 Tuesday May 5, 12:00 noon-2:00 p.m.

Vitamin B12 Status and Neuropsychiatric Disorders in HIV

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Summary:

Vitamin B12 deficiency may result in a number of neurologic and psychiatric disorders, including dementia and other neurocognitive dysfunction, myelopathy, peripheral neuropathy, and psychiatric symptomatology. HIV infected patients have been found to have a high rate of B12 deficiency. They also frequently develop a variety of nervous system disorders many of which are similar to those seen in patients with B12 deficiency. To evaluate the possible contribution of B12 deficiency to neurologic and neuropsychiatric signs and symptoms in HIV spectrum disease, 152 HIV seropositive individuals (104 asymptomatic, 38 AIDS Related Complex, 16 AIDS) and 58 high risk seronegative controls were studied with comprehensive psychiatric, neuropsychologic, and neurologic examinations. A subset of subjects (70 HIV seropositive) underwent clinical neurophysiologic, CSF, and MRI evaluations. Although there were significant neurologic/neuropsychiatric abnormalities in the HIV seropositive group, results indicate no significant relationship between serum B12 levels and the presence of psychiatric, neuropsychologic, neurologic, clinical neurophysiologic, or neuroradiologic disease. Contrary to some earlier reports, this study does not indicate that B12 deficiency has a significant role in neurologic/neuropsychiatric disease in HIV infection. B12 replacement, while obviously prudent in deficient patients, should not, therefore, be expected to reverse HIV-related nervous system dysfunction.

NR277 Tuesday May 5, 12:00 noon-2:00 p.m.

Elderly Medical Readmissions: Psychiatric Predictors

George Fulop, M.D., Psychiatry, Mt. Sinai Sch. Medicine, 1 Gustave Levy Pl Bx 1228, New York, NY 10029; David Huertas, M.D., Karen Pasternak, Peter M. Tafti, Howard Fillit, M.D., James J. Strain, M.D.

Summary:

Psychiatric comorbidity is noted in up to 56 percent of admissions to a geriatric medicine evaluation and treatment unit (GETU). Psychiatric predictors of readmission to a GETU were examined between 9/1/90 and 12/31/91. All 314 inpatients were prospectively screened by the Structured Clinical Interview for *DSM-III-R* (SCID). Geriatric Depression Scale (GDS), and the Mini-Mental State Examination (MMSE).

The majority of inpatients had a single admission – 183 (58 percent). The 58 readmissions comprised 93 multiple admissions (MA): one – N = 50 (16 percent), two – N = 16 (5 percent), three – N = 4(1.3 percent), four – N = 2 (.6 percent), or five – N = 1 (.3 percent) readmissions in the study timeframe.

Multiple admits (MAs) compared to single admits (SAs) were, respectively: Male 32 percent vs. 24 percent; White 32 percent vs. 44 percent, Black 34 percent vs. 26 percent, or Hispanic 34 percent vs. 29 percent; Education 7 vs. 6 years; and, mean Age of 82 vs. 82 years (All p # NS). MAs also had no significant difference in marital status, positive psychiatric family history (19 percent vs. 19.7 percent), outpatient treatment (16 percent vs. 12 percent), or hospitalization (3.5 percent vs. 4.4 percent). However, MAs vs. SAs had significantly more current (12 percent vs 5 percent, $p < 0.05$) and past (34.5 percent vs. 20 percent, $p < 0.03$) alcohol use. Significant proportions of geriatric patients had evidence of cognitive impairment (MMSE < 24), or depression (GDS > 10), but MAs did not significantly differ form SAs (55 percent vs 61.5 percent – MMSE < 24, and 43 percent vs. 36 percent – GDS > 10).

Conclusion: Current or past alcohol use appears to be associated with increased likelihood of multiple readmissions to a geriatric medicine unit. Identification and treatment of elderly alcohol use may impact on subsequent medical hospitalizations.

NR278 Tuesday May 5, 12:00 noon-2:00 p.m.

Evolution of Schizophrenia: A Psychiatric Emergency Room Perspective

Dianne Sena, M.S.W., CCHB, 411 Oak Street Suite 103, Cincinnati, OH 45219; Sean P. Stanton, Eugene Somoza, M.D.,

Summary:

Schizophrenics are overrepresented in young patients evaluated in Psych ER's, but underrepresented in geriatric groups. To understand this phenomenon we studied how the severity of their symptoms evolved with age, and how several epidemiological variables influence this relationship. The study population consisted of all patients evaluated at a VA Psych ER during a two-year period (N = 2170). BPRS items, suicidality, and several epidemiological variables (age, diagnosis, race, # of suicide attempts, and household composition) were measured. As expected, the age distribution of the 348 schizophrenics was significantly different form that of non-schizophrenics (N = 1822). Results showed that suicidality for schizophrenics decreased continuously with age. For example, those under 30 had a 119 percent higher rating than those over 60 ($p < 0.005$). The severity of several BPRS items (guilt feelings, bizarre thinking, flat affect, paranoid feelings, and hallucinations) were significantly lower in geriatric schizophrenics than in younger ones. The same pattern was observed when subscales of the BPRS measuring positive and negative symptoms of schizophrenia were analyzed. The positive symptoms decreased substantially (by 33.3 percent, $p < 0.05$) with age while the negative decreased less and did not reach statistical significance. The effects of race, household composition, and history of suicide attempts will be discussed. These results suggest that the decrease in schizophrenic symptom severity with age may contribute to the observed deficit in older schizophrenic patients seen in Psych ER's.

NR279 Tuesday May 5, 12:00 noon-2:00 p.m.

Quality of Life Following Liver Transplantation

Esteban Cirera, M.D., Psychiatry, Hospital Clinic, Villarroel 170, Barcelona 08036, Spain; Eduard Vieta, M.D., Juan De Pablo, M.D., Isabel Sanudo, M.D., Jose Visa, M.D.

Summary:

Forty-five of 67 adult patients surviving more than six months after undergoing orthotopic liver transplantation at the Hospital Clinic i Provincial de Barcelona between June 1988 and August 1990 answered a quality of life questionnaire (the Liver Diseases' Quality of Life Inventory, LDQLI) and Goldberg's General Health Questionnaire (GHQ). Overall quality of life, followed by physical appearance, mood, and appetite were perceived as much improved by more than 70 percent of the subjects. In contrast, almost 25 percent of patients felt that their tremor and strength had worsened. Fulminant hepatitis as cause of transplantation, as well as retransplantation, was significantly associated to a worse outcome with regard to quality of life. These patients reported a very low rate of psychopathology measured by the GHQ (9 percent). In view of these findings, liver transplantation seems to be a valid and beneficial intervention, not only in terms of survival, which has been reported elsewhere, but also in terms of the quality of this survival.

NR280 Tuesday May 5, 12:00 noon-2:00 p.m.

Psychiatric Aspects of Angiography and Angioplasty

Pascal Janne, M.D., Psychiatry, Univ of Louvain, UCL Mont-Godinne, B-5530 Yvoir 5530, Belgium-Europe; Christine Reynaert, M.D., Jean Costermans, Ph.D., Regnier Pirard, Ph.D., Jean Kinable, Ph.D., Xavier Renders, Ph.D.

Summary:

Little is known about anxiety during coronary angiography (C.A.) and percutaneous transluminal angioplasty (PTCA). Previous work showed the antidepressant and anxiolytic effects of denial in the coronary care unit. Is this also true in the catheterization ward?

Methods: 80 p^{ts} were involved in a prospective design and interviewed within 24 hrs before C.A. Among them, 12,5 percent underwent an IMMEDIATE PTCA whereas 35 percent further underwent an ELECTIVE PTCA. The remaining p^{ts} were reached either on a surgical procedure (15 percent) or on a drug regimen (18,75 percent). 15 (18,75 percent) p^{ts} had normal coronary arteries. State and trait anxiety, denial and Type A behavior ratings were assessed. We postulated (H1) a directly significant relationship between anxiety and illness seriousness as measured by ventricular ejection fraction, n^{br} of diseased vessels and previous myocardial infarction (PMI). H2 stated that elective PTCA would induce more anxiety. H3 stated that denial and anxiety would be reversely related as in Hackett & Cassem, Prince, Frazure, Smith studies.

Results: Unexpectedly H1 was rejected, because patients with 2 or 3 vessels disease or with PMI showed significantly less anxiety than the others (p = 0,022). H2 was accepted because previous angiography was associated with less anxiety. H3 was not rejected, but the results, even if significant, were not indicative of a very strong relationship (r = −0.27, p = 0,02). These data suggest either that denial could increase in proportion of illness's severity or, on the contrary, that illness seriousness itself could be the result of long-term denial.

NR281 Tuesday May 5, 12:00 noon-2:00 p.m.

A Most Simple Screening of Emotional Morbidity

Antonio Lobo, M.D., Psiquiatria, Hospital Clinico, San Juan Bosco 15, Zaragoza 50009, Spain; Maria Jesus Perez-Echeverri, M.D. Ricardo Campos, M.D., Javier Garcia-Campayo, M.D., Julian Izuzquiza, M.D., Carmen Monton, M.D.

Summary:

SPECIFIC PURPOSE: Hypothesis: A single question about the patient's mood is a good screening test of psychiatric morbidity in primary care (PC).

CONTENT: Description and preliminary results of an ongoing epidemiological study in Zaragoza, Spain.

METHODOLOGY: Two-phase screening. Representative, stratified sample (N = 1,500) of PC attendres (eight health care centers). First phase (lay interviewers): Specific question ('How is your mood?'). Screening with Spanish versions of GHQ-28, Mini-Mental, CAGE & Drugs Questionnaires. Second phase (clinicians): Standardized polivalent psychiatric interview (SPPI) (new interview built on the CIS, to assess patients on a specific multiaxial schema; permits the use of *DSM-III-R, ICD 10* and Goldberg & Bridges' diagnostic criteria for 'somatization.' Mean kappa = 0.8).

RESULTS: (N = 400): Prevalence, 27.9 percent of 'cases' (SPPI criteria). Somatization, duration of the symptoms 6 + months, 'neuroticism' and social problems were frequent among the 'cases'. To our knowledge, this is the first report of psychiatric morbidity in PC assessed on a specific multiaxial schema. Sensitivity of the single question about the patients' mood = 70 percent (GHQ = 86.4 percent). Positive predictive value = 88.5 percent (GHQ = 91.3 percent).

CONCLUDING STATEMENT: A single question about the patients' mood is effective in detecting emotional morbidity in PC.

NR281 Tuesday May 5, 12:00 noon-2:00 p.m.

The Role of EEG in Psychiatric Consultation

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Summary:

The role of electroencephalography (EEG) in psychiatric consultation has not been well studied. This study assessed general EEG use for organic mental disorders (OMD) on Consultation-Liaison (C/L) Services.

Methods: Chart review was performed on 100 consecutive psychiatric consultations on patients with OMD, not related to substance abuse, (*DSM-III-R* 290.XX, 293.XX, 294.XX, 310.XX). Volumes of EEG recommendations, consultee service response, and findings were compiled. Major outcome variables included change of diagnosis, treatment planning and other significant shifts in care following EEG.

Results: About 47 percent of consultations included an EEG recommendation. Of patients with EEG recommendations the most common physical diagnosis was CNS disease; the most common initial *DSM-III-R* diagnosis was atypical OMS (294.80). Common abnormal EEG findings included general and focal slowing and temporal epileptiform activity. Significant results were often unexpected. Higher than expected rates of organic personality disorder (310.10) were diagnosed. Examples of significant alterations in care following EEG were reported.

Conclusions: 1) EEG can be appropriately and usefully recommended by psychiatric consultants. 2) A significant proportion of EEG's yield unexpected and abnormal findings. 3) Significant alterations in psychiatric diagnosis or treatment may follow EEG.

NR283 Tuesday May 5, 12:00 noon-2:00 p.m.

The Psychiatric Emergency Service Utilization

Ole J. Thienhaus, M.D., Psychiatry, Univ of Cincinnati, 231 Bethesda, Cincinnati, OH 45267

Summary:

In a metropolitan psychiatric emergency service (PES), 200 patient contacts obtained through stratified random sampling, were analyzed in a prospective study design to determine defining descriptor variables of patients seen, to explore divergent views of chief complaints by clinicians versus patients, to establish an acuity profile of presenting pathology, and to identify alternative problem resolutions pursued by patients. Our results confirm that the majority of patients seen in PES are independently living individuals, are self-referred, and have chronic mental disorders. Suicidality and psychosis are significantly more often identified by clinicians than by patients as the pivotal problem. Patients by contrast see anxiety and depressive symptoms most often as the problems necessitating a visit to PES. In more than one third of cases, a visit to the emergency room was the method of first choice to deal with perceived distress, while 52 percent of patients first turned to their case-manager who then referred them to PES. The distress or crisis had lasted for over a week in 36 percent of the cases, suggesting a predominance of subacute problems and possibly a lack of ready access to alternative resources for resolution. Our data are presented as input for community-based mental health service research and development.

NR284 Tuesday May 5, 12:00 noon-2:00 p.m.

Non-Epileptic Seizures and Sexual Abuse

Kenneth R. Alper, M.D., Psychiatry, New York University, 550 First Avenue, New York, NY 10016; Orrin Devinsky, M.D., Daniel J. Luciano, M.D., Kenneth R. Perrine, Ph.D.

Summary:

Nonepileptic seizures (NES) are a common conversion symptom that must be distinguished from epilepsy in order to avoid the iatrogenic hazards of unnecessary anti-epileptic treatment and to initiate appropriate psychiatric intervention. A higher prevalence of a history of sexual abuse has been suspected in NES, although a controlled study comparing NES and patients with epilepsy has not yet appeared in the literature. Two hundred and seventeen patients admitted consecutively to a comprehensive epilepsy center were evaluated psychiatrically and with video EEG monitoring and placebo challenge to identify *DSM-III-R* conversion disorder presenting as NES. Forty-seven (21.6 percent) of the series were diagnosed with NES (78.7 percent female, mean age 32.1 years). These NES patients were compared to a group of 40 patients with definite partial complex epileptic seizures matched to the NES group with respect to age and gender composition. Seventeen patients with NES (36.2 percent) reported a history of sexual abuse compared to four (10 percent) of the Controls ($\chi^2 = 8.08$, ldf, $p < .005$). The severity of abuse appeared to also differ with seven NES patients reporting oral or vaginal penetration by a first degree relative and no controls reporting this occurrence. These preliminary data support the impression of sexual abuse as a determinant of NES.

NR285 Tuesday May 5, 12:00 noon-2:00 p.m.

Psychiatric Morbidity and Length of Hospital Stay

James J. Strain, M.D., Psychiatry, Mt. Sinai Sch. Medicine, 1 Gustave Levy Pl Bx 1228, New York, NY 10029; John S. Lyons, Ph.D., Jeffrey S. Hammer, M.D., Mary Eichmann, Ph.D., Marianne Fahs, Ph.D.

Summary:

INTRODUCTION: Cost offset studies have demonstrated the effectiveness of a psychiatric liaison intervention with elderly hip fracture patients with decreases in depression, organicity, and LOS. This study identifies the psychiatric morbidity and the timing of its assessment which correlates with LOS. *METHOD:* 452 patients over 65 years of age who were consecutively admitted for surgical repair of fractured hips from 7/1/87-6/30/89 at the Mount Sinai Hospital (MS) (NYC) and Northwestern Memorial (NW) (Chicago), were evaluated at admission/discharge/six and 12 weeks post discharge with the Mini Mental State (MMS), Hamilton Depression Rating (HDR), Geriatric Depression Scale (GDS), Spielberger State-Trait Anxiety Inventory (STAI), the Horn Disease-Staging Evaluation, all by trained raters who had achieved interrater reliability (kappa > .7). Statistical analyses were conducted with t and chi square tests for continuous and categorical variables, respectively. *RESULTS:* Admission HDR and GDS were correlated with increased LOS at MS ($r = .33504$, $p = 0.04$), ($r = .38421$, $p = 0.008$), and MMS at NW ($r = .51684$, $p = 0.007$). Discharge HDR, GDS, and STAI at MS correlated with increased LOS ($r = 35494$, $p = 0.02$), ($r = .46743$, $p = 0.0009$), ($r = .53835$, $p = 0.002$). Discharge MMS and HDR correlated with increased LOS at NW ($r = .59706$, $p = 0.002$), ($r = .49404$, $p = 0.007$). At six weeks there was no correlation with post discharge psychiatric morbidity and increased hospital LOS. Twelve-week post-discharge evaluation showed a correlation between GDS and increased LOS ($r = .44220$, $p = 0.05$). There was no increase in the cost of health services six and 12 weeks in the experimental group vs. the control indicating no transfer of costs to the ambulatory setting from shortened LOS. Psychiatric treatment is associated not only with decreased morbidity, but a decrease in LOS.

NR286 Tuesday May 5, 12:00 noon-2:00 p.m.

Fall Risk Assessment in a Psychiatric Service

Eduardo Rueda-Vasquez, M.D., Psychiatry, VA Medical Center, 1970 Boulevard, Salem, VA 24153; Frank Tellian, M.D.

Summary:

Fall risk assessments were performed on 2,632 patients admitted to a psychiatric service from January 1, 1989, through December 31, 1989. The scale used consisted of eight criteria. One point each was given to: (1) age above 65; (2) symptoms of dizziness, weakness, or hypotension; (3) visual or hearing impairment. Two points for: (1) incontinence and/or diarrhea; (2) history of previous falls. Three points for (1) cognitive deficit (confusion, disorientation); (2) uncooperativeness; and four points for ambulatory difficulties (neuromuscular, arthritic).

Potential scores ranged from 0 to 17. A total of 87 patients with scores of six or above suffered falls, and were thus categorized as "fall risk." Patient controls who did not fall had scores less than five. Eight patients with scores of 10 or above had multiple falls. The scores demonstrated a clear cut difference between controls and patients with fall risk (6 or above), and with risk of multiple falls (10 or above).

NR287 Tuesday May 5, 12:00 noon-2:00 p.m.

Lymphocytes in Alzheimer's Patients and Controls

Maurice W. Dysken, M.D., GRECC, VA Medical Center, One Veterans Drive, Minneapolis, MN 55417; Marcia D. Minichiello, M.A., James L. Hill, Ph.D., Stacy S. Skare, B.A., John T. Little, M.D., Susan E. Molchan, M.D., Trey Sunderland, M.D.

Summary:

Deficient immunoregulation has been postulated to play a role in the pathogenesis of Alzheimer's dementia, but research findings in this area have often been contradictory. Recently, lymphopenia was reported to be more prevalent in primary degenerative dementia patients than in control subjects. In addition, a decreasing number of total lymphocytes was found to be significantly correlated with increasing severity of dementia. In an attempt to replicate these findings, we studied 55 NIH Clinical Center patients (24 M, 31 F) who met criteria for *DSM-III-R* primary degenerative dementia and 41 healthy controls (21 M, 20 F) of comparable age and gender. Potential subjects with a significant current or past history of any major medical illness, abnormal neurological findings, or psychiatric disorders were excluded. There were no significant differences between Alzheimer patients and controls in baseline standard hematology tests, total protein, albumin, T4, TSH, cortisol concentrations, or WBC. No significant differences in total lymphocytes (M $\pm$ SD) were observed between patients (1,790 $\pm$ 553) and controls (1,786 $\pm$ 622). Furthermore, total lymphocytes were not significantly correlated with Global Deterioration Scale scores, Clinical Dementia Rating Scale scores, or duration of illness. These findings do not lend further support to an immune hypothesis for Alzheimer's dementia.

NR288 Tuesday May 5, 12:00 noon-2:00 p.m.

Measurement of Depression in Dementia

Barry S. Fogel, M.D., Psychiatry, Brown University, Box G-219, Providence, RI 02912; Brian R. Ott

Summary:

The presence of depression in dementia was evaluated in 50 dementia clinic outpatients using the Geriatric Depression Scale (GDS) and the Cornell Scale for Depression in Dementia (CDR). Patients' awareness of their cognitive deficits and their progression was assessed with a four-item clinician rated scale (the insight scale). SEverity of cognitive impairment was measured with the MMSE, and overall dementia severity was measured with the Clinical Dementia Rating Scale (CDR).

The insight scale had interrater reliability of .91 on a subsample of 25 patients, Cronbach's alpha was .85 in the full sample. The CDR and the GDS were correlated at .77 for patients with MMSE $\geq$22 and preserved insight (n = 14), the correlation was .15 for patients with MMSE $\leq$21 *or* poor insight (n = 36). The difference between the GDS and the CDR was modeled by multivariate linear regression including as independent variables, CDR, the MMSE, the insight scale, age, sex, education, and the diagnosis of Alzheimer's disease. With stepwise selection insight was the most significant variable; a model with the CDR and insight scale explained 49 percent of the variance. The findings strongly suggests that dementia patients with poor insight or more advanced dementia underreport depressive symptoms relative to observer-rated severity of depression; patients with early dementia and preserved insight tend to report depressive symptoms disproportionate to observer ratings.

NR289 Tuesday May 5, 12:00 noon-2:00 p.m.

Circadian Rhythms in Alzheimer's Disease: Clinico-Neuropathology

Andrew Satlin, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Edward G. Stopa, M.D., Ladislav Volicer, M.D., David Harper, B.S., Vickey Kuo-LeBlanc, B.S., Tom Edwards, Ph.D.

Summary:

Sleep-wake cycle disturbances and "sundowning" suggest that circadian rhythms may be disrupted in Alzheimer's disease (AD). This hypothesis is supported by our previous studies of locomotor and temperature rhythms in AD subjects, and by preliminary evidence of the efficacy of bright light therapy for sleep disturbances

in some AD patients. Our current study seeks neuropathologic correlations to these abnormalities. So far, 20 end-stage AD subjects and five age-matched controls have had continuous activity and temperature monitoring for 72 h. Cosinor analysis of circadian activity rhythms revealed marked disturbances, with decreased circadian correlation ($p = 0.002$), decreased inter-daily stability ($p = 0.0001$), and a 4 h phase delay ($p = 0.006$). Temperature rhythms were similarly delayed ($p = 0.004$), but in other respects were not different from controls.

Five subjects have come to autopsy, and were compared to four normal controls. All subjects had histologically confirmed AD, with mean plaque counts in the occipetal lobe of 32.98/sq mm (controls 0.575, $p = 0.04$). However, unlike the findings of Hinton et al, there was no difference in the ratio of degenerated to normal axons in the optic nerve (AD 0.021, controls 0.023). This result suggests that other structures subserving circadian rhythms may be responsible for the changes seen in function, and supports further attempts to correct circadian abnormalities and associated behavioral disturbances in AD using light acting through a presumably intact retinohypothalamic tract. Immunocytochemical studies of the SCN in these subjects are now being done.

NR290 Tuesday May 5, 12:00 noon-2:00 p.m.

Telephone Screening in Alzheimer's Disease

Jeanne Radcliffe, R.N., LCS, NIMH Bldg 10 RM 3D41, 9000 Rockville Pike, Bethesda, MD 20892; James Hill, Ph.D., Kathleen Dietrich, R.N., Marcia Minichiello, M.A., Georgia Latham, M.D., Brian A. Lawlor, M.D., Trey Sunderland, M.D.

Summary:

It is estimated that only one of every ten Alzheimer Disease (AD) research applicants is eventually accepted for medication protocols. Because the evaluation procedure is very time-consuming, we have developed a computer-assisted Geriatric Outpatient Telephone Screening (GOTS) to help screen subjects more efficiently. Modeled on the Global Deterioration Scale, a commonly used clinical rating scale which estimates the severity of dementia, the GOTS generates a prediction of a clinical GDS score based on responses to the cognitive and functional portions of the interview.

We tested the predictive value of this GOTS-GDS in 55 AD patients (37 females, 18 males, mean age $\pm$ SEM = 72 $\pm$ 1.3, range 50-90 years). The study was completed at two sites (NIMH and Mt. Sinai). In 44 of the 55 cases (80 percent), the GOTS-GDS was within one point of the clinical GDS, and the Pearson's correlation between the two scores was 0.445 ($p < 0.001$). The mean GOTS-GDS score tended to be lower than the actual GDS at both test sites.

Thus, the GOTS, a telephone screening of potential AD research subjects did provide valuable information which was closely related to the physician-derived GDS. While the correlation between the two scales was not perfect, the GOTS did tend to be more conservative in its estimate of the GDS, suggesting that outpatient AD subjects would not be unnecessarily excluded from a study because of a falsely high severity estimate of the telephone-screening GDS.

NR291 Tuesday May 5, 12:00 noon-2:00 p.m.

Age of Onset May Define a Clinical Subtype in Alzheimer's Disease

Brian A. Lawlor, M.D., Psychiatry, St. James Hospital, James's Street, Dublin 8, Ireland; Theresa Ryan, B.S., James Schmeidler, Ph.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

Summary:

Early onset Alzheimer's disease (<65 years) may be characterized by the presence of greater language and praxis difficulties, and a more malignant course, compared to late-onset (>65 years) cases. The issue of clinical heterogeneity and age of onset was examined in a large cohort of patients meeting NINCDS criteria for AD. Memory, orientation, language, praxis, and depression were measured using subscales of the Alzheimer Disease Assessment Scale (ADAS). The rate of disease progression was calculated as the annual change in the Blessed Dementia Score (BDS) from the baseline visit to the last visit available. When presenile ($n = 52$) were compared to senile-onset ($n = 54$) cases, presenile-onset patients had significantly greater language and praxis difficulties, and developed higher depression scores than the senile-onset cases. However, there was no difference in the rate of progression between the two groups. These findings lend support to the contention that an earlier age of onset may define a clinical subtype of AD, but do not support the notion that onset in the presenium is associated with a more rapid rate of progression.

NR292 Tuesday May 5, 12:00 noon-2:00 p.m.

Life Review in Group Therapy of Demented Elderly

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Summary:

This preliminary study examined the effects of structured life review on psychological well-being, self-esteem, and social functioning in group psychotherapy of older adults with chronic dementia, living in a retirement home. Participants with mild to moderate dementia (Folstein scores 22-25, ages 81-99) completed standardized instruments assessing levels of psychological and social functioning before and after the six-week group process (Self-esteem Scale, Rosenberg, 1965; Affect-balance Scale, Bradburn, 1969). All sessions were audiotaped and transcribed. Data analysis shows a marked increase in self-esteem, psychological well-being, and social functioning in six of the seven participants. Content analysis of sessions indicates that use of reminiscence and life review in brief group treatment may help older adults with moderate dementia maintain coherence and continuity in sense of self and identity. Further, the group process may provide critical opportunities for supportive interaction and relatedness among peers that contribute to increased levels of adjustment and social functioning. Participants may experience mastery, control, and satisfaction using reminiscence to review and reevaluate lifetime memories. Findings point to the adaptive value of life review processes in psychiatric treatment of older adults with chronic dementia. Developmental, research, and clinical implications are reviewed.

NR293 Tuesday May 5, 12:00 noon-2:00 p.m.

Depression: Anglo and African-American Caregivers

Jacobo E. Mintzer, M.D., Psychiatry, Medical University, 171 Ashley Avenue, 5th Fl IOP, Charleston, SC 29425; Carol Macera, Ph.D.

Summary:

The occurrence of dementia affects family members in many ways, including increased risk for mental health problems such as symptoms of depression (1). While a number of variables affecting depression among caregivers have been investigated, relatively little is known about the prevalence of depressive symptoms among caregivers from different ethnic groups living in the United States (2). Presented are the preliminary findings from baseline evaluation of a cross-cultural prospective study to assess mental health of white and African-American caregivers of demented patients in South Carolina. Eighty-three patients and their caregivers (63 white non-Hispanics and 20 African-American) were randomly selected for interview from the more than 5,000 demented patients

currently identified in the state of South Carolina Dementia Registry and area support groups. Mean age for patients was 76.9 years and for caregivers was 61.1 years. There was no statistically significant differences in patient or caregiver demographic characteristics (age, socio-economic status, education, and relationship to the patient). The sex distribution among patients was roughly equal, while the caregivers were primary females. Fifty percent of the patients in each group were considered mildly or moderately impaired, with the remaining 50 percent considered severely impaired according to the Global Deterioration Scale. Symptoms of depression among caregivers were studied using the Center of Epidemiological STudies of Depression Scale (CES-D). The results of this preliminary survey show significant differences in the prevalence of depressive symptoms among the two groups. African-American caregivers demonstrated statistically significant less depression than white caregivers when the data were analyzed using a cut-off value of 16 to differentiate among those that presented significant levels of depression. using this cut-off our sample showed that 62 percent of the white caregivers had significant symptoms of depression, while only 30 percent of the African-American caregivers exhibited symptoms of depression ($p < 0.05$). When a lower cut-off of 9 was utilized, significant values were also present, with 78 percent of the white caregivers compared to only 41 percent of the African-American caregivers presenting with comparable levels of depressive symptoms ($p < 0.05$). Similar patterns were found when CES-D mean values were compared (white mean CES-D score = 19.3, African-American mean CES-D score = 12.4, $p < 0.05$).

In addition other study variables such as measures of caregiver health status, burden, and living arrangements will be presented. These findings are in agreement with the author's previous findings on Hispanic populations (3). The significance of this study findings in the context of the available literature will be discussed.

NR294 Tuesday May 5, 12:00 noon-2:00 p.m.

The Geriatric Movement Disorders Assessment

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Summary:

The Geriatric Movement Disorders Assessment (GMDA) is an adaptation, for use in elderly populations, of three scales initially developed for the rating of neuroleptic-induced movement disorders in mixed-age patients. The Abnormal Involuntary Movements Scale, Simpson Extra Pyramidal Side Effect Scale, and the Barnes Akathisia Scale were condensed into one streamlined examination procedure requiring ten to 15 minutes to complete. Three geriatric research clinicians were trained in the use of the GMDA. Interrater reliability, as calculated by intraclass correlation coefficients for the total score of each of the GMDA subscales, was 0.89, 0.79, and 0.93, respectively. Tolerance of the GMDA examination by a population of elderly psychiatric inpatients was high with a completion rate of 97 percent. Thus, the GMDA is a reliable and well tolerated instrument for the assessment of movement disorders in the elderly. It is readily implemented in a clinical research setting and represents an important advance in standardizing the evaluation of akathisia, dyskinesia, and parkinsonism in geriatric populations.

NR295 Tuesday May 5, 12:00 noon-2:00 p.m.

Benzodiazepine Noncompliance of Older Adults

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Summary:

Benzodiazepines are commonly the first-line pharmacologic intervention for management of anxiety and sleep disturbance. However, a variety of side effects have been reported by older patients receiving benzodiazepines, including fatigue, cognitive impairment, depression, and ataxia precipitating falls. Notably, these effects are often more pronounced among older patients receiving long half-life benzodiazepines than among patients taking short half-life benzodiazepines. As cognitive impairment and affective symptoms have been associated with medication noncompliance among older adults, this study examined compliance with short and long half-life benzodiazepines among older patients living in the community. Medication compliance was assessed among 1,155 men and 1,942 women participants in the Iowa 65+ Rural Health Study. Results of an in-person interview revealed that 22.0 percent of respondents (26.7 percent of men, 20.5 percent of women) who had been prescribed benzodiazepines on a scheduled basis failed to comply with prescription instructions. Compliance rates did not differ significantly either between short and long half-life benzodiazepines nor across the age strata of older patients investigated. Anxiety symptoms and sleep disturbance did not distinguish compliant from noncompliant patients. These results suggest that while a sizable minority of older patients fail to comply with benzodiazepine regimens, medication noncompliance in this population cannot be attributed to age, drug half-life, or patient symptom distress.

NR296 Tuesday May 5, 12:00 noon-2:00 p.m.

Temporal Stability of Tardive Dyskinesia Status in Elderly Schizophrenic Patients

Paolo Decina, M.D., Psychiatry, S.M. Immacolata Hospital, Via Tiburtina 188, Guidonia 00012, Italy; Ferdinando Saraceni, m.d., Christos Hadjichristos, M.D., PierLuigi Scapicchio, M.D., Sukdeb Mukherjee, M.D.

Summary:

To examine the stability of tardive dyskinesia status (TD) in the elderly, 77 chronic schizophrenic inpatients (51 M, 26 F; mean age 64.9 years, SD 7.0, range 55-85) were evaluated for a range of demographic, clinical, and medication variables, and followed up over two years. At follow-up, the frequency of TD cases meeting research diagnostic criteria (52 percent) showed an insignificant increase from baseline (48 percent). However, while 56 (73 percent) of the 77 patients showed no change in TD status, 21 (27 percent) showed a fluctuating course. Of the 40 patients initially without TD, 12 (30 percent) went on to develop it over the two-year study period. Of the 37 with TD at initial evaluation, 9 (24 percent) remitted. Similarly, although in the patient group as a whole there was no overall change in Abnormal Involuntary Movement Scale (AIMS) global severity scores (1.9 vs 2.0), 32 percent of the patients showed an increase of one or more score point, and 27 percent showed a decrease of one or more score point. The only variable significantly related by stepwise multiple regression with these changes in severity scores was the initial symptom severity ($F[1,74] = 19.2$; $R^2 = 0.21$). Greater initial symptom severity was associated with both less improvement and worsening of dyskinesias at follow-up.

These results suggest that the temporal stability of TD status in the elderly is similar to that reported in younger populations, and is partly accounted for by the initial symptom severity of abnormal movements.

NR297 Tuesday May 5, 12:00 noon-2:00 p.m.

Diazepam Induced Impairment and Cognitive Decline

Nunzio Pomara, M.D., Geriatrics, Nathan S. Kline Inst., Building 37, Orangeburg, NY 10962; Dennis Deptula, Ph.D., Rajkumar Singh, M.D., David J. Greenblatt, M.D.

Summary:

We have reported previously that single 2.5 mg and 10 mg doses of diazepam produced measurable impairment in the elderly on the Buschke Selective Reminding Test (SRT), a test of verbal learning. In our previous study, 45 healthy volunteers between the ages of 60 and 79 were each administered single 2.5 mg and 10 mg doses of diazepam as well as placebo on three consecutive weeks under double-blind conditions. Just prior to drug administration and 1.5 hours following drug administration, the SRT was administered.

Twenty-two of these subjects returned to our center three years later for a follow-up visit during which they were again administered the SRT. Nine of the 23 subjects showed some decline in memory performance as indicated by the fact that they scored 0.5 standard deviations more poorly than at their drug-free baseline three years before. those demonstrating decline did not differ from those not showing decline on demographic variables, baseline cognitive performance, or plasma diazepam concentration during the drug test sessions. However, those who went on to show further decline in memory function were found to demonstrate more intrusion errors in response to 2.5 mg diazepam ($p < .05$). There was also a trend for this group to recall fewer words on the list after being administered 2.5 mg diazepam ($p < .10$).

This pilot study raises the possibility that elderly individuals showing greater memory impairment in response to a low dose of diazepam may also be more likely to show decline in memory as a function of time.

NR298 Tuesday May 5, 12:00 noon-2:00 p.m.

Use of Mental Health Services Before Nursing Home Admission

Barry W. Rovner, M.D., Psychiatry, Jefferson Med. College, 1025 Walnut St. Ste 301, Philadelphia, PA 19107; Pearl S. German, Sc.D.

Summary:

Community services such as home healthcare and psychiatric clinics are available to disabled elders and their families, although they may be underutilized. We examined the relationship of need for services for physical and behavioral symptoms, and their actual utilization among 454 new admissions to eight community nursing homes.

Families of demented patients more frequently required help with physical care than nondemented patients (79.8 percent vs 68.4 percent; $p < .01$). However, they were not more likely to receive such help (30.6 percent vs 28.6 percent; ns). The majority of all patients needing such help did not receive it prior to admission. Families of demented patients reported behavior disorders as reasons for admission more often than non-demented (31 percent vs 12 percent; $p < .001$). However, demented patients were no more likely to receive mental health services prior to admission. The overall use of mental health services for demented patients was extremely low (18.5 percent), whether for behavior disorder or for evaluation of dementia.

Community physical and mental health services may reduce the adverse effects of caring for community-residing physically and mentally disabled elderly, may prevent or postpone nursing home placement, and can reduce costs for caring for demented patients. However, they are underutilized. Methods to increase education and referral are necessary.

NR299 Tuesday May 5, 12:00 noon-2:00 p.m.

Validity of the Short Portable Mental Status Questionnaire Administered by Telephone

William H. Roccaforte, M.D., Psychiatry, Univ of NE Med. Center, 600 South 42nd Street, Omaha, NE 68198; William J. Burke, M.D., Steven P. Wengel, M.D., Barbara L. Bayer, M.S.N.

Summary:

The construct and criterion validity of a telephone version of the SPMSQ were assessed in 100 patients evaluated in an outpatient Geriatric Assessment Program. SPMSQ questions contained in the Adult Lifestyles and Function Interview were asked of the subjects by phone (Ph) and compared to those administered face-to-face (F) an average of eight days later.

Mean scores for both test versions increased with dementia severity. Total scores ($\bar{x}$ = 3.4-F, 3.1-Ph) correlated strongly (Pearson's $r = 0.82$, $p = 0.0001$). The mean score difference between the two versions was not affected by subject or collateral reports of hearing impairment.

When scores were adjusted for education and sex both test versions correlated strongly with Mini-Mental State Examination scores ($4 = 0.73$, $p = 0.001$-Ph; $r = 0.81$, $p = 0.0001$-F). Validity was further assessed by the tests' ability to distinguish cognitively intact and very mildly impaired (CDR-0 and 0.5) from those with a definite dementia diagnosis (CDR 1 and 2). Sensitivity, specificity and positive predictive value were 0.74, 0.79, and 0.88 for the phone test and 0.74, 0.91, and 0.94 for the live test, respectively.

The telephone-administered SPMSQ demonstrates construct validity relative to its face-to-face administration and to the MMSE. It shows criterion validity to a clinical diagnosis of dementia in an outpatient, geriatric medical population.

NR300 Tuesday May 5, 12:00 noon-2:00 p.m.

Psychiatric Symptoms in Two Types of Dementia

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Summary:

The Neurobehavioral Rating Scale (NRS), a 27-item observer-rated instrument, was used to identify the cognitive, psychiatric, and behavioral disturbances in 104 patients with either Alzheimer's disease (AD) or multi-infarct dementia (MID). Principal components analysis of the NRS ratings identified six factors: cognition/insight, agitation/disinhibition, behavioral retardation, anxiety/depression, verbal output disturbance, and psychosis. Each factor contained clinically related symptoms.

Among the patients with AD, symptoms on the agitation/disinhibition and psychosis factors were more severe in patients with more advanced dementia. Symptoms on the behavioral retardation and anxiety/depression factors were equally severe in patients with mild and advanced AD.

The data from a subgroup of 28 patients with AD and 28 patients with MID, matched for similar Mini-Mental State Exam score, education, and age, were examined further. The patients with MID demonstrated more severe signs of Behavioral Retardation and a trend for more severe Anxiety/Depression than those with AD. There was no difference between groups in the severity of Agitation/Disinhibition of Psychosis.

These results support the use of the NRS for structured assessment of psychiatric and behavioral disturbances. The nature and severity of psychiatric disturbance depends on the extent of dementia and the dementia subtype.

NR301 Tuesday May 5, 12:00 noon-2:00 p.m.

Odorant Specific Hyposmia in Alzheimer's Disease

Michael J. Serby, M.D., Psychiatry, Mt. Sinai Med. Center, One Gustave Levy Place Bx 1230, New York, NY 10029; Davina Kalkstein, B.A., Gwenn S. Smith, Ph.D., Michael Russell, M.D.

Summary:

Objective: Olfactory identification deficits have been demonstrated in all phases of Alzheimer's disease (AD). We have investigated the possibility that the ability to identify some specific odorants may be relatively preserved. If so, it may be instructive to characterize the nature of these odorants. *Methods: Odor identification was tested with the University of Pennsylvania Smell Identification Test. Each odorant had previously been subjectively rated by a control group with regard to five features: familiarity; intensity; irritation; pleasantness/unpleasantness; warmth/coolness. A total of 206 subjects were tested and classified as young (YC), ages 15-59, (n = 47); old controls (OC), ages 60-90 (n = 97); mildly impaired (Global Deterioration Scale 3) (n = 16); mild AD (GDS 4) (n = 22); moderate AD (GDS 5) (n = 24). WE clustered odorants that were identified most frequently ("best") and least frequently ("worst") and analyzed differences between clusters on the basis of the five features. Results:* The "best" odorants were significantly "cooler" than the "worst" odorants in YC ($p < .04$), OC ($p < .006$) and showed a trend in this direction in GDS 3 ($p < .08$). In contrast, AD showed no difference in features between their "best" and "worst" odorants. Early AD can be distinguished from OC based upon performance on four items (licorice, turpentine, paint thinner and lemon) with a sensitivity of 91 percent and a specificity of 83 percent. *Conclusions:* The AD process may involve some mechanism that compromises the ability to identify "cool" odorants. Certain odorants can be used to distinguish AD from normal aging and may be useful as early diagnostic markers.

NR302 Tuesday May 5, 12:00 noon-2:00 p.m.

Depression Among Korean Elderly Immigrants

Keum Y. Pang, Ph.D., Nursing, Howard University, 501 Bryant Street NW, Washington, DC 20059; Guojun Cai, M.D.

Summary:

This study is both qualitatively and quantitatively oriented exploratory anthropological research of depression. Forty-one elderly informants from Korean community were interviewed with DIS including Korean cultural specific questions in order to find the prevalence rate of major depression and the relationship between depression and somatization as well as culture related psychosocial factors. The results showed that major depression lifetime and current prevalence in Korean elderly population were 31.70 percent and 17.10 percent, respectively; General anxiety disorder were 36.60 percent and 14.60 percent, respectively; Somatization disorders were 9.80 percent and 7.30 percent, respectively. Strong evidence was found that there was very close overlapping relationship between major depression and GAD, and major depression and somatization disorders. Demographic differences, symptom distribution, social support system, explanatory model, and semantic networks of depression were studied and discussed in this paper.

NR303 Tuesday May 5, 12:00 noon-2:00 p.m.

TCAS, Orthostatic Monitoring and Falls in Nursing Homes

Blaine S. Greenwald, M.D., Psychiatry, Hillside Hospital, P.O. Box 38 Lowenstein Res Bld, Glen Oaks, MD 11004; Elisse Kramer-Ginsberg, Ph.D., Susy Abraham, M.D., Richard A. Hodder, M.D.

Summary:

Recent reports on prevalence of and increased mortality associated with depression in nursing homes suggest the need for more aggressive case-finding and treatment. Consequently, cyclic antidepressant prescription, already common in nursing homes, may be expected to increase. However, little is known about actual antidepressant treatment practices in long-term care facilities, despite their frequent prescription. Orthostatic hypotension, a common cardiovascular side effect of these agents, poses extraordinary risks in this trail population. To ascertain whether orthostatic hypotension was monitored, medical charts of residents prescribed cyclic antidepressants (n = 45, mean age = 85.5 +/−7 years) in a 784-bed nursing home were systematically reviewed. Orthostatic blood pressure was independently measured according to recommended guidelines. Number of falls/resident during cyclic antidepressant therapy over the past six months were recorded. Chart review indicated that orthostatic blood pressures had **not** (i.e., 0 percent) been monitored. Actual postural blood pressure assessments revealed that 44 percent of residents met standardized criteria for orthostatic hypotension. A total of 61 percent of treated residents had at least one documented fall. Orthostatic hypotension was significantly associated with falling ($p < .05$). Blood pressure changes and falls were not associated with age, sex, cognitive ratings, and number of medical illnesses. Nortriptyline dose did not correlate with mean blood pressure decrement. Findings suggest a need in nursing homes for (1) vigorous education about and possibly mandated monitoring of orthostatic hypotension as a cyclic antidepressant side effect; (2) cautious use of these agents, especially in residents with additional risk factors for falling; and (3) introduction of newer antidepressants with little or no cardiovascular side effects.

NR304 Tuesday May 5, 12:00 noon-2:00 p.m.

Delirium: Detecting Mild Cases by Measuring Change

Ira R. Katz, M.D., Psychiatry, Medical Coll. of PA, 3200 Henry Avenue, Philadelphia, PA 19129; Laura Sands, Ph.D., Richard Harner, Ph.D., Suzanne Doyle, R.N.

Summary:

Delirium and related toxic or metabolic encephalopathies can occur with varying degrees of severity. Standard approaches to diagnosis require the observation of symptoms that emerge in the pathological state. This may, however, not be sensitive enough to allow the identification of mild cases. Accordingly, we have been evaluating an approach to case identification that is based upon repeated tests of cognitive performance and measures of the EEG background in elderly subjects. We calculate prediction intervals that characterize the magnitude of expectable within-subject change, in medically stable subjects, and, hence, allow the definition of excessive change as a categorical variable. Using this approach, we find that the ratio of the prediction interval tot he sample S.D. is <1 for fingertapping, simple reaction time, continuous performance, pattern recognition/memory, digit symbol substitution and measures of percent theta, alpha, and beta in the EEG background. Thus, with these measurements, it is possible to detect significant change in test performance and EEG for subjects who are still in the normal range. These methods show promise for clinical use in monitoring vulnerable patients.

NR305 Tuesday May 5, 12:00 noon-2:00 p.m.

Serotonin in Parkinson's Disease and Depression

Lawrence H. Price, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Elinore F. McCance-Katz, M.D., Kenneth L. Marek, M.D.

Summary:

Evidence for serotonin (5-HT) dysfunction in Parkinson's disease (PD) includes studies of cerbrospinal fluid levels of the 5-HT metabolite, 5-hydroxyindoleacetic acid, which may be up to 50 percent lower in PD patients and 70 percent lower in depressed PD patients compared to controls. Fluvoxamine, a 5-HT reuptake inhibitor, has demonstrated antidepressant efficacy. Serotonin dysfunction in the

pathophysiology of PD and depression was studied via a controlled trial of fluvoxamine in treatment of depression in PD and tryptophan (TRP) depletion testing in remitted, depressed PD patients. METHOD: Subjects with idiopathic PD and major depression participated in an eight-week, double-blind, placebo-controlled trial of fluvoxamine. Hamilton Depression Rating Scale and Beck Depression Inventory were used to assess treatment response. Motor symptoms were monitored with Unified Parkinson's Disease Rating Scale and Abnormal Involuntary Movements examination. Remitted, depressed PD patients underwent TRP depletion which acutely decreased 5-HT levels. Behavioral and motor changes were studied. RESULTS: Depression in two thirds of fluvoxamine treated patients remitted. Depression worsened in two thirds during TRP depletion. All experienced worsened motor symptoms during the TRP depletion test. CONCLUSIONS: Fluvoxamine may be an effective antidepressant treatment in PD patients. 5-HT dysfunction may be important in the pathoetiology of depression and motor disturbances of PD.

NR306 Tuesday May 5, 12:00 noon-2:00 p.m.

Access to Hospice Programs in End-Stage Dementia: A National Survey of Hospice Programs

Patricia Hanrahan, Ph.D., Psychiatry, University of Chicago, 5841 S. Maryland Avenue, Chicago, IL 60637; Daniel J. Luchins, M.D., Todd J. Segneri, B.A.

Summary:

Care of end-stage dementia is a significant clinical problem for which alternative modes of care are needed. Although many family and professional caregivers of demented patients prefer a hospice alternative (Luchins & Hanrahan, 1991) the availability of this alternative has not been formally studied. Hospices in the 1988 National Hospice Directory were surveyed (N = 1,559), response rate: 27 percent or 418 programs. Follow-up mailings are in progress. RESULTS: Although Alzheimer's disease is the fourth leading cause of death (Katzman, 1976), less than one-half of 1 percent of patients in hospice had a primary diagnosis of dementia. Hospices with a larger program size were more likely to serve dementia patients (T-test = 3.06, df = 366, $p < .004$), with the average number of patients served among programs that included dementia patients being twice as high. The major obstacle to providing hospice for severely demented patients was the difficulty in predicting their survival time as survival time in advanced dementia is highly variable. Providing clinical care for dementia patients was otherwise feasible as 55 percent of the hospice programs served patients whose dementia was secondary to cancer or AIDS.

NR307 Tuesday May 5, 12:00 noon-2:00 p.m.

Schizophrenic Dementia Revisited

William B. Lawson, M.D., Psychiatry, North Little Rock VA, 2200 Fort Roots Drive, North Little Rock, AR 72114; Nancy Lyon, Ph.D., Craig N. Karson, M.D.

Summary:

We previously reported that a number of schizophrenics become demented. One hundred ten *DSM-III-R* positive, mostly elderly, schizophrenic patients (mean age = 60 + 10) were surveyed using the Neurobehavioral Cognitive Status Exam (NCSE). Eighty-two percent met criteria for dementia. Most were impaired on half of the subscales. We studied in depth ten younger patients (mean age = 49.4 range = 42-67) meeting criteria for dementia from a locked ward of 30. Their length of stay was 29 years (range 7-44). All had greater than an eighth grade education, pronounced positive and negative symptoms, and all but one did not have a history of lobotomy or ECT. Five had a history of polydispsia and hyponatremia, and were the only such patients on that ward. Seven had received clinical diagnoses of dementia. Five that were evaluated showed abnormal EEG's and single photon emission tomography by clinical determination. The SPECT scan showed consistently frontal hypoperfusion. Severe dementia that is diagnosible using standard clinical assessments can be found in elderly chronic schizophrenic patients. Cognitive impairment of a less severe nature occurs frequently and is qualitatively similar to severe impairment.

NR308 Tuesday May 5, 12:00 noon-2:00 p.m.

Heritability of Personality Disorder

W. John Livesley, M.B., Psychiatry, Univ of BC, 2255 Wesbrook Mall, Vancouver BC V6T 2A1, Canada; Douglas N. Jackson, Ph.D., Kerry L. Jang, M.A., Phillip A. Vernon, Ph.D.

Summary:

The study reports a classic twin study designed to estimate the heritability of basic dimensions of personality disorder. The genetic contribution to personality disorder has received little detailed attention in the research literature which typically reports no more than familial concordance rates. This provides little quantitative information on the size of genetic or environmental influences. Subjects, 32 monozygotic and 39 dizygotic twin pairs completed the Dimensional Assessment of Personality pathology Questionnaire—a self-report questionnaire that measures 18 factor analytically based dimensions of personality disorder (Livesley, Jackson & Schroeder, 1989). General population subjects were used because the responses of this population to questions of psychopathology have consistently been shown to be similar to those obtained form clinical samples. Biometrical analyses using structural equation model fitting techniques (Heath, Neale, Hewitt, Eaves & Fulker, 1989) estimated a model that allows for direct gene action (h^2), the effects of shared life experiences (c^2), and unshared life experiences (e^2). Moderate heritabilities were found for most dimensions of personality disorder. These values were consistent with previous reports of the heritability of normal personality traits. The magnitude of heritabilities was not consistent across all dimensions. The traits also suggest that environmental events, particularly nonshared events, are important in the etiology of personality disorder.

NR309 Tuesday May 5, 12:00 noon-2:00 p.m.

Bupropion Therapy in Chronic Fatigue Syndrome

Paul J. Goodnick, M.D., Psychiatry, University of Miami, D79, 1400 NW 10 Avenue #304A, Miami, FL 33136; Ricardo Sandoval, M.D., Andrew Brickman, Ph.D., Nancy G. Klimas, M.D.

Summary:

Chronic fatigue syndrome (CFS) includes many symptoms of major depression. For this reason, many antidepressants have been used. More recently, bupropion, an antidepressant with a dopaminergic and a relatively activating clinical profile, was found effective in two cases of CFS (Goodnick, 1990). For this reason, an open trial with nine CFS patients (criteria of Holmes et al, 1988) previously unresponsive to fluoxetine was pursued at a dose of 300 mg/day. A total of 7F & 2M with a mean age of 43.3 ± 8.1 years were rated on the Beck Depression Inventory (BDI) and Hamilton Depression RAting Scale (HDRS) at baseline, four wks, and eight wks. Measures of plasma HVA and MHPG were completed at baseline and four weeks; immune studies were also done midstudy. The HDRS improved from 19.7 ± 7.4 to 12.5 ± 10.9 ($t = 4.80$, $p < .01$), and BDI, from 19.8 ± 15.1 to 14.3 ± 16.0 ($t = 2.48$, $p < .05$) after eight weeks. %improved 40 percent in HDRS; fall in plasma HVA correlated significantly with improved response ($r = .96$, $p < .01$). Total plasma MHPG fell during treatment (1.8 ± 2.0, $t = 2.37$, $p < .05$). T1 monoclonal antibody levels fell during treatment ($p < .05$); increases in natural killer cells correlated inversely

with increases in plasma free MHPG ($r = -.88$, $p < .05$). These results indicate that bupropion may be an effective treatment for CFS, even in those previously not responding to other antidepressants. Perspectives concerning mechanism of bupropion and immune response will be discussed.

NR310 Tuesday May 5, 12:00 noon-2:00 p.m.

Affective Processes, Immune Dysfunction and Health

Steven E. Keller, Ph.D., Psychiatry, UMDNJ Medical School, 185 South Orange Avenue E501, Newark, NJ 07103; Steven J. Schleifer, M.D., Jacqueline Bartlett, M.D., Haftan Eckholdt, M.A.

Summary:

A major question in psychoimmunology is whether immune alterations seen with various psychological paradigms are clinically relevant. Specifically, are psychological alterations related to subsequent immune changes and in turn are those immune changes related to subsequent disease occurrence? We have been investigating psychological, immunological, and health variables in 600 randomly accrued adolescents at six month intervals over the past several years. We now report on preliminary longitudinal analyses of a cohort subset of 226 subjects. The average age of the subjects was 16; 82 percent were African Americans and 14 percent Hispanic, fifty-five percent were male. Sixteen percent of the subjects met criteria for major depressive disorder, and there was a wide range of scores for the other psychosocial variables. The immune variables were in the normative range. Approximately 30 percent of the subjects had minor physical illness findings. Regression analyses, controlling for age race and sex revealed that depressed mood ($p < 0.08$) and syndromal depression ($p < 0.03$) at Time 1 was related to illness at Time 2 and that decreased WBC, number of B cells, activated T cells and lower PWM responses at Time 1 were independently associated with increased disease at Time 2 ($p < 0.05$ in all cases). Finally, MDD and HDRS at Time 1 were associated with lower B and T cell function at Time 2 ($p < 0.05$ in all cases). These preliminary analyses suggest a PNI model of affective alterations leading to immune dysfunction which in turn leads to increased illness.

NR311 Tuesday May 5, 12:00 noon-2:00 p.m.

Eustress of Humor Associated Laughter Modulates Immune System Components

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Summary:

Stress or negative emotion has been associated with immunosuppression, partially modulated by increased neuroendocrine hormones such as epinephrine, corticotropin, and cortisol. We have previously reported that the eustress of humor associated laughter decreases or attenuates these and other hormones, and increases spontaneous lymphocyte blastogenesis and natural killer cell activity. To further investigate the effects of humor associated laughter on immunological response we studied ten healthy male subjects for change in peripheral blood mononuclear cells expressing membrane antigens [activated T cells (CD3±DR+), uncommitted T cells with helper and suppressor markers (CD4+8+), T cell helper/suppressor ratio (CD4+/CD8+), natural killer cells (CD57+8+), B cells (CD19+)]; immunoglobulins (IgG, IgA, IgM); complement (C3) and gamma interferon (IFN-γ). The experimental group viewed a preselected 60 min humor video. Blood samples were obtained through an iv catheter before (baseline), during (intervention), after (recovery) and the next day. Data were analyzed using multivariate ANOVA. Within group effects showed a significant increase in the experimental subjects for CD3+DR+ ($p = 0.007$), CD4+8+ ($p = 0.016$), CD57+8+ ($p = 0.013$), IgA ($p = 0.015$) and IFN-γ ($p = 0.024$). Simple contrasts with baseline showed significant increases in CD4+/CD8+ at recovery ($p < 0.001$), IgG during intervention and the next day ($p < 0.01$), IgM during intervention ($p < 0.05$), CD19+ at recovery and next day ($p < 0.001$), and C3 the next day ($p < 0.01$). Plasma volume, hematocrit and total serum protein showed no significant change over the time points studied. Although further research is needed to elucidate these effects on the composite immune response, these data suggest that humor associated laughter may be capable of immunomodulation.

NR312 Tuesday May 5, 12:00 noon-2:00 p.m.

Stress and Immunity in Adolescents

Jacqueline Bartlett, M.D., Psychiatry, UMDNJ-NJ Med School, 185 South Orange Ave. RM E501, Newark, NJ 07103; Steven Schleifer, M.D., Haftan Eckholdt, M.A., Melissa K. Demetrikopoulos, M.S., Steven E. Keller, Ph.D.

Summary:

Studies in adults have found altered, primarily decreased, immunity in relation to stressful life events or level of perceived distress. We are studying stress-immune relationships among inner city adolescents. Data are reported on 306 healthy adolescents (age 15.9 ± 1.7, 89 percent African American, 49 percent female) attending a local high school or adolescent health clinic. Past year life events (Coddington Life Events Scale, CDLES), distress (Perceived Stress Scale, PSS) and a battery of immune measures were studied.

CDLES (mean 15.8 ± 10.8) and PSS (21.8 ± 7.3) were intercorrelated ($r = 0.22$, $p < 0.0001$). Regression analyses tested the effects on immunity of age, sex, race, CDLES, and, concurrently, PSS. Regressions revealed an independent association of PSS with increased WBC's (F 5.0, $p < 0.03$) and CD4+ (T helper) cells ($F = 4.1$, $p < 0.05$). CDLES predicted increased percent T cells ($F = 9.8$, $p < 0.002$), T helper ($F = 7.4$, $p < 0.007$), activated T ($F = 4.1$, $p < 0.05$), T inducers of help ($F = 14.5$, $p < 0.0002$) and T inducers of suppression ($F = 7.6$, $p < 0.006$), and decreased percent B cells ($F = 8.2$, $p < 0.004$). No alterations in functional immune measures (PHA, ConA, and PWM mitogen response, NK activity) were found.

Stressful life events and, to a lesser extent, perceived stress were associated with increased circulating T lymphocyte subtypes. These findings are comparable to those found in some models of acute stress in adults.

NR313 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Race Bias in Child Psychiatry versus the Juvenile Justice System?

Stuart L. Kaplan, M.D., Rockland Child Psych Ctr, Convent Road, Orangeburg, NY 10962; Joan Busner, Ph.D.

Summary:

In response to several studies suggesting racial bias in the admission of proportionately more white children and adolescents to the child and adolescent mental health system than to the juvenile justice system, this study was designed to test whether whites would be overrepresented compared to blacks in mental health facilities and underrepresented compared to blacks in juvenile corrections facilities when ethnic distribution in the general population was controlled. *Method:* Ethnicity, age, and sex of 10- to 18-year-olds admitted in a one-year period to NY State-operated psychiatric and correctional facilities were converted into rates per 100,000 population using New York State U.S. census data and compared. *Results:* There were no meaningful differences in population-corrected admission rates between blacks, whites, and Hispanics in

the NY State mental health system. In contrast, there was a vast preponderance of blacks in the NY State juvenile corrections system. The systems have different points of entry: A total of 100 percent of juvenile justice versus 17 percent of mental health admissions were court-referred. *Conclusion:* The analysis of demographic variables fails to support an allegation of racial bias in admission to the child and adolescent public mental health system in New York State.

NR314 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Prescribing Practices of Child Psychiatrists

Stuart L. Kaplan, M.D., Rockland Child Psych Ctr, Convent Road, Orangeburg, NY 10962; Robert Simms, M.D., Joan Busner, Ph.D.

Summary:

Although there have been several surveys of psychoactive medication prescribing practices for adult psychiatric outpatients, there have been no studies of the prescribing practices of child psychiatrists for children attending psychiatric outpatient or day treatment programs. We report the first survey of this type. From a total of 1483 cases seen during 1990, the charts of a randomly selected sample of 171 medicated and 169 nonmedicated children from two large public psychiatry systems in New York and Ohio were reviewed using a comprehensive instrument that assessed present and past five Axis-*DSM-III* and *DSM-III-R* diagnoses, present and past medications, responses to medication, reasons for use and reasons stopped, demographic variables, and psychiatric history such as previous treatment and hospitalizations. More salient results were as follows: disorders most often treated with medication were psychosis, major depression, and ADHD. Antipsychotic medication was used to treat disorders other than psychosis. Between 9 percent (New York) and 20 percent (Ohio) of patients were medicated. Patients with a history of hospitalization were more likely to now receive medication. In New York, children of single parent families were more likely to be medicated; in Ohio, males were more likely to be medicated. Medication usage by diagnosis was similar across the two settings.

NR315 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Bupropion Treatment of Adolescent Depression

David E. Arredondo, M.D., Brookside Hospital, 11 Northwest Blvd., Nashua, NH 03063; Melissa Streeter, John P. Docherty, M.D.

Summary:

This presentation will summarize the initial results of an ongoing, prospective, flexible dose (50 mg BID to 100 mg TID), open trial of bupropion in a sample of newly hospitalized adolescents who met *DSM-III-R* and K-SADS criteria for major depressive disorder. Following a one- to two-week washout period, those patients who did not respond to standard milieu treatment, including individual and group therapy, were started on bupropion. Clinical response was measured by the Beck Depression Inventory, Hamilton Rating Scale for Depression, brief Symptom Inventory, Clinical Global Impressions Scale, and K-SADS Global Assessment Scale. These assessments were done at baseline, at two-week intervals for the first two months of the study, and monthly thereafter. By the one-month follow-up, significant improvement on all measures was apparent; and these gains were maintained post-hospitalization. Ongoing assessments of drug side effects indicated that the drug was well tolerated. Although the long-term effects are still unknown, these results suggest an important role for bupropion in the treatment of adolescent depression.

NR316 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Conduct Disorder, Oppositional Defiant Disorder and Mood Disorder in Adolescents

David E. Arredondo, M.D., Adol. Psych., Brookside Hospital, 11 Northwest Blvd., Nashua, NH 03063; Stephen F. Butler, Ph.D.

Summary:

Two-hundred and twenty-three consecutively admitted adolescent inpatients were systematically assessed for conduct disorder (CD) and oppositional defiant disorder (ODD) using *DSM-III-R* and the Schedule for Affective Disorders and Schizophrenia in School Aged Children (Kiddie SADS) criteria. Twenty-six percent met criteria for CD and 12 percent met criteria for ODD.Compared with other patients in the sample, patients with a diagnosis of CD were significantly more likely to meet criteria for an affective disorder. Specifically, these patients were more likely to have a diagnosis of major depression ($P < .01$). *Of those patients meeting criteria for conduct disorder, there was an overall affective disorder comorbidity rate of 69 percent. Major depression occurred in 33 percent of these patients, bipolar disorder in 25 percent, affective psychosis in 5 percent, and dysthymic disorder in 9 percent. Similar analyses for adolescents with ODD revealed much lower incidence of affective disorders and no psychotic disorders. These data support development of a separate diagnostic category of affective conduct disorder.*

NR317 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Follow-up of Fifty-Four Obsessive Compulsive Children

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

Summary:

Fifty-four consecutive pediatric patients with obsessive compulsive disorder (OCD) who participated in controlled clomipramine trials and then received a variety of interim treatments, were reevaluated two to seven years after initial contact. Despite multiple treatment interventions in three-quarters of the patients, at follow-up 23 (43 percent) of the subjects still met diagnostic criteria for OCD, and only six (11 percent) were totally asymptomatic (three of those were on medication), supporting previous reports of the chronicity and intractability of the illness. Thirty-eight (70 percent) were on psychoactive medication at the time of follow-up; however, there were no significant associations between follow-up OCD status and type of interim treatment(s). As a group, they were improved at follow-up, although ten (19 percent) subjects were unchanged or worse. A poor initial clinical response to clomipramine, presence of parental Axis I psychiatric diagnosis, high expressed emotionality, and family dysfunction all correlated significantly with higher OCD symptom scores at follow-up. Of the five (9 percent) who were rated as worse than at baseline, all had severe comorbid diagnoses at follow-up which may have contributed to their poor outcome.

NR318 Tuesday May 5, 3:00 p.m.-5:00 p.m.

The Adult Outcome of Child Psychiatric Inpatients: Diagnosis and Mental Health Service Utilization

Michael S. Lundy, M.D., Psychiatry, Univ of South Carolina, P.O. Box 202, Columbia, SC 29202; Bruce M. Pfohl, M.D.

Summary:

Forty-one (41) adults (27 M, 14 F) who were psychiatrically-hospitalized during childhood were interviewed by telephone, using

the Diagnostic Interview Schedule. Subjects comprised a representative, non-random sample of the 170 nonretarded persons treated at the University of Iowa during early childhood, between 1970 and 1982. All members of the group of 170 were inpatients *before, but not after* the age of 12. Follow-up intervals ranged from eight to 19 years, with a mean of 14 years. Mean age at follow-up was 24 years. Specific *DSM-III* adult diagnoses were generated from the interview. Twenty-one (21) subjects were found to have one or more major psychiatric disorders (schizophrenia, bipolar disorders I & II, dysthymia, bulimia, post-traumatic stress disorder, substance abuse, panic disorder, generalized anxiety disorder, and obsessive compulsive disorder); the remaining 20 had no disorder or only minor psychiatric disorders (sexual dysfunction, social phobia, and simple phobia). Only four subjects had been psychiatrically-hospitalized as adults, and only two additional subjects had outpatient treatment; all persons receiving treatment as adults had at least one major psychiatric disorder. Although a majority of subjects had mental illness as adults, no specific childhood psychiatric diagnosis or broader diagnostic category predicted either the *presence or absence* of major adult psychiatric disturbance, specific adult psychiatric diagnosis, or adult diagnostic category.

NR319 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Outcome: Home Based Child Psychiatric Treatment

Edwin J. Mikkelsen, M.D., Mass Mental Health Center, 74 Fenwood Road, Boston, MA 02115; Gerald M. Bereika, Ph.D., Wayne J. Stelk, Ph.D., Julie C. McKenzie, M.Ed.

Summary:

This study reports discharge and one-year follow-up data for a home based program that is designed to be an alternative to psychiatric hospitalization for children and adolescents. The program utilizes the homes of specially trained lay persons (mentors) who work in conjunction with a multidisciplinary treatment team. All subjects were either diverted from or admitted from psychiatric hospitals. Basic demographic data: 43 percent female, 57 percent male, average age 12.6, and average length of stay 16.3 days. Discharge data: N = 122, 91.8 percent planned, 8.2 percent unplanned, 73.8 percent returned to parental home, 14.8 percent to less restrictive settings, 4.9 percent to comparable restrictive settings, and 6.8 percent to more restrictive settings.

One year follow-up results are as follows: N = 70, living with parents 45.7 percent, living with extended family 12.9 percent, living with friends 4.3 percent, residential treatment 17.1 percent, foster care 15.8 percent, other 2.9 percent. A total of 61.4 percent received an average of 7.5 months of outpatient treatment post discharge. Six patients were psychiatrically hospitalized within the year following discharge (48.7 average bed days per patient). These data compare favorably with the results form follow-up studies of psychiatrically hospitalized children and adolescents, which will be reviewed in the presentation.

NR320 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Chronicity in Child Psychiatric Disorders

Atilla Turgay, M.D., Psychiatry, Wayne State University, 951 E. Lafayette, Detroit, MI 48207; Edward Gordon, M.D., Martin Vigdor, Ph.D.

Summary:

This prospective clinical study examined the correlates of treatment resistance and chronicity in 100 consecutive admissions to a residential treatment center in New York State which has an average length of stay greater than two years. They were compared to an age and sex matched group of 100 outpatients who had never had a psychiatric admission, from among consecutively referred patients to an acute care children's hospital. NIMH criteria for "chronicity" and "treatment resistance" in child psychiatric disorders and *DSM-III-R* were used. Seven risk factors were found to be statistically significant ($p < 0.05$-0.0001) in chronic, treatment resistant patients: male gender; older age; the presence of conduct disorder, attention-deficit hyperactivity disorder, and dysthymia; multiple diagnosis; the presence of developmental disorders, speech and language disorders, and chronic pediatric illness; use of psychoactive drugs, (especially two or more drugs); the presence of multiple abnormalities in EEG, and dynamic brain mapping. Strategies for prevention of chronicity and treatment resistance will be outlined in the paper.

NR321 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Major Depression and Dysthymia in Children

Tova Ferro, B.A., Psychology, SUNY at Stony Brook, Stony Brook, NY 11794-2500; Patricia Grayson, Ph.D., Gabrielle A. Carlson, M.D., Daniel N. Klein, Ph.D.

Summary:

The present study attempted to draw distinctions between major depression without dysthymia (MD), dysthymia without major depression (dy), and double depression (Dd) with a sample of 55 child inpatients meeting criteria for either a current MD, dy, or Dd. Best estimate diagnoses were made using information gathered by the Kiddie-Schedule for Affective Disorders and Schizophrenia for School-aged Children, the Social Adjustment Inventory for Children and Adolescents (SAICA), rating scales, and observation on the inpatient unit. Preliminary analyses found differences between groups in comorbidity, suicidality, and impairment of peer and family relationships. Results suggest that the relationship between the three disorders is complex and varies according to the domain under examination. Externalizing disorders were present in 100 percent of the dy group compared to approximately 60 percent in the MD and Dd groups ($X = 7.73$, $p < .02$). On the other hand, a trend found the MD (73 percent) and Dd (80 percent) groups to exhibit more suicidality than the dy group (43 percent) ($X = 5.14$, $p < .08$). An overall analysis of peer relationships was found to be significant ($F = 3.45$, $p < .04$), however post hoc tests revealed no significant differences between groups. Regarding family relationships, the ANOVA was significant ($F = 5.14$, $p < .01$), with the MD group (mean = 1.72; SD = .64) significantly less impaired than both the dy (mean = 2.4; SD = .66) and Dd (mean = 2.2; SD = .46) groups (a score of one on the SAICA indicates mild impairment; two indicates moderate impairment). No differences appeared for demographic variables, other social adjustment scores, or symptomatology. It appears that the presence of a MD plays an important role in the expression of depressive symptomatology, whereas in terms of impairment, chronicity seems to be the determining factor.

NR322 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Axis I/II Disorder and Adolescent Sexual Behavior

Wade C. Myers, M.D., Psychiatry, Univ of Florida, P.O. Box 100234 JHMHC, Gainsville, FL 32610; Roger C. Burket, M.D.

Summary:

This study explores the relationship between psychiatric disorders and adolescent sexual behavior. Forty psychiatrically hospitalized adolescents were evaluated for *DSM-III-R* Axis I and II diagnoses using the Diagnostic Interview for Children and Adolescents, the Schedule for Affective Disorders and Schizophrenia (panic disorder and agoraphobia only), and the Structured Interview for *DSM-II-R* Personality Disorders. A sexual history and behaviors instrument developed by the authors was used to determine type and frequency of sexual activity. Two-thirds (64 percent) of the sample were sexually active. The sexually active subjects, in com-

parison to the sexually abstinent subjects, were more likely to have: 1) conduct disorder (63 percent vs. 33 percent), 2) ADHD (63 percent vs. 33 percent), 3) substance abuse (75 percent vs. 55 percent), 4) passive aggressive personality disorder (63 percent vs. 22 percent), 5) histrionic personality disorder (50 percent vs. 22 percent), and 6) borderline personality disorder (38 percent vs. 22 percent). There was a trend for the sexually active subjects to have more Axis I disorders than the sexually abstinent subjects ($x = 3.4$ vs. $x = 2.6$). There were significantly more Axis II disorders in the sexually active group ($x = 2.7$ vs. $x = 1.2$; $t = 1.26$, $df = 23$, $p = 0.02$). Exploring the relationship between psychopathology and adolescent sexual activity may be useful in: 1) identifying youthful populations involved in high-risk sexual behaviors, 2) developing a better understanding of adolescent psychopathology, and 3) implementing treatment and prevention plans.

NR323 Tuesday May 5, 3:00 p.m.-5:00 p.m.

School Performance and Mental Health in Refugees

Cecile Rousseau, M.D., Psychosocial, Child REsearch Center, 6875 LaSalle Blvd, Verdun QC H4H 1R3, Canada; Aline Drapeau, MS.C., Ellen Corin, Ph.D.

Summary:

Refugees tend not to seek professional help for the emotional problems faced by their children who are at high risk. The previously reported association between school performance and mental health in the general population suggests that refugees' children at risk could be identified within the school system. However, these studies have not accounted for cultural differences which may affect the specificity of preventive measures. The aim of this research was to compare the association between school performance and emotional difficulties for refugees' children from different cultural origins. Subjects were 120 refugees' children, aged 8 to 12, born in Southeast Asia or Central America and living in Montreal. In order to maximize cultural validity, emotional difficulties were evaluated in descriptive (Achenbach's CBCL and Valla's Dominique) rather than diagnostic terms. Results indicate that the relationship between school performance problems and emotional difficulties is stronger for Central American compared to Southeast Asian refugees' children. They also emphasize that refugees are not an homogeneous group and that some ethnic groups may be more stigmatized by their school environment than others.

NR324 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Mood and Altered Immunity in Adolescents

Jacqueline Bartlett, M.D., Psychiatry, UMDNJ Medical School, 185 South Orange Avenue E501, Newark, NJ 07103; Steven Schleifer, M.D., Steven E. Keller, Ph.D.

Summary:

We investigated affective states and immunity in 306 healthy adolescents (mean age 15.9 ± 1.7). A total of 157 were female; 261 African-American, 45 Latino. Affects were assessed using the Ilfeld Psychiatric Symptom Index (**IPSI**) and its subscales [depression (**DEP**), cognitive disturbance (**COG**), anxiety (**ANX**), anger (**ANG**)]. Immune measures included lymphocyte subsets, mitogen response (PHA, ConA, PWM), and NK activity. All analyses controlled for age, gender, and race.

IPSI was associated with decreased activated T cells (F 3.4, $p < 0.05$), ConA (F 6.8, $p < 0.01$), PWM (F 4.0, $p < 0.05$), and PHA (F 4.1, $p < 0.05$). Regressions testing the (highly intercorrelated) individual subscales showed an association of **COG** with decreased ConA (F 7.6, $p < 0.006$), PWM (F 4.3, $p < 0.04$), and PHA (F 3.3, $p < 0.08$), and possibly lower NK activity (F 3.1, $p < 0.08$) and T cells (F 3.1, $p < 0.08$). **ANX** predicted lower ConA (F 9.9, $p < 0.002$), PHA (F 4.2, $p < 0.04$), and PWM (F 3.0, $p < 0.09$), and lower activated T cells (F 3.6, $p < 0.06$). **ANG** predicted lower ConA (F 5.9, p lt 0.02), PWM (F 5.4, $p < 0.02$), and PHA (F 4.2, $p < 0.04$). **DEP** did not predict any immune measures. The above associations, with exception of **COG** effects on NK activity (F 5.4, $p < 0.02$), were no longer found when all four subscales were entered into the same model.

These findings in a nonpatient sample suggest the presence of specific and nonspecific immune changes in relation to affective disturbances in adolescents.

NR325 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Psychopathology and Outcome in Juvenile Offenders

Hans Steiner, M.D., Child Psychiatry, Stanford University, 750 Welch Road, Palo Alto, CA 94304; William Huckaby, Ph.D.

Summary:

Incarceration of juvenile offenders represents a unique opportunity for treatment and prevention of recidivism and cost to society. While predictive studies have been done on adult offenders, it is uncertain which variables best predict adolescent adjustment to incarceration, facilitate ward participation in education and therapeutic programs, and predict recidivism.

A total of 400 wards were studied at baseline and at various stages of follow-up (mean age: 16 +/−1.2 years; average length of stay: 461 +/−368 days; mean length of commitment: 983 +/−632 days; 44 percent white, 28.5 percent black, 22 percent Hispanic, 5.5 percent other). Instruments included: standard psychiatric examinations, yielding *DSM-III-R* diagnoses; interviews covering drug abuse; observer and self-report ratings of adaptive variables including distress, restraint, and defensiveness (based on Weinberger's typology). Cross-sectional regression analyses suggest that reduction of distress and increase of repressive defensiveness are significant determinants of restraint. Short length of stay and repressive defensiveness related positively to successful adaptation to incarceration. Restraint significantly predicted lower mean reoffense ratio and less severe crimes committed at follow-up. Intensity and chronicity of drug abuse had no predictive value. These findings suggest novel diagnostic and treatment approaches and have implications for the study of adaptation in adolescents.

NR326 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Evidence That D2 Dopamine Receptor Alleles Do Not Influence Severity of Tourette's Syndrome

Joel Gelernter, M.D., Psychiatry, 116A, Yale Univ Sch of Med, 950 Campbell Avenue, West Haven, CT 06516; David Pauls, Ph.D., James Leckman, M.D., Kenneth K. Kidd, Ph.D., Roger Kurlan, M.D.

Summary:

It has recently been proposed that the A1 allele of the TaqI polymorphic system at the D_2 dopamine receptor gene (DRD2) either predisposes to alcoholism or influences its severity; evidence against this hypothesis has also been presented by ourselves and others. Comings et al. (1991; *JAMA* 266:1793-1800) have also suggested that this same allele influences the severity of Tourette syndrome (TS), a claim based on an observed increase in A1 carrier frequency among severe TS patients compared to controls and less severe TS patients. We have previously demonstrated that DRD2 is not linked to TS, establishing that it cannot be the major locus determining whether one gets TS.

If DRD2 influences the severity of TS, then among affected family members, those with the A1 allele should have more severe disease than those without it. We studied DRD2 alleles in patients with TS or chronic multiple tics (CMT) in four extended kindreds

segregating TS. (CMT is considered a less severe manifestation of the same genetic liability which may give rise to TS.) Individuals from one of these kindreds had already been typed for our earlier linkage study. We evaluated severity in two ways. First, considering the whole sample (59 individuals with TS and 22 with CMT), we studied allele frequency by diagnosis. A1 allele frequency in the TS group was 0.27; in the CMT group it was 0.18 ($\chi^2 = 0.94$, $p < 0.33$: NS). (As these individuals were related, these figures are not directly comparable with population figures.) Second, we evaluated a subset of the sample using a derivative of the Yale Global Tic Severity Scale composed of subscales concerning number, frequency, and severity of motor and phonic tics, rated separately. We divided this sample (N = 17, 9 with TS, 8 with CMT) by presence or absence of the A1 allele. The A1 carriers (N = 7; all heterozygotes) had an average severity score of 11.3; the A2 homozygotes had an average severity score of 14.2. These data do not support DRD2 alleles as a factor for severity of TS.

NR327 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Segregation Analysis of ADD

Stephen V. Faraone, Ph.D., Child Psychiatry, Mass General Hospital, ACC-725 15 Parkman Street, Boston, MA 02135; Joseph Biederman, M.D., Wei Chen, M.D., Belinda R. Krifcher, B.A., Kate Keenan, B.A., Cindy Moore, B.A.

Summary:

Although family, twin, and adoption studies suggest that genetic factors are involved in attention deficit hyperactivity disorder, further evidence is needed to demonstrate that its familial transmission is consistent with known genetic mechanisms. We applied segregation analysis to a sample of 257 children and their 808 first degree relatives. Interviews of subjects with *DSM-III-R*-based structured interviews provided the basis for psychiatric diagnosis. We analyzed these family data with the mixed model, as implemented in the computer program POINTER and a Class A regressive logistic model as implemented in the computer program REGTL. our results indicate that the familial distribution of *DSM-III-R* attention deficit hyperactivity disorder can be attributed to the effects of a single major gene. We can reject multifactorial polygenic transmission, nonfamilial environmental transmission, and cultural transmission.

NR328 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Adolescent Sex Offenders: Admitters and Deniers

Diane K. Shrier, M.D., Psychiatry, UMDNJ-NJ Med. School, 215 South Orange Avenue, Newark, NJ 07103; Robert L. Johnson, M.D.

Summary:

Data are reported on 54 adolescents accused of a sexual offense (rape or aggravated sexual assault). Twenty-five (46.9 percent) admitted to having committed the offense, while 29 (53.7 percent) denied the offense. The entire sample and each subgroup (admitters and deniers) were compared to a nonoffending control sample of 33 adolescents matched by age and race. The 54 adolescent offenders were referred from family court to an adolescent medicine clinic for medical and psychosocial assessment and triaged for counseling, referral for mental health services, or out of home interventions. The offenders were given a three part computer-coded form: 1) demographics, school history, family information, peer relationships, psychiatric and juvenile justice history, alcohol and drug use history; 2) sexual history, including sexual molestation experiences; 3) history of the specific offense(s). The control sample completed parts one and two of the form. Few differences were noted between the controls and offenders except that offenders had fewer friends, began sexual activity at an earlier age, and were less likely to use birth control. Significant differences between the admitters and deniers and between each subgroup and the controls are presented and discussed.

NR329 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Clomipramine for Chronic Stereotypy/Self-Injury

H. Jordan Garber, M.D., Psychiatry, Allegheny General Hosp., Allegheny Neuropsych Inst., Oakdale, PA 15071; John J. McGonigle, Ph.D., Gregory T. Slomka, Ph.D., Edith Monteverde, B.A.

Summary:

Self-injurious and stereotypic behaviors often cause physical complications in patients with developmental disabilities. Features of anxiety and similarities to compulsions led to our open trial of clomipramine in 11 consecutive referrals (ages 10-20, mean [sd] = 15 [3.6]; ten males, one female) for chronic stereotypic or self-injurious behaviors (duration 1-10 years, mean [sd] = 9.3 [5.9]. Findings included acute (lacerations, contusions) and chronic (unhealed fracture, callous formation) injuries; four and noninjurious stereotypy. Behaviors limited self-care, education or socialization, with > daily frequency, and required physical restraint (e.g. head banging, aggressive tantrums). Mental retardation was present in ten patients (three moderate, two severe, five profound); four had infantile autism, two had cerebral palsy, and six had prior epileptic events. Clomipramine started at 25 mg/day was increased to a maximum of 3 mg/kg/day, based on improvement (range 25-125 mg/day, mean [sd] = 70 [37]). Behavioral management remained constant; patients on lithium or anticonvulsants had unchanged blood levels. Responses to clomipramine were determined from changes in observed frequencies of each target behavior, with lengths of follow-up from one month to one year. A total of 10/11 patients (91 percent) had > 50 percent decreases in frequencies of all target behaviors; three had > 90 percent decreases in all target behaviors; three with other-directed aggression had > 90 percent decreases in frequency of aggression. No seizures or cardiovascular complications occurred. Hypomania, sedation, constipation, and eneuresis were managed with dosage reduction, lithium, or fluoxetine substitution.

NR330 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Anabolic Steroids: Dosage and Psychiatric Effects

Donald A. Malone, Jr., M.D., Psychiatry, Cleveland Clinic, 9500 Euclid Ave. Desk P68, Cleveland, OH 44195; Robert J. Dimeff, M.D.

Summary:

Anabolic steroid (AS) use has only recently been found to be common among athletes. Psychiatric side effects to these agents have recently been reported, and the question of whether AS can produce dependence is controversial. A total of 164 bodybuilders were given a Scheduled Clinical Interview for *DSM-III-R* (SCID), a Buss-Durkee Hostility Index (BDHI), and a Symptom Checklist 90R (SCL-90R). Also obtained were AS use history, AS dependence status according to *DSM-III-R,* and urine toxicology results. A total of 31 subjects tested positive for AS use of which accurate dosages were obtained for 28. Testosterone dosage equivalents were determined for other AS by utilizing anabolic potency. Regardless of the cutoff point used, dosage categories did not differ in scores on the SCL Global Severity Index (Wilcoxon p-value > 0.05), SCL Hostility Subscale ($p > 0.05$), or BDHI total score ($p > 0.05$). Dosage categories also did not differ with regards to their likelihood for steroid dependence (Fisher's exact p-value > 0.05). In addition, dosage categories did not differ with regard to psychiatric diagnoses (exact chi-square p-value > 0.05). Non-AS user controls did not differ significantly form current AS users with regard to psychi-

atric diagnosis or psychological test scores. In conclusion, the dose of AS used does not appear to predispose AS users to a greater likelihood of psychiatric symptomatology or AS dependence at commonly used dosages.

NR331 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Naltrexone in the Treatment of Alcohol Dependence

Joseph R. Volpicelli, M.D. Psychiatry, University of Penn., 3900 Chestnut Street 6178, Philadelphia, PA 19104; Bruce J. Berg, M.D., Arthur I. Alterman, Ph.D., Motoi Hayashida, M.D., Charles P. O'Brien, M.D.

Summary:

Recent reviews of alcohol rehabilitation programs report that relapse rates often exceed 50 percent within the first three months after beginning intensive inpatient or residential treatment. The high relapse rate has prompted a search for pharmacological agents that may act as an adjunct to psychosocial alcohol rehabilitation programs.

A new pharmacological approach to the treatment of alcoholism is suggested by biochemical and behavioral studies demonstrating an interaction between alcohol and opiates. Several animal studies have shown that opiate antagonists such as naltrexone or naloxone will decrease alcohol drinking. The data suggest that naltrexone may be a helpful adjunct in reducing alcohol drinking and loss of control over alcohol drinking.

In our study involving 70 alcohol dependent male veterans, naltrexone decreased craving, mean drinking days, and relapse rates. It seemed to be particularly effective in decreasing drinking in subjects who had at least one slip, that is, naltrexone helped stop the "loss of control" over drinking observed among placebo-treated subjects. In addition, naltrexone was well tolerated with few side effects and no deleterious effects on mood and psychopathology.

In summary, our study provides preliminary support to the clinical utility of naltrexone as an adjunct to the treatment of alcohol dependence and supports the hypothesis that alcohol is reinforcing in part because of its effects on opioid systems.

NR332 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Pergolide, Bromocriptine Trial in Cocaine Addicts

Robert Malcolm, M.D., Psychiatry, Med. Univ of S.C., 171 Ashley Avenue, Charleston, SC 29425; Joem Phillips, PAC; Kathleen Brady, M.D.

Summary:

Preliminary investigations have indicated that dopamine agonists (DAs) may be useful in the treatment of cocaine withdrawal. The present study is an open label comparison of three treatment conditions: pergolide, a selective DA, minimally studied for use in cocaine withdrawal; bromocriptine; and a no medication group. Males and nonpregnant females between the ages of 21 and 50 enrolled in a 30-day treatment program for substance abuse who met *DSM-III-R* criteria for cocaine dependence were studied. Exclusion criteria included alcohol, sedative, or opioid withdrawal requiring treatment. Treatment groups were compared for mean length of stay in hospital (MLS), number of discharges against medical advice (AMA), and on a self-report Visual Analog Craving Scale prior to treatment and again between days 7 and 10. The pergolide group had MLS of 25.1 days with one AMA discharge (6 percent). The bromocriptine group had a MLS of 26.4 days with one AMA discharge (6 percent). The no medication group had a MLS of 16.2 days with four of 11 (36 percent) AMA discharges. T-test comparisons between both pergolide and no medication MLS ($t = 3.44$, $p \leq 0.002$) and bromocriptine and no medication MLS ($t = 2.83$, $p \geq 0.009$) indicated significant differences. One factor ANOVA indicated a between group significant difference in craving scores ($df = 2$, $F = 5.697$, $p = 0.008$). Mean change in craving scores in the pergolide group was 31.8, in the bromocriptine group was 24.0, and in the no medication group was 7.9 Using a Scheffe F test, the pergolide change scores were significantly greater than either bromocriptine or no medication group ($p \geq 0.05$). In summary, both DAs appeared to have a highly significant clinical effect on lengthening hospital stay and reducing AMA discharges when compared with no medication. There is evidence that pergolide may have been most effective in reducing craving. This latter finding is suggestive only, since baseline craving scores differed across groups.

NR333 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Ethanol Blood Levels in Older versus Younger Males

Thomas P. Beresford, M.D., Psychiatry, Univ of Michigan, 400 E. Eisenhower Ste. A, Ann Arbor, MI 48104; Michael Lucey, M.D., Linda Demo-Dananberg, B.S.N., Katherine Harris, B.A., Kimberly Brown, M.D.

Summary:

Previous research suggests that older persons reach higher blood alcohol levels than do younger persons owing to the decreased volume of distribution seen in the elderly as total body water decreases. This view was based on only one study, however, and did not take route of administration into account. We administered ethanol (0.3 gm/kg body weight) to 12 older (>60 years) and 12 younger (<40 years) non-alcoholic, adult males and measured serial blood levels of ethanol over the next three hours. The ethanol was given on three occasions: intravenously, and orally both in a fed and in a fasted state. We then measured the areas under the curves for a statistical comparison of the two age groups. While the older men achieved slightly higher blood levels in all three states, there was no statistical difference between the two age groups in the comparisons of the areas under the three curves. This finding was contrary to previous knowledge. AT the same time, route of administration made no difference when comparing the two age groups. These data suggest that the lessened drinking reported for elderly persons may have more to do with decreased central nervous system tolerance or with an increased acute sensitivity to ethanol rather than with an altered pattern of ethanol distribution.

NR334 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Decreased Tolerance to Ethanol Related to Age

Thomas P. Beresford, M.D., Psychiatry, Univ of Michigan, 400 E. Eisenhower Ste. A, Ann Arbor, MI 48104; Linda Demo-Dananberg, B.S.N., Katherine Harris, B.A., Kimberly Brown, M.D., Michael Lucy, M.D.

Summary:

Longitudinal studies have noted that drinking decreases with age. To the best of our knowledge, however, there have been no studies on the mechanism of this phenomenon. We administered the equivalent of two drinks (0.3 gm ethanol/kg body weight) to 12 older (>60 years) and 12 younger (<40 years) non-alcoholic, adult males. The ethanol was given on three separate days, first intravenously, and then orally first in a fed and then in a fasted state. Resulting blood alcohol values did not differentiate the two groups. Simultaneously, we measured a series of intoxication parameters in order to assess the effects of ethanol in the two age groups. These included measures of gait and balance, of reaction time, of a series of cognitive challenges such as rotatable letters and picture identification, and of subjective moods states. These were administered at baseline, at 30 minutes (the peak ethanol concentration), and at 100 minutes (midway down the ethanol decay curve). Baseline responses to most measures were similar between the two

groups. Peak responses showed a greater change from baseline for the younger subjects. By contrast, however, the elderly subjects usually failed to return to baseline on most measures during the recovery period. Differences among the latter were most striking for measures of gait, reaction time and the subjective sensation of fatigue; these were statistically significant. These data suggest 1) that elderly drinkers are less resilient to the acute effects of ethyl alcohol and 2) that younger drinkers, with greater changes from baseline and significantly more rapid recovery, demonstrate a significantly greater acute tolerance to the effects of ethanol. Understanding the mechanism for this age related change may shed light on the mechanism(s) of alcohol tolerance more generally.

NR335 Tuesday May 5, 3:00 p.m.-5:00 p.m.

A New Elderly Specific Screening Test: (MAST-G) Michigan Alcoholism Screening Test

Frederic C. Blow, Ph.D., Psychiatry, Univ of Michigan, 400 E. Eisenhower Ste. A, Ann Arbor, MI 48104; Kirk J. Brower, M.D., John Schulenberg, Ph.D., Linda Demo-Dananberg, B.S.N., James P. Young, M.S., Thomas P. Beresford, M.D.

Summary:

Current screening instruments have been shown to do poorly in identifying alcoholism among older adults. We developed a new screening instrument to address this clinical need. Items were developed based on a literature review of alcoholism among the elderly, a critique by a panel of alcoholism treatment professionals, and a focus group discussion by recovering older alcoholics. The 94 items of the initial instrument were tested on a heterogeneous sample of 840 older adults. The preliminary Michigan Alcoholism Screening Test (MAST-G) was then reduced using a combination of item and factor analysis. The reduced instrument, consisting of 32 items, was refined using a stratified sample of 305 elderly subjects that included five groups: 1) those currently meeting criteria for alcohol dependence, but not in treatment; 2) those currently in treatment for alcoholism, 3) those with a previous history of alcoholism and currently in recovery, 4) social drinkers, and 5) abstainers. The diagnosis of alcohol dependence (DSM-III-R) was used as the validation standard. This process yielded a final version of 24 items. Psychometric properties of this new instrument are superior to other screening tests for identification of elderly alcoholics. The MAST-G has a sensitivity of 93.9 percent, specificity of 78.1 percent, positive predictive value of 87.2 percent, and negative predictive value of 88.9 percent. In addition, factor analysis identified five underlying symptom domains: Loss and Loneliness, Relaxation, Dependence, Loss of Control with Drinking, and Rule-Making. To our knowledge, the MAST-G is the first elderly-specific alcoholism screening measure to be developed with items unique to older problem drinkers.

NR336 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Location of Inpatients with Comorbid Disorders

Frederic C. Blow, Ph.D., Psychiatry, Univ of Michigan, 400 E. Eisenhower Ste. A, Ann Arbor, MI 48104; Brenda Booth, Ph.D., Cynthia Cook, Ph.D., J.C. Fortney, M.A.

Summary:

Previous reports have indicated that both the frequency of alcoholism comorbidity among patients with psychiatric disorders and, conversely, the frequency of psychiatric comorbidity among patients with alcoholism, varies depending on whether patients are treated in a general psychiatric or in an alcoholism setting. This study included 68,337 primary psychiatric and 67,433 primary alcoholism inpatients admitted to VA Medical Centers nationwide during fiscal year 1990. Data were obtained from the VA database, the patient treatment file. Of those patients admitted with a primary psychiatric diagnosis, 15.2 percent had a secondary diagnosis of substance abuse; of those with a primary diagnosis of substance abuse, 21.7 percent had a secondary psychiatric diagnosis. Not surprisingly, specific concurrent diagnoses varied depending on primary diagnosis. A secondary diagnosis of alcohol dependence was listed most frequently for those patients admitted primarily for schizophrenia (28.9 percent), major depression 919.1 percent), bipolar disorder (11.8 percent), and psychosis (10.3 percent). In contrast, of those admitted with a primary diagnosis of alcoholism, relatively few had a secondary diagnosis of schizophrenia or other psychosis (6.8 percent and 2.3 percent, respectively), somewhat more had a secondary diagnosis of bipolar disorder (5.8 percent), but a quarter (25.2 percent) had a secondary diagnosis of major depression. Because patients included in this study were not admitted for inpatient treatment of the secondary diagnosis anytime during the year of the study, it is highly probable that many with comorbid disorders did not receive timely treatment of their secondary diagnosis. Results of this study suggest possible differences in admissions policies and that patients with comorbid conditions may not be receiving needed treatment.

NR337 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Effect of Alcoholism Comorbidity on Depression

Timothy I. Mueller, M.D., Psychiatry, Brown University, Duncan Bldg 345 Blackstone Blvd, Providence, RI 02906; Philip W. Lavori, Ph.D., Martin B. Keller, M.D.

Summary:

The NIMH-Collaborative Depression Study has prospectively followed a cohort of 616 treatment seeking subjects with RDC major depressive disorder (MDD) from five centers in the United Sates for up to 13 years. Twenty-five percent (151 total) of this sample had a lifetime diagnosis of alcoholism at intake in addition to depression. All subjects were assessed for activity of alcoholism during the follow-up. The interplay of the alcoholism activity and the MDD course was evaluated in the 151 subjects who had both diagnoses compared tot he 465 who had MDD only. This was accomplished through an analysis of the week by week transitions from one level of psychopathology (MDD) to another level conditioned on the activity of alcoholism. For the ten years of analyzed data, alcoholism activity increased the transitions to more severe MDD and decreased the transitions to less severe MDD. Subjects who had recovered from active alcoholism behaved similarly to subjects who had no lifetime diagnosis of alcoholism in term of worsening of MDD. However, they showed greater improvement in MDD than subjects who had MDD alone. These data have implications for treatment of and research with people with co-morbid depression and alcoholism.

NR338 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Subject Ratings and Catecholamines During Intravenous Cocaine

Jeffery N. Wilkins, M.D., VAMC Brentwood 116A2, Wilshire & Sawtelle Blvds, Los Angeles, CA 90073; Koonlawee Nademanee, M.D.; David Setoda, B.S., James Gaffield, B.S., Martin A. Josephson, M.D.

Summary:

Three subjects meeting *DSM-III-R* criteria for cocaine dependence received randomized, double-blind infusions of saline, 30, 60, or 90 mg cocaine in the West Los Angeles VAMC Clinical Research Center. The infusions were conducted as part of a study investigating the effects of cocaine on cardiovascular function. Serial venous plasma samples were collected, stored at −70°C, and assayed for cocaine (Coc), dopamine (DA), norepinephrine (NE), epinephrine (Epi), cortisol, and prolactin (HPrl). High pressure liq-

uid chromatography with electrochemical detection was used for catecholamine analysis, and radioimmunoassay was used for hormone analysis. During the first two hours post infusion, the subjects were interviewed using Likert scales for "high" and "craving". **Results:** Cocaine "high" was maximal for all subjects during the 90 mg condition, minimal to moderate during the 60 mg condition, and negative during the 30 mg and saline conditions. Peak "high" ratings occurred at two minutes post infusion and corresponded to peak Coc levels. DA levels increased 100 percent to 200 percent from baseline (with peak values at 8 minutes) in all subjects at 60 mg, and 40 percent and 400 percent from baseline in two subjects at 90 mg; no DA changes were seen in the 30 mg and saline conditions. Circulating Epi followed a pattern identical to DA. The one subject who did not manifest DA and Epi response to 90 mg cocaine reported maximal craving at 15 minutes. This subject's HPrl increased by 150 percent by 30 minutes, which contrasted with the 80 percent decrease in HPrl seen in the subject who had a 400 percent DA increase. Cortisol was stimulated in all subjects from 100 percent to 400 percent at 30 minutes after the 90 mg and 60 mg infusion. These preliminary results suggest interactions between the subjective experience of cocaine euphoria and measures of plasma Coc, DA, Epi, and cortisol in cocaine-dependent subjects.

NR339 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Schizophrenia and Substance Abuse Typology

Richard N. Rosenthal, M.D., Psychiatry, Beth Israel Med Center, First Avenue at 16th Street, New York, NY 10003; David J. Hellerstein, M.D., Christian Miner, Ph.D.

Summary:

Two weeks after admission to an inpatient dual-diagnosis psychiatric unit, data were collected on 30 patients who met SADS-RDC criteria for schizophrenia or schizoaffective disorder, but also had concurrent addictive disorders. Twenty-nine patients abused cocaine (M = 5.0 yrs; sd = 4.8), 26 abused marijuana (M = 11.6 yrs; sd = 8.3), and 28 abused alcohol (M = 12.6 yrs; sd = 8.3). Most (76.6 percent) had prior substance abuse treatment. Most had never worked, and almost all (90.0 percent) fell into Hollingshead's "unskilled" category. Patients had M = 9.9 years since the onset of schizophrenia (sd = 5.7). Most (86.7 percent) were rated as markedly disturbed on at least one SANS or SAPS subscale. Eight patients (26.7 percent) met criteria[1] for the negative syndrome and five (16.7 percent) had the positive syndrome. A very high proportion (56.7 percent) of patients presented with mixed syndromes, compared with 34.6 percent of Andreasen and Olsen's[1] original Iowa sample (z = 1.97; p .05, two-tailed). A significant relationship exists between syndrome type and years post-onset [1-way ANOVA, F = 6.78; df = (2,26); p = .003], but in contrast with non-addicted schizophrenics[2], addicted patients with the negative syndrome had fewer years post-onset than those with mixed (Tukey HSD, p = .015) or positive (Tukey HSD, p = .007) syndrome. Discussion will focus upon the implications for treatment and prognosis of dually-diagnosed schizophrenics.

NR340 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Personality Disorders and Multiple Substance Use

Michael O'Boyle, M.D., Psychiatry, Univ of Texas Med Branch, D 29, Galveston, TX 77550; Adel A. Wassef, M.D., Laurence R. Schweitzer, M.D.

Summary:

DSM-III-R personality disorder diagnoses of individuals meeting criteria for multiple substance dependence were compared to those dependent on a single substance. Ninety-nine subjects in a substance abuse treatment program received *DSM-III-R* axis I diagnoses by structured interview (SCID-P). Fifty-eight had a history of multiple substance dependence, 41 of dependence on a single substance. Those dependent on multiple substances were more likely to receive additional axis I diagnoses such as major depression. To control for the effect of these disorders on personality measures, 29 subjects with current axis I diagnoses in addition to substance dependence were excluded from the personality analysis. Subjects completed the Personality Disorder Questionnaire Revised (PDQ-R), which yielded *DSM-III-R* axis II personality disorder diagnoses. Fifty-seven of the 70 remaining subjects received at least one personality disorder diagnosis. While personality disorder diagnoses were common in both groups, multiply dependent subjects were significantly more likely to receive dramatic cluster diagnoses, especially those of borderline or antisocial personality disorder. The results are consistent with the idea that multiple substance dependence is associated with greater personality pathology within the dramatic cluster.

NR341 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Sleep, Depression and Aging in Alcoholics

James E. Shipley, M.D., Psychiatry, University of Michigan, 1500 East Medical Ctr Drive, Ann Arbor, MI 48109; Michael Aldrich, M.D., Philip Kroll, M.D., Rajiv Tandon, M.D., Kirk Brower, M.D.

Summary:

Sleep complaints are prominent in alcoholics, but the pathophysiology of these changes is not well understood. We studied 46 alcoholics by DIS after a two-week drug free period. On night 1, eight of 40 patients (20 percent) had an apnea + hypopnea index $\geq$ 10 events/h. These were older (50.8 vs. 39.8 y, $p < .01$), but they did not show evidence of excessive sleepiness, having a sleep latency of 61.0 vs. 44.8 min (NS). Among all patients having any scorable obstructive apnea-hypopnea events, we found that increased age was associated with an increase in the sum of obstructive apneas and hypopneas, and also with an increase in the amount of time spent in such events. On night 2, 38 nonapneic alcoholics had consistently impaired sleep continuity and lighter sleep than 20 controls. REM latency was shorter in the patients (46.8 vs. 66.4 min, $p < .05$) and REM percent was increased (25.1 vs. 21.1, $p < .05$), but they did not differ in REM activity or REM density. Age and REM latency were negatively correlated in both controls ($r = -0.47$, $p < .05$) and patients ($r = -0.39$, $p < .05$). Controls tended to have stronger correlations between age and various measures of sleep depth and quality. This may be due to "premature aging" in alcoholics, resulting in consistently poor sleep in patients regardless of age. Patients tended to show positive correlations between age and REM percent ($r = 0.34$, $p < .05$), REM activity ($r = 0.40$, $p < .05$) and REM density ($r = 0.31$, $p < .06$), while controls did not. Sleep variables were not predictive of whether patients would maintain sobriety vs. relapse as assessed after a mean of 5.3 months post-sleep.

Alcoholism may include an increased risk for mild sleep apnea, especially in the older patient. The findings of shortened REM latency, increased REM percent, and a disease-specific association of age with increased REM pressure suggest potential overlap with the pathophysiology of major depression.

NR342 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Familial Alcoholism in Schizophrenia versus Schizotypy

Leonard Handelsman, M.D., Psychiatry, VA Medical Center, 130 West Kingsbridge Road, Bronx, NY 10468; Jeremy Silverman, Ph.D., David P. Bernstein, Ph.D., Larry J. Siever, M.D., Kenneth L. Davis, M.D.

Summary:

Phenomenological psychophysiological, and family genetic evidence links schizotypal personality disorder (SPD) to schizophrenia. We examined the possibility that the presence of familial alcoholism, but not the manifest expression of alcoholism or addiction in probands, is a risk factor for having schizophrenia rather than SPD. Psychiatric (and addictive) histories of parents and siblings (over 18) of SADS/RDC-determined schizophrenics (relatives = 744) and of SIDP-determined SPDs (relatives = 83) and other personality disorders (PDs) (relatives = 199) were ascertained by FH-RDC criteria using the family history method with the ratings and final consensus made blind to proband information. Schizophrenic probands had no lifetime alcohol or drug abuse. PD probands were included with lifetime but not current abuse. The risk of alcoholism in relatives of the nonalcoholic, non-addict schizophrenics was higher than in relatives of the SPD probands (morbid risk = 0.135 vs. 0.052, $Z = 2.06$, $p < .05$), but slightly lower than in relatives of probands with other PDs (morbid risk = 0.135 vs. 0.157, $Z = -0.76$, NS). The pattern of comorbid PD's cannot explain the findings. Familial alcoholism, or a factor for which it is a proxy, may be a "second-hit" which converts a vulnerability for SPD into schizophrenia. The possible confounding effects of familial alcoholism on familial studies of schizophrenia spectrum disorders will be discussed.

NR343 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Cocaine Precipitation of Opiate Withdrawal

Susan M. Stine, M.D., Psychiatry, VA Medical Center, 960 Campbell Avenue, West Haven, CT 06516; Sally Satel, M.D.

Summary:

In our clinical programs we observed that many opiate addicts reported typical opiate abstinence symptoms after using cocaine. In order to study this phenomenon, we constructed a 16-item, clinician-administered questionnaire to evaluate opiate withdrawal symptoms that are precipitated by cocaine. The 29 subjects were 93 percent male, 50 percent black, and had an average age of 38. Most subjects had experienced opiate withdrawal after cocaine use (79 percent), although they were not in opiate withdrawal while using the cocaine. Of those already in mild opiate withdrawal, 35 percent stated that cocaine relieved opiate withdrawal and that relief occurred only while they were high from the cocaine administration and lasted ½to one hour. After this period opiate withdrawal symptoms were even more severe than those usually experienced. Thus, this effect appears to be one of cocaine-induced euphoria, masking opiate withdrawal rather than relief of withdrawal itself. The interaction of cocaine and opiates is highly significant for clinical treatment programs. We conclude that cocaine precipitates and/or exacerbates opiate withdrawal symptoms. This work is continuing and data from a larger sample size will be presented. These results will be discussed in terms of the specific symptoms reported, time interval between opiate and cocaine use, and possible neurobiological explanations for this observation.

NR344 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Panic Disorder with Comorbid Alcohol Abuse

Juan M. Segui, M.D., Psiquiatria, Hospital Alianza, Virgen De Monserrat 193bis, Barcelona 3o3a 08011, Spain; Luis C. Salvador, M.D., Jaume Canet, Ph.D., Carmen Aragon, Ph.D., Christian Y. Herrera, M.D.

Summary:

INTRODUCTION: There is a relationship between panic disorder (PD) and alcohol abuse/dependence (AA/D). Alcohol problems appear in 7 percent to 35 percent of patients with PD (Kushner et al, 1990).

MATERIAL & METHODS: A total of 148 patients with *DSM-III-R* criteria for PD were consecutively assessed with the SCID-P, ASI subscale for alcoholism, Hamilton ANxiety and Depression scales, PASS, RDC family history, Marks' Social Phobia scale, SCL-90, EPQ, and GAS.

RESULTS: A total of 18.90 percent of PD had alcohol problems. A total of 10.1 percent fulfilled criteria for AA and 8.8 percent fulfilled criteria for AD. PD appears after AA/D in 78.6 percent of this subgroup of patients. The age of onset was 19.9 ± 6.19 years for AA/D and 26.9 ± 9.58 for PD. The PD patients with AA/D (AA/D + PD) presented the following characteristics when they were compared with the rest of PD patients: 1). Higher rate of males ($p > 0.001$). 2) Family history of AD ($p > 0.05$). 3) Higher global clinical severity ($p > 0.001$). 4) Higher consume of the following substances; tobacco ($p > 0.001$), caffeine ($p > 0.01$), cocaine ($p > 0.001$), and cannabis ($p > 0.01$). 5) WOrsening of panic attacks with alcohol ($p > 0.01$). 6) Higher introversion ($p > 0.05$).

NR345 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Alcohol Dependence with Comorbid Panic Disorder

Juan M. Segui, M.D., Psiquiatria, Hospital Alianza, Virgen De Monserrat 193bis, Barcelona 3o3a 08011, Spain; Luis C. Salvador, M.D., Jaume Canet, Ph.D., Carmen Aragon, Ph.D., Christian Y. Herrera, M.D.

Summary:

INTRODUCTION: There is a relationship between alcohol dependence (AD) and panic disorder (PD) (Kushner et al, 1990). According to the prevalence studies, PD is present in 4.8 percent to 38 percent of patients with AD.

MATERIAL & METHODS: One hundred patients with *DSM-III-R* criteria for AD were consecutively assessed with the SCID-P, ASI interview, a semi-structured interview for alcoholism, RDC family history, and GAS.

RESULTS: Twenty-seven percent of AD patients presented PD. The former was prior to AD in 22 percent of the patients. The age of onset was 17.94 ± 9.04 years for AD and 27.69 ± 8.99 for PD. A total of 70.4 percent referred a worsening of panic attacks with alcohol. The AD patients with PD (AD + PD) presented the following characteristics when they were compared with the rest of AD patients: 1) Family history of PD ($p > 0.05$). 2) Older age when first treated for AD ($p > 0.05$). 3) Higher academic level ($p > 0.01$). 4) Poorer general functioning ($p > 0.01$) and clinical severity ($p > 0.001$). 5) Higher comorbidity with mood disorders ($p > 0.01$) mainly dysthimic disorder ($p > 0.001$).

NR346 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Fluoxetine and Counseling in Cocaine Abuse

Lino Covi, M.D., NIDA ARC, P.O. Box 5180, Baltimore, MD 21224; Judy M. Hess, M.A., Charles A. Haertzen, Ph.D., Jerome J. Jaffe, M.D.

Summary:

In a double-blind, randomized, placebo-controlled trial of 12 weeks duration, single drug cocaine abuses were treated on a three times a week outpatient visit schedule. At each visit they were interviewed regarding drug usage and observed urines obtained and analyzed for drugs of abuse. Weekly, a variety of inventories and scales were administered. Treatment consisted of 50 minutes, twice a week, individual interpersonal counseling by Master's level counselors and double-blind assignment to one of three dosage levels of fluoxetine (20, 40, or 60 mg) or active placebo (diphenylhydramine 12.5 mg). Sixty-two subjects began the study, but only 34 were sufficiently compliant to permit valid comparisons.

Fourteen of these were on placebo, ten achieved a blood level of fluoxetine/norfluoxetine above 100 ng/ml and, another ten a blood level of fluoxetine/norfluoxetine below 100 ng/ml. Analyses of variance for repeated measures showed significant improvement over time in all treatment groups for the measures of amount of cocaine use, urine positivity for drugs of abuse, and cravings. However, differences were found in mood measures favoring fluoxetine. These results are interpreted as indicating a strong effect of counseling and no additional effects of fluoxetine treatment.

NR347 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Dopamine Receptor MRNA in Prenatal Cocaine Exposure

Andrea De Bartolomeis, M.D., ETB, NIMH, 9000 Rockville Pike, Bethesda, MD 20892; Mark C. Austin, Ph.D., Linda P. Spear, Ph.D., David Pickar, M.D., Jacqueline N. Crawley, Ph.D.

Summary:

Clinical studies of infants born to mothers who used cocaine during pregnancy suggest that in utero exposure to this drug may result in behavioral and neurological abnormalities.

Animal models of gestational cocaine exposure point toward the involvement of the dopaminergic system, e.g. an increase of striatal D2 receptor binding. We investigated the effects of prenatal cocaine exposure on messenger RNA for striatal dopamine receptors.

Pregnant Sprague-Dawley rats were treated on gestational days 8 to 20 with daily subcutaneous injection of cocaine hydrochloride 40 mg/kg/3cc; daily subcutaneous injection of 0.9 percent saline and feeding paired to cocaine group; or no injection and ad libitum access to lab chow.

Offspring were sacrificed at postnatal day 21. In situ hybridization histochemistry using cDNA oligonucleotide probes for D1 and D2 receptors was carried out on 12 μ brain sections from anterior to posterior caudate nucleus and nucleus accumbens. Computerized analysis of the autoradiographic images demonstrate no significant differences in mRNA concentrations in any of the areas quantitated among the experimental groups. This finding suggests that the reported increase in D2 receptor binding after prenatal cocaine may not be the result of an increase in gene transcription, but rather that a different molecular mechanism may be responsible for upregulation of this receptor. Other dopaminergic and nondopaminergic mechanisms may mediate the behavioral and neurological abnormalities associated with the prenatal cocaine syndrome in rodent models.

NR348 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Comorbidity of Alcoholism and Depression in Smokers

Kathleen N. Franco, M.D., Psychiatry, Univ of Vermont, Burlington, VT 05405; John Hughes, M.D., Joanne Astill, M.D., Linda Inatsuka, B.A., Bettina Bailey, M.S.W., John E. Helzer, M.D.

Summary:

Alcoholism, smoking, and illicit drug dependence are associated with an increase in medical and psychiatric problems and with increased use of medical resources. Studies indicate a significant number of general hospital patients may have such dependence problems. This study administers self-questionnaires (MAST, BDI) and the *DSM-III-R* checklist sequentially to general hospital admissions. Data from the initial sample indicate 55 percent of those who smoke greater than 16 cigarettes per day had elevated MAST scores as compared to 12 percent of nonsmokers. One-third of the smokers scored greater than 13 on the BDI in contrast to 1 percent of the nonsmokers. BDI and MAST scores were correlated ($r = 0.45$) to each other but not to elevated caffeine consumption. This study suggests smokers are at increased risk for alcoholism and depression and that clinicians should carefully assess for these disorders in patients who smoke.

NR349 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Beer Advertising Spending Not Related to Teen Drinking

Paul A. Kettl, M.D., Psychiatry, Penn State-Hershey, P.O. Box 850, Hershey, PA 17033; Michelle Sredy, B.S.

Summary:

Beer advertising expenditures more than doubled between 1970 and 1988. It has been alleged that the number and content of beer ads leads to an increase in teen drinking. We sought to explore if this rise in beer advertising was linked to an increase in the number of teens drinking, or drinking regularly by age 17.

Total yearly per capital beer advertising expenditures between 1970 and 1989 (in constant 1987 dollars) did not at all correlate with: 1) the percentage of teenagers (age 12 to 17) who had any experience with alcohol as measured by nine NIDA surveys between 1972 and 1988 ($r = -0.12$, NS) or by 15 yearly senior student surveys from 1975 through 1989 ($r = 0.03$, NS); 2) the yearly percentage of senior high students who used alcohol in the past 30 days (from 1975 to 1988)[1]: ($r = -0.41$, NS); 3) the yearly percentage of senior students who are occasional heavy drinkers (i.e., took 5 or more drinks at one time in the two weeks before the survey) from 1975 to 1988 ($r = 0.00$, NS). Instead, yearly beer advertising expenditures did significantly correlate with per capita *adult* consumption of beer from 1970 through 1989 ($r = 0.57$, $p = 0.008$).

Thus, the increase in beer advertising over the last 20 years is not associated with an increase in the number of teenagers who try alcohol, or who drink regularly by age 17.

NR350 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Voice-Based Computer Interview for Drug Dependence

David R. Gastfriend, M.D., Addiction Services, Mass General Hospital, MGH-ACC 812, Boston, MA 02114; Michael Brown-Beasley, M.A., Janel Hackney, Emily Gerber, B.A., Lee Baer, Ph.D., David Mee-Lee, M.D.

Summary:

The Recovery Attitude and Treatment Evaluator (RAATE) assesses resistance and obstacles to chemical dependence treatment. The RAATE patient questionnaire's 94 true/false statements demonstrate good psychometric properties and reliability. We computerized the RAATE to offer the questions via high fidelity digitally recorded human voice and to recognize patient responses spoken into the computer's microphone. Sixty-eight consecutive adults seeking addictions treatment were randomized to one of four formats ($N = 17$ per group): (1) conventional paper "output"/pencil "input," (2) computerized screen text output/mouse-selected input, (3) voice output/mouse-input, and (4) voice output/patient voice input.

The voice/voice version yielded the shortest mean duration of administration. Patients reported high satisfaction ratings, confidence that answers were accurate, and perceived their responses to be useful in treatment planning. Group mean ratings did not significantly differ by version. There was a statistical trend in which the voice-based versions reduced intra-group variability on test duration and patient confidence.

Computerized voice-interactive interviewing is feasible and may shorten test durations, increase uniformity of administration, increase access for vision-impaired or foreign language speakers, and increase data entry efficiency and accuracy. An important ben-

efit in behavioral assessment is the ability to provide a consistent, controlled and nonjudgemental interview interaction.

Supported by NIDA Grants DA 06116, DA 07693, and OTI T100022

NR351 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Comparative Validity of Five Alcoholism Typologies

William R. Yates, M.D., Psychiatry, University of Iowa, 500 Newton Road Meb 2-126D, Iowa City, IA 52242; Ann I. Fulton, B.S.W.

Summary:

Background: Clinicians and researchers disagree as to the best method to subtype subjects with alcoholism. **Objective:** The objective of this study was to compare and rank the descriptive validity of five typologies in a series of subjects with *DSM-III-R* alcohol abuse or dependence admitted to inpatient treatment facilities. **Method:** One hundred fourteen men and 60 women were interviewed using the Diagnostic Interview Schedule, personality Diagnostic Questionnaire, and Schuckit Alcoholism Outcome Scale. The five typology systems applied were presence or absence of 1) primary alcoholism, 2) drug abuse or dependence, 3) antisocial personality disorder, 4) early onset alcoholism, and 5) parental alcoholism. Twenty-six external phenomenology and severity variables were examined for each typology. **Results:** The null hypothesis of no validity difference between the five typologies was rejected (Friedman rank chi square = 21.3, $p < .001$). The rank order (mean rank) from best to worst typology was presence or absence of: Drug abuse/dependence (2.11), antisocial personality disorder (2.36), early onset alcoholism (3.17), primary alcoholism (3.22, and parental alcoholism (4.14). **Conclusion:** Documenting *DSM-III-R* axis I drug abuse/dependence comorbidity and *DSM-III-R* axis II antisocial personality disorder comorbidity is a valid alcoholism typology strategy for clinical and research purposes.

NR352 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Mood State Changes in Withdrawal from Methadone

Philip D. Kanof, M.D., Psychiatry, University of Arizona, 1501 North Campbell Avenue, Tucson, AZ 85724; Marvin Aronson, Ph.D., Robert Ness, Ph.D.

Summary:

Prospective studies were conducted to delineate the clinical characteristics of mood state changes that occur in stable opioid-dependent patients undergoing therapeutic detoxification from methadone maintenance treatment. Twenty-four patients participated in a blinded protocol for gradual dosage reduction that included weekly assessments of affective state, using the Profile of Mood States (POMS), and of signs and symptoms of opioid withdrawal. Sustained increases in POMS scores of greater than 20 points were observed in 12 of the 24 patients during the course of detoxification. The emergence of symptoms of dysphoria was accompanied by insomnia, loss of appetite, and somatic complaints consistent with opioid withdrawal, but with only minimal levels of objective signs of opioid withdrawal. Greater changes from baseline in mood state and opioid withdrawal measures occurred in patients who were unable to complete the detoxification regimen. Restabilization on methadone of patients who failed detoxification resulted in a prompt reduction in symptoms of dysphoria and of opioid withdrawal. The results indicate that the development of an organic mood syndrome is a common occurrence, and is associated with a poor outcome in patients undergoing slow detoxification from methadone maintenance treatment. Pharmacological strategies aimed at preventing the emergence of this syndrome may enhance the success rates for therapeutic detoxification regimens.

NR353 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Schizophrenia and Drug Abuse: Clinical Correlates

William B. Lawson, M.D., Psychiatry, North Little Rock VA, 2200 Fort Roots Drive, North Little Rock, AR 72114; Jeff Clothier, M.D., Jimo'Lea Angel, R.N., Craig N. Karson, M.D.

Summary:

Substance abuse is common among schizophrenic patients. Over half may abuse alcohol and nearly 17 percent may be cocaine abusers. We initiated an eight-week Schizophrenia/Addiction Treatment (SCAT) program. Thus far, 54 patients have entered the program. Upon entering the SCAT program, they receive a SCID and clinical *DSM-III* diagnosis, SANS, PANS, and substance abuse questionnaire. They also receive a dementia workup, neuropsychological assessment, single photon emission tomography (SPECT) scan, and EEG. Eight patients were diagnosed with schizophrenia when they had other disorders, including major depression, and post-traumatic stress disorder (PTSD). Four black patients, but no whites, with PTSD previously were misdiagnosed. Because of cocaine's effects on dopamine receptor function,we compared cocaine abusers vs. patients who only abused alcohol. Cocaine abusers (6/9) were more likely to be intolerant of neuroleptics due to parkinson effects than alcohol abusers (0/28, $p < .05$). We will be reporting the findings from SPECT and the correlation with neuropsychological performance. Dual diagnosis programs provide an excellent laboratory for examining the effects of substance abuse on the schizophrenia process. The effects of substance abuse on misdiagnosis and race, as well as the neuropsychiatric effects of cocaine need further evaluation.

NR354 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Predicting Antidepressant Response in Alcoholics

Edward V. Nunes, M.D., Psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; Patrick J. McGrath, M.D., Jonathan W. Stewart, M.D., Frederic M. Quitkin, M.D.

Summary:

The nosology of depressive syndromes in substance abusers is a current focus of controversy. Ongoing work at our center suggests imipramine is effective in about 50 percent of depressed alcoholics, supporting self-medication model. This report seeks to identify predictors of success with this approach in a 12-week open label trial. Patients currently met *DSM-III-R* criteria for alcohol abuse or dependence and for major depression or dysthymic disorder which was primary (antedated any substance abuse), or persisted during six months of abstinence in the past, or was secondary but chronic. Sixty patients had a minimum adequate imipramine trial of $\geq$4 weeks and $\geq$150 mg per day. Among baseline demographic, diagnostic, and severity measures only race (nonwhites did worse) and baseline Hamilton Depression Scale (higher scores did worse) were significant predictors ($p < .05$) of success, defined as improved mood and substantial reduction in alcohol intake and morbidity. Baseline measures of alcohol severity were not strongly predictive of outcome. We expected that primary depression would be characteristic of self-medicators. Surprisingly, the success rate was slightly higher when drinking antedated depression. Implications for the nosology and treatment of comorbid depression and alcoholism will be discussed.

NR355 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Automated Assessment of Cocaine Craving

Sharadha Raghavan, M.D., Psychiatry, Univ of California, 401 Parnassus Ave Bx CAS-0984, San Francisco, CA 94143; Roy King, M.D., Guenther Knoblich, B.S., Christopher Flowers, B.S., Leslie Fried-Behar, Ph.D.

Summary:

Cocaine craving as a concept has yet to be delineated as an event arising from a particular set of conditions. Recent animal models of craving implicate increased central dopaminergic activity underlying a craving event. In this study, 11 patients with cocaine dependence diagnosed by the SCID underwent in-depth personality and drug use assessment. Their urge to use (craving) was assessed using the Stanford Cocaine Craving Scale (SCCS), administered to the subjects via a small hand-held computer, the Casio PB1000, programmed to beep at different times during the day and ask questions about presence of craving, what contributed to it, and what helped resist it. It also asked questions about three different mood states, namely, happy/sad, anxious/relaxed, and excited/calm. It was hypothesized, on the basis of the relationship between dopamine activity and incentive motivation, that excited mood would predict craving attacks. Using the SCCS, we showed diurnal variation in craving and, as hypothesized, prior to craving attacks subjects reported heightened levels of excitement. We also investigated attribution of craving attacks by the subjects which will be reported in this presentation. This methodology used to study cocaine craving provides a good tool for future research in characterizing the phenomenology and neurochemistry of not only cocaine craving but also that of other drugs.

NR356 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Neuroendocrine Effects of Anabolic Steroids

Tung-Ping Su, M.D., ETB/BPB, Bldg 10/3N238, 9000 Rockville Pike, Bethesda, MD 20892; Michael Pagiliaro, R.N., David Pickar, M.D., David R. Rubinow, M.D.

Summary:

To evaluate the central and peripheral effects of anabolic steroids (AS), 20 normal male subjects participated in a double-blind, placebo-controlled trial of methyltestosterone (MT). Subjects received three days each of placebo (P), low dose MT (40 mg/day) (LD-MT), high dose MT (240 mg/day) (HD-MT), and placebo withdrawal (W). Mood and behavioral ratings were obtained daily, plasma at the end of each three day period, and CSF at the end of P and HD-MT. ANOVA-R and post hoc comparisons revealed significant ($p < .05$) decreases during HD-MT and W in plasma levels of reproductive hormones (testosterone (T), free T, DHT, estradiol, SHBG, LH, and FSH) and thyroid hormones (T3, T4, TBG). TSH and free T4 were both significantly increased during HD-MT. The usually coordinated secretion of IL-1 and IL-2 was disturbed during HD-MT, with a significant decrease in IL-1 and increase in IL-2. During HD-MT, self-ratings of distractibility were significantly correlated with cortisol, DHEA, and CSF ACTH, and the highly correlated relationships observed in CSF between endorphin, CTH, vasopressin, and somatostatin during P disappeared. In sum, even short-term AS administration strongly influences HPG, HPT, HPA, and immune activity as well as behavior.

NR357 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Evaluation of Treatments for Cocaine Abuse

Hari K. Khalsa, M.D., Neuropsychiatry, UCLA, 1100 Glendon Suite 763, Los Angeles, CA 90024; M. Douglas Anglin, Ph.D., Alphonso Paredes, M.D.

Summary:

The purpose of this study was to assess the effectiveness of existing modalities for the treatment of cocaine abuse. Data were collected from 300 cocaine dependent male subjects seeking treatment at the West Los Angeles Veterans Administration Medical Center; 275 patients were voluntarily admitted to an inpatient program (condition 1), and 75 agreed to be randomly assigned to one of three treatment conditions (25 in each): 21 day inpatient (condition 2, and equivalent to condition 1), outpatient clinic (condition 3), or referral to community self-help groups (condition 4). The subjects have been followed for two years. Three major instruments to evaluate treatment effectiveness have been used: the "Cocaine Natural History Interview," the "Treatment Evaluation Form," and the "Treatment Summary Form." Time-series techniques have been applied to compare post-assignment behaviors across the four conditions and to assess treatment effectiveness, including the course of cocaine and other drug abuse and associated behaviors. Overall, treatment interventions seem to be effective as they result in a decrease in the level of cocaine and other drug use, a decrease in deviant behaviors, and in an increase in socially desirable behaviors. Duration of treatment has been found to influence outcome more than other treatment characteristics such as intensity, structure, or program orientation. Patient individual characteristics have not been found to significantly affect treatment outcome in our study. This is the first study with a large enough sample to provide data that can serve as the basis for modifying existing cocaine treatment approaches to increase their effectiveness in helping addicted patients.

NR358 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Biology and Phenomenology of Cocaine Withdrawal

Ananda Pathiraja, M.D., Psychiatry, Medical Col. of Georgia, 1515 Pope Street, Augusta, GA 30912; Donatella Marazziti, M.D., Bruce I. Diamond, Ph.D., Richard L. Borison, M.D.

Summary:

In order to correlate the parameters of cocaine use and the linkage between cocaine withdrawal and "post-cocaine depression," we studied ten male patients in the initial two-week period of withdrawal from cocaine. Ham-D scores and 3H Imipramine binding of these patients were compared with that of nine healthy controls. Interpretation of our data by Pearson Analysis showed statistically significant correlations between HAM-D scores and period of use ($r: +0.83$, $p < 0.05$). 3H Imipramine binding was found to be negatively correlated with period of cocaine use ($r: -0.64$), number of days of abstinence ($r: -0.78$) and HAM-D scores ($r: -0.66$). We did not find any relationship between cocaine craving and other correlates. When compared with normal volunteers, patients had a significant lower B Max score ($434 + 274$ vs 1020 ± 95 $p < 0.0001$) and kd (0.54 ± 0.20 vs $1.14 \pm$ $p < 0.0001$) values. These results indicate the presence of decreased imipramine binding activity at the presynaptic site during cocaine withdrawal which may be due to the effect of the drug or alternatively, a result of concomitant depression which may be primary or secondary in origin.

NR359 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Fluoxetine Study in Depressed Alcoholics

Jack R. Conelius, M.D., Psychiatry, WPIC Univ of Pitts, 3811 O'Hara St. Room 1092, Pittsburgh, PA 15213; Barry W. Fisher, M.D., Ihsan M. Salloum, M.D., Marie D. Cornelius, Ph.D., James M. Perel, Ph.D., Joan G. Ehler, M.D.

Summary:

Serotonergic mechanisms have been implicated in the etiology of depressive disorders and of alcoholism. The selective serotonergic agonist fluoxetine has demonstrated efficacy in the treatment of depression, and has suggested efficacy in the treatment of alcoholism. However, no trials with any selective serotonin agonist have been reported in patients who display both depression and alcoholism. In this study, 12 patients with *DSM-III-R* diagnoses of major depressive disorder and alcohol dependence were treated openly for eight weeks with fluoxetine, with doses ranging from 20

mg. to 40 mg. po qAM. Six of these patients had made suicide attempts shortly before admission to the hospital. Detoxification and a subsequent one-week washout period had been completed prior to entry into the study. Prominent baseline depressive severity following washout was demonstrated on the Beck Depression Inventory (Mean = 16.3) and the Hamilton Depression Scale (Mean = 17.1) Mean alcohol consumption in the week prior to admission was 38.8 drinks, as measured on the timeline scale. Weekly ratings of symptoms were performed for eight weeks. Statistically significant improvements on the paired student T test were observed on the Beck (Δ = 10.6 points, $p < .005$), the Hamilton (Δ = 6.8 points, $p < .01$), and the timeline scale (Δ = 36.8 drinks, $p < .0005$). These findings suggest promise for fluoxetine in treating the depressive symptoms and excessive alcohol intake of depressed alcoholics. Large, double-blind, placebo-controlled studies with serotonergic medications are warranted in depressed alcoholics.

NR360 Tuesday May 5, 3:00 p.m.-5:00 p.m.

The D2 Dopamine Receptor Gene and CSF HAV

David Goldman, M.D., NIAAA Bldg 10 3C102, Lab of Neurogenetics, 9000 Rockville Pike, Bethesda, MD 20906; Michael Dean, Ph.D., Gerald L. Brown, M.D., Riitta Tokola, M.D., Matti Virkkunen, M.D., Markku Linnoila, M.D.

Summary:

A population genetic association was reported between a D_2 dopamine receptor genotype and alcoholism, and later, other psychiatric disorders. However, efforts to establish genetic linkage in families have been unsuccessful and there is emerging evidence for large interpopulation differences in allele frequencies for the Taq1 RFLP used in these studies. If the genetic association is mediated by altered D_2 receptor function, then alcoholics and others who are deviant in dopamine function might be expected to show the strongest association. Also, if the population association should be stronger when alcoholics and nonalcoholics are matched for ethnicity.

We, therefore, evaluated the D_2/Taq1 polymorphism in 29 impulsive, violent alcoholics Finns, 17 nonimpulsive, violent alcoholic Finns and 36 Finnish controls free of mental disorders, alcoholism, and substance abuse. There were no allele frequency difference between healthy, nonalcoholic controls (0.21), alcoholics (0.12), and impulsive alcoholics (0.17). As a measure of brain dopamine function, in 37 of the alcoholics, we measured homovanillic acid in lumbar cerebrospinal fluid. We also measured the serotonin and norepinephrine metabolites 5-hydroxyindoleacetic acid and 3-methoxy-4-hydroxyphenylglycol. There was no significant relationship between the D_2/Taq1 genotype and the concentrations of the monoamine metabolites in these violent, alcoholic Finns, or in an additional 24 American Caucasian alcoholics. The homovanillic acid results ($\pm$SEM) are given in the following table:

D_2 Genotype	A1A1,A1A2	A2A2	t =
Finns	166.4 ± 17.2, n = 11	143.8 ± 12.3, n = 26	1.027
Americans	176.5 ± 15.0, n = 10	174.2 ± 17.1, n = 14	−0.455

NR361 Tuesday May 5, 3:00 p.m.-5:00 p.m.

The Characteristics of Triply Diagnosed Patients

Eric C. Strain, M.D., Psychiatry, Johns Hopkins FSK MC, 4940 Eastern Avenue, Baltimore, MD 21224; Dan Buccino, M.S.W., Chester W. Schmidt, M.D., George E. Bigelow, Ph.D.

Summary:

This study determined the prevalence and characteristics of patients who carry diagnoses of cognitive impairment, substance abuse, and a major mental illness (the triply diagnosed) in a day hospital population. The charts of all patients admitted over a one-year period (n = 145) were reviewed for *DSM-III-R* diagnoses, demographic characteristics, and psychosocial concomitants. The triply diagnosed constituted 26 percent of the population, and were significantly different ($p < 0.05$) from the non-triply diagnosed on several measures: They were younger (38 versus 45 years), had more inpatient (6.6 versus 4.8) and substance abuse (0.76 versus 0.36) treatment episodes, and had more problems with noncompliance with treatment (82 percent versus 60 percent) and involvement with the legal system (39 percent versus 22 percent). They also had higher rates of living in supervised housing (39 percent versus 18 percent) and being homeless (16 percent versus 6 percent), and were more frequently diagnosed with schizophrenia/psychotic disorder (63 percent versus 18 percent). The triply diagnosed are a population with high healthcare needs who utilize a wide variety of mental health resources and have poor compliance with treatment. Identification of these problematic patients can be useful in focusing attention upon their diverse requirements, and they represent a highly prevalent population which needs further study.

NR362 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Benzodiazepine Sensitivity in Sons of Alcoholics

Deborah S. Cowley, M.D. Psychiatry, Univ of Washington, 1959 NE Pacific Street, Seattle, WA 98195; Peter P. Roy-Byrne, M.D., Richard Ries, M.D., David J. Greenblatt, M.D., R. Dale Walker, M.D., Daniel W. Hommer, M.D., Herman H. Samson, Ph.D.

Summary:

To examine the role of the GABA-benzodiazepine receptor system in risk for alcoholism, we studied acute sensitivity to diazepam in sons of male alcoholics (SOAs; n = 18) and controls (n = 18).

SOAs and controls were given intravenous diazepam and placebo vehicle on two separate days in random order in four logarithmically increasing doses (25, 25, 50, and 100 μg/kg; cumulative doses 25, 50, 100, 200 μg/kg) 15 minutes apart. Self-rated sedation, saccadic eye movement velocity (SEV), feelings of being "drugged," "high," and "intoxicated" were assessed at baseline and after each dose. The ARCI-MBG Scale, measuring pleasurable responses to sedatives, was completed at baseline and after dose 3.

Compared with controls, SOAs showed greater increases in pleasurable mood with diazepam ($F = 10.9$, $p = 0.002$) and trends toward greater increases in feeling "high" ($F = 3.4$, $p = 0.07$) and "intoxicated" ($F = 3.6$, $p = 0.06$). Groups did not differ in sedation or feeling "drugged." SOAs also showed trends toward less diazepam-induced reduction in saccadic eye movement velocity at doses 3 ($F = 3.1$, $p = 0.08$) and 4 ($F = 3.0$, $p = 0.09$). These preliminary data suggest differences between SOAs and controls in responses to diazepam. In particular, SOAs are more likely to report pleasure with diazepam, a finding which may be attributable to different expectations of, or central nervous system response to, benzodiazepines.

NR363 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Treating the Cocaine Abusing Schizophrenic

Douglas M. Ziedonis, M.D., Psychiatry, Yale University, 9904 Howard Avenue, New Haven, CT 06519; Ismene Petrakis, M.D., Teresa Richardson, R.N., Thomas R. Kosten, M.D.

Summary:

Cocaine abuse is a clinical problem in the treatment of schizophrenics and new treatment approaches are needed. This 12-week outpatient open label study compares 12 cocaine abusing schizophrenics treated with desipramine (DMI, 100 mg to 150 mg) and antipsychotic agents to 15 treated with only antipsychotic agents

(no DMI). Of note, the dosage of DMI is lower than usual because of the altered metabolism when used in combination with neuroleptics. All 27 patients participated in a new dual diagnosis program with psychotherapy which integrated substance abuse relapse prevention approaches and social skills training (psychiatric symptom and medication management). The average patient was a 30-year-old, single, unemployed, black (67 percent) male (59 percent). Compared to the non-DMI treatment group, the DMI treated group had better 12-week retention (83 percent versus 53 percent), more patients with at least six weeks of abstinence (58 percent versus 40 percent), fewer cocaine positive urines during the last month of treatment (12 percent versus 42 percent), and a higher percentage of program attendance during the last two months (62 percent versus 44 percent). Integrating pharmacotherapy and psychotherapy approaches appears to improve outcomes. Desipramine may have an important role in treating schizophrenic cocaine abusers, and double-blind studies using desipramine should be undertaken. Supported by NIDA R18-DA06190.

NR364 Tuesday May 5, 3:00 p.m.-5:00 p.m.

ADHD Subgroups in Opiate Dependent Adults

Christian Y. Herrera, M.D., Psychiatry, Clinical Quiron, Pasaje Maluquer 7, Barcelona 08022, Spain; Juan M. Segui, M.D., Luis C. Salvador, M.D., Jaime Canet, Ph.D., Viviana Torresi, Ph.D., Isabel Rabella, Ph.D.

Summary:

INTRODUCTION: ADHD has been often related to alcoholism, antisocial personality, and schizophrenia. Its relationship to opiate dependence has been studied by few authors. No studies have differentiated its adult residual form from ADHD as previous history only opiate dependents.

OBJECTIVES: To determine adult and previous ADHD prevalence and its clinical correlations in a severe opiate dependent outpatient population.

METHOD: A total of 104 adult subjects were evaluated by a senior psychiatrist to assess: previous and present history of ADHD. Instruments used: Research Diagnostic Criteria for Axis I and *DSM-III-R* for Axis I and Axis II diagnosis. Utah University Criteria for Adult ADHD, and the Addiction Severity Index (ASI).

RESULTS: 1.—High prevalence of Adult ADHD: 42 percent and previous ADHD: 18 percent. 2.—Adult ADHD patients showed the following significant data (compared to those presenting only previous ADHD): a) Higher unemployment rate ($p < 0.02$). b) More family history of opiate dependency ($p < 0.03$) and delinquency ($p < 0.05$). c) Higher learning disabilities ($p < 0.01$) and conduct disorders ($p < 0.001$) rates. d) More medical pathology ($p < 0.01$) and HIV positives ($p < 0.01$). e) More delictive acts ($p < 0.001$), drug dealing ($p < 0.01$) and younger age at first police contact ($p < 0.02$).

NR365 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Social Network and Methadone Treatment Outcome

Leslie Goehl, M.A., Psychiatry, Columbia University, 722 West 168 St Box 35, New York, NY 10032; Edward V. Nunes, M.D., Frederic M. Quitkin, M.D.

Summary:

Social support is thought to improve drug abuse outcome. However, the potential negative impact of social networks has received less study. A consecutive series of 70 methadone maintenance patients was evaluated and followed prospectively for three months with weekly urine drug screens. Baseline evaluation included measures of mood (Positive/Negative Affect Scale) stress (Stress Ladder) perceived social support (Interpersonal Support Evaluation List; Social Network Index) and drug use among network members. Although perceived social support was correlated with positive affect ($r = .59$, $p < .01$), and stress with negative affect ($r = .46$, $p < .01$), the proportion of drug positive urines did not correlate with any measures of affect, stress, or perceived social support. However, patients with at least one drug user among the closest four significant others had 63 ± 38 percent positive urines versus 35 ± 36 percent positive among those without a drug using significant other ($T = 3.2$, $p < .002$). Thus, substance use in the social network had a substantial negative impact on treatment outcome. Consistent with the traditional "persons, places, and things," this suggests interventions should separate patients from their drug using significant others or teach patients coping skills to reduce their influence, and get the significant others into treatment.

NR366 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Defining Benzodiazepine Dependence

Stef M. Linsen, M.D., Psychiatry, Nijmegen University, P.O. Box 9101, Nijmegen 6500HB, The Netherlands; Christopher J. Kwik, M.D., Marinus H. Breteler, Ph.D., Frans G. Zitman, M.D.

Summary:

Aim: Because of the growing concern about benzodiazepine (BZ) dependence, generally accepted criteria for (aspects of the) BZ-dependency syndrome are becoming more and more desirable. We reviewed the literature for the existence of such criteria.

Methods: A Medline/Psychlit literature search was carried out first using the keywords BZ and anxiety, and BZ and insomnia, followed by substance abuse disorder, substance dependence, substance use disorder, and substance withdrawal. The search concerned the period January 1985 until 1992. It was noted for each paper whether and how dependence and its aspects were specified.

Preliminary results: A total of 420 papers were included. In 40 percent no specification of dependence (addiction), withdrawal, craving, rebound, tolerance and/or euphoria was given. In the other papers wide variations of the specifications were found. Taken together, in the papers, 180 symptoms associated with (aspects of) BZ dependence could be found. When made operational, rebound, withdrawal, and relapse overlapped considerably. The set of *DSM-III-R* criteria for dependence in general was seldom used.

Conclusion: No consensus exists concerning the definition of BZ-dependence and about many aspects of this syndrome.

NR367 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Psychiatric Syndromes in Anabolic Steroid Users

Harrison G. Pope, M.D., McLean Hospital, 115 Mill Street, Belmont, MA 02178; David Katz, M.D., Harlyn Aizley, M.Ed.

Summary:

A growing literature has suggested that anabolic androgenic steroids—drugs taken by athletes to gain strength and muscle mass—can cause significant psychiatric effects in some users. To further explore this issue, we conducted a controlled study of body builders recruited from gymnasiums in Boston and Los Angeles. To date, 101 body builders have been interviewed using the Structured Clinical Interview for *DSM-III-R*, together with a variety of other measures.

Preliminary data from this sample confirm the impressions of earlier studies: overall, 31 percent of anabolic steroid users described either a manic episode, a hypomanic episode, or major depression in association with steroid use or steroid withdrawal, as compared to a 6 percent incidence of such syndromes in nonusers.

Another syndrome of interest in several of these subjects was "bigarexia nervosa," a belief that they appeared small and weak when they were in fact large and muscular. Seven subjects, all

steroid users, experienced this syndrome to the degree that they declined social invitations, refused to be seen in public, or wore baggy sweat clothes even in the heat of summer to avoid being seen as small. This "reverse form" of anorexia nervosa may be one factor which induces bodybuilders to use anabolic steroids.

NR368 Tuesday May 5, 3:00 p.m.-5:00 p.m.

M-CPP and Yohimbine in Alcoholics and Controls

John H. Krystal, M.D., Psychiatry, Yale University, West Haven VA Medical Center, West Haven, CT 06516; Elizabeth Webb, M.a., Henry R. Kranzler, M.D., Ned Cooney, Ph.D., George R. Heninger, M.D., Dennis S. Charney, M.D.

Summary:

A previous report by Binkelfat and his associates suggested that the 5-HT partial agonist, m-chlorophenylpiperazine (MCPP), produced behavioral effects similar to acute alcohol ingestion in some recently detoxified alcoholic patients. The alcohol-like effects were associated with increased craving, suggesting that 5-HT systems may play an important role in the early relapse to alcohol use in some recently detoxified alcoholics. The current study attempted to replicate and extend the initial findings by comparing the MCPP response of recently detoxified alcoholic patients to placebo and the α-2 adrenoceptor antagonist, yohimbine. *METHODS:* In an ongoing study, healthy subjects (n = 10) and male inpatients meeting *DSM-III-R* criteria for alcohol dependence and alcohol free for a minimum of ten days (n = 11) completed three test days in a randomized double-blind design. Test days consisted of MCPP (0.1 mg/kg, i.v. over 20 minutes), yohimbine (0.4 mg/kg, i.v. over 10 minutes + 10 minute saline infusion), or saline were administered. High, similarity to the behavioral effects of drugs of abuse, anxiety, mood responses, and craving were assessed with visual analog scales before and following infusion. Blood was sampled to measure MHPG, prolactin, growth hormone, and cortisol responses. *RESULTS:* Neither MCPP, placebo, nor yohimbine consistently produced craving for alcohol in the patient group. In patients, MCPP, but not placebo or yohimbine, was identified as producing alcohol-like effects during infusion which were gone by the completion of MCPP infusion. Also, neither patients nor healthy subjects exhibited panic attacks or dissociative experiences following MCPP or yohimbine. Hormonal analyses are pending. *IMPLICATIONS:* While these findings may support a role for 5-HT systems in the mood enhancing effects of alcohol, they do not support a role for either 5-HT or noradrenergic systems in the regulation of craving for alcohol in recently detoxified alcoholics under laboratory conditions.

NR369 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Comorbid Substance Use and Psychiatric Disorders

Norman S. Miller, M.D., Psychiatry, Univ of Illinois, 912 South Wood Street, Chicago, IL 60612; Beth M. Belkin, M.D., Robert Gibbons, Ph.D.

Summary:

Clinical psychiatrists blind to the study diagnosed substance use disorders in psychiatric inpatients in a private psychiatric hospital at rates similar to those found in studies of nonprivate psychiatric patients. According *DSM-III-R* criteria for Axis I and Axis II disorders, 200 patients consecutively discharged were examined prospectively for concomitant substance use and psychiatric disorders. Fifty-nine (30 percent) patients with combined substance use and psychiatric disorder (dual diagnosis) on Axis I were significantly more likely to be males 54 percent (females 46 percent) compared to psychiatric only (nondual diagnosis), males 37 percent (females 63 percent). No significant differences were found for mean age, 34 and 33 years, mean length of stay, 25 and 31 days, and discharge type between combined and psychiatric diagnoses only, respectively. Of those 59 (30 percent) patients with combined disorders, 38 percent had substance use diagnoses on Axis I, 64 percent on Axis II. Significantly greater number of substance use diagnoses were associated with Axis II diagnoses. Of the 141 (70 percent) patients with psychiatric only diagnoses, 87 percent had diagnoses on Axis I and 37 percent on Axis II. Polysubstance use disorder was most common at 47 percent and 46 percent among Axis I and Axis II disorders, respectively.

NR370 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Butyrylcholinesterase Activity in Cocaine Abusers

David A. Gorelick, M.D., Addiction Research, NIDA, P.O. Box 5180, Baltimore, MD 21224; Linda Weinhold, Ph.D., Raymond Woosley, M.D., Fengue Du

Summary:

The major metabolic pathway for cocaine in humans is hydrolysis by the plasma enzyme butyrylcholinesterase (BChE) (also called pseudocholinesterase). In normal populations, BChE activity varies with genotype, sex, age, and body weight. BChE activity might also vary in cocaine users, resulting in differences in response to cocaine. We studied plasma BChE activity (by the method of Ellman, et al.) in seven cocaine-dependent volunteers housed on a locked research ward for five to nine weeks. Pairs of samples (collected 72 hours apart) were drawn after admission ($\geq$4 days from last drug use) and again prior to discharge. During the interim, subjects also received IV cocaine as part of another study. All BChE values were within the range of published norms, with no significant change over time. There were no significant differences in BChE activity associated with age, body weight, height, or current or lifetime self-reported use of cocaine, alcohol, or heroin. There was a trend for BChE activity to correlate with serum liver transaminase levels. These findings suggest that cocaine abusers have normal plasma BChE activity and that such activity remains stable over time, even with exposure to cocaine.

NR371 Tuesday May 5, 3:00 p.m.-5:00 p.m.

PICA Behavior in the Mentally Retarded

Barbara C. Witkowski, Ph.D., Psychiatry, Cooper Hospital, 3 Cooper Plaza Suite 403, Camden, NJ 08103; Thomas S. Newmark, M.D.

Summary:

Pica, the ingestion of nonfood substances, is one of the most frequently occurring dysfunctions in children and adults with mental retardation. This study surveyed the entire population (N = 1010) of residents at Vineland Developmental Center (VDC), a New Jersey state institution for females with developmental disabilities. Ages ranged from 17 to 96 years, and levels of retardation ranged from mild to profound.Inclusion criterion was any client who was observed to engage in pica within the preceding year.

A data collection instrument, the Pica Survey, was used for this research.

Results indicated that 169 or 16.7 percent were identified as engaging in pica within the preceding year. Age and level of mental deficit were highly related to pica. Pica decreased with increasing age; 94 percent of those with pica were profoundly retarded. They were somewhat discriminating in their choice of pica items, with paper, string, and clothes the most popular. A relatively high number of pica clients were also identified as having iron deficiency or seizure disorder. Medications, particularly anticonvulsants and neuroleptics, were associated with pica; however, no medication was prescribed specifically to treat pica. Treatments included behavioral interventions. The study should increase the awareness of pica in the mentally retarded.

NR372 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Bright Light Therapy for Bulimia Nervosa

Raymond W. Lam, M.D., Psychiatry, University of B.C., 2255 Wesbrook Mall, Vancouver, BC V6T2A1; Elliot M. Goldner, M.D., Leslie Solyom, M.D., Ronald A. Remick, M.D.

Summary:

Objective: Light therapy is used to treat winter depressions, but anecdotal reports suggest that it may also be beneficial for bulimia. We report preliminary results from a controlled study of dim versus bright light therapy in patients with bulimia nervosa.

Methods: Ten female patients who met *DSM-III-R* criteria for bulimia nervosa underwent a six-week randomized, counter-balanced, crossover light therapy study during the winter. Each subject completed two weeks of prospective baseline monitoring of mood and eating, followed by two-week periods of daily early morning light therapy using: 1) ½hour of 10,000 lux white fluorescent light, and 2) ½hour of 500 lux red fluorescent light. Pretreatment expectation ratings were no different for the two conditions.

Results: The bright white light condition reduced binge/purge episodes by 43 percent compared to 12 percent with the dim red light ($p < 0.007$). The bright white light also produced greater changes in Eating Attitudes Test scores ($p < 0.03$). There was no significant difference between the two conditions in change scores on the 29-item Hamilton Depression Rating Scale, SAD version (HAM-SAD), but both light conditions significantly reduced Ham-SAD scores. There were no order effects of treatments.

Conclusions: These results suggest that bright light therapy is an effective treatment for bulimia nervosa, and that the clinical effect of therapeutic light on bulimia may be independent of changes in mood.

NR373 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Dissociation and Sexual Abuse in Eating Disorder

Kathleen Jordan, M.S.N., University of Michigan, 1500 East Medical Center Dr, Ann Arbor, MI 48109; Mark A. Demitrack, M.D., Vivian Folsom, S.W., Dean D. Krahn, M.D., Karen Nairn, R.N., Frank W. Putnam, M.D.

Summary:

The development of severe adult dissociative psychopathology has been suggested to have a specific link with histories of childhood abuse. Because we have previously shown that eating disordered inpatients report significant levels of dissociative experience, we sought to determine whether those patients with more severe dissociative symptoms would also show higher rates of childhood sexual abuse.

A series of 99 consecutively evaluated eating disorder patients from the inpatient and outpatient services of the Michigan Eating Disorders Program were asked to participate. Ninety-eight patients completed the Dissociative Experiences Scale (DES) and 95 completed the Finkelhor Sexual Life Events Questionnaire (SLEQ). Fifty-one patients completed both instruments ($n = 7$, anorexia nervosa, $n = 51$, bulimia nervosa, and $n = 10$ eating disorder, NOS). Of these, 25 patients reported a history of childhood sexual abuse. The median score on the DES for the abused group was 16.3, while the median DES score in the group of non-abuse subjects was 6.5 ($p < .003$, two tailed Mann-Whitney U-test).

These results confirm our previous findings of high rates of self-reported dissociative experiences in patients with eating disorders. Moreover, the data show that eating disordered subjects with a childhood history of sexual abuse report significantly higher levels of dissociative experience. These findings are compatible with the hypothesis that childhood abuse experiences may be an important precursor for the development of adult dissociative psychopathology. Furthermore, these data add to a growing literature suggesting that the behavioral sequelae of abuse may cut across established diagnostic boundaries to produce clinically evident dissociative experiences.

NR374 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Predicting Continued Abstinence in Bulimia Nervosa Over Two Years

Allan S. Kaplan, M.D., Psychiatry, Toronto General Hospital, 200 Elizabeth Street, Toronto Ontario M5G 2C4, Canada; Marion P. Olmsted, Ph.D.

Summary:

This study examines a sample of 50 patients with bulimia nervosa treated for ten weeks in a day hospital group psychotherapy program (DHP) for eating disorders and who were re-interviewed two years after discharge. These patients were categorized into three groups: a group that was completely symptom free throughout the two-year follow-up ($N = 12$; 24 percent of total), a group that binged and vomited throughout the follow-up ($N = 13$, 26 percent of total), and a group that was intermittently symptomatic over the two years ($N = 25$, 50 percent of total), and was omitted from this analysis. Seventy-five percent of the patients in the continually abstinent group were abstinent for the four weeks prior to discharge, while only 23 percent of the symptomatic group were abstinent prior to discharge ($p < .03$). The two extreme groups were compared on a variety of admission and discharge demographic, symptom, attitudinal weight, and mood related variables to predict symptom status over the two-year follow-up.

Seven variables differentiated the two groups. At admission, the abstinent group were bingeing and vomiting less, had lower "Bulimia" and higher "Drive for thinness" scores on the EDI, and were closer to their highest ever weight than were the symptomatic group. At discharge, the abstinent group were bingeing and vomiting less. Stepwise discriminate function based on these seven variables showed that admission vomiting frequency, "Drive for Thinness," and percent below highest weight, and discharge binge frequency accounted for 71 percent of the variance in group membership ($p < .0001$).

In this study, continued abstinence over two years was predicted by disorder specific symptoms and not psychological functioning. The fewer symptoms patients had at discharge, the more likely they were to be symptom free over the follow-up period. These results have implications for understanding the natural history of bulimia nervosa and how it is altered by intensive treatments.

NR375 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Open Trial of Fluvoxamine in Bulimia Nervosa

Jose L. Ayuso-Gutierrez, M.D., Hospital San Carlos, Isaac Peral SN, Madrid 28040, Spain; Monica Palazon, M.D., Jose L. Ayuso-Mateos, M.D.

Summary:

We designed an open-label trial to measure the efficacy of fluvoxamine, a potent and selective serotonin re-uptake inhibitor in the treatment of bulimia nervosa. Twenty consecutive referrals of bulimic patients who met *DSM-III-R* criteria were treated in a fixed-dose study with fluvoxamine for eight weeks. After a seven-day washout period, patients received 50 mg. of fluvoxamine during the first week, 100 mg. during the second, and 150 mg. through the end of the eight-week study. Patients were monitored with the following instruments: EDI, Severity Index of the Bulimic Condition, CGI, Binge Eating Episodes, Bulimic Behavior Diary, and Hamilton Scale for Depression. Of the 20 patients admitted, one dropped out after seven weeks of treatment. Comparing baseline data and the measures at the end of the treatment, there were significant ($P < 0.01$) changes of the scores of the EDI, CGI and number of binge eating episodes. As early as between the baseline period and the

first week of treatment, significant differences were observed on the EDI ($p < 0.05$) and number of binge eating episodes ($p < 0.01$). The results indicate that fluvoxamine was associated with statistically significant improvement in most of the measures used, and that the drug was well tolerated.

NR376 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Weight and Reproductive Function in Bulimia

Theodore E. Weltzin, M.D., Eating Disorders, WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213; Judy Cameron, Ph.D., Sarah Berga, M.D., Walter H. Kaye, M.D.

Summary:

Even though most women with bulimia nervosa are at a normal weight, more than 50 percent have abnormal menstrual function. In patients with anorexia nervosa, abnormal reproductive function is known to be related to weight *loss*. It has not been known why patients with bulimia nervosa, who are at normal weight, have disturbed menstrual function.

Thirteen women with bulimia nervosa and six healthy volunteers were studied. Subjects underwent q 15 minute determinations of plasma luteinizing hormone (LH) for an entire 24-hour period. Analysis of LH secretion was done using cluster pulse analysis.

Bulimics and controls were matched for age and weight. Bulimics were no different than controls for mean LH concentration, LH pulse frequency and area under the LH curve. For patients with bulimia we found that weight as a percent of *previous* high weight (percent PHW) positively correlated with LH pulse frequency ($n = 13$, $r = .70$, $p < .01$). Bulimics less than 85 percent PHW ($n = 5$) had fewer LH pulse in 24 hours (2.8 ± 3.6) compared to bulimics who were $\geq$85 percent of PHW ($n = 8$, 13.5 ± 2.4, $t = 6.54$, $p < .01$) and healthy volunteer women (9.8 ± 3.7, $t = 4.10$, $p < .01$). We also found that bulimics whose current weight was <85 percent of PHW had more severe ratings on the Eating Disorder Inventory and Speilberger State-Trait Anxiety Inventory compared to controls at the $p = .05$ level.

We have found that menstrual function in normal weight bulimic patients is also related to body weight. However, reproductive function appears to be related to *previous high* body weight. These data suggest that the high incidence of reproductive dysfunction in bulimic women may be linked to some having too low a current body weight in relationship to their past highest weight.

NR377 Tuesday May 5, 3:00 p.m.-5:00 p.m.

The Seasonality of Eating Disorders

Timothy D. Brewerton, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; Dean D. Krahn, M.D., Todd A. Hardin, M.D., Thomas A. Wehr, M.D., Norman E. Rosenthal, M.D.

Summary:

Seasonality appears to be an important clinical feature of affective illness and other related disorders thought to involve serotonin dysregulation, such as bulimia nervosa (BN) and anorexia nervosa (AN). We therefore administered the Seasonal Pattern Assessment Questionnaire (SPAQ) to 151 female patients (pts) with *DSM-III-R* defined eating disorders (BN: $n = 102$; AN: $n = 28$; BN + AN: $n = 21$) studied at three locations (NIMH: $n = 47$; MUSC, $n = 44$; UM, $n = 60$) and compared them with 54 female controls studied at NIMH. There was a statistically significant difference in Global Seasonality Scale (GSS) scores among the four diagnostic groups ($p < 0.0001$, ANOVA). Pts with BN + AN had significantly higher GSS scores than both controls and pts with AN alone ($p < 0.05$, Bonferroni t-test). Pts with BN alone had significantly higher GSS scores than controls in the NIMH and UM samples only. These results suggest that pts with BN, regardless of the presence of AN, have higher degrees of seasonal variation of mood and neurovegetative symptoms than healthy controls. This supports the hypothesis that BN and seasonal affective disorder (SAD) involve similar pathophysiological mechanisms, possibly involving serotonin (5-HT) dysregulation. In addition, more research exploring the possible role of phototherapy in the treatment of eating disorders is warranted.

NR378 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Stimulation of the Hypothalamic-Pituitary-Adrenal Axis by Bulimic Behaviors

Margaret Altemus, M.D., LCS, NIMH Bldg 10 Rm 3D41, 9000 Rockville Pike, Bethesda, MD 20892; Julio Licinio, M.D., Libby Jolkovsky, Philip W. Gold, M.D.

Summary:

Patients with bulimia nervosa have reductions in indices of thyroid and sympathetic nervous system activity when they stop bingeing, suggesting that bingeing and vomiting have an activating or arousing function. In the present study we wished to explore whether the arousal producing hormone CRH, which drives the hypothalamic-pituitary-adrenal (HPA) axis, is also stimulated by bingeing and vomiting. To address this question we measured plasma ACTH and cortisol secretion over 24 hours in ten women with bulimia nervosa studied both while they were actively bingeing and again after six weeks without bingeing and in ten controls. Compared to controls, active bulimics showed a significant reduction in mean 24 hr ACTH levels ($5.8 \pm .6$ vs. $4.0 \pm .6$ pg/ml, $p < .05$) and at rend toward higher mean 24 hr cortisol levels ($8.1 \pm .4$ vs. $9.9 \pm .9$ μg/dl, $p = .1$). After six weeks without bingeing and vomiting, ACTH and cortisol secretion returned to normal. In addition, there was a negative correlation ($p < .05$) between mean 24 hr ACTH and cortisol in both active bulimics and controls, consistent with increased adrenal sensitivity to ACTH known to occur with prolonged HPA axis stimulation. In conclusion, there seems to be a subtle, chronic activation of the HPA axis in actively bingeing and vomiting bulimics, resulting in increased adrenal responsiveness to ACTH and mild hypercortisolism.

NR379 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Delayed Gastrointestinal Transit Time in Eating Disordered Patients: A Radiographic Study

Arnold E. Andersen, M.D., University of Iowa, 500 Newton Road, Iowa City, IA 52242; Neell Kamal, M.D., William E. Whitehead, M.D., Twafik Chami, M.D., F.A. Rosell, R.N., M. M. Schuster, M.D.

Summary:

Eating disordered patients often complain of gastrointestinal (GI) distress. The psychological vs. physiological basis for these complaints has not been well studied. This study investigated ten anorectic and 18 bulimic subjects as well as ten normal weight controls for gastrointestinal transit time. Methodology consisted of five days of ingestion of 20 radiopaque markers followed by radiograph of the abdomen on the sixth day. GI transit time was calculated by standard methods. All of the anorectic and 67 percent of bulimic patients complained of constipation or bloating. Whole gut transit time was significantly longer in anorectic patients (66.6 hours) and bulimic patients (66.5 hours) compared to controls (38.0 hours) ($p < .05$). Mouth to cecum transit time showed a trend toward increased number of minutes in both anorectic and bulimic patients. No significant correlation was found between whole gut transit time and body mass index across all subjects. These data confirm the common complaints of constipation and bloating in eating disordered patients and support a physiological basis for the complaints, namely delayed GI transit time. Although it is doubtful that delayed

transit time is a pre-existing physiological condition, it may contribute to the perpetuation of eating disorders by the inhibition of gastric emptying through rectal distension and by the aggravation of fear of fatness due to enteroceptive sensations of bloating.

NR380 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Psychopathology and Severity of Obesity

Enos D. Martin, M.D., Psychiatry, Penn State University, 500 University Drive, Hershey, PA 17033; Tjiau-Lin Tan, M.D., Louis F. Martin, M.D., Lowell D. Mann, M.D.

Summary:

The Minnesota Multiphasic Personality Inventory (MMPI) was administered to 411 moderately and severely obese patients. Significant psychopathology was evidenced both within our sample and in comparison to a normal control group (N = 93). We also separated the total obese population into two treatment option groups: the Supplemented Fast and Behavior Modification (SFBM) group and the Gastric Bypass Surgery (GBPS) group. For individual scales, mean T-scores were significantly higher than controls ($p < 0.01$) for the total group of obese patients on six out of eight scales: 1-Hs (Hypochondriasis), 2-D (Depression), 3-Hy (Conversion Hysteria), 4-Pd (Psychopathic Deviate), 7-Pt (Psychasthenia) and 8-Sc (Schizophrenia). The scale with the highest mean value was 4-Pd. The mean number of pathologically elevated scales per obese individual was 1.8 versus 0.5 for controls ($p < 0.01$). Also, as a group, the obese had significant elevations (≥ 70) on the eight major MMPI scales. The four highest in order of percent patients with significant elevations were: 2-D (32.4 percent), 3-Hy (30.7 percent), 4-Pd (29.9 percent) and 1-Hs (26.8 percent). There were no significant differences, however, in the degree of psychopathology between the SFBM and GBPS groups, despite the fact that the groups differed significantly in degree of obesity, i.e., the GBPS group is significantly heavier than the SFBM group. This suggests that the severe obesity seen in the GBPS group is related more to familial factors, including genetic predisposition and family eating patterns.

NR381 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Nociception in Bulimia Nervosa During Treatment

Nancy M.C. Raymond, MD., Psychiatry, University of Minn., Bx 393 UMHC 420 Delaware St SE, Minneapolis, MN 55455; Patricia L. Faris, Ph.D., James E. Mitchell, M.D., Elke D. Eckert, M.D.

Summary:

Basic research has supported an involvement of the vagus nerve in the relay of both satiety and nociceptive information from the periphery to the CNS. In patients with bulimia nervosa, binge eating episodes may be partially explained by abnormalities in the processing of satiety-related information. Therefore, if the vagus nerve is involved in the pathophysiology of bulimia nervosa, then the decrease in the perception of satiety might be accompanied by a decrease in nociceptive perception evidenced by an increase in nociceptive thresholds.

Our research group has found significant elevations in pain thresholds in women with bulimia nervosa ($n = 27$, repeated measure ANOVA, $p < 0.01$). These data also show a significant negative correlation between pain detection thresholds and frequency of vomiting episodes ($R^2 = 0.151$, $p < 0.05$). Currently, we are assessing pain thresholds in bulimic patients being treated in a ten-week group therapy program. In our initial group ($n = 6$), the frequency of binge/purge episodes per week decreased during treatment by 89 percent. Inversely, pain detection thresholds increased by 24 percent. Thresholds in controls remain constant over time. A larger sample is now being examined. These preliminary findings indicate that an abnormality in vagal tone may contribute to the ongoing pattern of binge/purge behavior.

NR382 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Life Events and Anorexia Nervosa

Netta Horesh, Ph.D., Psychiatry, Chaim Sheba Medical Ctr., Tel Hashomer 52621, Israel; Eli Lepkifker, M.D., ALlen Apter, M.D.

Summary:

Despite the growing literature on the relationship between sexual abuse and eating disorders, there are almost no reports of the effects of nonsexual, negative childhood experiences on the development of such disorders. The present study examined the association between different kinds of stressful life events (SLE) in childhood and adolescence and the development of anorexia nervosa. Fifteen adolescent inpatients with anorexia nervosa were compared with 79 adolescent, nonanorectic, psychiatric inpatients and 40 healthy adolescents for SLE throughout their lives. We used a semistructured interview based on the life event and family background scales developed by Pfeffer. ANOVAs and t-tests indicated that the anorectic patients showed significantly higher negative life event scores than healthy controls in all the areas examined. In addition, the anorectics reported significantly more negative life events concerning parents than patients with other psychiatric diagnoses. The results of the study emphasize the importance of SLE as precursors of psychopathology in adolescence, and more specifically—the contribution of negative experiences with parents to the development of anorexia nervosa.

NR383 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Interhemispheric Coordination and Affect Discrimination in Disruptive Behavior Disorder

Daniel F. Shreeve, M.D., Psychiatry, Wilford Hall USAF, 315 Argo Avenue, San Antonio, TX 78236

Summary:

Children's social adjustment requires not only the understanding of verbal instructions but also the comprehension of nonverbal messages. Whereas children are generally inaccurate decoding nonverbal signals, several authors postulate that the ADHD child may be especially disadvantaged based upon a right hemisphere defect (1). Alternatively interhemispheric transfer of information may particularly affect the discrimination of emotional cues (2).

In a research study of 12 children with disruptive behavior disorder, scores on the Profile of Nonverbal Sensitivity (PONS) are compared to a tactile test of interhemispheric coordination, the Haptic Transfer Test (HTT), and to hemispheric arousal measured by ipsilateral skin conductance level. The Pearson Product Moment statistic is significant for the relationship between PONS score and proficiency on the HTT ($p < .04$). This was not found in eight controls. Skill on the HTT also correlates inversely with "false alarms" in recognizing negative (hostile) signals in experimental subjects. The relative difference between right versus left skin conductance level is proportional to errors in those signals which combine body posture use with voice intonation ($p < .004$) in inpatients. Scales for hyperactivity or conduct disorder do not correlate with experimental variables in the inpatient subjects.

NR384 Tuesday May 5, 3:00 p.m.-5:00 p.m.

Child/Parent Perceptions of Psychiatric Treatment

Spyros J. Monopolis, M.D., Psychiatry, Frances Scott Key Med Ctr, 8116 Bellona Avenue, Towson, MD 21204; John Minas, Ph.D., John Myhill, Ph.D., Melinda B. Stein, Ph.D., Timothy Whalen, Chester W. Schmidt, M.D.

Summary:

This is a preliminary report on perceived symptom change and probable treatment side effects among children and parents. Our outpatient sample (N = 29; ages four to eight years, $\bar{X}$ = 9 years) consisted of three groups—depression 31 percent, ADHD 52 percent, both 17 percent. They received psychotherapy, antidepressents and/or stimulants. Psychiatric evaluations, self-reports and standardized instruments were used. The initial phase of data analysis involved χ^2, multiple correlation and ANOVA procedures. Depression symptom improvement was reported by 62 percent of children and 79 percent of parents ($p < .006$). ADHD symptom improvement was noted by 79 percent of youths and 90 percent of parents (high agreement). Probable medication side effects were reported by 35 percent of youngsters and 38 percent of parents ($p < .005$). Clinically, 55 percent of children were moderately ill, 55 percent minimally improved, and 41 percent showed moderate drug efficacy. The BPRS-C did not correlate significantly with severity of illness or improvement. It showed significant negative correlation with drug efficacy ($p < .01$). Treatment groups did not differ in regard to severity to illness, improvement, drug efficacy, or psychopathology. Clinical measures did not predict child or parent perception of symptom change. However, drug efficacy showed significant correlation with parent perception of ADHD symptom change ($p < 0.1$). Additional data will be presented on self-reports of pathology, treatment, and compliance. Further data analysis will include log-linear and multiple regression techniques and post hoc comparison tests.

NR385 Wednesday May 6, 9:00 a.m.-10:30 a.m.

BRAINBLAST: Voxel Processing for 3-D Brain Studies

Nancy C. Andreasen, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; Victor W. Swayze, M.D., Ted Cizadlo, M.S., Greg Harris, M.S., James Erhardt, Ph.D., William Yuh, M.D.

Educational Objectives:

To describe methods for three dimensional study of the human brain that produce high fidelity rendering of surface anatomy, and to discuss applications of this method to the study of the normal brain and mental disorders.

Summary:

Recent advances in magnetic resonance imaging now permit rapid acquisition of very thin slices (i.e., 1.5 mm). This in turn permits the development of image processing techniques that provide precise three-dimensional anatomical reconstructions that resemble formalin-fixed brains in visual detail. We have developed a software program, BRAINBLAST, that applies voxel processing techniques to the near cubic voxels acquired through these new advances. BRAINBLAST is then used to perform an "*in vivo* autopsy" on each image. Steps (and methods) involved are: removing the brain (edge detection), stacking the slices (reconstruction in z dimension), removing CSF (histograming), dissecting away blood vessels (connectivity heuristic), and highlighting sulci/gyri (surface normals). BRAINBLAST permits the investigator to manipulate the 3-D image in a variety of ways: rotation, resampling in multiple planes, capacity to "write on" images in one plane and telegraph to corresponding positions in other planes, visualization of internal three-dimensional structures, capacity to redissect, and capacity to measure areas and volumes. Applications include: study of individual normal variations in sulcal/gyral patterns, measurement of volumes of subregions using anatomic landmarks rather than arbitrary ones, evaluation of structure/function relationships in the normal and diseased brain, and teaching/learning neuroanatomy.

References:

1. Vannier MW, Brunsden BS, Hildebolt CF, et al: Brain surface cortical sulcal lengths: Quantification with three-dimensional MR imaging. *Radiology,* 180:479-484, 1991.

2. Toga AW: *Three-dimensional neuroimaging.* Raven Press, New York, 1990.

NR386 Wednesday May 6, 9:00 a.m.-10:30 a.m.

D3 Receptor Polymorphism and Schizophrenia

Marc-Antoine Crocq, M.D., Psychiatry, Centre Hosp Special, 27 Rue Du 4e R.S.M., Rouffach 68250, France; Lars Lannfelt, M.D., Pierre Sokoloff, Ph.D., Antonia Mayer, Ph.D., Jean-Charles Schwartz, Ph.D., Jean-Paul Macher, M.D., Marie-Pascale Martres, Ph.D., Yann Hode, M.D., Fabrice Duval, M.D.

Educational Objectives:

To discuss the possibilities and pitfalls of genetic association studies in psychiatry, specifically in the case of complex and heterogeneous disorders such as schizophrenia.

Summary:

Objective: The recently cloned human D3 dopamine receptor may play a role in schizophrenia because it is mainly expressed in limbic structures and is a target for neuroleptics. We investigated the association between schizophrenia and a two-allele polymorphism, characterized by a point mutation (A to G) in the 5′ end of the D3 receptor gene leading to a Serine (allele 1) to Glycine (allele 2) amino-acid substitution in the N-terminal part of the receptor protein, and creating a BalI restriction site. *Method:* We studied 48 DSM-III-R schizophrenic inpatients with a chronic course, and 49 healthy controls without psychiatric history. The D3 genotype was determined by PCR amplification of a 462 bp fragment in the 5′ end of the gene and subsequent BalI cleavage. *Results:* In this population, the distribution of the three possible genotypes (i.e., 1-1; 1-2; 2-2) differed between controls and schizophrenics (N = 19; 28; 2 and 22; 18; 8 respectively). Specifically genotype 2-2 was associated with an excess of schizophrenics (Fisher's exact test, P = 0.04). *Conclusion:* The data suggest that D3 dopamine receptor polymorphism might play a role in the expression of schizophrenic illness. We emphasize that the results are preliminary and need to be confirmed by research with more individuals.

References:

1. Sokoloff P, Giros B, Martres MP, et al: Molecular cloning and characterization of a novel dopamine receptor (D3) as a target for neuroleptics. *Nature* 347:146-151, 1990.

2. Giros B, Martres MP, Sokoloff P, Schwartz JC: cDNA cloning of the human dopaminergic D3 receptor and chromosome identification. *C R Acad Sci Paris* 311:501-508, 1990.

NR387 Wednesday May 6, 9:00 a.m.-10:30 a.m.

Withdrawn

NR388 Wednesday May 6, 9:00 a.m.-10:30 a.m.

Genetic Studies in Schizophrenia: An Update

Mihael H. Polymeropoulos, M.D., LBG, NIMH, 2700 M.L. King Jr. Avenue SE, Washington, DC 20032; Hong Xiao, M.D., Timothy Crow, M.D., Lynn Delisi, M.D., Carl R. Merrill, M.D.

Educational Objectives:

To discuss a strategy for genome-wide search for a major locus associated with schizophrenia, using highly informative markers;

to address practical issues such as marker availability, progress in mapping and rates of genotyping.

Summary:

Findings from twin, adoption, and family studies have suggested that schizophrenia is an inherited disorder. Several models of inheritance have been proposed, including autosomal recessive, dominant, pseudoautosomal, and polygenic. While the mode of inheritance is debated, it is clear that schizophrenia exhibits phenotypic variability, even within affected members of the same family. Such an uncertainty in diagnostic classification can have a tremendous impact on the outcome of genetic linkage studies. One way to minimize the effect of uncertain diagnostic classifications is to limit the study to affected sib-pairs and their parents when both of the siblings can be diagnosed with schizophrenia with a high degree of confidence. Given the complexities in the mode of inheritance, the size of the sample becomes an issue. A total of 171 individuals were typed with 70 markers and, for those markers that resulted in inconclusive data, typing was expanded through to an additional 130 individuals. Results on a number of markers along with the effects of sample size will be presented.

References:

1. Weber and May: *Am. J. Hum. Genet.* 44:388-396, 1989.

2. Smeets et al: *Hum. Genet.* 83:245-251, 1989.

NR389 Wednesday May 6, 9:00 a.m.-10:30 a.m.

IQ and Brain Size in Schizophrenics and Normals

Michael A. Flaum, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; Dan S. O'Leary, Ph.D., Victor W. Swayze, M.D., Randy Alliger, Ph.D., Gregg Cohen, M.S., Nancy C. Andreasen, M.D.

Educational Objectives:

To present the methods, results and implications of a study of the relationship between IQ and several measures of brain volume ascertained with MRI, in a large group of schizophrenic and normal subjects.

Summary:

The literature on the relationship between brain size and IQ has been controversial.[1] A recent study using MRI demonstrated a significant positive relationship in a group of 40 normals.[2] We examined the relationship between IQ and volumes of several brain structures/regions in a sample of 71 normal controls and 74 DSM-III-R schizophrenic subjects who underwent IQ testing (full WAIS-R) and MRI in our laboratory. All subjects were scanned on a 1.5 Tesla G.E. Signa scanner, with the same protocol (both PD and T-2 weighted sequences, with 5mm coronal slices and a 2.5mm gap). All tracings were performed by a single rater, blind to diagnosis, using a semi-automated method, yielding volumetric estimates of 23 separate brain structures/regions.

Results: The controls had significantly higher IQ scores than did the patients (FSIQ 116 ± 14 vs. 88 ± 14). For the control group, Pearson correlations (with height partialled) yielded significant positive correlation coefficients between FSIQ and each of the following volumes: cranium, cerebrum, cerebellum, temporal lobe, thalamus and hippocampus. No relationship was noted in the controls between IQ and volumes of the ventricular system or lenticular nuclei. In contrast, among the schizophrenic group, there were no significant correlations between either verbal or performance IQ and any of the measures of brain volume. These results may provide continuing confirmation for an early neurodevelopmental defect in schizophrenia.

References:

1. Van Valen L: Brain size and intelligence in man. *American Journal of Physical Anthropology.* 40:417-424, 1974.

2. Willerman L, Schultz R, Rutledge NJ, Bigler ED: In vivo brain size and intelligence. *Intelligence.* 15:223-228, 1991.

NR390 Wednesday May 6, 9:00 a.m.-10:30 a.m.

Obligate Carriers of Schizophrenia

Merilye C. Waldo, Ph.D., Psychiatry, Univ of Colo. HSC, 4200 E. Ninth Ave. Box C268-71, Denver, CO 80262; Alice Madison, M.D., Ellen Cawthra, R.N., William Byerley, M.D., Marina Myles-Worsley, Ph.D., Larry Adler, M.D.

Educational Objectives:

By the end of this presentation the audience should have a rudimentary understanding of the importance of P50 auditory sensory gating in schizophrenia research, and of the usefulness of combining this methodology with obligate carrier analysis of schizophrenic families.

Summary:

Schizophrenia itself may have too low a penetrance to provide a reliable phenotype in most families for linkage studies. It would be desirable to identify other biological manifestations of genes that convey risk for schizophrenia. One approach to this problem, used for genetic studies of large pedigrees, is to identify obligate carriers of the disorder as subjects with evidence of schizophrenia both in their offspring and in their ancestors. Neurobiological deficits in these obligate carriers would be candidates for markers of genes that convey risk for schizophrenia. One such marker is loss of auditory sensory gating of the P50 wave, rare in individuals from the general population (10%-15%) and common in schizophrenia (85%-90%). We studied 22 nuclear families, which comprise both parents and one schizophrenic offspring. In all families, at least one parent had the P50 gating deficit; 95% of the schizophrenics also showed the deficit. In 86% of the families, at least one parent had a known ancestral history of schizophrenia. Of the 22 parents with schizophrenic ancestors, 86% had the P50 gating deficit, whereas their spouses without family histories of schizophrenia had only a 8% incidence of gating deficit (Chi Square 17.4, 1 d.f., $p = .00003$). In the families with no known history of schizophrenia, at least one of the parents demonstrated a sensory gating deficit. The P50 gating deficit may be an alternative phenotypic marker for genetic studies of schizophrenia.

References:

1. Waldo M, Carey G, Myles-Worsley M, Cawthra E, Adler L, Naganoto H, Wender P, Byerley W, Plaetke R, Freedman R: Co-Distribution of a Sensory Gating Deficit and Schizophrenia in Multi-Affected Families (In Press).

2. Waldo M, Cawthra E, Adler L, Dubester S, Staunton M, Nagamoto H, Baker N, Madison A, Simon J, Scherzinger A, Derebing C, Gerhardt G, Freedman R: Multiple Factors in the Pathogenesis of Schizophrenia: Abnormalities in Sensory Gating, Hippocampal Volume and Dopamine Metabolism in Schizophrenics and Their Sibling (In Press).

NR391 Wednesday May 6, 9:00 a.m.-10:30 a.m.

P500 Amplitude Discriminates Between ADD Subtypes

R. Scott Smith, M.A., Psychology, Univ of Texas El Paso, Psychiatry 116A/940 Belmont St., Brockton, MA 02401; Jon F. DeFrance, Ph.D., Stephen F. Sands, Ph.D., Lloyd Smith, B.A.

Educational Objectives:

To come

Summary:

The DSM-III recognized two diagnoses of attention deficit disorder: attention deficit disorder with hyperactivity (ADHD) and attention deficit disorder without hyperactivity (ADD). The DSM-III-R only recognizes the diagnoses of ADHD. To empirically evaluate the unidimensional utility of the DSM-III-R, event-related potentials (ERPs) were recorded simultaneously with the administration of a visual continuous performance task (CPT) from 62 children. The groups consisted of 26 ADHD, 17 ADD, and 19 normal controls (NC). ERPs were recorded from 28 electrode sites using an extended 10/20 system. A late positivity (P500) to target CPT trials was elicited. P500 topographic differences between groups were evidenced by significance probability mapping. These topographic differences between groups were largest at parietal electrode sites. MANOVA indicated a significant group by electrode site interaction ($F = 6.18$, $p < .005$) among ADHD, ADD, and NC. P500 amplitude was then subjected to a discriminate function analysis. The three groups were correctly classified by the discriminate function analysis in over 90% of all cases. This separation was obtained solely on the basis of P500 amplitude, without the aid of behavioral data. These findings suggest that the bidimensional approach employed by the DSM-III is more appropriate than the current unidimensional approach of the DSM-III-R.

References:

To come.

NR392 Wednesday May 6, 9:00 a.m.-10:30 a.m.

Neonatal Hypoxic Exposure Results In Hyperactivity

Bruce I. Diamond, Ph.D., Psychiatry, Medical Col. of Georgia, 1515 Pope Street, Augusta, GA 30912; Morris J. Cohen, Ed.D., Jian Wang, B.S., Karen L. Campbell, B.A., Richard L. Borison, M.D.

Educational Objectives:

To learn conditions where hypoxia may play a role in neuropsychiatric conditions as well as the most relevant neurochemical mechanisms and pathological substrates underlying hyperactivity attention deficit disorders.

Summary:

Hypoxic injury has been implicated in several neurological and behavioral disorders. In this study, the second day after birth, male Sprague Dawley rats were randomly assigned to either 0 (room air), 30 minutes or 60 minutes of 6% oxygen and balanced nitrogen at 34°C in a closed chamber. This model simulates hypoxia-ischemic injury in the developing fetus or pre-term infant. Rats were tested for spontaneous and apomorphine-induced activity and sterotypy 85 days later. Animals were sacrificed, their brains removed and dopamine as well as norepinephrine were measured by HPLC. Norepinephrine levels were significantly ($p < .05$) elevated from controls in the nucleus accumbens and striatum, whereas dopamine levels were elevated in the caudate nucleus and decreased in the nucleus accumbens. These changes occurred with an increase in spontaneous activity and stereotypy that correlated with time of hypoxic exposure. Apomorphine only increased activity and sterotypy in control animals. These results suggest that neonatal hypoxia leads to the development of hyperactivity whose pathology may be due to abnormal catecholamine function.

References:

1. Johnston MV, Silverstein FS: New insights into mechanisms of neural damage in the developing brain. *Pediatric Neurosci,* 12: 87-89, 1986.

2. Shawitz BA: The sequelae of hypoxic-ischemic encephalopathy. *Seminars in Perinatology* 11: 180-190, 1987.

NR393 Wednesday May 6, 9:00 a.m.-10:30 a.m.

Association of ADHD with Generalized Resistance to Thyroid Hormone in 18 Kindreds

Peter Hauser, M.D., NIKKD MCEB RM 8D14, Natl Inst of Hlth Bldg 10, 900 Rockville Pike, Bethesda, MD 20892; Alan J. Zametkin, M.D., Pedro Martinez, M.D., Benedetto Vitiello, M.D., A. James Mixson, M.D., Bruce D. Weintraub, M.D.

Educational Objectives:

To demonstrate the effect of mutations in the human beta thyroid receptor gene on behavior and to postulate a molecular model for the pathogenesis of attention deficit hyperactivity disorder.

Summary:

The syndrome of generalized resistance to thyroid hormone (GRTH) is characterized by elevated levels of triiodothyronine (T3) and thyroxine (T4), inappropriately nonsupressed levels of thyroid-stimulating hormone (TSH) and resistance of pituitary and peripheral tissues to the action of thyroid hormone. GRTH is a disease with a primarily autosomal dominant inheritance and linkage to the human beta thyroid receptor (hTRβ) gene has been demonstrated. To date, we have identified 13 distinct mutations located in exons 9 and 10 of the hTRβ gene in 13 of 18 unrelated kindreds with GRTH. Various somatic and neuropsychiatric manifestations of GRTH, including symptoms of hyperactivity, have been observed, but the association of ADHD with GRTH has not been systematically assessed. In the present study, we evaluated the presence of ADHD and other psychiatric disorders in our 18 kindreds with GRTH. The study population consisted of 49 affected and 55 unaffected family members comprising a total of 52 adults (≥18yrs) and 52 children (<18 yrs). Each child and one of the parents were interviewed by a child psychiatrist who was blind with respect to the diagnosis of GRTH using the DICA (parent or child version). Adults were interviewed about their own symptomatology by a psychologist, blind with respect to the diagnosis of GRTH, using the SADS and a ADHD symptom checklist designed to evaluate the presence of childhood and adult ADHD. Our results demonstrate that, for adults and children combined, 61% (30/49) of patients affected with GTHR met criteria for the diagnosis of ADHD compared with 13% (7/55) of unaffected family members ($p < 0.0001$). Further, the mean ADHD symptom score was 2.5 fold higher in the affected patient group as compared with the group of unaffected family members (7.0 vs. 2.8, $p < 0.0001$). Other psychiatric diagnoses were not significantly different between the two groups. These data suggest that ADHD is strongly and specifically associated with GRTH. This is the first defined molecular model of ADHD and may provide new insights into the basic pathogenesis of this disorder.

References:

1. Usala et al.: A base mutation of the c-erbA-beta thyroid hormone receptor in a kindred with generalized thyroid hormone resistance. *J. Clin. Invest.* 85:93-100, 1990.

2. Parilla et al.: Characterization of seven novel mutations of the c-erbA-beta gene in unrelated kindreds with generalized thyroid hormone resistance. *J. Clin. Invest.* 88:2123-2130, 1991.

NR394 Wednesday May 6, 9:00 a.m.-10:30 a.m.

The Continuity Between Childhood and Adult Depression: Longitudinal Study of Depressed Children as Adults

Christina A. Sobin, Ph.D., Psychiatry, Columbia Col. of Phys., 722 West 168th Street Box 14, New York, NY 10032; Jacqueline Martin, R.N., Philip Adams, Ph.D., Myrna M. Weissman, Ph.D.

Educational Objectives:

To demonstrate knowledge of Puig-Antich's original findings, the clinical syndrome of childhood depression and its subtypes, and the continuity into adulthood of childhood depression and associated social functioning deficits.

Summary:

Ten years ago, Joaquim Puig-Antich et al. evaluated 447 children between the ages of 6 and 17 using unmodified Research Diagnostic Criteria. Two-hundred and four (204) were found to meet full criteria for major depressive disorder. Puig-Antich et al. (1985) also reported that following remission, peer and sibling relationships of depressed children continued to be disrupted. We are re-interviewing these patients who are adults and obtaining current and lifetime diagnoses using the SADS-LA and other instruments including the Social Adjustment Scale—Interview Retrospective Version, Family History Epidemiologic, and self-administered questionnaires.

This presentation will provide a brief review of Puig-Antich et al.'s original findings and a report of our early follow-up results. Among the first subjects recontacted, seven suicides were found in the depressed children, and none in the psychiatric or normal controls (Rao, Weissman, Martin & Hammond, 1991). This yielded a suicide rate of 4.4%. Suicide occurred an average of 6.7 years following the onset of first major depressive episode. Initial diagnostic data on approximately 30 subjects will be used to compare diagnoses and social adjustment at times 1 and 2. We predict higher rates of adult depressive-spectrum illnesses for those children diagnosed as depressed at time 1, and continuing deficits in social functioning. Longitudinal findings impact treatment indications for depressed children, as well as our practical and conceptual understanding of adult depressive illness.

References:

1. Bao U, Weissman M, Martin J, Hammond R: Childhood depression and risk of suicide: A preliminary report of a longitudinal study. *Journal of the American Academy of Child Psychiatry,* 1991 (in press).

2. Ambrosini P, Puig-Antich J: Major depression in children and adolescents. In Shaffer D, Erhard A & Greenhill L (eds) *The Clinical Guide to Child Psychiatry.* New York, Free Press, pp 182-191, 1985.

NR395 Wednesday May 6, 9:00 a.m.-10:30 a.m.

Anxiety Disorders in 30 Alcoholic Adolescents

Duncan B. Clark, M.D., Psychiatry, Western Psych. Inst., 3811 O'Hara Street, Pittsburgh, PA 15213; Rolf G. Jacob, M.D., Oscar Bukstein, M.D., Juan E. Mezzich, M.D.

Educational Objectives:

1) To review the importance of recognizing comorbid anxiety disorders, especially PTSD in adolescents with alcohol abuse and dependence; 2) To describe the correlates of anxiety disorders in this population, including implications for assessment and treatment.

Summary:

Thirty adolescents with a history of alcohol abuse or dependence (mean age of 15.4 ± 1.5; 15 female, 15 male) were carefully assessed for anxiety disorders using a modified K-SADS. Thirteen (43%) had anxiety disorder diagnoses. Posttraumatic stress disorder was the most common (eight cases). In four PTSD cases, the adolescents had a history of sexual and/or physical abuse by a family member. In the four other PTSD cases, two adolescents were raped, one was in a motor vehicle accident, and one was severely beaten by a gang. In 11 (85%) of these 13 cases, an anxiety disorder presented before alcohol abuse or dependence. Adolescents with both an anxiety and an alcohol disorder frequently had had a wish to die (77%), suicidal ideas (62%), and suicide attempts (46%). In many of these adolescents, chronological as well as perceived relationships showed that anxiety disorders, particularly PTSD, contributed to the development and morbidity of alcohol abuse and dependence. Cases will be presented and discussed.

Supported by the NIAAA Grant AA08746-02.

References:

1. Bukstein OG, Brent DA, Kaminer Y: Comorbidity of substance abuse and other psychiatric disorders in adolescents. *Am J Psychiatry* 146:1131-1141, 1989.

2. Brown GR, Anderson B: Psychiatric morbidity in adult inpatients with histories of sexual and physical abuse. *Am J Psychiatry* 148:55-61, 1991.

NR396 Wednesday May 6, 9:00 a.m.-10:30 a.m.

Childhood Abuse and Neglect in BPD

Joel F. Paris, M.D., psychiatry, Jewish General Hospital, 4333 Cote Ste Catherine Road, Montreal PQ H3T 1E4, Canada; Hallie Zweig-Frank, Ph.D., Jaswant Guzder, M.D.

Educational Objectives:

To present findings of a study comparing childhood experiences of abuse and neglect in borderlines vs. non-borderline personality disorders.

Summary:

Female borderline (n = 78) and non-borderline (n = 72) personality disorder patients were given a semi-structured interview to assess abuse during childhood, as well as the Parental Bonding Index which measured neglect. Seventy-three percent of the borderlines experienced childhood sexual abuse, compared with 46% of the controls ($p<.002$). However, when the two groups were compared for the perpetrators of abuse, the differences were significant only for relatives outside the immediate nuclear family and for non-relatives. Borderlines also reported significantly more physical abuse ($p<.05$).

A discriminant function using sexual abuse, physical abuse, neglect, and histories of early separation or loss classified borderline patients correctly at 70%. The coefficients showed that sexual abuse was the strongest discriminating variable.

The findings confirm the earlier studies (1, 2) which show that childhood sexual abuse is particularly common in BPD, but suggest that such experiences do not correspond to incest within the nuclear family.

References:

1. Ogata SN, Silk KR, Goodrich S, et al.: Childhood sexual and physical abuse in adult patients with borderline personality disorder. *Am J Psychiatry* 147:1008-1013, 1990.

2. Herman JL, Perry JC, van der Kolk BA: Childhood trauma in borderline personality disorder. *Am J Psychiatry* 146:490-495, 1989.

NR397 Wednesday May 6, 12 noon-2:00 p.m.

Biochemical Effects of Clozapine and Haloperidol

Alan I. Green, M.D., Psychiatry, Harvard Med. School, MMHC 74 Fenwood Road, Boston, MA 02115; Mohammed Y. Alam, M.D., Roger A. Boshes, M.D., Kathleen M. Pappalardo, B.S., Mary E. Fitzgibbon, B.S., Joseph J. Schildkraut, M.D.

Summary:

This presentation reports data on similarities and differences between effects of clozapine (CLOZ) and haloperidol (HAL) and plasma catecholamines and metabolites in eight treatment-resistant schizophrenic patients who underwent a 2½-6 week neurolep-

tic-free period before being treated with CLOZ, and 11 chronic schizophrenic/schizoaffective patients with acute exacerbations who underwent a five-to-seen day neuroleptic-free period before being treated with HAL. Following CLOZ treatment, plasma levels of homovanillic acid (pHVA) and 3-methoxy-4-hydroxyphenylglycol (pMHPG) decreased significantly ($p<.05$) with clinical response, whereas plasma levels of dopamine (pDA) and norepinephrine (pNE) increased significantly ($p<.05$). Following HAL treatment, levels of pHVA increased during the first week of treatment before falling to baseline, while levels of pMHPG fell; similarly, levels of pDA increased during the first week of treatment and then decreased (like pHVA) and pNE decreased (like pMHPG). The sustained increases in pDA and pNE with CLOZ but not HAL may be related to the unusual clinical effects of CLOZ. The possible contribution of the CLOZ-induced pDA elevation toward an understanding of CLOZ's reported potential for decreasing cocaine self-administration in animals and substance abuse in man (Chorus and Cole, personal communication, 1992) will be discussed.

NR398 Wednesday May 6, 12 noon-2:00 p.m.

Does Psychosis Contribute to Water Intoxication?

Morris B. Goldman, M.D., Psychiatry, Univ of Chicago Med Ctr, 446 Lenox, Oak Park, IL 60302; Daniel J. Luchins, M.D., Gary L. Robertson, M.D., Donald Hedeker, Ph.D., Javaid Javaid, Ph.D., Robert C. Marks, M.D.

Summary:

Our previously described defects in secretion of the antidiuretic hormone and regulation of desire for water were sufficient to account for basal hyponatremia in stable, polydipsic, hyponatremic psychotics, but too mild to account for their epidodic water intoxication. To determine if water intoxication could be caused by psychotic exacerbations, we administered the psychotimimetic, methylphenidate, to male polydipsic schizophrenics with ($n=9$) and without ($n=6$) a history of water intoxication, and to age-matched normal males ($n=11$). Schizophrenics were stabilized on fluphenazine prior to the study. Parameters were measured every 15 minutes from 30 minutes prior to infusion of 0.5 mg/kg of drug (given over 30 seconds), and for the next 120 minutes. Plasma vasopressin and desire for water increased significantly in all three groups (ANOVA with repeat measures), though the vasopressin increase was greatest in normals ($p<.01$). The increase in plasma vasopressin was related to the severity of drug-induced psychosis in schizophrenics ($r=.62$, $df=15$, $p<.007$). We conclude that psychotic exacerbations may worsen water imbalance in schizophrenia, but polydipsic patients with a history of water intoxication appear no more susceptible than those without such a history. While mild drug-induced epigastric symptoms may account for some of our findings, this is unlikely to explain the entire response in schizophrenic subjects. (Supported by NIMH IR29 MH 43618-O1A1 and the Scottish Rite Foundation.)

NR399 Wednesday May 6, 12 noon-2:00 p.m.

Idazoxan Augmentation of Neuroleptic Therapy: Antagonist Strategies in the Pharmacotherapy of Schizophrenia

Robert E. Litman, M.D., ETB, NIMH 10/4N214, 9000 Rockville Pike, Bethesda, MD 20892; Walter W. Hong, M.D., Rolando Gutierrez, M.D., Manji Husseini, M.D., William Z. Potter, M.D., David Pickar, M.D.

Summary:

The atypical neuroleptic, clozapine's, superior therapeutic efficacy over typical neuroleptics has been attributed to its antagonism of nondopaminergic receptors combined with dopamine receptor blockade. In a crossover, placebo-controlled, double-blind study comparing fluphenazine and clozapine treatment, we found that clozapine significantly reduced total and both positive and negative symptoms, and greatly enhanced indices of noradrenergic turnover, including increased urinary excretion of norepinephrine and normetanephrine. The latter biochemical effects reflect clozapine's unique pharmacology as an α_2 adrenergic antagonist.

To investigate further whether clozapine's therapeutic efficacy is related to its α_2 antagonist properties, we administered oral idazoxan, a potent, highly selective α_2 receptor antagonist, to six patients with schizophrenia on chronic fluphenazine treatment under placebo controlled, double-blind conditions. Compared to fluphenazine alone, combining idazoxan (mean dose 120 mg/day) with fluphenazine (mean dose 28 mg/day) resulted in a significant decrease in total symptoms ($p<0.05$) and a decrease in negative symptoms approaching significance ($p<0.07$). Positive symptoms were not significantly decreased, but clinically observable reductions in positive symptoms were observed in three patients. These data suggest that balance between dopaminergic and noradrenergic neurotransmission is important for clozapine's mechanism of action, and that augmentation of typical neuroleptic treatment with α_2 receptor antagonists may improve antipsychotic response in schizophrenia.

NR400 Wednesday May 6, 12 noon-2:00 p.m.

Schizophrenia: MRI Temporal Volumes and Neuropsychology

Paul G. Nestor, Ph.D., Psychiatry, Brockton VAMC, 116A 940 Belmont, Brockton MA 02401; Martha E. Shenton, Ph.D., Robert W. McCarley, M.D., Jennifer Haimson, Robert S. Smith, M.A., Ron Kikinis, M.D.

Summary:

To examine the neuropsychological correlates of MRI temporal lobe abnormalities (TL) in schizophrenia (SZ), 15 SZs were administered the Wisconsin Card Sorting Test (WCST), the Wechsler Memory Scale-Revised (WMS-R), and the Wechsler Adult Intelligence Scale-Revised (WAIS-R). Quantitative semi-automated MRI image processing techniques acquired from a 1.5 Tesla magnet were used to obtain volumes of left and right TL, and grey matter within the superior temporal gyrus (STG), hippocampus, and parahippocampus gyrus (PHG). Reduced volume in TL structures correlated with poorer scores on the WCST, Verbal Paired Associates of the WMS-R, and the Similarities subtest of the WAIS-R, but not with performance on other neuropsychological tasks. Poorer WCST correlated with reduced volume in the left ($r=.69$, $p<.01$) and right ($r=.62$, $p<.05$) PHG and left ($r=.71$, $p<.01$) and right ($r=.67$, $p<.01$) STG. A similar pattern of significant correlations was found between TL structures and Similarities and Verbal Paired Associated. Thus, reduced TL volume may be related to impairments in categorization, as measured by the WCST, and semantic processing, as measured by Similarities and Verbal Paired Associates. Moreover, putative frontal lobe indicators (WCST) may reflect TL damage in SZ, perhaps as a consequence of damaged projections to the frontal lobe.

NR401 Wednesday May 6, 12 noon-2:00 p.m.

Temporal Lobe in schizophrenia

Patrick E. Barta, M.D., Psychiatry, Johns Hopkins University, 600 N. Wolfe Street 3-166, Baltimore, MD 21205; Godfrey D. Pearlson, M.D., Richard E. Powers, M.D., Rajiv Menon, M.B., Stephanie Richards, Larry E. Tune, M.D.

Summary:

We extended our prior MRI study of temporal lobe morphology in schizophrenia[1] in an enlarged sample of 41 DSM-III-schizophrenics and 52 screened normal controls. Groups were matched

on age, sex, race and family SES. Schizophrenics had significantly fewer years of education, leading us to covary on this measure. MRI parameters were identical to our prior study. Ratings were carried out blindly by a neuropathologist using our former RO1 definitions, with the addition of new measures for anterior and posterior superior temporal gyrus (STG).

After accounting for intracranial volume and education, schizophrenics showed significantly reduced volume of both amygdalae, left anterior STG, left posterior STG and left entorhinal cortex. These results show more lateralization than our prior report. The lateralized finding in posterior STG is consistent with the hypothesis of Crow, implicating the planum temporale in schizophrenia. 3-D reconstructions of the planum temporale from volumetric MRI data, and quantified measures of this region will be shown.

NR402 Wednesday May 6, 12 noon-2:00 p.m.

Genetic Transmission of Familial Schizophrenia

Martin Alda, M.D., Psychiatry, University of Ottawa, 1145 Carling Avenue, Ottawa Ontario K1Z, 7K4, Canada; Alain Labelle, M.D., Maria Dvorakova, Ph.D., Barry Jones, M.D., Petr Zvolsky, M.D., Hope Fraser, B.Sc., Jean-Michel Le Melledo, M.D., Paul Cameron, B.Sc.

Summary:

Linkage analysis is an important tool for detecting major-gene effects in etiology of familial diseases. However, its application in research of schizophrenia has produced ambiguous or negative results. This can be ascribed partly to the lack of information about the role of genetic factors in schizophrenia and about the mode of inheritance. Results of segregation analyses of large samples of families have not been compatible with single-gene transmission. However, families for linkage studies are selected based on high numbers of affected relatives. Such families can represent an extreme on the continuum of genetic loading, but they may also be a distinct subgroup. We have investigated the mode of inheritance of schizophrenia in 25 moderately large pedigrees with high prevalence of the disease. The diagnoses in relatives were based on the RDC/DSM-III-R criteria. A total of 92 subjects were diagnosed with an illness from the spectrum of schizophrenia-related disorders; 224 subjects were healthy. The analysis used a single-gene model with incomplete penetrance and the maximum-likelihood procedure for parameter estimation. The dominant model with incomplete penetrance (maximum penetrance = 0.7) fits the data significantly better than the recessive model. Even better fit is obtained if the age-of-onset distribution in subjects born after 1945 is modelled separately (earlier onset). The results further indicate that if no ascertainment correction is applied, the gene frequency will be overestimated, inflating proportions of homozygotes among affected subjects.

NR403 Wednesday May 6, 12 noon-2:00 p.m.

Focal Temporal Lobe Abnormalities in Schizophrenia

Manuel F. Casanova, M.D., Psychiatry, Medical Coll. of Georgia, 1515 Pope Street, Augusta, GA 30912; Daniel R. Weinberger, M.D., E. Fuller Torrey, M.D., Bagao Xu, Jay Sobus, Behnam Pourdeyhimi, Ph.D.

Summary:

Recent neuroimaging studies have reported significant volume reductions of temporal lobes in patients with schizophrenia. A major portion of the reported tissue "loss" was further localized to the gray matter by using either isodensity pixel counting or a semi-automated optical threshold detection method. In order to better evaluate the nature of this finding (i.e., diffuse vs. focal), we analyzed the shape of the temporal lobes of 21 monozygotic twin pairs discordant for schizophrenia. According to previous studies, generalized structural abnormalities cause reduction in size but leave the basic conformation of the structure intact. Focal or multifocal tissue "loss," however, results in both size reduction and distortions in shape. Paired t-test analysis of shape description factors from the latter series showed significance or a trend towards the same in 20 out of 84 comparisons. Those results are consistent with bilateral focal or multifocal distortions of the temporal lobes of patients with schizophrenia. Furthermore, given that the experimental and control groups were matched completely for inherited genome and partially for postnatal environment, differences in temporal lobe morphology suggests the occurrence of a lesion during prenatal brain development.

NR404 Wednesday May 6, 12 noon-2:00 p.m.

Early-Onset Temporal Lobe Lesions in Schizophrenia

Manuel F. Casanova, M.D., Psychiatry, Medical Coll. of Georgia, 1515 Pope Street, Augusta, GA 30912; Denise Evans, M.D., Ramon E. Figueroa, M.D., Kathleen A. Crapanzano, M.D., Nathan DeVaughn, B.S.

Summary:

Recent neuroimaging studies indicate that both right and left temporal lobe volumes are reduced in patients with schizophrenia. This volumetric reduction appears to be the result of focal or multifocal gray matter abnormalities. Since early in life brain growth, or lack thereof, influences the overlying skull configuration, we attempted to elucidate the time of onset of the temporal lobe lesion in patients with schizophrenia by quantifying the angulation of their petrous ridges. Anatomically, the petrous bone defines the posterior extent of both the middle cranial fossa and the temporal lobes. The subject population consisted of 22 patients with schizophrenia (DSM-III-R criteria) and 17 age-matched controls. An inclined PA view of the skull was taken and the petrous ridge angulation measured against a reference line passing through the cristae galli and the insertion of the anterior nasal spine. Statistical analysis revealed significant differences between the angulation of the petrous ridge on the right side (t-test, $T = 2.22$, $p < 0.05$). The results suggest that the observed temporal lobe reduction of patients with schizophrenia is due to a prenatal or early postnatal brain lesion that altered the normal developmental pattern of the skull with the resultant asymmetry persisting into adulthood.

NR405 Wednesday May 6, 12 noon-2:00 p.m.

Rating of Medication Influences in Schizophrenia

Tasha Mott, M.A., Psychiatry, St. Lukes Roosevelt, Schizophrenia Frog 428 W. 59st, New York, NY 10019; Peter J. Weiden, M.D., Marcella Lennon, M.D., Dodi Goldman, M.A., John Ragone, M.D., Bruce Rapkin, Ph.D.

Summary:

Goals: Noncompliance is a major issue for schizophrenic outpatients. Despite this, there is no standardized measure for assessing attitudinal and behavioral factors related to neuroleptic noncompliance. The Rating of Medication Influences (ROMI) was developed to address this need.

Methods: There are three major parts to the ROMI: perceived reasons for compliance, perceived reasons for noncompliance, and rater judgment of factors not amenable to self-report (e.g. paranoia). Using the ROMI, a research team comprised of five raters conducted 25 interrater reliability sessions with schizophrenic patients participating in a longitudinal study on neuroleptic compliance. A kappa coefficient was computed for each possible paring of the five raters.

Results: Six of the seven items (86%) assessing perceived reasons for reported compliance and 10 out of 14 items (71%) rating perceived reasons for noncompliance achieved adequate

(.70 – 1.0) kappa coefficient scores. In contrast, the 11 rater judgment items only obtained marginal or inadequate kappa coefficients.

Conclusions: Our results show that: 1) it is feasible to reliably rate patient perception about their reasons to continue or stop neuroleptic medication, and 2) rater judgment on a cross-sectional interview for noncompliance is unreliable. We have used these results to update the ROMI so it can better assess patients' willingness and/or reluctance to take neuroleptic medication.

NR406 Wednesday May 6, 12 noon-2:00 p.m.

Validity of Diagnostic Criteria for Schizophrenia

Gerhard Lenz, M.D., Psychiatry, University of Vienna, Wahringer Gurtel 18-20, Vienna A1090, Austria; Kenneth Thau, M.D., Christian Simhandl, M.D.

Summary:

One aim of the Vienna follow-up study was to investigate the temporal stability and predictive validity of different diagnostic criteria for functional psychoses. Two hundred representative first hospital admissions (1980-1982) were documented with PSE and followed up seven years later (1987-1989). All patients were diagnosed simultaneously with polydiagnostic procedure (DSM-III, RDC, ICD, St. Louis, Taylor, Vienna Research Criteria).

The stability coefficient for diagnostic criteria for schizophrenia between first admission and follow-up was 88.9% for Taylor criteria, 88.2% for VRC, 86.4% for DSM-III, 80.0% for ICD and for St. Louis criteria and 77% for RDC.

Residual syndrome and/or psychotic symptomatology was used to identify the predictive validity of various diagnostic criteria for schizophrenia: DSM-III 0.81; St. Louis 0.81, RDC 0.77; VRC 0.74; ICD 0.70; Taylor 0.64. The power of diagnostic criteria to predict a residual syndrome and/or psychotic symptomatology at follow-up is increased if the diagnostic criteria already include a time factor (DSM-III, St. Louis criteria) or if prediction is based on the presence of formal thought disorder (VRC).

NR407 Wednesday May 6, 12 noon-2:00 p.m.

Illness Severity and Homelessness in Schizophrenia

Carol L.M. Caton, Ph.D., Psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; Lewis A. Opler, M.D., Patrick E. Shrout, Ph.D., Boanerges Dominguez, M.P.H., Frederic I. Kass, M.D., Paula F. Eagle, M.D.

Summary:

Are schizophrenic patients who become homeless more severely ill than those who do not? We explored this question in a case-control study of 100 homeless and 100 never-homeless young adult men with a history of at least one psychiatric hospitalization who met criteria for schizophrenia or schizoaffective disorder on the Structured Clinical Interview for DSM-III-R (SCID). The majority of subjects were African-American or Hispanic, unemployed, and single. Measures of illness severity included symptom ratings on the Positive and Negative Syndrome Scale (PANSS), concurrent alcohol and/or drug abuse, and Global Assessment of Functioning. Patterns of mental health service utilization and treatment compliance were also assessed.

Findings revealed that homeless schizophrenic men had significantly higher ratings on both positive and negative symptoms than domiciled subjects. Although alcohol abuse affected nearly half of subjects in both groups, homeless men were significantly more likely to abuse illicit drugs. Homeless men were more functionally impaired and were significantly less likely to comply with prescribed psychopharmacologic treatments. We explore severity of illness and homelessness in relation to life history variables such as onset of psychosis and substance abuse, premorbid functioning, and patterns of prior mental health service use. We discuss the implications of study findings for mental health policy.

NR408 Wednesday May 6, 12 noon-2:00 p.m.

Assessing Frontal Lobe Dysfunction

Kenneth Podell, Ph.D., Psychiatry, Med. College of Penn., 3200 Henry Avenue, Philadelphia, PA 19129; Michael Zimmerman, B.A., James L. Rebeta, Ph.D., Andrea Menezes, M.A., Elkhonon Goldberg, Ph.D.

Summary:

Frontal lobe dysfunction is common in neuropsychiatric disorders. The Executive Control Battery (ECB) has been designed to elicit the cognitive symptoms of frontal lobe dysfunction: perseverations, stereotypy, echopraxia, and disinhibition. We used discriminant analyses to compare two ECB subtests (Competing Programs: CP, and Graphical Sequence: GS) with the Wisconsin Card Sorting Test (WCST), the standard test of frontal lobe functions. ECB and WCST were given to 22 chronic schizophrenics (CS, DSM-III-R diagnosis); eight patients with isolated frontal lesions (FL, verified on MRI or CT); and 22 matched healthy volunteers (HV). The CS/HV classification was 86% (100% HV and 73% CS) correct with the combination of CP and GS subtests of ECB; 84% (100% HV and 68% CS) correct with the WCST Number of Categories; and 77% (91% HV and 64% for CS) correct with the WCST Perseverative Responses. The values for the FL/HV classification were 93% (100 HV and 75% FL); 90.00% (100% HV and 62% FL); and 90.00% (1005 hv and 62% FL), respectively.

Combined GS and CP subtests of ECB have superior sensitivity, and equal specificity, to both WCST indices. They are also shorter to administer: 30 minutes for GS and CP combined, and 40 minutes for the WCST.

NR409 Wednesday May 6, 12 noon-2:00 p.m.

Haloperidol Decanoate and Nicotine Alter Cell Surface Antigens in Rats: Implications for Schizophrenia

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Summary:

There is evidence of immunological abnormalities being present in schizophrenia. Many patients have been treated with haloperidol, a DA receptor blocker. Also, the incidence of smoking among schizophrenic outpatients (88%) is higher than among the general population (Hughes et al., 1986). We examined the change in peripheral and splenic blood mononuclear cell populations in rats treated repeatedly with either haloperidol decanoate (HAL), nicotine (NIC) or both. After 28 days of treatment, trunchal and splenic blood was collected. Lymphocytes were stained for Class II MHC, CD4, CD5 and CD8 antigens. Cell counts were analyzed by low cytometer. Chronic HAL resulted in an increased secondary population of CD4 cells, as well as increased fluorescence of a secondary population of CD5 cells, but suppressed a medium population of CD8 cells. Chronic NIC resulted in suppression of fluorescence of the primary population of Class II MHC, CD5 cells and of a medium population of CD8 cells, and skewed the distribution of CD4 cells. NIC/HAL resulted in separation of three populations of CD4 cells and a decrease in CD8 cells of medium brightness. Thus, chronic stimulation with a dopaminergic antagonist or cholinergic agonist altered immune responsiveness and should be considered in immunological studies of schizophrenia.

NR410 Wednesday May 6, 12 noon-2:00 p.m.

Clozapine-Induced Changes in Liver Enzymes

Robert A. Leadbetter, M.D., Psychiatry, Western State Hospital, P.O. Box 2500, Staunton VA 24401; Michael S. Shutty, Ph.D., Diane Pavalonis, M.S.N.

Summary:

Clozapine has recently been introduced for treatment-resistent schizophrenia. A number of toxic adverse reactions, including agranulocytosis, seizures, orthostatic hypotension, and weight gain have been noted. No systematic human studies have examined changes in liver enzymes with clozapine treatment, despite transient increases in transaminase enzymes noted in one study.[1] Another report noted clozapine-induced cholestatic jaundice.[2] We studied 17 patients by monitoring changes in liver enzymes six months before and six months after clozapine treatment. We found no significant change in SGOT, SGPT, LDH, and total bilirubin. However, elevation did occur in alkaline phosphatase ($t = 5.82$, $df = 16$, $p < .001$). Across all patients the mean alkaline phosphatase increased from 78 IU/1 to 102 IU/1. Seven patients had clinically significant elevations in alkaline phosphatase. Results of alkaline phosphatase isoenzyme profile and gamma GT suggest these observed elevations were from the liver. In these patients, a significant positive association between clozapine dose and alkaline phosphatase was noted, controlling for time (partial $r = 0.45$, $p < .009$). Possible etiologies include cholestatic jaundice associated with inhibition of bile secretion, a direct cytotoxic effect on the peribiliary cells in the liver, or a hypersensitivity reaction.

NR411 Wednesday May 6, 12 noon-2:00 p.m.

Monitoring Haloperidol Levels in Acutely Ill Schizophrenics

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Summary:

Forty-one acutely ill inpatients diagnosed with schizophrenia by DSM-III criteria completed at least two weeks of treatment with haloperidol. The initial dose was 5 mg. b.i.d. Dose was adjusted each week after determination of serum haloperidol level by radioimmunoassay (target range 8 to 25 ng/ml). At the end of one week's treatment, levels in seven subjects were below the range, with 27 subjects in range, and seven subjects above range. The ratios of blood level to medication dose (LDR) in these three groups were different (means of 0.86 ± 0.45, 1.56 ± 0.62, and 3.52 ± 1.34, respectively; $F_{2,38} = 24.5$, $p < 0.0005$). These differences in LDR were not explained by age or medication compliance prior to admission. Haloperidol level and LDR at week one were positively associated with rate of symptom reduction during the first week of treatment. During the second week, LDR increased in 22 subjects (mean change in level of 6.94 ± 7.42 ng/ml), and in 18 subjects, LDR decreased (mean change in level of -5.33 ± 8.50 ng/ml). *Summary:* There is clinically significant variability in haloperidol levels between subjects on similar doses of medication during the early weeks of treatment. Serial measurement of serum haloperidol levels should be considered in "routine" clinical care of schizophrenic patients, not just for those who do not respond to treatment.

NR412 Wednesday May 6, 12 noon-2:00 p.m.

Basal Ganglia in Discordant Schizophrenic Monozygotic Twins

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Summary:

MRI analysis of monozygotic (MZ) twins discordant for schizophrenia provides a unique opportunity to assess extragenetic morphological changes in the brain T1 weighted, 2mm, contiguous coronal MRI scans were obtained from 7 MZ twin pairs. Morphometry was performed on a computer image analysis system.

The volume of the right lentiform nucleus is significantly bigger in affected than in unaffected twins ($p < 0.03$, paired t-test); moreover, the right lentiform nucleus is larger than the left in every affected individual ($p < 0.002$). In unaffected twins left and right side did not differ ($p < 0.7$).

We found no significant difference in the volume of the caudate nucleus either within individuals (right vs. left) or between affected and unaffected twins. The basal ganglia measurements are particularly intriguing because they show one larger parenchymal structure (right lentiform nucleus) in affected individuals, but no difference in the caudate nucleus in the same individuals. These data partially confirm reports of enlargement of basal ganglia structures on MRI in schizophrenia. Interpretation of the results, especially the lateralization, is obscure.

NR413 Wednesday May 6, 12 noon-2:00 p.m.

Insight and Treatment Compliance in Schizophrenia

Paul H. Lysaker, Ph.D., Psychology, VA Medical Center, VAMC Psychology Service 116B, West Haven, CT 06516; Morris D. Bell, Ph.D., Robert M. Milstein, M.D., Joseph B. Goulet, M.S., Gary J. Bryson, M.A.

Summary:

Poor insight is a phenomenon commonly observed in schizophrenia. Research to date has suggested that poor insight in acute phases of schizophrenic illness is associated with poorer medication compliance and heightened levels of psychopathology. This study examined the relationship of poor insight to psychopathology and compliance with a psychosocial rehabilitation program in 85 schizophrenic subjects in a stable phase of disorder. Insight was measured using the insight item from the Positive and Negative Syndrome Scale (PANSS). Results suggest the PANSS insight item was a valid and reliable measure. Poor insight was not found to be related to heightened levels of psychopathology, but was negatively related to the number of weeks of participation in a 26-week psychosocial rehabilitation program and to ratings of social skills and poor personal presentation at a job placement after one month. Poor insight also appeared to be positively related to cognitive disorganization as measured by the Gorhams proverbs test and negatively related to intelligence. These results suggest that in a stable phase of schizophrenia poor insight may predict poorer compliance with psychosocial rehabilitation programs and be related to cognitive impairment.

NR414 Wednesday May 6, 12 noon-2:00 p.m.

Work Capacity in Schizophrenia

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Summary:

Impairment in work functioning is both a defining characteristic and enduring feature of schizophrenia. Little is known about the nature of this impairment. It is not known if work behavior is uniformly impaired or if various domains of work function are differentially affected. This study examined five domains of work behavior of 38 schizophrenic subjects placed in a supported work program. Subjects' behavior was sampled in weeks 1, 3, and 13

using the Work Personality Profile and compared with norms from a general rehabilitation population. In week 3, subjects performed well on measures of work skills (68th percentile), work motivation (65th percentile), work conformance (72nd percentile), and personal presentation (66th percentile), and more poorly on social skills at work (45th percentile). Performance scores did not differ significantly from weeks 1 to 3. Performance in week 3, however, provided a stronger prediction of work performance in week 13, than did week 1. These findings suggest individuals with schizophrenia suffer the greatest impairments in social skills at work, yet perform as well as other disability groups in other areas of work performance. Implications for psychiatric rehabilitation, and the value of multiple on-site evaluations of work performance over time are discussed.

NR415 Wednesday May 6, 12 noon-2:00 p.m.

Abnormal Splenial Shape in Schizophrenia

Robert M. Bilder, Ph.D., Psychiatry, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004; Regina Graham, Lauren Broch, Ph.D., Jeanine Springer, Jeffrey A. Lieberman, M.D.

Summary:

Altered size and shape of the corpus callosum in schizophrenia have been reported, but conflicting findings and complex interactions with sex have made it difficult to specify the abnormality. We assessed mid-sagittal magnetic resonance (MR) images of 52 schizophrenic/schizoaffective disorder, 23 affective disorder, and 15 healthy control subjects. We rated the shape of the splenium on a five-point scale (with low ratings for a more "tubular" and high ratings for more "bulbous" shape). The means of six raters' judgments (ICC = .91) were used to test for group differences. ANOVA revealed a significant main effect of group on shape ratings ($F_{2,87} = 5.66$, $p < .005$), and post-hoc tests confirmed that the schizophrenia group had significantly lower mean ratings than controls, while the affective group had intermediate values. Given unequal sex distributions across groups, and a nonsignificant trend for females to have more bulbous splenia across groups, we analyzed ratings among males alone, and found virtually identical group effects. The results corroborate prior reports that callosal shape may be altered in schizophrenia, but fail to support the suggestion that this reflects the absence of normal sexual dimorphism. The findings have implications for neurodevelopmental models of psychiatric illness.

NR416 Wednesday May 6, 12 noon-2:00 p.m.

Neuropsychological Manifestations of Hyponatremia in Chronic Schizophrenia Patients Who Exhibit Water Intoxication Syndrome

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Summary:

No empirical studies have documented specific neuropsychological effects of hyponatremia in patients who exhibit water intoxication. We examined the neuropsychological functioning of nine schizophrenic inpatients with the syndrome of psychosis, intermittent hyponatremia and polydipsia. Standardized measures were selected that possess demonstrated sensitivity to brain impairment. Patients were assessed on two occasions following laboratory blood work: once during hyponatremia (serum sodium 130 mmol/l) and once during normonatremia (serum sodium 136 mmol/l). Data analysis involved comparison of neuropsychiatric performance during hyponatremia versus baseline. The repeated measures MANOVA revealed a significant overall effect ($f = 41.85$, $df = 2$, $p = .02$). Significant mean comparisons ($p < .02$) revealed deficits during hyponatremia involving orientation, mental flexibility and verbal fluency but not memory or sustained attention. Patients were more impaired during hyponatremia on tasks requiring processing speed and spontaneous production of responses whereas performance on tasks requiring repetition of, or attention to, previously given information was unchanged across conditions. These findings have treatment implications for interventions that require patient participation to limit fluid intake.

NR417 Withdrawn

NR418 Wednesday May 6, 12 noon-2:00 p.m.

Plasma Clozapine and Clinical Response in Treatment Refractory Schizophrenics

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Summary:

Recent research indicates that a relationship may exist between clozapine plasma levels and clinical response. In this study the relationships between clozapine dose, plasma levels and therapeutic response were examined. Neuroleptic nonresponsive schizophrenic patients were titrated to and maintained on clozapine 500mg/day for a minimum of six weeks. Pretreatment and BPRS ratings at weeks 3, 6, 12, 24, 39, and 52 of treatment and weekly clozapine plasma levels for six weeks were obtained. Data from 43 DSM-III schizophrenic or schizoaffective subjects with a mean age of 28.02 ± 5.31 (69.2% Males/30.8% Females) were analyzed. Treatment response was defined as a 20% decrease in BPRS total score plus either a post-treatment CGI scale rating of mildly ill (3) or a post treatment BPRS score of 35 or less. No relationships between BPRS ratings at treatment weeks 3, 6, 12, 24, 39 and 52 and clozapine levels at weeks 3 and 6 clozapine levels were found. These results do not show any relationship between dose, plasma levels and response to clozapine. Since clozapine is actively metabolized to various intermediate forms that may have biologic activity, future studies may need to examine more than just the parent compound. These and other findings will be presented and discussed.

NR419 Wednesday May 6, 12 noon-2:00 p.m.

Positive and Negative Symptoms of Schizophrenia

John J. Boronow, M.D., Sheppard-Pratt Hospital, 6501 N. Charles Street, Towson, MD 21204; Norman B. Ringel, M.A., Frederick Parents, Ph.D.

Summary:

Positive and negative symptoms can occur simultaneously, or to the exclusion of one another. The nature of their interrelationship, if any, has been controversial. We therefore prospectively rated 107 chronic RDC schizophrenic inpatients using the BPRS and a 24-hour time-sampling measure called ROUNDS. A composite score of positive and negative symptoms on the BPRS was generated, after the model of Kay. We were able to replicate some of Kay's findings with the PANSS: 1) a normal distribution of scores around a mean of 0; 2) a positive correlation between positive and negative symptoms ($r = .319$); 3) the inversion of this correlation when global severity was partialed out ($rx.y = -.145$). However, we could not confirm the existence of typologically pure subsets. To explore this further, we plotted the frequency of positive versus negative symptoms on a three-dimensional histogram called a bivariate kernel

density estimator. This revealed the presence of two distinct subsets: high negative/high positive and low negative/low positive, but neither high positive/low negative nor low positive/high negative. A distance weighted least squares smoothing surface, generated by plotting positive and negative symptoms against the ROUNDS variable Relatedness, showed that Relatedness decreases when *either* positive or negative symptoms increase. We conclude that pure subtypes of positive and negative symptoms are rare in this sample, and that any bimodality that may occur in the distribution of patients is along a symptom severity axis, and not with respect to positive and negative symptoms per se. Graphical displays will be presented and implications discussed.

NR420 Wednesday May 6, 12 noon-2:00 p.m.

Neuropsychological Deficits and Withdrawal

John J. Boronow, M.D., Sheppard-Pratt Hospital, 6501 N. Charles Street, Towson, MD 21204; Norman B. Ringel, M.A., Faith Dickerson, Ph.D., Frederick Parents, Ph.D.

Summary:

Negative symptoms in schizophrenia have been associated with cognitive deficits. We explored this in a sample of 58 RDC schizophrenic inpatients, who were rated on the BPRS and a 24-hour time-sampling measure called ROUNDS. In addition, subjects received the WAIS-R, WRAT, and Luria-Nebraska Neuropsychological Battery (LN). All measures used in the analyses reflected a clinically optimal state. No ROUNDS variables correlated with the WAIS-R and WRAT. The ROUNDS variable Passive Solo, a measure of autistic withdrawal, correlated with eight LN subtests ($.30<r<.43$, $p<.05$-$.01$): Writing, Arithmetic, Intellectual Processes, Pathognomonic Scale, Left Frontal, Left Parietal, Right Sensory and Right Temporal. A factor analysis supported the association of most of these subtests with each other and with Passive Solo. A stepwise multiple regression of the eight subtests on Passive Solo resulted in only Left Frontal contributing to the R of .43, $p<.001$. When the BPRS Withdrawal Factor and a measure of clinical limit-setting interventions were entered into the multiple regression along with Left Frontal, the R rose to .7, $p<.001$. None of the LN subtests correlated with simultaneously derived BPRS measures of negative symptoms, nor contributed significantly to a multiple regression on the BPRS Withdrawal actor. However, they did correlate with several positive symptoms. When the variance from positive symptoms was partialed out of Left Frontal, it did not contribute significantly to the multiple regression. We conclude that in this sample, the autistic withdrawal measured by Passive Solo is related to Left Frontal dysfunction, but that this may reflect a confounding effect of positive symptoms, which could also derive from a Left Frontal deficit and cause behavioral withdrawal.

NR421 Wednesday May 6, 12 noon-2:00 p.m.

Family History of Schizophrenia

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Summary:

Familial factors in schizophrenia, and the genetic predisposition that these factors imply, have been well established in both family and twin studies of schizophrenia. Familial schizophrenia has been found to be associated with more negative symptoms, neurological abnormalities, increased CSF monoamine concentrations, poor premorbid functioning and CT scan abnormalities. The authors evaluated demographic, behavioral, and biochemical data in a sample of 61 male, drug-free, schizophrenic patients. The 21 patients with a first- or second-degree family history of schizophrenia exhibited higher CSF monoamine concentrations of homovanillic acid (HVA), 3-methoxy-4-hydroxyphenylglycol (MHPG), and 5-hydroxyindoleacetic acid (5-HIAA), poorer premorbid functioning on the Premorbid Adjustment Scale (PAS) [Cannon-Spoor et al., 1982], and higher performance IQ scores on the WAIS-R. Familial schizophrenic patients did not differ from nonfamilial schizophrenics in age, age of onset, or duration of illness. In contrast to previous findings, however, familial schizophrenia was associated with less psychopathology; i.e., both negative and positive symptoms. In an attempt to consolidate these findings into a comprehensive model, multivariate analyses are being pursued and will be presented.

NR422 Wednesday May 6, 12 noon-2:00 p.m.

Loading Versus Standard Haloperidol Decanoate Dosing

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Summary:

Haloperidol decanoate (HLD) dosing strategies are evaluated in 27 schizophrenic patients (pts). Group 1 ($n=16$) initially received a "loading-dose" strategy (20 $\times$ daily oral HL dose), which based on prior work, should achieve the rapid attainment of plasma concentrations (Cps) comparable to those from oral HL. Group 2 ($n=11$) received HLD in a more conservative fashion, which was based on the product's labeling. HL Cps were measured by HPLC. The statistics reported are within group measurements using ANOVA. The Clinical Global Impressions (CGI) Scale was used to evaluate safety and efficacy. Group 1 mean $\pm$ SD: Oral HL Dose $= 19 \pm 7.0$ mg/day; Cps $= 8.5 \pm 7.1$ ng/mL; HDL/HL dose ratio $= 20.9 \pm 6.1$; and HLD dose for first month $= 410 \pm 68$ mg. Group 2: Oral HL $= 39 \pm 20$; Cps $= 22 \pm 13$; HLD/HL dose ratio $= 6.4 \pm 4.7$; HLD dose for first month $= 217 \pm 87$ mg; and oral overlapping HL dose $= 22 \pm 15$ (in 8 subjects). During the first month of HLD therapy, Cps in Group 1 ranged from 5.4 ± 1.1 (Day 14), to 8.5 ± 3.0 (Day 21), to 6.6 ± 4.8 (Day 28) ng/mL. Cps on Day 14 were significantly lower than on prior oral HL, but equivalent on days 21 and 28 ($p<0.05$). CGI Severity of Illness data for Group 1 suggest that responses to HL were maintained or extended: 4.4 ± 1.3 (oral baseline); 3.9 ± 1.6 (Day 14); 3.6 ± 1.4 (Day 21); 3.4 ± 1.1 (Day 28) [$p<0.01$]. Group 1 CGI side effects did not significantly change. Group 2 pts had significant reductions in Cps following conversion to HLD. In 8/11 pts oral overlapping therapy yielded Cps $= 14 \pm 11$ (Day 14); 13 ± 7 (Day 21); 14 ± 11 (Day 28) ng/mL [$p<0.02$]. In 3 pts in Group 2 without oral HL overlap, Cps $= 1.5 \pm 0.4$ (Day 14) and 0.8 ± 0.5 (Day 28), [$p<0.02$]. Group 2 pts receiving both HLD *and* oral HL had CGI responses which suggested a trend towards clinical worsening ($p=0.08$) while side effects slightly decreased ($p<0.05$). The three Group 2 pts without oral overlapping therapy demonstrated clinically significant deterioration. Data for months 2 and 3 of depot therapy will be presented. A "loading-dose" strategy is most likely to maintain previous oral HL Cps and clinical benefit.

NR423 Wednesday May 6, 12 noon-2:00 p.m.

Neuropsychology in Schizophrenia: State or Trait?

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Summary:

Neuropsychological profiles of unmedicated patients with schizophrenia have indicated a selective deficit in memory and learning, particularly for verbal material. The present report addresses the issue of the temporal stability of neuropsychological functioning.

Detailed testing was administered twice to two independent samples meeting DSM-III-R criteria for schizophrenia. In Study 1, which addressed short-term stability, 20 medication-free patients were tested before and after treatment (median interval = 3 months). In Study 2, long-term follow-up was obtained on a second sample of 25 patients who had previously undergone baseline evaluation while off medication, and for 22 healthy controls (median interval = 1.5 years). For both studies, repeated evaluation yielded nearly identical shape for baseline and retest profiles. There was a slight improvement at retest for patients and controls, but no interactions between profile shape, diagnosis and time. This pattern of results suggests longitudinal stability of neuropsychological function in schizophrenia. Test performance off medication during an acute phase of the illness appears to largely reflect underlying trait rather than state features. These findings are placed in the context of clinical status, medication, and neuroimaging.

NR424 Wednesday May 6, 12 noon-2:00 p.m.

Linkage Exclusion Between Schizophrenia and Candidates

Ann E. Pulver, Sc.D., Psychiatry, Johns Hopkins University, 1615 Thames Street, Baltimore, MD 21231; Maria Karayiorgou, M.D., Nicola Diemarchi, M.D., Stelios Antonarakis, M.D., David Housman, Ph.D., Laura Kasch, Haig Kazazian, M.D., Malgorzata Lamacz, Ph.D., K. Lasseter, B.A., Deborah Meyers, Ph.D., Jurg Ott, Ph.D., Paula Wolyniec, M.A., Gerald Nestadt, M.D., Elango Ramu, John McGrath, M.A., Barton Childs, M.D.

Summary:

Our group has been involved in an epidemiologic-genetic investigation of schizophrenia in a large systematic sample of patients admitted to 15 hospitals in Maryland. Individuals from 51 families in which there are at least two individuals with schizophrenia have been included in the study. Linkage analysis using polymorphic markers in a subgroup of 20 families is currently being performed. To date family members have been genotyped for 150 markers. Our model for linkage analyses is complex and includes age-dependent penetrance and phenocopies; it is unique in that we have been able to incorporate information previously derived from our sample regarding factors which influence the relative's morbidity risk (Pulver et al 1989; 1990; 1991; and Wolyniec et al 1992).

Our initial strategy involves two complementary lines of approach: 1) the testing of specific candidate genes including any markers suspected to be linked and 2) an effort to systematically scan the entire genome. We have now tested for linkage in several candidate gene regions (i.e. dopamine receptor genes. Marfan syndrome gene and the pseudoautosomal region), and the data permit exclusion of these regions in a set of families (LOD < -2 at a recombination fraction of >0.05.)

NR425 Wednesday May 6, 12 noon-2:00 p.m.

Familial Risk and Mania in Schizophrenia

Ann E. Pulver, Sc.D., Psychiatry, Johns Hopkins University, 1615 Thames Street, Baltimore, MD 21231; Kung-Yee Liang, Ph.D., Lawrence Adler, M.D., Paula Wolyniec, M.A., John McGrath, M.A., Gerald Nestadt, M.D., Barton Childs, M.D.

Summary:

Risk for schizophrenia among first-degree relatives of schizophrenic probands obtained from an epidemiologic sample using family history methods was examined to determine whether a history of manic symptoms in the proband was associated with familial risk. The results of this study of the first-degree relatives of 381 schizophrenics suggested that the relatives of male probands with mania had 2.25 increased risk for schizophrenia when compared with the relatives of male probands without mania. Similarly, the relatives of female probands with mania had a 5.86 increased risk when compared with the relatives of female probands without mania.

NR426 Wednesday May 6, 12 noon-2:00 p.m.

Neurochemistry Studies in Schizophrenic Patients

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Summary:

More than 2/3 of elderly schizophrenic patients and almost half of the affective disorder patients residing in a state-supported chronic institution show poor cognitive function compatible with a diagnosis of dementia. Examination of brain specimens from these schizophrenic patients who reached autopsy did not reveal any of the neurohistological findings known to correlate with a clinical picture of dementia (plaques, tangles, Lewy bodies, infarcts), and none of the tissue specimens showed reactivity with ALZ-50. Furthermore, AchE and ChAT activity in the demented schizophrenic patients was found to be similar to the enzyme's activity in nondemented schizophrenic patients and in normal controls, but higher than AD patients. This underscores the notion that dementia in elderly schizophrenic patients is not the result of superimposed SDAT or any other histologically known dementing illness. To further investigate the biological substrate of dementia in elderly schizophrenic patients, we will present data regarding catecholamine tissue levels, nicotinic receptor binding and SI in brain tissue from schizophrenic patients.

NR427 Wednesday May 6, 12 noon-2:00 p.m.

Diazepam Binding Inhibitor-Like Immunoreactivity and Sleep EEG in Schizophrenia

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Summary:

This study examined the relationship between cerebrospinal fluid (CSF) Diazepam-Binding Inhibitor-like immunoreactivity (DBI-ir) and sleep polysomnography in schizophrenic patients. Twenty-eight drug-free male schizophrenic patients (DSM-III-R) underwent a three-night polysomnography evaluation and a lumbar puncture. CSF DBI-ir correlated positively with rapid eye movement (REM) sleep latency and stage 4% sleep, and correlated negatively with stage 15 sleep and REM density. CSF DBI-ir did not correlate significantly with duration of sleep or sleep latency. Negative symptoms also correlated negatively with CSF DBI-ir. CSF DBI-ir did not correlate significantly with sleep EEG measures in 17 patients who were evaluated on haloperidol as well. While there were positive relationships between CSF DBI-ir and sleep measures, the relationships between CSF DBI-ir and schizophrenic behavior were negative.

The results of this first study of the relationship between endogenous DBI and sleep in humans suggest a different physiological role for DBI than concluded from pharmacological studies. However, the absence of similar sleep data in normals precludes more specific conclusions.

NR428 Wednesday May 6, 12 noon-2:00 p.m.

Clozapine Versus Haloperidol Blockade of M-CPP in Schizophrenia

John H. Krystal, M.D., Psychiatry, Yale University, West Haven VA Medical Center, West Haven, CT 06516; John P. Seibyl, M.D., Laurence Karper, M.D., Joseph Erdos, M.D., Ma-Li Wong, M.D., George R. Heninger, M.D., Dennis S. Charney, M.D.

Summary:

Interest in serotonergic (5-HT) contributions to the symptoms of schizophrenia has increased in light of recent findings that the 5-HT partial agonist, *m*-chlorophenylpiperazine (MCPP), increases positive symptoms in unmedicated schizophrenic patients, perhaps via 5-HT_{1C} receptor activation. Clozapine, a drug that potently blocks both the 5-HT_{1C} and 5-HT_2 receptors, has been reported to be more effective in reducing positive symptoms than typical neuroleptics in patients refractory to typical neuroleptics. The purpose of this study is to compare the ability of four weeks of clozapine and haloperidol treatment to block the psychogenic and anxiogenic effects of MCPP controlling for the effects of MCPP in these patients while neuroleptic-free. *Methods:* In an ongoing study, schizophrenic patients completed MCPP (0.1 mg/kg, iv, over 20 min.) and placebo testing in a randomized order following a two-week neuroleptic washout period and repeated MCPP and placebo testing following four weeks of treatment with haloperidol 20 mg/d (n = 9) or clozapine 600-800 mg/d (n = 5). Behavior was assessed using the BPRS and anxiety measured with a clinician-rated visual analog scale. Blood was sampled for hormonal analyses. *Results:* Haloperidol treatment did not significantly reduce MCPP-induced increases in positive symptoms (as assessed by the BPRS Thought Disorder Factor), anxiety, or increases in prolactin, growth hormone, or cortisol. Clozapine blocked both the behavioral and neuroendocrine effects of MCPP in all patients studied to date. *Implications:* These findings suggest that excessive stimulation of 5-HT receptors, perhaps the 5-HT_{1C}, results in increases in positive symptoms that are blocked by clozapine but not by haloperidol. These findings have implications both for predicting patients who would benefit by from the addition of clozapine and the design of novel treatments for refractory schizophrenia.

NR429 Wednesday May 6, 12 noon-2:00 p.m.

Ritanserin Blockade of M-CPP Effects in Schizophrenia

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Summary:

M-chlorophenenylpiperzaine (MCPP) is a serotonin (5-HT) partial agonist that transiently increases positive symptoms in schizophrenic patients. Clozapine, a 5-HT_{1C} and 5-HT_2 antagonist, produces greater blockade of MCPP effects than haloperidol. However, the numerous neurotransmitter receptor subtypes blocked by clozapine makes it difficult to infer the mechanism of its enhanced efficacy in blocking MCPP effects. The purpose of the current study was to determine whether ritanserin, a drug that selectively blocks 5-HT_2 and 5-HT_{1C} receptors reduces MCPP-induced exacerbation of anxiety and psychosis in schizophrenics. *Methods:* In an ongoing study, six schizophrenic patients who were neuroleptic-free for at least two weeks prior to testing completed four test days in a randomized balance order in which patients received ritanserin (10 mg p.o. or placebo) one hour prior to MCPP (0.1 mg/kg, iv, over 20 minutes or saline). Behavioral responses were measured with the BPRS and a clinician-rated visual analog anxiety scale pre- and 210 minutes post-MCPP infusion. Plasma hormones were also measured during this period. *Results:* In the first six patients, six of six subjects had MCPP-induced increases in anxiety and positive symptoms, as assessed by the BPRS Thought Disorder Factor Scores. Ritanserin reduced MCPP-induced increases in positive symptoms in four of six subjects. Ritanserin also reduced MCPP-induced anxiety in six of six subjects. Hormonal results are pending. *Implications:* These data replicate the finding that MCPP increases positive symptoms and anxiety in neuroleptic-free schizophrenic patients. They also indicate that ritanserin reduces both the psychotogenic and anxiogenic effects of MCPP in these patients. Blockade of MCPP effects by ritanserin implicate the 5-HT_2 and 5-HT_{1C} receptors in the modulation of positive symptoms and, perhaps, in the enhanced efficacy of clozapine.

NR430 Wednesday May 6, 12 noon-2:00 p.m.

Effects of the NMDA Antagonist, Ketamine in Humans

John H. Krystal, M.D., Psychiatry, Yale University, West Haven VA Medical Center, West Haven, CT 06516; Laurence Karper, M.D., John P. Seibyl, M.D., Richard Delaney, Ph.D., Glenna Freeman, B.S., George R. Heninger, M.D., Malcolm B. Bowers, M.D., Dennis S. Charney, M.D.

Summary:

NMDA antagonists such as PCP have been reported to produce behavioral effects that have been likened to schizophrenia. This study will report on an important initial step in evaluating the PCP model of schizophrenia, characterizing the behavioral, cognitive, and neuroendocrine effects of ketamine in healthy human subjects. *Methods:* In an ongoing study, 10 healthy subjects have completed three test days over two weeks during which ketamine (0.1 mg/kg, 0.5 mg/kg) or placebo was administered intravenously over 40 minutes. Behavioral and neuroendocrine assessments were made prior to, during, and following ketamine infusion. *Results:* Ketamine had no effects on the Mini-Mental Status Examination Scores over the doses studied. Ketamine dose-dependently transiently increased the positive symptoms of schizophrenia, assessed by the BPRS Thought Disorder Factor Score; the negative symptoms of schizophrenia, assessed by the BPRS Withdrawal-Retardation Factor Score; and produced alterations in perception similar to those reported in schizophrenia and dissociative disorders, assessed by the Wisconsin Perceptual Aberration Scale and the Clinician-Rated Assessment of Dissociative States. Ketamine dose-dependently impaired frontal lobe function as assessed by increased perseverative error on the Wisconsin Card Sort and decreased verbal fluency. Ketamine also selectively and dose-dependently impaired object recall after a 10-minute delay without impairing immediate recall or recall after a five-minute delay. Neuroendocrine responses to ketamine will be presented at the meeting. *Implications* These data suggest that NMDA receptor blockade produces behavioral alterations similar to those observed in schizophrenic patients, including increases in the positive and negative symptoms of schizophrenia and impairments in frontal and tempero-hippocampal function. They suggest that alterations in NMDA function may contribute to the neurobiology of schizophrenia and dissociative disorders.

NR431 Wednesday May 6, 12 noon-2:00 p.m.

Stabilization and Depot Neuroleptic Dosages

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Summary:

Goals: Little is known about optional neuroleptic dosing during the immediate post-discharge (stabilization) phase in schizophre-

nia. We studied the patterns of depot neuroleptic dosing during this phase.

Methods: The Treatment Strategies in Schizophrenia (TSS) study is a multicenter two-year, double-blind, maintenance dosage study. These data only use the first part of the TSS protocol. After discharge, patients were stabilized on open-label fluphenazine decanoate (FZD) (permissible range 12.5 to 50 mg every two weeks). We analyzed depot neuroleptic records for all TSS patients successfully stabilized (N = 202). Two blind raters categorized the dosage patterns. Pre- and-post stabilization BPRS and CGI scores were compared for the final dosage pattern groups.

Results: There were five patterns of depot neuroleptic dosing: Pattern A (HIGH) (n = 30, 15%) was a very rapid increase to the maximum dose (>37.5mg of biweekly). Pattern B (INTERMEDIATE) (n = 36, 18%) was a gradual increase to an intermediate FZD dose (>12.5mg). Pattern C (LOW) (n = 33, 16%) was a low dose (> or = 12.5 mg FZD) administration. Pattern D (UP) (n = 52, 25%) represented a dosage raising after a lower stabilization dose had been established. Pattern E (DOWN) (n = 51, 25%) was coded when a dosage lowering occurred after an initial higher stabilization dose. Not surprisingly, the patients with HIGH and UP patterns remained most ill at the end of stabilization. Contrary to expectations, however, the DOWN group did not improve a much as other dosage patterns.

Significance: The post-discharge period in schizophrenia has significant risks of relapse, depression, and suicide. Better understanding of the psychopharmacology of depot neuroleptic dosing during stabilization period may help improve outcome during this critical time period.

NR432 Wednesday May 6, 12 noon-2:00 p.m.

Effects of Haloperidol on Negative Symptoms

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Summary:

After five weeks of haloperidol, positive symptoms in naive-treated schizophrenic patients, substantially subsided. Negative symptoms, although with a different temporal pattern, decreased after the fifth week of haloperidol treatment; specifically, a decrease was seen in anhedonia and affective flattening, whereas avolition-apathy and attentional impairment presented no changes. Alogia showed a decrease during the third week and a trend to return to placebo scores during weeks 4 and 5. Changes in affective flattening, alogia and attentional impairment correlated with changes in positive symptoms. During placebo, plasma homovanillic acid (HVA) correlated with negative symptoms and with changes presented by negative symptoms between the first and the fifth treatment week. These data show that negative symptoms respond differentially to neuroleptics and suggest that avolition-apathy may represent a different behavioral component of the schizophrenia process.

NR433 Wednesday May 6, 12 noon-2:00 p.m.

Neuropsychology in First-Episode Schizophrenia

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Summary:

First-episode patients with schizophrenia provide an opportunity to examine the characteristics of illness prior to the effects of neuroleptic and anticholinergic medication, as well as of chronicity. We have previously identified a selective deficit in memory and learning against a background of generalized impairment using a comprehensive neuropsychological battery. In this study we compare the profiles of 33 first-episode (FE) (neuroleptic naive) patients with 66 previously treated (PT) schizophrenics and 87 normal controls. Both patient groups were impaired compared with controls, particularly for verbal memory and learning. Neuropsychological level of impairment was highly similar for FE and PT groups in those areas most typically associated with schizophrenia (abstraction, memory, verbal skills); other functions tended to be performed better by the FE group. Since this FE group had no prior neuroleptic or anticholinergic exposure, these findings suggest that drug effects are not sufficient to explain the memory and other deficits found in patients with schizophrenia. Furthermore, the neuropsychological impairments appear to be present early in the course of illness.

NR434 Wednesday May 6, 12 noon-2:00 p.m.

Phenomenology and Functioning in Schizophrenia

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Summary:

While the role of negative symptoms in patients with schizophrenia is generally associated with poor premorbid adjustment and functional outcome, the role of positive symptoms is less clear. A sample of 107 patients meeting DSM-III-R criteria for schizophrenia were assessed using the Brief Psychiatric Rating Scale, Scale for the Assessment of Negative Symptoms, Scale for the Assessment of Positive Symptoms, Premorbid Adjustment Scale and Quality of Life. Factor analysis of the BPRS, SANS and SAPS revealed a four factor structure: 1) negative; 2) thought-disorder/bizarre behavior; 3) hallucinations and Schneiderian delusions; 4) grandiosity/paranoid delusions. Patients could be clustered into three groups using these factors, and the clusters differed in functioning. Cluster 1 (high on negative, moderate on other factors) had worse premorbid and current functioning. Cluster 3 (high on factor 3) had fair premorbid functioning and best current functioning, and Cluster 2 patients (high on factors 2 and 4) had the best premorbid functioning and intermediate social functioning, but were as bad as Cluster 1 patients in occupational functioning. We conclude that negative symptoms are indeed associated with poor premorbid and current functioning, but that the role of positive symptoms is more complex and may vary in subtypes.

NR435 Wednesday May 6, 12 noon-2:00 p.m.

Predictors of Noncompliance in Schizophrenia

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Summary:

Goals: To assess predictors of future neuroleptic noncompliance at the time of discharge from the hospital.

Methods: These results are part of an ongoing longitudinal study of noncompliance in schizophrenia. Criteria for this study were that the patient suffer from schizophrenia and improve enough to be treated as an outpatient. Assessments were done by independent research raters at discharge and one and six months post-discharge. Study variables included level of functioning (GAS), global psychopathology (CGI), objective side effects (ESRS), subjective distress from EPS, and Neuroleptic Dysphoria (Van Putten and May). The analysis reports correlational measures for the first 76 patients who completed six-month follow-ups.

Results: **Side Effects:** Subjective distress from akinesia at discharge, predicted outpatient noncompliance at 1 month ($r = .34$, $h = 58$, $p < .005$) but not at 6 months. In contrast, during the outpatient phase akathisia was the strongest side effect correlate of noncompliance ($r = .50$ $n = 40$ $p < .01$). **Psychopathology:** Neuroleptic-refractory patients were more likely to stop their medicines briefly after discharge ($r = .33$, $n = 56$, $p < .01$). This phenomenon was not correlated with global compliance scores, but represented transient medication discontinuation. In contrast, neuroleptic-responsive patients become progressively less willing to remain on a neuroleptic regimen ($r = .29$, $n = 68$, $p < .01$).

Conclusions: Distress from akinesia is associated with future (not immediate) noncompliance. Persistence of schizophrenic symptoms at discharge predicts episodic and transient medication discontinuation. Neuroleptic-responsive patient seem to show a different course. They are more likely to develop, over time, an increased desire to stop their medication.

NR436 Wednesday May 6, 12 noon-2:00 p.m.

Clinical Review of Clozapine Treatment in a State Hospital

William H. Wilson, M.D., Oregon Health Sc. Univ., Dammasch State Hosp Bx 38, Wilsonville, OR 97070

Summary:

We recently reported a review of the medical records of the first 37 individuals to begin clozapine treatment at a state hospital. The review period covered a 13-month period, centered around the month in which clozapine treatment began. All of the patients had long histories of schizophrenia poorly responsive to antipsychotic medication. Clozapine treatment was generally well tolerated, although the rate of seizures (8%) was slightly higher than expected. Psychotic symptoms (measured with the BPRS) decreased, as did symptoms of tardive dyskinesia (measured with the AIMS). Thirty-four of the patients remained hospitalized after six months of treatment. However, indicators of social function within the hospital (hospital privilege level, passes to the community, violent episodes, seclusion and restraint) all showed marked improvement, beginning with the introduction of clozapine, and continuing throughout the review period.

This poster extends that follow-up to a six-month follow-up of 75 patients, and a one-year follow-up of the 37 patients previously reported.

NR437 Wednesday May 6, 12 noon-2:00 p.m.

Organic Memory Pathology and Schizophrenia

Avraham Calev, Ph.D., Psychiatry, Suny at Stony Brook, Health Sciences Center T-10, Stony Brook, NY 11794; Donald O'Donnell, M.A., Lynn Delisi, M.D., Olga Van Iyl, M.D.

Summary:

A battery consisting of memory tasks that had been shown to be sensitive to schizophrenic memory pathology and to post-ECT patients' amnesia, which focuses on retention over 48 hours, was administered to patients who had an early schizophrenia spectrum diagnosis during their first hospitalization. Testing was done not later than two years after their first admission whether patients were in remission or not. Neuroleptic (haloperidol) and anti-cholinergic (benzotropines) blood levels, as well as magnetic resonance imaging (MRI) measurements of total ventricular size, total brain size and right and left temporal lobe sizes were taken. The examiner was blind to the patients' drug levels and brain measures. It was found that both anticholinergic medication and ventricular size *independently* affected retention over time. Memory measures, not including retention, were affected by anti-cholinergic medication, but enlarged ventricles did not show a significant effect on these tasks. These results suggest that a problem in retention is part of the schizophrenic organic pathology and that anticholinergic drugs add to this pathology.

NR438 Wednesday May 6, 12 noon-2:00 p.m.

Schizophrenia Spectrum: Delusions and Diagnoses

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Summary:

There is hope that clinical data collected in genetic research may be useful in validating diagnostic categories in the schizophrenia spectrum. As part of an ongoing linkage study of schizophrenia, we examined interview material from 31 relatives (of schizophrenic probands) who received a DSM-III-R diagnosis of a nonaffective psychotic disorder or schizotypal or paranoid personality disorder. Six exhibited episodic or chronic delusions that resulted in diagnostic dilemmas. Case vignettes that raise the following questions will be presented: (a) when are transient psychotic symptoms in individuals with schizotypal or paranoid personality disorder of sufficient intensity or duration to warrant a separate 'psychotic' diagnosis; (b) how 'plausible' must a delusion be in a given culture for the diagnosis of delusional disorder to be more appropriate than atypical psychosis in the absence of associated symptoms; and (c) what degree of functional impairment would suggest schizophrenia in an individual with nonbizarre delusions? We conclude that the schizophrenia spectrum includes a range of delusional presentations, not all of which are easily or reliably captured by our current classification system. We recommend that published reports of similar studies include descriptions of the clinical features of ambiguous cases.

NR439 Wednesday May 6, 12 noon-2:00 p.m.

Schizophrenia Subtypes: Stability Over Time

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Summary:

While the traditional subtypes of schizophrenia can be diagnosed reliably, there has been much discussion about their stability over time. Bleuler himself considered the subtypes to be unstable and this position has been supported (Tsuang, 1981, Kendler, 1985).

Seventy pairs of comprehensive diagnostic evaluations (including the SADS) were completed on 49 schizophrenic patients with an average intervening interval of 33 months. Each assessment was done independently by two raters. Final diagnoses, including subtype determination, were made at a consensus conference under the leadership of a senior diagnostician. Of the 70 pairs of sequential evaluations, 33 received the same subtype diagnosis and 37 were rediagnosed. There was no difference for duration of illness or evaluation interval between the two groups. The overall Kappa coefficient for repeat evaluations was .3.1. The Kappas for the individual subtypes, from the first evaluation to the second, were .33 (chi square 9.998, $df = 1$, $p = .0016$) for disorganized, .32 (chi square 7.824, $df = 1$, $p = .0052$) for paranoid and .28 (chi square 6.588, $df = 1$, $p = .0103$) for undifferentiated schizophrenia. No differences were found between stable and unstable groups with regard to formal thought disorder (as measured by the TLC), negative symptoms (as measured by the SANS) or any of the RDC "A" criteria.

While these findings have implications for our understanding of the natural history of schizophrenia, they also suggest that cross-

sectional studies using subtype evaluations should be critically evaluated.

NR440 Wednesday May 6, 12 noon-2:00 p.m.

Schizophrenia: Premorbid Adjustment

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Summary:

Premorbid adjustment in schizophrenia (SZ) is thought important 1) as a predictor of current pathology and course, and 2) as a psychosocial expression of brain pathology preceding psychosis. To improve the validity and reliability of its measurement, we interviewed 12 chronic male SZ veterans and their first-degree relatives, plus normal controls (NCLs) matched for age and social class of origin using the Cannon-Spoor et al. Premorbid Adjustment Scale (PAS), combined with objective data from school records. PAS reliability for two interviewers for SZs was rho = .98, $p<.001$ (1 tail). Overall PAS scores, based on all informant sources, were significantly poorer in SZs than in NCLs ($p<.001$ 2 tail). Worse premorbid adjustment in SZ predicted 1) worse current clinical state (GAS, rho = −.50, p = .05 1 tail); 2) more current negative symptoms (SANS, rho = .59, p = .02 1 tail); and, 3) poorer current level of functioning (degree of independent living, rho = .65, p = .01 1 tail, duration of hospitalization, rho = .61 $p<.02$ 1 tail). Additionally, worse premorbid adjustment in SZ was associated with 1) larger ventricular brain ratio (VBR), when controlled for age, (n = 7, rho = .72, $p<.04$ 1 tail); and, lower premorbid IQ in SZ was associated with 1) larger VBR, (n = 4, rho = −.95, $p<.03$ 1 tail); 2) larger lateral ventricular volume, normalized for head size, (n = 4, rho = −.97, $p<.02$ 1 tail); and, 3) lower P300 amplitude at the T3 (left temporal) electrode site (n = 5, rho = .89, $p<.05$ 2 tail). We conclude that premorbid adjustment, rigorously measured, is poorer in SZs than in NCLs and is predictive of psychosocial and biological pathology in SZ.

NR441 Wednesday May 6, 12 noon-2:00 p.m.

Follow-Up of Clozapine Treated Schizophrenics

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Summary:

Acute double-blind trials in treatment-refractory schizophrenics, have shown clozapine to be more effective than standard antipsychotics in ameliorating both positive and negative symptoms. Several investigators have followed patients for longer periods and report that the rate of improvement increases with time. The aim of the present study was to determine if clozapine treatment improved quality of life and/or decreased hospitalization. We did a follow-up of 29 treatment-refractory schizophrenics treated with clozapine who we reported on previously (1991). After a six-week trial of clozapine 11/29 (38%) were considered to be improved based on Kane's definition of response (1988). At follow-up, 24 of the original 29 patients remained on clozapine and had been receiving it for a mean of 26.5 ± 3.7 months (23 to 34 months). Of the 24 patients still on clozapine, 13 (54%) were considered to be responders. When compared with the same period of time before treatment with clozapine, we found that the patients were living more independently, had higher rates of employment, and had a significant decrease in number and duration of hospitalizations. Despite its high cost, it appears that clozapine improves quality of life and decreases medical costs.

NR442 Wednesday May 6, 12 noon-2:00 p.m.

Sexual Functioning of Schizophrenic Women

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Summary:

Many clinicians think schizophrenic patients have very limited (if any) overt sexual activity. Opinions on this topic are founded mostly in case reports and old descriptions.

Sixty-one schizophrenic women (DSM-III-R diagnosed, 18-45 years old, mean age-34 years, both inpatients and outpatients) were interviewed with a clinician-rated battery of instruments (PANSS, Carpenter's criteria and Axis V of DSM-III-R) and with a semi-structured questionnaire related to their sexual behavior, including questions on premorbid and present sexuality, sexual dysfunctions, perversions, victimizations, contraception, motherhood and health problems linked to sexuality.

The first results indicated that a large proportion of these patients had usual sexual activity. Whereas 5% had never had sexual intercourse, the mean age at first sexual intercourse was 19. Forty-nine percent had sexual intercourse in the previous month, 46% had a permanent partner and 48% had children, with a mean of 1.8 children. On the other hand, experiences of venality in sexual relationships were found in 18% and sexual victimization was frequent (rape in adulthood and sexual abuse in childhood).

In addition, our results suggest an age cohort effect, the younger generations of schizophrenic women more and more closely resembling the general population in several characteristics of their overt sexual behavior.

NR443 Wednesday May 6, 12 noon-2:00 p.m.

Clozapine Improves Sensory Gating More Than Haldol

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Summary:

Introduction: Deficits in the ability to filter extraneous sensory information has been hypothesized to be a factor in the pathophysiology of schizophrenia (McGhie and Chapman, 1961; Venables 1964). Prepulse inhibition (PPI) of the acoustic startle response (ASR) has been proposed as an experimental method to quantitatively study hypothetical sensory filtering defects. Schizophrenics have been reported to have decreased PPI of the ASR compared to normals (Braff et al., 1978). Studies with animal models of schizophrenic sensory filtering deficits shows that spiperone reverses the deficits, but that clozapine has an "inverted U" shaped dose response with low doses reversing deficits but not high doses (Swerdlow et al, 1990). *Method:* Data will be presented from clinical trials of schizophrenics who have been tested for sensory filtering with the ASR PPI in a double-blind, randomized, crossover trials five weeks of Haldol, placebo, and clozapine. *Results:* Preliminary analysis suggests that five weeks of clozapine improves sensory gating in schizophrenic patients to a greater extent when compared to five weeks of haloperidol. *Implications:* Atypical antipsychotics might enhance information processing in schizophrenia.

NR444 Wednesday May 6, 12 noon-2:00 p.m.

Quantity and Quality: Work Effect on Schizophrenia

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Summary:

Although work figures importantly in psychiatric rehabilitation programs, little is known about whether the amount the patient works or how well the patient works influences outcome. To address this question, 43 subjects with SCID-determined schizophrenia were offered 20 hours per week of paid work over six months. Work quality was monitored on-site using the Work Personality Profile and symptoms were rated using the Positive and Negative Syndrome Scale bi-weekly. At baseline and five-month follow-up the Quality of Life (QOL) scale was administered. Multiple regression revealed work hours but not work quality during the first month predicted amount of work performed during the next four. Using hierarchical regression, relation of work quantity and quality to outcome measures was assessed controlling for baseline values. Better social skills at work were associated with lower level of negative symptoms at follow-up ($R^2 = .15$). Surprisingly, better work social skills predicted poorer perceived quality of life ($R^2 = .10$), and greater hours worked predicted less satisfaction with perceived amount of friendship in life at follow-up ($R^2 = .10$). The QOL findings seem to contradict the hypothesis that productive activity improves quality of life, but may be artifactually related to subjects' disappointment about ending work involvement.

NR445 Wednesday May 6, 12 noon-2:00 p.m.

Cortical CSF and Neuropsychological Function

Daniel S. O'Leary, Ph.D., University of Iowa, 200 Hawkins Drive 2911 JPP, Iowa City, IA 52242; Nancy C. Andreasen, M.D., Michael A. Flaum, M.D., Victor Swayze, M.D., James Ehrhardt, M.D., William Yuh, M.D.

Summary:

The neuroanatomical basis of the cognitive deficits characteristic of schizophrenia and normal aging is unknown. Using calibrated visual ratings with established reliability, we assessed the amount of cerebrospinal fluid (CSF) surrounding the brain on coronal MRI scans in 56 normal controls and 86 schizophrenic patients. The patients had significantly more CSF over frontal and temporal lobes, but not over parietal/occipital lobes, and significantly worse performance than controls on a standard neuropsychological battery. Multiple regression analyses assessed the relationship between a global measure of surface CSF and test performance. Age, height, diagnoses, and ventricular volumes were included in the analyses. Surface CSF was significantly related to VIQ, PIQ, verbal and non-verbal learning and memory, and measures of attention. The relationship between increased surface CSF and neuropsychological performance was similar in controls and patients, and increased surface CSF accounted for most of the subtle age-related decline in performance in our normal controls. Ventricular volume showed little relationship with neuropsychological function, although increased ventricular size was associated with worse performance in patients only on verbal memory measures. These results indicate that increased cortical CSF seen in both schizophrenia and normal aging is more strongly associated with neuropsychological impairment than is ventricular enlargement.

NR446 Wednesday May 6, 12 noon-2:00 p.m.

Validation of Schizophrenia Spectrum Personality

Gerald Nestadt, M.D., Psychiatry, Johns Hopkins University, 1615 Thames Street, Baltimore, MD 21231; John Hanfelt, Kung-Yee Liang, M.D., Paula Wolyniec, M.A., John McGrath, M.A., Malgorzata Lamacz, Ph.D., Ann E. Pulver, Sc.D.

Summary:

Research into the genetics of schizophrenia has revealed the importance of a spectrum of conditions that may be indicative of the underlying genetic diathesis for this condition. Important among these are specific personality disorders, paranoid, schizoid and schizotypal. Despite operational criteria in the DSM-III-R, demonstration of a valid phenotype for use in genetic analyses is lacking. We will present the results from a study in which all the relatives in multiplex families of schizophrenic probands were examined using a modified SID-P (Stangl, et al. 1985) interview with each relative and an informant. A total of 598 relatives were examined in this way. Latent class analytic techniques (Clogg, 1977) were employed to study the inter-relationships of the individual DSM-III personality disorder criteria. The results reveal that all the DSM-III-R paranoid and schizoid features are strongly related to each other, and the degree to which an individual belongs to each disorder is related to the number of criteria he/she meets. For schizotypal personality disorder, two distinct groups of criteria emerge. External validation of these classes will be valuable.

NR447 Wednesday May 6, 12 noon-2:00 p.m.

Eye Movements: Bipolar Disorder and Schizophrenia

Allen Y. Tien, M.D., Psychiatry, Johns Hopkins University, Hampton House 624 N. Broadway, Baltimore, MD 21205; Godfrey Pearlson, M.D., Milton Strauss, Ph.D.

Summary:

Abnormal eye movements are associated with schizophrenia, but important issues remain. One is the neurobiological nature of the abnormality, and relationship to specific brain areas or systems. Another is the specificity to schizophrenia, for example, whether subjects categorized as bipolar also manifest similar deficits. In general, a diagnostically specific *smooth pursuit* abnormality appears present in schizophrenia, but *saccadic eye movements* have not been studied as extensively. What is known suggests a deficit in schizophrenia in saccadic eye movements thought to be under the control of frontal lobe/basal ganglia circuits. There are, however, no known reports on saccadic performance in bipolar patients.

In this study, saccadic performance was assessed in bipolar ($N = 23$) as well as schizophrenic patients ($N = 19$), and compared to normal subjects ($N = 24$). Performance on an anti-saccade task, in which subjects consciously make a saccade opposite to a target stimulus, was studied. Mean error rates were compared as a proportion of total trials. Mean error rate for the schizophrenic group was 0.58 ± 0.24, bipolar group 0.38 ± 0.31, and normal group 0.10 ± 0.09. The significance level for t-test comparisons between the schizophrenic and normal groups was $p < .001$, between bipolar and normal groups $p < .001$, and schizophrenic and bipolar groups $p < .023$. These results suggest overlap of deficits in brain function in schizophrenia and bipolar disorder.

NR448 Wednesday May 6, 12 noon-2:00 p.m.

Situational Feature Detection and Schizophrenia

Patrick W. Corrigan, Psy.D., Psychiatry, University of Chicago, 5841 S. Maryland Box 411, Chicago, IL 60637; Michael F. Green, Ph.D., Rosemary Toomey, M.A.

Summary:

Social situations are comprised of several schematized features including characteristic actions, roles, rules, and goals. These features vary in level of abstraction, with rules and goals representing the more abstract components of the situation. Given that schizophrenic patients have more difficulty processing abstract phenomena, these patients should be able to recognize the actions and roles specific to a social situation better than the rules and goals of that interaction. To test this hypothesis, 25 PSE diagnosed schizophrenic patients and 15 normal controls completed the Situational Features Recognition Test, an instrument in which the four types of features have been matched for item difficulty. In addition, sub-

jects completed measures of information processing, intelligence, and symptomatology. Results showed that schizophrenic patients are less sensitive to situational features than normal controls. Moreover, schizophrenic patients are less sensitive to the goals that define a situation than the actions, roles, or rules. Results also indicated that the schizophrenic subjects recognition of schematic features interacts with the content of the specific situation. Findings from a correlational analysis showed that feature recognition of schizophrenic patients is associated with sustained attention, short-term recognition memory, verbal intelligence, and level of positive and negative symptoms. These findings have implications for understanding the social cognitive deficits that underlie the interpersonal dysfunctions of schizophrenia.

NR449 Wednesday May 6, 12 noon-2:00 p.m.

Patient Rejection and Relapse in Schizophrenia

Uriel Heresco-Levy, M.D., Ezrath Nashim Hospital, Jerusalem Israel, 1500 Waters Pl. Bronx Psy Ctr, Bronx, NY 10461; Daniel Brom, Ph.D., David Greenberg, M.D.

Summary:

The purpose of this study was to evaluate, in an Israeli sample, two economic methods of measuring family attitudes that may be relevant to prognosis in schizophrenia. Fifty single, key relatives of 50 DSM-III-R stable chronic schizophrenic outpatients were assessed. Relatives' ratings were obtained on: 1) The Patient Rejection Scale (PRS), a self-report scale reported to predict relapse in U.S. samples, 2) a four-item questionnaire in which the treating physicians, blind to PRS scores, rated the degree of rejection, criticism, hostility and emotional overinvolvement (EOI) of the relatives. PRS response distribution was similar to that found in the original New York sample. PRS total scores positively correlated with physicians' ratings on each of the first three items of the questionnaire ($p<.01$) but not with EOI scores. The number of psychotic exacerbations registered among the patients during a three-year period correlated positively with both PRS ($p<.05$) and the questionnaire items ($p<.01$) scores. Physicians' ratings of rejection also correlated with the number of rehospitalizations ($p<.01$). These findings suggest that family rejection: 1) may be predictive of relapse, 2) can be assessed using the PRS and staff rating instruments, 3) may not be positively correlated with EOI.

NR450 Wednesday May 6, 12 noon-2:00 p.m.

Modules to Train Social Skills in Schizophrenics

Robert P. Liberman, M.D., Psychiatry, UCLA-Camarillo, P.O. Box 6022, Camarillo, CA 93011; Charles J. Wallace, Ph.D., Sally J. MacKain, Ph.D.

Summary:

While social skills training has been shown to be effective in improving the functioning of schizophrenics and in reducing their relapse rates, obstacles to the widespread application of this modality come from inadequate specification of the training procedures. The objective of this study was to evaluate the effectiveness and replicability of highly prescribed and operationalized, psychoeducational "modules" to improve the social and instrumental skills of severely mentally ill patients. Staff in seven facilities conducted modules for rooming, medication self-management, and recreation for leisure with 108 schizophrenic patients, following two days of formal training and periodic consultation. Each module's effectiveness was measured by patients' knowledge and performance and staff's accuracy in conducting the modules was measured by directly observing them and rating their fidelity to the module manual. Patients significantly improved their skills with no significant erosion over a one-year follow-up period in state hospital and community mental health facilities. Fidelity to the module manual was good except in one facility where departure from the manual procedures was associated with no improvement in patient's skills. The modules appear to be "user-friendly" and applicable to a wide array of mentally disabled patients, professional and paraprofessional staff, and facilities.

NR451 Wednesday May 6, 12 noon-2:00 p.m.

P300 and Temporal Lobe Structures in Schizophrenia

Robert W. McCarley, M.D., Psychiatry, VAMC Harvard Med. School, 940 Belmont Street, Brockton, MA 02401; Martha E. Shenton, Ph.D., Brian F. O'Donnell, Ph.D., Robert S. Smith, M.A., Ron Kikinis, M.D., Ferenc A. Jolesz, M.D.

Summary:

Amplitude reduction and left < right topographic asymmetry of the P30 component of the event-related potential (ERP) to novel, task-related auditory stimuli have been consistently reported in schizophrenia (SZ). We combined P300 recordings with the use of semi-automated MRI image processing techniques to examine the relationship between abnormalities in P300 amplitude and specific temporal grey matter regions of interest (ROI) in 15 male, right-handed subjects with SZ (DSM-III-R and RDC criteria). The P300 component was recorded using an auditory oddball paradigm at 28 electrode sites. Grey matter volumes computed on 1.5 mm MRISPGR images included the anterior and posterior superior temporal gyrus (STG), hippocampus, amygdala, and parahippocampal gyrus. Pearson correlation coefficients were calculated between P300 amplitude (300 to 400 ms mean value at T3, C3, Cz, C4, and T4) and MRI volumes. In SZ subjects, volume reductions in the left but not right posterior superior temporal gyrus (STG), which includes Heschl's gyrus and the planum temporale, were associated with both P300 amplitude reduction ($r>.54$ at T3, C3 and Cz, $p<.05$) and left < right topographic amplitude asymmetry ($p<.05$). Medial temporal lobe ROIs did not correlate with P3 amplitude. These data suggest 1) a left posterior STG generator site for P300, 2) abnormalities of this site in SZ, and 3) a left-right asymmetric gradient of influence of the left posterior STG generator site on scalp-recorded P300 voltages with maximal influences near T3 and minimal near T4.

NR452 Wednesday May 6, 12 noon-2:00 p.m.

Abnormal N2 in Schizophrenia and MRI Limbic Volumes

Brian F. O'Donnell, Ph.D., Psychiatry, Brockton VAMC, 116A 940 Belmont, Brockton, MA 02401; Martha E. Shenton, Ph.D., Robert W. McCarley, M.D., Dean Salisbury, Ph.D., Ron Kikinis, M.D., Ferenc A. Jolesz, M.D.

Summary:

The N2 (N200) is a negative-going event-related potential (ERP) associated with violation of stimulus expectancy. It is usually followed by a P3 component, although their anatomic generators may differ. We studied the N2 component in 15 schizophrenic and 14 control subjects using an auditory oddball paradigm and recording EEG from 28 channels. Peak amplitude of the N2 was measured from difference ERPs (rare-frequent). N2 amplitude was reduced both at midline (Fz,Cz,Pz,Oz) and coronal (T5,P3,Pz,P4,T6) sites (Group difference on mixed ANOVAs, $p<.05$). Six of the patients had values less than any of the normal control subjects. We next examined the correlation between N2 reduction measured along a coronal chain (T5,P3,Pz,P4,T6) with volumetric MRI measurements of temporal lobe structures. N2 reduction, especially at T5, was markedly correlated with left anterior superior temporal gyrus ($r=0.72$, $p;<.01$) and left anterior hippocampus/amygdala volume reduction ($r=0.66$, $p<.01$), and, to a lesser extent T6 was correlated with volume reduction in right posterior hippocampus. These

results 1) provide the first evidence from quantitative MRI of N2 sources, 2) point to the N2 potential as useful as a possible indicator of medical temporal lobe damage (P3 reduction is associated only with neocortical left posterior STG volume reduction,) and 3) the extent of normal-Sz separation on N2 suggests N2 may be useful in differentiating schizophrenics from normals.

NR453 Wednesday May 6, 12 noon-2:00 p.m.

Cognitive Activated Prism SPECT in Schizophrenics

Joel L. Steinberg, M.D., Psychiatry, VA Medical Center, 4500 South Lancaster Road, Dallas, TX 75216; Michael D. Devous, Ph.D., David L. Garver, M.D., Joachim D. Raese, M.D., Rodrick R. Gregory, M.D.

Summary:

Medication-free schizophrenic subjects underwent SPECT scanning, using a high-resolution (6-8mm) three-headed tomograph (PRISM). Tc-99m HMPAO was injected through an intravenous line while the subjects were engaged in performance tasks. For each subject, PRISM data were acquired for the Wisconsin Card Sort Task (WCS) to provide a cognitive challenge for dorsolateral prefrontal cortical activity, and for the Number Matching Task (NM) to control for nonspecific brain activation. Three-dimensional surface images of the brain were reconstructed by the PRISM computer system. A value of approximately 70 percent of the highest pixel value in the data set was used as the threshold value for the three-dimensional rendering to display the surface. Deficits previously described in the metabolic activity/rCBF in dorsolateral prefrontal cortex during WCS compared with NM are dramatically demonstrated by this new three-dimensional technique.

NR454 Wednesday May 6, 12 noon-2:00 p.m.

Brain Potentials to Complex Tones in Schizophrenia

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Summary:

Brain event-related potentials (ERPs) of psychotic patients were measured during a dichotic Complex Tone Test. ERPs were recorded at midline and homologous sites over each hemisphere. Comparison of ERP data for eight psychotic patients (DSM-III-R diagnoses: four schizophrenic, two schizoaffective, one paranoid delusional, one schizotype/bipolar) and 20 normal controls, who had comparable behavioral accuracy data, revealed the following results: (1) patients had smaller N1 amplitude than normals ($p<.01$) and this was most evident bilaterally at frontocentral sites ($p<.05$); (2) patients had smaller amplitudes of P350 ($p<.01$) and P550 ($p<.05$); (3) P550, identified with the classical P3 component, showed a Group X Hemisphere interaction ($p<.05$), with less P3 over the left than right hemisphere of patients but not normals. Smaller N1 and P3 in patients is consistent with prior findings for schizophrenic patients. Although preliminary, the finding of less P3 over left than right hemisphere of patients, which was most evident at central and parietal sites, is of particular interest given recent ERP and imaging findings of left temporal deficits in schizophrenia. This abnormal P3 asymmetry has not been found in groups of depressed or manic patients and may, therefore, be specific to schizophrenia-spectrum disorders.

NR455 Wednesday May 6, 12 noon-2:00 p.m.

Extrapyramidal Symptom Scale: A Factor Analysis

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Summary:

The Extrapyramidal Symptom Rating Scale (ESRS) is widely used in clinical trials of neuroleptic drugs for the assessment of parkinsonism, akathisia, dystonia and tardive dyskinesia (TD). Previous studies have established its validity and excellent inter-rater reliability.

Method: The ESRS includes subscales for neuroleptic-induced parkinsonism, dystonia and TD. The subscale for parkinsonism consists of eight items assessing expressive automatic movements, bradykinesia, rigidity, gait and posture, tremors, akathisia, sialorrhea and postural stability. The subscale for TD consists of seven items assessing dyskinetic movements of the tongue, jaw, mouth and lips, trunk, upper and lower extremities, and other regions. Principal components factor analysis of the ESRS was carried out on data from 327 chronic schizophrenic outpatients participating in multicenter clinical trials of neuroleptic drugs, including haloperidol, fluphenazine, fluspirilene, pimozide, chlorpromazine, remoxipride, and risperidone.

Results: The existence of two factors for neuroleptic-induced parkinsonism was confirmed: (1) hypokinesia and (2) hyperkinesia. Also, three factors for TD were confirmed: (1) buccolingual masticatory movements, (2) movements of the extremities and (3) truncal movements.

Conclusion: The factor structure of the Extrapyramidal Symptom Rating Scale is of interest as it appears to be compatible with recent findings suggesting different pathophysiological significance of dyskinetic movements in different body areas.

NR456 Wednesday May 6, 12 noon-2:00 p.m.

Negative Symptoms as Medication Side-Effects

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Summary:

Some investigators have suggested that negative symptoms associated with schizophrenia may represent, at least partially, side effects caused by neuroleptic medication (i.e., akinesia). The present work examined this possibility by exploring the relationship between chlorpromazine (CPZ) equivalence levels and negative symptoms. This was done with both a general negative symptom index as well as with specific negative symptoms. Chronic male schizophrenics ($N=28$) were assessed with the Positive and Negative Syndrome Scale (PANSS), an assessment instrument that yields positive and negative symptom scores as well as a general psychopathology score. Results indicated that CPZ equivalence dose was significantly related to the overall negative symptom index as well as to specific negative symptoms. It appeared that some (blunted affect and emotional withdrawal), but not all (stereotyped thinking and passive-apathetic social withdrawal) negative symptoms could represent neuroleptic side effects. These results will be discussed in terms of their relevance to the concept of negative symptoms. Specifically, an attempt will be made to highlight the ways in which medication side effects may be associated with the expression of different negative symptoms.

NR457 Wednesday May 6, 12 noon-2:00 p.m.

Compliance in Patients with Schizophrenia

Patricia G. Carrion, M.D., Medical School, University of Texas, 1300 Moursund #141, Houston, TX 77030; Alan C. Swann, M.D., Heather Kellert, M.A.

Summary:

Patients with schizophrenia have increased relapse rates associated with failure to take prescribed medication and failure to maintain regular attendance with an aftercare facility (Caton et al., 1985; Goldstein et al., 1978; Hogarty et al., 1979; Serban and Thomas, 1974). It was hypothesized that outpatients who participate in a biopsychosocial medication/education group would have increased compliance in both of these areas. The group model includes a focus on education about medication, coping skills and social support. Relapse identification and prevention is stressed, subjects were 85 patients with schizophrenia. Fifty-six patients were seen monthly in one of six biopsychosocial groups. The remaining 29 outpatients were seen individually either monthly or every other month by a clinician. Chi square analyses revealed that participants in the biopsychosocial group setting were more likely to maintain regular attendance in the first two months of the investigation than were individually seen patients. However, no difference in rates of attendance were observed for the three months following the initial two months studied. Reasons for why the hypothesis was not supported are discussed.

NR458 Wednesday May 6, 12 noon-2:00 p.m.

Cyclic Nucleotides and Neurotransmitter Metabolites in CSF of Clozapine-Treated Schizophrenics and Normal Controls

Emile D. Risby, M.D., Psychiatry, Emory University, 1701 Uppergate Drive, NE, Atlanta, GA 30322; Robert Risinger, M.D., Mark Stipetic, B.S., Zachary Stowe, M.D., Samuel C. Risch, M.D.

Summary:

Abnormalities in the regulation central neurotransmitter systems are proposed in schizophrenia. While cerebrospinal fluid (CSF) concentrations of monoamine metabolites may reflect presynaptic release of central monoamines, CSF concentrations of cyclic nucleotides may reflect post-synaptic neurotransmitter activation. Lumbar punctures were performed on 12 clinically stable clozapine-treated schizophrenic patients and 18 controls. CSF was assayed for homovanillic acid (HVA), 5-hydroxyindoleacetic acid (5-HIAA), 3-methoxy-4-hydroxyphenylglycol (MHPG), cyclic adenosine monophosphate (cAMP), and cyclic guanosine monophosphate (cGMP). There were no group differences between the controls and the schizophrenics in any of the metabolite or cyclic nucleotide measures; however, cGMP was positively correlated with HVA and 5-HIAA in both controls (HVA and cGMP, $r=.59$, $p<.03$; 5-HIAA with cGMP, $r=.54$, $p<.04$; $n=12$) and schizophrenics (HVA with cGMP, $r=.70$, $p<.02$; 5-HIAA with cGMP, $r=.68$, $p<.02$; $n=10$). In addition, HVA was correlated with 5-HIAA in both groups (in normals: $r=.66$, $p<.01$; schizophrenics: $r=.92$, $p<.001$). Brief Psychiatric Rating Scale scores were not strongly correlated with any of the CSF measures. Although CSF concentrations of cyclic nucleotides and monoamine metabolites did not distinguish clozapine-treated schizophrenic patients from normal controls, the data suggest that concentrations of CSF cGMP may be a valid index of central serotonergic and/or dopaminergic activity.

NR459 Wednesday May 6, 12 noon-2:00 p.m.

Effects of Pay for Work on Rehabilitation Outcome

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Summary:

Schizophrenia is associated with poor work rehabilitation outcomes. Most often patients are offered volunteer or unpaid work readiness programs as a first step in rehabilitation. This may be less effective if pay leads to greater participation, and greater participation leads to better outcomes. This study examines the effect on work performance and clinical status of paying subjects an hourly wage for participation in a 26-week supported-work program. *Method:* 77 subjects with schizophrenia were assigned work placements and randomized to a pay ($3.40/hr) or no-pay condition. Symptom assessment (PANSS) was done at intake and five-month follow-up, and work performance and symptoms were monitored weekly. *Results:* Paid subjects performed significantly more hours of work and more weeks of work than unpaid subjects. Participation for pay and no-pay Ss were respectively Week 1: 98%, 32%; Week 5: 75%, 10%; Week 13: 50%, 5%; Week 26: 32%, 2%. Paid subjects had lower symptom scores on the PANSS "depressive cluster" of symptoms with a significant relationship between weeks worked and improvement. *Implications:* Pay improves rehabilitation outcomes in schizophrenia. Pay increases the likelihood of beginning and remaining in a work program. Greater participation has significant clinical effects and improves quality of life.

NR460 Wednesday May 6, 12 noon-2:00 p.m.

Pyramidical Model of Schizophrenia: Replication

Morris D. Bell, Ph.D., Psychology, VA Medical Center, VAMC Psychology Service 116B, West Haven, CT 06516; Paul H. Lysaker Ph.D., Robert M. Milstein, M.D., Joseph B. Goulet, M.A.

Summary:

A pyramidical model of schizophrenia has been presented by Kay and Sevy (1990) based on a factor analysis of the Positive and Negative Syndrome Scale (PANSS). They found factorial validity for negative and positive syndromes and identified excitement, depressive and cognitive components as well. They suggested that subtypes and syndromes can be mapped along these dimensions presented in a pyramidical model. The present study replicates their analysis using a sample of 76 subjects with schizophrenia recruited for rehabilitation. Despite divergent demographic characteristics between the samples, a five-factor equimax rotation of PANSS data produces strikingly similar dimensions. Direct comparisons of factor loadings between the original factor analysis and our replication are presented. Discussion focuses on significant points of agreement and important differences in the symptoms assigned to each cluster. How these dimensions relate to rationally derived models of positive and negative syndromes is also reviewed. For example, unusual thoughts and somatic concern listed as general symptoms in the PANSS fall into the positive syndrome, while difficulty in abstract thinking identified as a negative symptom on the PANSS is part of a cognitive component independent of negative or positive syndromes. Implications for subtyping and other methods of examining the heterogeneity of schizophrenia are considered.

NR461 Wednesday May 6, 12 noon-2:00 p.m.

Genetic and Social Influences on Schizophrenia

Frederic J. Sautter, Ph.D., Psychiatry, Tulane Univ Sch of Med, 1430 Tulane Ave., New Orleans, LA 70112; Barbara McDermott, Ph.D., John Cornwell, Ph.D., Patricia Houterloot, M.S.W., Alicia Borges, B.A.

Summary:

Genetic factors are accepted as being important in the etiology of schizophrenia. Studies also indicate that psychosocial factors may influence the course of schizophrenia. There are few data

relevant to the interaction of genetic and psychosocial factors. Previous data from our laboratory indicate that familial and nonfamilial schizophrenics respond differently to social network effects. This longitudinal study utilized structural equation modeling to define the causal relationship between social network factors, psychological variables and psychotic symptoms in 72 RDC schizophrenics. We hypothesized that different mathematical models would be required to predict the evolution of psychotic symptoms in the familial and nonfamilial groups. This hypothesis was supported as the constructed models indicate that social networks have a different impact on the two groups. In the familial group, the relationship between social network factors and psychotic symptoms was mediated by psychosocial factors (Bentler-Bonnet Nonnormal goodness of Fit statistic (BBNN) = .984). In the nonfamilial group there were no mediating psychosocial effects, as social network factors had a direct causal relationship with psychotic symptoms (BBNN = .995). These data indicate that the interaction of psychosocial variables and genetic factors warrant further study, and they suggest that psychosocial factors may have an especially strong influence on familial schizophrenia.

NR462 Wednesday May 6, 12 noon-2:00 p.m.

Cognitive Deficits in Familial Schizophrenia

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Summary:

A number of studies have indicated significant neuropsychological differences between familial and nonfamilial schizophrenia. In an ongoing study of recent-onset schizophrenia, 23 familial and 28 nonfamilial (i.e. sporadic) RDC schizophrenics were rated for psychotic symptoms and administered a range of neuropsychological tests. While both the familial and nonfamilial groups evidenced significant neuropsychological deficits, the two groups produced entirely different patterns of cognitive deficits. Cognitive deficits in the nonfamilial group were profound and appeared to reflect a generalized cognitive deficit. The neuropsychological test results of nonfamilial patients were highly intercorrelated ($p<.04$ to $p<.01$), and there was a significant relationship between those deficits and negative symptoms ($p<.05$). A different pattern of intellectual deficits was evidenced by the familial group: these test results suggested significant cognitive impairment but test scores were not highly intercorrelated. These data suggest the presence of a number of selective cognitive deficits in the familial group, and these deficits were not related to the intensity of psychotic symptoms. These data demonstrate that the heterogeneity of schizophrenia may be validly reduced by subtyping on the basis of family history of schizophrenia, and they suggest that while nonfamilial schizophrenia is characterized by generalized cognitive deficits, familial schizophrenia is associated with more selective impairments.

NR463 Wednesday May 6, 12 noon-2:00 p.m.

Neuropsychology in Relatives of Schizophrenics

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Summary:

We compared neuropsychological functioning in 32 nonpsychotic siblings and children of schizophrenics with 60 normal controls. Scores were adjusted for age, sex, and education. Using linear combinations of these adjusted variables, we created profiles of 10 neuropsychological functions: abstraction, auditory attention, motor, perceptual-motor, mental control, learning, verbal memory, visual memory, spatial and verbal ability. Relatives had worse performance and/or higher impairment rates (>1.5 SD below control mean) in abstraction, verbal memory, verbal learning, and attention ($p's<.05$), even though overall verbal and spatial abilities were equated with controls. Cluster analysis was used to examine our hypothesis that relatives comprise two classes, those with and without the schizophrenia genotype. One cluster ("non-carriers"), comprising 69% of relative, had essentially normal profiles. "Carriers" (31%) had an abnormal profile; they were significantly worse than controls in abstraction, verbal memory, learning, mental control, and auditory attention ($p's<.05$). The two clusters did not differ in age, sex, parental SES, SANS or SAPS scores, but "carriers" had lower education than "noncarriers" ($p = .01$). Lower educational attainment implies an effect of the schizophrenia genotype because scores were adjusted for education and there were no differences in parental SES. Our results further suggest that neuropsychological deficits may be useful as neurobehavioral markers for schizophrenia.

NR464 Wednesday May 6, 12 noon-2:00 p.m.

Long-Term Mazindol Treatment of Schizophrenia

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Summary:

Preliminary data suggest mazindol may be a useful adjunct to neuroleptic medication in treating negative schizophrenic symptoms, including affective flattening, withdrawal, and alogia. Mazindol is a long-acting agent that blocks dopamine (DA) reuptake at the DA transporter site. We tested the long-term clinical responses of positive and negative symptoms to mazindol augmentation of neuroleptic in outpatient schizophrenics. *Methods:* In an ongoing study, patients who participated in a placebo-controlled trial of mazindol augmentation of typical antipsychotic medications received open-label mazindol (2-4 mg/day) in addition to typical neuroleptics. Brief Psychiatric Rating Scale (BPRS), Positive and Negative Symptom Scale (PANSS), AIMS, Webster EPS ratings, and fasting prolactin and HVA were obtained biweekly for four to six months of mazindol treatment. *Results:* Patients receiving mazindol demonstrated a 25%-30% reduction of BPRS and PANSS negative symptom ratings compared to their baseline. No increases in positive symptoms were noted in any patients. There was a modest reduction of extrapyramidal side effects with mazindol. Subjectively, patients experienced increased mood, energy, and affective reactivity and requested to be maintained on the medication. No patients developed tolerance to the beneficial effects of mazindol. *Conclusions:* Mazindol may be a useful adjunct to standard neuroleptic medication for long-term treatment of refractory negative symptoms in stable outpatient schizophrenics.

NR465 Wednesday May 6, 12 noon-2:00 p.m.

Neuropsychiatry of Impulsivity and Aggression

Maxim Frenkel, M.D., Psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; Cecile Durlach-Misteli, M.D., Bonnie Aronowitz, M.A., Eric Hollander, M.D., Michael Leibowitz, M.D., Enrico Fazzini, D.O., Lee Cohen, M.D., Andrew Levin, M.D., Lawrence Rubin, M.D.

Summary:

Recent studies have suggested that impulsive and aggressive populations may differ on a number of dimensions. Neurological and neuropsychological impairment, among other factors, may differentially contribute to the development of impulsive or aggressive

behavior. Adolescent and adult inpatients hospitalized for impulsive or aggressive behavior were administered a neuropsychological battery and a neurological evaluation. On neuropsychological measures, 29% of impulsive adolescents showed deficits on tasks assessing frontal lobe/executive functions, while aggressive adolescents did not. In contrast, 33% of impulsive and 57% of aggressive adults demonstrated frontal lobe/executive function difficulties. On neurological measures, 85% of all adults and 53% of all adolescents demonstrated high orbitofrontal (OF) scores. In addition, 69% of the adults and 33% of the adolescents scored positive on the temperolimbic (TL) battery. None of the adults but 26% of the adolescents were soft sign positive. Overall aggressive patients had higher OF and TL scores than impulsive patients. Impulsivity and aggression may be the behavioral correlates of a progressive disorder characterized by early OF signs with subsequent TL involvement. Other results are also discussed in light of developmental factors.

NR466 Wednesday May 6, 12 noon-2:00 p.m.

Bupropion Use in Patients at Risk for Seizures

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Summary:

Bupropion is an effective antidepressant medication that has been reported to have an associated risk of precipitating seizure events in patients without known risk factors for seizures at a rate of 0.3%-0.9%. In patients with conditions predisposing for seizures (e.g. head trauma, cerebrovascular insults, degenerative neurologic disease, etc.), the risk of seizures from bupropion has been considered significantly higher, particularly at higher dosages, and limited the use of this medication in those patients. At a specialized neuropsychiatric facility, 17 patients (ages 20-83, mean[sd] = 58.3 [20.8], seven males, 10 females) have been treated with bupropion (daily dose range 75-450 mg, average = 200 mg) for organic mood disorders (closed head injury n = 4, cerebrovascular events n = 10, SDAT n = 2, SLE cerebritis n = 1). Duration of bupropion treatment ranged from five days to greater than six months (two patients discontinued initial treatment due to increased anxiety) with clinical improvement in mood evident in 13/15 patients remaining on drug. No seizure events occurred in any of these patients. Although sample size limits statistical interpretation, these cases suggest that bupropion may be safely used in patients at risk for seizures, particularly at lower dosages. Controlled studies of dose and duration effects with larger samples of patients at risk for seizures are needed to establish the relative efficacy and safety of bupropion.

NR467 Withdrawn

NR468 Wednesday May 6, 12 noon-2:00 p.m.

Reliability of Schizophrenia Symptom Assessment

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Summary:

The validity of the diagnosis of schizophrenia is dependent upon the reliability of assessment of its constituent symptoms. Although numerous studies have evaluated the reliability of diagnoses generated with structured interviews, few have studied the relative reliability of the individual symptom assessments made as part of such structured interviews. The present study utilizes data obtained from pairs of independent diagnosticians participating in SADS interviews of 71 schizophrenic patients to evaluate the reliability of assessment of a number of symptoms currently under study for the DSM-IV criteria for schizophrenia. Inter-rater intraclass correlation coefficients (ICC's), calculated for each symptom/item, suggest differences among the reliabilities of various symptoms.

Among seven items evaluating delusions, five revealed ICC's above .75 ($df = 50$, $p < .001$). Among four negative schizophrenia symptoms assessed, ICC's ranged from .56 for "blunted affect" ($df = 50$, $p < .001$) to .74 for "loss of interest or pleasure" ($df = 53$, $p < 001$). Formal thought disorder ICC's ranged from .39 for "illogical thinking" ($df = 49$, $p = .002$) to .62 for both "impaired understandability of speech" ($df = 50$, $p < 001$) and "loosening of associations" ($df = 49$, $p < .001$). At the time of presentation, the data will include over 200 patients previously assessed with SADS interviews.

NR469 Wednesday May 6, 12 noon-2:00 p.m.

Indices of Gender Effects in New Onset Schizophrenia

Sally R. Szymanski, D.O., Research, Hillside Hospital, P.O. Box 38, Glen Oaks, NY 11004; Jeffrey A. Lieberman, M.D., Jose M.A. Alvir, Dr. PH., Margaret Woerner, Ph.D., Miranda H. Chakos, M.D., Amy R. Koreen, M.D.

Summary:

Gender effects in chronic schizophrenia in course and outcome have been described. Female chronic schizophrenics have been reported to have higher homovanillic acid and prolactin levels on neuroleptic treatment. The effect of biologic variables in determining gender differences in first-episode schizophrenics was examined in this study.

Fifty-four first-episode RDC schizophrenic patients were followed for one year. Weekly plasma neuroleptic, homovanillic acid and prolactin levels, provocative methylphenidate infusion testing and a brain magnetic resonance imaging scan were obtained.

The sample consisted of 54 patients, 53% male. An increased psychotogenic response to the methylphenidate infusion was seen in females. The effect of gender on plasma HVA level change from baseline to week one was highly significant. Mean plasma prolactin levels during weeks one to six were significantly greater in females than males during the first six weeks of the study. No statistically significant gender difference in prolixin levels was seen. Qualitative MRI ratings showed gender differences in third ventricular enlargement at the level of a statistical trend with females having smaller third ventricles.

These results indicate a greater sensitivity in females to neuroleptic blockade all of which is superimposed on less brain pathomorphology. These differences in biologic factors could play a role in female schizophrenics' better treatment response and outcome as compared to males.

NR470 Wednesday May 6, 12 noon-2:00 p.m.

Gender Effects in Clozapine Treated Patients

Sally R. Szymanski, D.O., Research, Hillside Hospital, P.O. Box 38, Glen Oaks, NY 11004; Jeffrey A. Lieberman, M.D., Simcha Pollack, Ph.D., Margaret Woerner, Ph.D., S. Masiar, M.D., A. Safferman, M.D.

Summary:

Gender differences in chronic schizophrenia have been reported in age of onset and neuroleptic response, with females having a superior course of illness. Female schizophrenics are reported to have higher plasma HVA and prolactin levels than males. Whether

the same pattern of gender effects exists in neuroleptic nonresponsive, clozapine-treated schizophrenics remains a clinical question.

Gender differences in a group of neuroleptic nonresponsive schizophrenics who were treated with clozapine for six weeks were examined. Patients were rated for psychopathology and side effects at regular intervals, with weekly plasma homovanillic acid, prolactin, and clozapine levels collected.

The treatment response of 71 DSM-III-R schizophrenics and schizoaffective patients was examined with an early onset of illness was observed in the females with no significant difference in duration of illness prior to clozapine initiation noted. Initially, females had a poorer response to clozapine, but no difference was noted after six weeks. More gait and tremor side effects in females were observed. Mean weekly plasma clozapine levels were significantly higher in females than males with no significant dosage difference. Mean weekly prolactin levels were higher in females, although no difference in HVA levels was noted.

Patterns of gender effects in clozapine-treated chronic schizophrenics are markedly dissimilar to those reported in neuroleptic-treated patients. Therefore, these clozapine-treated female schizophrenics may represent a distinct clinical subgroup of female schizophrenics.

NR471 Wednesday May 6, 12 noon-2:00 p.m.

The Positive and Negative Syndrome Scale Structure in Adult and Geriatric Schizophrenia

Leonard White, Ph.D., Clinical Neurology, Pilgrim Psychiatric, Box A Building 11 CNC, West Brentwood, NY 11717; Michael Parrella, Ph.D., Philip D. Harvey, Ph.D., Peter Powchik, M.D., Michael Davidson, M.D.

Summary:

The purpose of this study was to examine the controversy concerning the structure of schizophrenic symptoms and the effects of aging upon symptoms. The Positive and Negative Syndrome Scale (PANSS) was originally presented in terms of a three-factor structure, but more recently a seven-factor structure was derived. We have re-examined published PANSS data and have conceptually derived a five-factor structure. The method of confirmatory factor analysis (CFA) was used to evaluate which of the alternative models provides the best fit to empirical data and to examine similarity of fit across adult and geriatric patients. PANSS data were available from two schizophrenic (DSM-III-R criteria) inpatient cohorts: 1) adult (N = 240, X age = 33.1); geriatric (N = 415 X age = 76.6). Data from each cohort were subjected to CFA analysis using EQS statistical software to obtain contrasting goodness-of-fit indices among the alternative structure models. Results from each cohort revealed the five-factor model as best fitting. Multisample CFA confirmed that this model applied equally well to both adult and geriatric cohorts (Non-normed fit index = .991). We conclude that the five factors of Negative, Positive, Excitement, Depression, and Cognition provide the best fit description of schizophrenic symptoms in both adult and geriatric inpatients.

NR472 Wednesday May 6, 12 noon-2:00 p.m.

Neuropsychobiological Correlates of Tardive Dyskinesia

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Summary:

Introduction: Several studies suggest that the subgroup of schizophrenic patients who develop tardive dyskinesia (TD) with neuroleptic treatment tend to have more negative symptoms, cognitive impairments and structural brain abnormalities.

Methods: We studied 100 consenting DSM-III-R schizophrenic patients from the community. Using the AIMS scale we identified 12 out of 100 patients who had a score of 2 or more for involuntary movements. We then compared the TD group (N = 12) with the non TD group (N = 88) on clinical features, neuropsychological performance and MRI brain structure measures.

Results: The TD group had significantly higher mean negative symptom score on the SANS ($p<.001$), but were not different on positive symptoms, family history of psychosis, or frequency of perinatal brain insults. The TD group was significantly worse on several cognitive functions (verbal and performance TQ, trail making A and B, Know Cube immediate, verbal fluency and figural memory (Wechsler). Finally, the TD group was not different on MRI brain measures (cerebral volume, lateral and third ventricular volumes).

Discussion: The findings suggest that TD is associated with clinical as well as brain structural and functional variables that could be used to predict vulnerability to neuroleptic-induced TD.

NR473 Wednesday May 6, 12 noon-2:00 p.m.

Significant Decrease in Psychopathology Within Three Days of Haloperidol Treatment in Patients with Chronic Schizophrenia

Rene S. Kahn, M.D., Psychiatry, Bronx VAMC, 130 West Kingsbridge Road, Bronx, NY 10468; Robert G. Stern, M.D., Michael Davidson, M.D., Philip D. Harvey, Ph.D., Seth H. Apter, Ph.D., Kenneth L. Davis, M.D.

Summary:

It was hypothesized that neuroleptics produce an early, large and specific antipsychotic effect. After two drug-free weeks, DSM-III-R chronic schizophrenic inpatients were treated with haloperidol 20 mg/d. BPRS and CGI ratings were performed on the last drug-free day (baseline) and on day 3, 8, 15, 22, 29 and 36 of treatment. Patients showing a decrease of at least one CGI point from baseline at day 36 were defined as "responders," and those without such a change as "non-responders." There were 17 responders and 29 non-responders. Repeated measures ANOVA with one repeated measure, time (baseline, day 3) and one between subjects factor, Group (responders and non-responders) showed a significant Group by Time interaction for total BPRS ($F = 7.207$; $df = 1,45$; $p<0.05$) and CGI scores ($F = 10.331$; $df = 1,44$; $p<0.005$). Within Group Paired t-tests between scores obtained at day 3 and at baseline showed that responders had a significant reduction in total BPRS ($p<0.005$) and psychotic symptoms ($p<0.05$) as well as in anergia and anxiety clusters by the third day of treatment. The decrease in total BPRS and CGI scores by day 3 represented almost 50% of the total improvement achieved by day 36.

These findings have relevance to clinical practice and to the understanding of the mechanism of action of neuroleptics.

NR474 Wednesday May 6, 12 noon-2:00 p.m.

Placebo-Controlled Treatment of Prodromal States

William C. Wirshing, M.D., Psychiatry, West LAVA Med Center, 11301 Wilshire Blvd, Los Angeles, CA 90073; Stephen R. Marder, M.D., Theodore Van Putten, M.D., Kathleen Johnston-Cronk, M.S., Joanne MacKenzie, R.N., Jim Mintz, Ph.D., Robert P. Liberman, M.D., Malca Lebell, Ph.D.

Summary:

Lower than conventional maintenance doses of depot neuroleptics cause fewer untoward side effects but may result in a higher rate of schizophrenic relapse. In a five-year prospective study we examined the potential mitigating effects of early, symptom-tar-

geted, neuroleptic supplementation on this higher relapse liability. Subjects were stabilized on low-dose fluphenazine decanoate (5-10mg every two weeks) and then randomized to receive either oral fluphenazine supplementation or placebo (in double-blind fashion), at the first sign of prodromal symptoms. Supplementation continues throughout each prodromal period until subjects have either restabilized or an exacerbation intervenes. To date, 81 patients meeting DSM-III-R criteria for schizophrenia have been entered, and of these 36 have developed prodromes (as defined by pre-established and operationalized criteria) during four years of formalized evaluation. Within this randomized subgroup, only 26 have remained ee of either prodromal or exacerbated symptoms for 12 or more weeks. For this more clinically stable group, neuroleptic supplementation during prodromes has resulted in longer survival to exacerbation [p = 0.013 (log likelihood statistic)], fewer prodromes ending in exacerbation (37% vs 50%), and a greater percentage of subjects remaining exacerbation-free (50% vs 14%, p = 0.049 chi square). However, only 30% of all exacerbations detected were preceded by an identified prodromal period. Taken together, these results suggest that: 1) treating prodromal symptoms with supplemental neuroleptics does decrease relapse rates and 2) our method for detecting prodromal episodes was relatively insensitive.

NR475 Wednesday May 6, 3:00 p.m.-5:00 p.m.

L-365,260: A CCK-B Antagonist Blocks CCK-4-Panic

Jacques Bradwejn, M.D., Psychiatry, St. May's Hospital, 3830 Lacombe Avenue, Montreal PQ H3T 1M5, Canada; Diana Koszycki, M.A., Anne Couetoux, M.D., Hank van Megen, M.D., Johan den Boer, M.D., Herman Westenberg, Ph.D., Chris Karkanias, M.Sc., Jeremy Haigh, Ph.D.

Summary:

Cholecystokinin (CCK) is a neurotransmitter found in high quantities in mammalian brain that contains CCK receptors, mainly of the B subtype. CCK-4, a CCK_B receptor agonist, reliably induces panic attacks in panic disorder (PD) and to a much lesser extent in normals, suggesting an enhanced sensitivity to CCK-4 in PD. The present study investigated the effects of pretreatment with L-365,260, a CCK_B antagonist, on CCK-4 induced panic attacks in PD. Patients were treated with L-365,260 (10 or 50 mg PO) or placebo 90 minutes before a challenge with a submaximal dose of I.V. CCK-4 (20 μg). Twenty-four patients were entered; three patients received a single challenge, and 21 patients were challenged on two occasions according to a double-blind, incomplete block design. The panic rate following challenge with CCK-4 was as follows: 13/15 (placebo), 5/15 (10 mg), and 0/15 (50 mg); ($P<.01$ for 10 mg and 50 mg against placebo). The adjusted mean (±SD) sum intensity scores on the Panic Symptom Scale were 37.2 ± 15.6 (placebo), 25.7 ± 16.3 (10 mg) and 12.4 ± 15.9 (50 mg). Differences between 50 mg and placebo were statistically significant ($P<.01$), and differences between 10 mg and placebo approached significance ($P=.07$). These data demonstrate that L-365,260 can block CCK-4-induced panic. The clinical efficacy of this CCK_Bantagonist in PD warrants investigation.

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Behavioral and Cardiovascular Effects of Four Doses of CCK-4

Jacques Bradwejn, M.D., Psychiatry, St. Mary's Hospital, 3830 Lacombe Avenue, Montreal PQ H3T 1M5, Canada; Diana Koszycki, M.A., Anne Couetoux, M.D., Lawrence Annable, D.S., Scott Reines, M.D., Chris Karkanias, M.Sc.

Summary:

Exogenous CCK is anxiogenic in humans and animals. Pretreatment with CCK_B antagonists markedly attenuates anxiogenic-like effects of CCK receptor agonists in rodents and monkeys. To determine whether CCK_B antagonists can reverse the effects of CCK agonists in humans an appropriate challenge dose must be selected. Thus, we compared four doses (10, 15, 20, 25 μg) of CCK-tetrapeptide (CCK_4) and placebo (saline) in panic disorder patients (12M; 17F; mean age = 34.8 yrs) in a double-blind, balanced incomplete block design. CCK_4 or placebo were given i.v. on two separate days. Significant dose effects with strong linear effects were found for the number of symptoms ($P<.0001$), sum intensity of symptoms ($P<.0001$), and 15 of 18 symptoms on the Panic Symptom Scale ($P<.05$ to $P<.0001$). Linear effects for blood pressure ($P<.05$) and heart rate ($P<.001$) were significant. Significant dose effect for heart rate was also noted ($P<.01$). The panic rate was: 0/11 (placebo), 2/12 (10 μg), 7/11 (15 μg), 9/12 (20 μg), and 9/12 (25 μg). These results demonstrate that CCK-4 dose-dependently produces panic attacks and increases in cardiovascular indices. The 20 μg dose of CCK-4 (ED_{75}) might be appropriate for efficacy studies of CCK_B antagonists and other potential antipanic drugs in panic disorder patients.

477 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Personality Disorder and OCD

Donald W. Black, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; Russell V.R. Noyes, M.D., Bruce M. Pfohl, M.D., Rise B. Goldstein, M.S.W., Nancee Blum, M.S.W.

Summary:

We compared the frequency of DSM-III personality disorder in 32 obsessive-compulsive volunteers and 33 psychiatrically normal controls, as well as their first-degree relatives, all of whom were interviewed blind to proband status (i.e., case versus control). Obsessional probands were more likely than control probands to have a personality disorder, but among obsessionals, compulsive personality was not the most frequent disorder. No differences in the frequency of personality disorders were found in first-degree relatives, including compulsive personality. No differences were found between the groups on obsessional, hysterical, or oral character traits as measured by the Lazare-Klerman-Armor Inventory. The findings confirm that personality disorders, but not compulsive personality per se, are highly prevalent among obsessionals, and that there is little support for the existence of a relationship between compulsive personality and obsessive-compulsive disorder.

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A Comparison of Fluvoxamine, Cognitive Therapy and Placebo in the Treatment of Panic Disorder

Donald W. Black, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; Robert Wesner, M.D., Wayne Bowers, Ph.D.

Summary:

Seventy-five outpatients with moderate to severe panic disorder were randomly assigned to eight weeks of fluvoxamine, cognitive therapy, or placebo. Fifty-five patients completed the treatment protocol. Fluvoxamine was found to be an effective and well-tolerated treatment for panic using both clinician and patient rated variables. Subjects receiving cognitive therapy also improved, but this improvement did not significantly differ from the experience of the placebo group for most comparisons. Fluvoxamine was superior to cognitive therapy for many ratings, but cognitive therapy was not superior to fluvoxamine on any rating. Fluvoxamine also produced improvement earlier than cognitive therapy. At the main comparison point (week 4), 57% of patients receiving fluvoxamine were rated moderately improved or better versus 40% of the cognitive therapy group, and 19% of the placebo group. At that point, 44% of the

fluvoxamine recipients versus 26% of cognitive therapy, and 5% of placebo recipients were free of panic attacks.

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Effects of Fluvoxamine on Panic Disorder

Rudolf Hoehn-Saric, M.D., Psychiatry, Johns Hopkins University, 115 Meyer, 600 N. Wolfe St., Baltimore, MD 21205; Daniel R. McLeod, Ph.D.

Summary:

Several reports suggest that selective serotonin reuptake blockers are helpful in the treatment of panic disorder (PD). The aim of the study was to compare fluvoxamine with placebo in 50 PD patients using an eight-week, double-blind parallel design. Weekly assessment included a panic diary (frequency and severity), the Montgomery-Asberg Depression Scale, the Clinical Anxiety Scale and the Sheehan Disability Scale. While both groups improved on all measures, the fluvoxamine group experienced significantly less frequent major panic attacks from the third week on, and significantly lower ratings on anxiety, depression and disability from the sixth week on. The severity of major, and the severity and frequency of minor attacks remained unaffected by fluvoxamine.

The results indicate that: 1) Participation in a drug study, even without additional psychotherapy, led to significant improvement in all patients; 2) Fluvoxamine lowered the number but not the severity of panic attacks; 3) The effects of fluvoxamine on anxiety, depressive mood and disability differed from placebo only after six weeks of treatment, at which period the placebo group either showed no further improvement or a reversal of symptoms; 4) Minor panic attacks differed from major panic attacks in their response to fluvoxamine. They may not necessarily represent a milder form of panic attacks.

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Panic Disorder in Schizophrenic Patients

Jean M. Chignon, M.D., Psychiatry, Hopital Louis Mour, 178 Rue Des Renovillers, Colombes 92701, France; Patrick Hardy, M.D., D. Levy, M.D., C. Epelbaum, M.D., J. Ades, M.D., A. Feline, M.D.

Summary:

Considering the importance of anxiety in schizophrenic disorders and the conflicting interpretations, it is surprising that very few systematic studies have been done on specific anxiety disorders in schizophrenic patients.

This study describes the prevalence and phenomenology of panic attacks and panic disorder in patients suffering from schizophrenia. We included all patients who met DSM-III-R criteria for schizophrenia without any associated mood disorder. Forty consecutive patients, either inpatient ($n=21$) or outpatient ($n=19$), were interviewed with a semi-structured diagnostic instrument allowing the use of DSM-III-R criteria. Mean age of the patients was 29.9 years (SD:8.4), and mean duration of schizophrenic disorders was 430.0 weeks (SD:426,3).

Among these 40 schizophrenic patients, 19 (47.5%) suffered currently from recurrent panic attacks and 14 (35%) of them from panic disorder. The prevalence of panic disorder is higher in patients with paranoid type of schizophrenia than in other types (90% vs 16.7%; corrected $Chi2=6.60$, $p<.01$). Although, the Montgomery and Asberg Depression Rating Scale (M.A.D.R.S.) mean score was found similar in different subtypes of schizophrenia, we found that schizophrenic patients with comorbid panic disorder had significantly higher scores than patients without a history of panic (16.7 ± 9.4 vs 10.3 ± 8.6, $p<.10-3$).

So, it appears that the prevalence of panic disorder is high in schizophrenic patients and seems to be associated with depressive symptomatology in this population, even in the absence of defined current depressive disorders.

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Chest Pain in Generalized Anxiety Disorder

Cameron S. Carter, M.D., Psychiatry, U.C. Davis, 4330 V. Street, Sacramento, CA 95817; Richard J. Maddock, M.D.

Summary:

The presence of chest pain as a symptom in patients with generalized anxiety disorder was investigated in a psychiatric sample using a structured interview. Of 30 sequentially evaluated patients meeting DSM-III-R criteria for G.A.D., 16 (53%) reported a history of chest pain. Five of these patients also had a history of panic attacks; however, four of the five reported that their pain occurred independently of their panic attacks. Ten of these patients reported that their chest pain episodes were associated with episodes of excess worry. Nine had sought medical evaluation for their pain. These findings suggest that chest pain may be a common symptom in G.A.D. and should be considered for inclusion in the diagnostic criteria for this disorder. The pattern of utilization of medical care was comparable in this sample of patients with G.A.D. and a group of patients with panic disorder recruited in a similar manner. Patients with chest pain and normal coronary arteries are frequently found to have panic disorder. These results suggest that G.A.D. might also be a common finding in chest pain patients with no demonstrable coronary disease. Future studies of coronary-artery-disease-negative patients with chest pain should include assessments for the presence of G.A.D.

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Body Dysmorphic Disorder: Can It Be Psychotic?

Susan L. McElroy, M.D. Psychiatry, Univ Cincinnati Col Med., 231 Bethesda Avenue ML559, Cincinnati, OH 45267; Katharine A. Phillips, M.D., Paul E. Keck, Jr., M.D., Harrison G. Pope, Jr., M.D., James I. Hudson, M.D.

Summary:

Controversy exists as to whether body dysmorphic disorder (BDD) can present with psychotic features. Is BDD purely a nonpsychotic disorder, as classified in DSM-III-R, and its psychotic counterpart—delusional disorder, somatic type—an entirely separate diagnostic entity? Or does BDD have a psychotic subtype that represents a form of the primary disorder? To address this question, 18 patients who met DSM-III-R criteria for BDD were compared with 12 patients who met criteria for BDD except that their preoccupations were of delusional intensity. Delusional patients did *not* differ significantly from nondelusional patients on demographics, phenomenology, course, associated psychopathology, family history, or treatment response. For instance, both delusional and nondelusional groups responded preferentially to serotonin uptake blockers: eight (53%) of 15 nondelusional patients responded to clomipramine or fluoxetine compared with six (75%) of eight of the delusional patients. In contrast, neither group responded to neuroleptics: none of 16 patients (including seven with delusional preoccupations) responded, including two delusional and two nondelusional patients who received pimozide. We conclude the BDD and the BDD variant of delusional disorder, somatic type, significantly overlap or may even be the same disorder, and that DSM-IV should consider a psychotic subtype of BDD.

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Social Phobia: Efficacy of Brofaromine Versus Placebo

Mats Humble, M.D., Psychiatry, Danderyd Hospital, S-Danderyd 18288, Sweden; Tom Fahlen, M.D., Charlotte Koczkas, M.D., Heimo L. Nilsson, Ph.D.

Summary:

The efficacy of nonselective MAO inhibitors in social phobia has been demonstrated, but the mechanism of action remains undetermined. Brofaromine is a selective reversible MAO-A inhibitor, also inhibiting 5-HT reuptake. Thus, its clinical profile in social phobia may have implications for serotonergic mechanisms in social phobia.

Seventy-seven patients (45 male, 32 female) with social phobia (DSM-III-R) were randomly and double-blindly treated with brofaromine (mean age 37.2 yrs) or placebo (mean age 38.4 yrs) for 12 weeks. Exclusion criteria were history of panic attacks and ongoing depressive episode. Clinical efficacy was measured by Clinical Global Improvement (CGI), Liebowitz Social Phobia Scale (LSPS) and Hamilton Anxiety Scale (HAS). Intent-to-treat analysis was performed. After 12 weeks of treatment 79.4% of the brofaromine patients were much or very much improved (CGI) compared to 25.6% in the placebo group ($p<0.0001$). In the LSPS there was a significant reduction in favour of brofaromine for anxiety ($p<0.003$) and for avoidance ($p<0.0002$). The reduction in HAS was also in favor of brofaromine compared to placebo ($p<0.005$). Eight patients were withdrawn from the study (lack of efficacy 1; poor tolerability ; other 1). The side effects were mostly mild and decreased with time; most frequent were sleep disturbances.

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Amine Profiles in OCD

Jose A. Yaryura-Tobias, M.D., Bio-Behavioral Psych., 935 Northern Blvd, Great Neck, NY 11561

Summary:

The serotonergic hypothesis for obsessive compulsive disorder (OCD) is based on the efficacy of clomipramine (CMI), a strong serotonin (5-HT) reuptake blocker in the treatment of OCD. However, CMI not only blocks 5-HT reuptake, but also norepinephrine (NE). For this reason, it was hypothesized that more than one neurotransmitter may be involved in OCD physiopathology. Fifty-two drug-free patients diagnosed with OCD (DSM-III-R) and 48 normal controls underwent a blood amine profile (5-HT, NE), 5-hydroxyindolacetic acid (5-HIAA), dopamine (DA), and epinephrine (E). Within each subject group, correlations were computed among amine levels. Compared with the control group, there were significantly higher correlations between most of the amines, while virtually no significant correlations were found in the control group. The significant covariations among the neurotransmitters in the OCD group suggest that a change in one amine produces a change in another and it is the balance or relationship among themselves that is important rather than one in particular. The nature of the covariance needs further exploration.

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Social Functioning in Anxiety Disorders

Catherine Mancini, M.D., Psychiatry, McMaster Univ Station A, 3G Outpatient Dept. Bx 2000, Hamilton Ontario L8N 3Z5, Canada; Michael Van Ameringen, M.D., David Streiner, Ph.D., Georgina Stogios, Lara Kubilius, B.A., Shirley Davies, B.Sc.N., Elizabeth Ward, Reg.N., Dorothy Donison, Reg.N.

Summary:

To determine level of social functioning, 165 consecutive patients admitted to an anxiety disorders clinic were assessed using the Structured Clinical Interview for DSM-III-R (SCID) with the Global Assessment of Functioning Scale (GAF), the Social Adjustment Scale-Self Report (SAS-SR) and the Sheehan Disability Scale, as well as other measures of anxiety and depression. Results of the SAS-SR were compared with those obtained by Weissman et al. (1978). Sex, level of education, occupation and history of previous suicide attempt(s) did not predict level of impairment. Patients who had received previous treatment for their anxiety disorder, had a concurrent major depression or a lifetime diagnosis of major depression, and patients with a lifetime diagnosis of alcohol and/or substance abuse had statistically significant higher levels of functional impairment when compared with patients with no previous treatment, no concurrent or lifetime diagnosis of depression, and no lifetime diagnosis of alcohol and/or substance abuse. Patients with a primary diagnosis of social phobia had significantly higher scores on the SAS-SR and Sheehan Disability Scale when compared with the other anxiety disorders. Higher levels of social impairment in anxiety disorder patients was associated with the presence of other comorbid psychiatric illness as well as the presence of social phobia.

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Placebo Response Rates in OCD Pharmacologic Trials

Jane L. Eisen, M.D., Psychiatry, Butler Hospital, 345 Blackstone Blvd., Providence, RI 02906; Steven A. Rasmussen, M.D.

Summary:

Results from multicenter clomipramine double-blind trials have led investigators to believe that obsessive compulsive disorder (OCD) has a minimal placebo response. However, more recent OCD efficacy studies using newer serotonin reuptake blockers have had higher placebo response rates. In an effort to systematically evaluate placebo response in OCD, we compared the placebo response rates between clomipramine, fluvoxamine and sertraline with the criteria for response being a greater than 35% improvement of baseline Yale-Brown OC (YBOCS) score. Only 2% of those receiving placebo in the clomipramine trial improved (47 probands on placebo with one responder). The rate was 22% for fluvoxamine (four probands out of 18 on placebo) and 25% for sertraline (two probands out of eight on placebo). Baseline severity of illness as measured by the YBOCS was similar in the three trials and therefore could not account for the difference found between medications in frequency of placebo response. There was no significant difference in baseline YBOCS scores between placebo responders and nonresponders across studies, which excluded the possibility that those on placebo were less symptomatic at study entry. An analysis of the clinical characteristics of the placebo responders vs. nonresponders will be presented. While the explanation for the increase in frequency of placebo response with the newer agents is not clear, this change indicates that OCD is less specifically responsive to pharmacologic intervention than has been previously considered.

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Predictors of Placebo Response in Panic Disorder

Mark D. Fossey, M.D., Psychiatry, Med Univ of SC & VAMC, 109 Bee Street, Charleston, SC 29401; R. Bruce Lydiard, M.D., Michele T. Laraia, M.S.N., Joseph J. Zealberg, M.D., Alex Morton, Pharm.D., James C. Ballenger, M.D.

Summary:

The ability to predict who will respond to placebo has important implications for the design of clinical drug trials. This study examined 32 patients with panic disorder (22 females, 10 males) who received double-blind placebo for up to 12 weeks. The Tridimensional Personality Questionnaire (TPQ), Hamilton rating Scales for Anxiety and Depression and the Global Phobia Scale were administered at baseline, and results were correlated with the number of panic-free weeks during the study and the Clinician's Global Rating (CGR) at termination. The Total Harm Avoidance scale (THA) of the TPQ as well as harm avoidance subscales for Fatigability & Asthenia (HA4) and Fear of Uncertainty (HA2) had significant negative correlations with number of panic-free weeks ($r = -0.44$, $p<.02$; $r = -0.44$, $p<.02$; $r = -0.38$, $p<.05$ respectively) but did not correlate with improvement on the CGR at termination. There was a trend for HA4 scores to be negatively correlated with completion of the study ($r = -0.35$, $p<.07$). These results indicate that panic patients scoring high on the THA, HA2, & HA4 scales of the TPQ are less likely to be panic-free in response to placebo. Placebo recipients with high scores on HA4 may be more likely to terminate studies early.

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Prevalence of Anxiety Disorders in Asthmatics

Vijaya L. Boppana, M.D., Psychiatry, Queens Hospital Center, 82 68 164 St. N. Bldg 4th Flr., Jamaica, NY 11432; Basawaraj Karajgi, M.D., Arthur Rifkin, M.D., Jean Fleischman, M.D.

Summary:

A high prevalence rate for panic disorder appears in patients with chronic obstructive pulmonary disease (1). Conversely, a statistically significant, high prevalence of asthma and bronchitis occurs in patients with panic disorder. Our study looks at the prevalence rate of anxiety disorders in adult patients with asthma. Twenty-five patients attending a pulmonary clinic were interviewed using the Structured Clinical Interview Schedule for DSM-III-R (six men, aged 44-68 years, mean 56.5 ± 19.9 and 19 women, aged 27-78 years, mean 50.95 ± 13.6). Patients rated the severity of their asthmatic attacks on a 10 c.m. Visual Analogue Scale and rated various fears, including agoraphobia on a fear questionnaire. Seventeen patients had panic disorder and seven of these patients had agoraphobia. In most instances, the panic attack and agoraphobia were related to fear of having an asthmatic attack. One other patient had panic attacks without meeting full criteria for panic disorder. This total of 17 patients (68%) having panic disorder contrasts with 1.5% in the general population (2). Seven patients (28%) had agoraphobia of markedly troublesome severity, as compared with 2.2 per 1,000 in the general population. These high prevalence rates of panic disorder and agoraphobia, especially in relation to asthmatic attacks, have treatment implications.

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Major Depression with Panic Disorder Responds to Nefazodone

Rejean Fontaine, M.D., Research Center, Louis H. Lafontaine Hosp, 7401 Hochelaga St., Montreal Quebec H1N 3M5, Canada; Benoit Dassylva, M.D., Alfonso Ontiveros, M.D., Robert Elie, M.D.

Summary:

According to several studies, major depression involving atypical features like panic attacks and agoraphobia tends to respond poorly to tricyclic antidepressants, while a better response was reported with monoamine oxidase inhibitors (MAOI's). We are reporting a double-blind, placebo-controlled trial of nefazodone versus imipramine in the treatment of major depression with panic disorder. We enrolled 56 patients with these diagnosis (DSM-III-R) who had this condition for at least one month and a minimal score of 22 on the first 17 items on the Hamilton Depression Scale. They were then randomly assigned to nefazodone, imipramine or placebo in a trial of six weeks duration.

Results: Analysis of covariance showed that nefazodone was significantly better than imipramine or placebo on the HAM-D total score and on factors of the SCL-90 ($p<0.05$). This finding was unexpected. Moreover, nefazodone acts mostly on the serotonergic system, and drugs with a similar mechanism of action were poorly tolerated in patients suffering from panic attacks. Further placebo-controlled studies are needed comparing nefazodone to MAOIs to further support this finding.

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OCD in Harvard/Upjohn Anxiety Research Project (HARP)

Kerrin White, M.D., Psychiatry, Providence VA Hospital, 830 Chalkstone Avenue, Providence, RI 02908; David Shera, M.S., Gail Steketee, Ph.D., Ingrid Dyck, B.A., Linda Langford, B.A., Alan Gordon, M.D.

Summary:

The Harvard/Upjohn Anxiety Research Project (HARP) is a large ($N = 712$) multicenter, prospective, longitudinal, three-year follow-up study of patients with panic disorder with or without agoraphobia, agoraphobia without panic, social phobia, or generalized anxiety disorder. Though obsessive compulsive disorder (OCD) alone was not one of the five target diagnoses necessary for inclusion, its frequent occurrence as a comorbid diagnosis was anticipated and therefore a small number of Ss with "OCD only" without any of the target diagnoses were added for comparison.

Among the first 636 HARP Ss for whom intake data have been analyzed, 86 have had a lifetime diagnosis of comorbid OCD; the addition of 16 "OCD-only" Ss brings the total number of HARP Ss with OCD to 102. Most ($N = 73$) of these derived from the large McLean Hospital site, which may have contributed to some of their characteristics such as a frequent history of psychiatric hospitalization (present in 40%).

At intake, OCD presented as one of the earliest-onset and most chronic of the anxiety disorders. Its presence was associated with relatively greater impairment of functioning. Affective disorders (primarily depression) frequently coexisted, in about half the cases, but no more often with OCD than with other anxiety disorders.

"OCD-only" proved a misnomer, since all but one of the 16 Ss in this group had comorbid psychiatric diagnoses, largely depressive. This group had a 1:1 sex ratio in contrast to the 2:1 preponderance of females in the larger HARP sample of Ss with other anxiety disorders plus comorbid OCD, and the HARP sample as a whole.

Over the first 18 months of prospective follow-up, about one-third of all OCD Ss showed enough improvement to no longer meet full criteria for the diagnosis. This proportion was similar for men versus women and for those who had OCD comorbid with another anxiety disorder versus those with "OCD only." Most received some degree of putatively effective antiobsessional somatotherapy (i.e. serotonergic antidepressants) and/or some behavior therapy.

491 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Alprazolam Discontinuation Effects of Carbamazepine

Ehud Klein, M.D., Psychiatry, Rambam Medical Center, BAT-GALIM, Haifa 35254, Israel; Varda Colin, M.D., John Stolk, M.D., Robert H. Lenox, M.D.

Summary:

Discontinuation of chronic benzodiazepines, most notably alprazolam, has been reportedly associated with a symptom profile characteristic of physiological withdrawal, although this often has been difficult to differentiate from reemergent anxiety symptomatology. We (EK) were among the first to report in an uncontrolled study that carbamazepine was effective in reducing withdrawal symptoms following alprazolam discontinuation. This present study was designed to examine the efficacy of carbamazepine as adjunctive treatment during a controlled alprazolam discontinuation in two different patient populations. Forty patients with panic disorder (PD) and 40 patients with generalized anxiety disorder (GAD) according to DSM-III-R criteria received alprazolam (open-label phase) for eight to 11 weeks in doses ranging from 1.5-6 mg/day according to clinical needs. Thirty-six PD and 35 GAd patients successfully completed phase 1 and entered the second phase of the study. Carbamazepine or placebo was added in a randomized, double-blind fashion with no change in alprazolam dose for the first week, followed by a single-blind dose reduction of alprazolam, 25% every third day. Thirty-five percent of patients completed the study, achieving a zero dose of alprazolam for at least four weeks. Carbamazepine significantly reduced the plasma concentration of alprazolam; altering the apparent clinical course of withdrawal. We will discuss our outcome variables, characterizing the extent of withdrawal experienced, based upon physiological measures, behavioral ratings and plasma hormone determinations.

492 Wednesday May 6, 3:00 p.m.-5:00 p.m.

High Prevalence of Obsessional Habits in a Cohort of Italian High School Students

Mario Guazzelli, M.D., c/o Pietro Pietrini M.D., Lab. of Neurosc. Bldg 10, 9000 Rockville Pike RM 6C414, Bethesda, MD 20892; Alfonso Ceccherini Nelli, M.D., Luigi F. Bardellini, M.D., Elisabetta L. Balsamo, M.D., Pietro Pietrini, M.D.

Summary:

Recent studies revealed that the prevalence of obsessive compulsive disorder (OCD) is higher than previously thought in both the general population (2.5%; Karno et al., *Arch. Gen Psychiatry,* 45:1094, 1988) and adolescents (2%; Flament et al., *J Am Acad Child Adolesc Psychiatry* 27:764, 1988). When "subtle obsessional habits" (OH), rather than clinical OCD, are considered, an impressive prevalence of up to 46% has been reported. To evaluate the prevalence of OH among Italian adolescents, we administered the Italian version of the self-reporting Leyton Obsessional Inventory-Child Version to 9,488 high-school students (age range 14-20 yrs., mean $\pm$ SD 16.2 $\pm$ 2; male/female ratio 47/53%) in Pisa. The aims of the project were explained to teachers and students in each school. Students completed the anonymous questionnaire during school-time, thus minimizing the risk of "group-work". Among the 7,941 (84%) students who returned a completed questionnaire, 1,217 (15.3%) reported presence of various OH with variable degrees of severity. OH were more frequent and severe in females than in males ($p<.0001$), and in younger individuals ($p<.03$); frequency of severe OH was significantly lower in the senior level classes ($p<.0001$). In 507 (6.4%) subjects, OH was severe enough to interfere with the everyday activities. Our findings show a high prevalence of OH among Italian adolescents, and are consistent with recent surveys in the U.S. Interference with everyday activities, as admitted by more than 6% of the subjects, may contribute to difficulties in school career and deserves further investigation and pursuit of possible support strategies.

493 Withdrawn

494 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Personality and Benzodiazepine Sensitivity

Deborah S. Cowley, M.D., Psychiatry, Univ of Washington, 1959 NE Pacific Street, Seattle, WA 98195; Peter P. Roy-Byrne, M.D., David J. Greenblatt, M.D., Daniel W. Hommer, M.D.

Summary:

A model of personality recently formulated by Cloninger links variation in traits of novelty seeking, harm avoidance, and reward dependence with differences in the function of CNS neurotransmitters. To examine the relationship between these personality traits, anxiety disorders, and the GABA-benzodiazepine system, we tested acute sensitivity to diazepam (DZ) in patients with panic disorder (PD; $n=18$), GAD ($n=12$), and control subjects ($n=21$). Personality traits were measured using the Tridimensional Personality Questionnaire (TPQ). Subjects received I.V. DZ or placebo one week apart in randomized order in four logarithmically increasing doses 15 minutes apart, yielding DZ doses of 25, 25, 50, 100 μg/kg (cumulative dose 25, 50, 100, 200 μg/kg). Saccadic eye movement velocity (SEV) was measured at baseline and after each dose. A log-linear model was used to calculate the effective dose (ED30) and DZ concentration (EC30) required to reduce SEV by 30% (the upper limit of SEV reduction in controls). Anxious patients (PD and GAD) had significantly higher harm avoidance scores than controls ($F=13.1$, $p<0.0001$). There were no significant correlations between ED30 or EC30 and any personality dimension within the diagnostic groups. The combined group ($n=51$) showed significant inverse correlations between novelty seeking and ED30 ($r=-0.28$, $p=0.04$) and EC30 ($r=-0.30$, $p=0.04$). These findings suggest an association between the GABA-benzodiazepine receptor system and novelty seeking. This is consistent with prior studies of effects of benzodiazepines on exploratory behavior in animals and the sedation threshold in extroverts.

495 3:00 p.m.-5:00 p.m.

Hyperfrontality and Serotonin in OCD

Eric Hollander, M.D., Psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; Concetta Decaria, M.S., Lisa Cohen, M.A., Mohammed Islam, M.D., Dan J. Stein, M.D., Maxim Frenkel, M.D.

Summary:

PET and SECT scan studies of OCD demonstrate increased frontal lobe activity and blood flow that correlate with OCD severity. Behavioral exposure and serotonin agonists increase cortical blood flow, especially to frontal lobes. Fluoxetine treatment decreases frontal lobe blood flow. Thus, hyperfrontality is associated with obsessionality and harm avoidance. We found that a subgroup of OCD patients ($N=50$) studied with a neuropsychological test battery had frontal lobe (executive function/set-shifting) abnormalities (Trails A, B, B-A). In addition, male OCD patients had a significant negative correlation between peak change in prolactin response to m-CPP, and frontal impairment (Trails B-A) ($R_{sq}=.366$, $n=26$, $p=.033$). Thus, patients with greater hyperfrontality had more impairment of serotonin function. This suggests that harm avoidance, obsessionality and anticipatory anxiety may be mediated by serotonin dysfunction and hyperfrontality, and effective treatments appear to normalize both hyperfrontality and serotonin dysregulation.

496 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Neuropsychiatric Impairment in Social Phobia

Eric Hollander, M.D., Psychiatry, Columbia University, 722 West 168th Street, New York, NY 10032; Concetta Decaria, M.S., Sari

Trungold, B.A., Lisa Cohen, M.A., Maxim Frenkel, M.D., Frank Schneier, M.D., Dan J. Stein, M.D., Michael R. Liebowitz, M.D.

Summary:

To investigate whether patients with social phobia have evidence of neuropsychiatric impairment, a neurological soft-sign examination and neuropsychological test battery were performed in 13 social phobics, and the findings were contrasted with those from 31 healthy volunteer and 80 OCD patient controls. In contrast to normals, social phobics had significantly more left-sided ($p = .026$), cube-drawing ($p = .001$) and mirror-movement ($p = .029$) soft signs. On neuropsychological testing, social phobics had significantly poorer performance on visuospatial memory (BVRT) ($p = .000$) and frontal (Trails A, B, B-A) ($p = .003$) tasks than did normals. Thus, there was evidence for both right hemispheric visuospatial impairment, and frontal impairment in social phobic patients. However, OCD patients also had increased neurological soft signs, and neuropsychological deficits suggestive of right hemispheric visuospatial and frontal-executive function impairment, and social phobics did not significantly differ from OCD patients on the most part on these measures. Thus, neuropsychiatric impairment was not selective for social phobics. These findings were most prominent in males, and both social phobia and OCD are anxiety disorders with high male prevalence. Neuropsychiatric impairment may predispose to the development of adult anxiety disorders in males.

497 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Lactate Sensitivity in Sleeping Panic Patients

Harold W. Koenigsberg, M.D., Psychiatry, New York Hospital, 21 Bloomingdale Road, White Plains, NY 10605; Charles P. Pollak, M.D., Jeffrey Fine, M.D., Tatsu Kakuma, Ph.D.

Summary:

In spite of a series of careful physiological and neuroendocrine studies of sodium lactate-induced panic attacks in panic disorder (PD) patients, the mechanism of lactate sensitivity is poorly understood. Cognitive as well as purely biological models have been proposed. To further explore the mechanism, we administered sodium lactate and control dextrose-saline infusions to 15 PD patients and 12 normal controls during sleep, taking advantage of the opportunity that sleep provides for closely monitoring shifts in state of arousal. Both PD subjects and normals showed a significant ($p < .03$) arousal response to lactate administered during stage 3-4 sleep; but not to control solution. The PD subjects were significantly more sensitive to lactate. Within 2.5 minutes after lactate infusions, the sleep of PD subjects became significantly lighter, while the sleep of normals did not become lighter until 10 minutes after the infusion ($p = .03$ and .02, respectively for the 5.0-7.5 and 7.5 to 10.0 minute time intervals). When the rate of awakenings per infusion for each group and each substance was examined, we found a similar pattern. These findings suggest, but do not establish, a differential biological sensitivity to lactate in PD patients.

498 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Social Phobia, Personality Traits and Brofaromine

Tom R. Fahlen, M.D., Psychiatry, Fridhemsgatan 35, S-Kungalv 44233, Sweden; Helmo L. Nilsson, Ph.D.

Summary:

Seventy-seven patients with social phobia (DSM-III-R) were randomly and double-blindly treated with the new reversible and selective MAO-A inhibitor brofaromine and placebo for 12 weeks. Exclusion criteria were a history of panic attacks and an ongoing major depressive episode. In one centre 63 patients were specifically studied for personality traits. At inclusion 60% of these had an avoidant personality disorder (DSM-III-R). The occurrence of this diagnosis was reduced from 62% to 19% in the brofaromine group during treatment, compared with a drop from 59% to 44% in the placebo group. A number of dysfunctional personality traits, examined with a questionnaire before and after treatment, was reduced significantly more in the brofaromine group than in the placebo group. Fifty-four percent of the patients had mood disorder: major depressive disorder in full remission (48%) and dysthymia (17%). The severity of the social phobia was not related to the occurrence of mood disorders. However, the dysfunctional personality traits and the diagnosis avoidant personality disorder were significantly more common in the mood disorder subgroup than in the non mood disorder group. There was a trend to more marked treatment response in the major disorder subgroup than in the non mood disorder subgroup.

499 Wednesday May 6, 3:00 p.m.-5:00 p.m.

The Effects of Buspirone on Sleep, Anxiety and PTSD

Patrick E. Ciccone, M.D., Psychiatry, Univ of PA-Phil VAMC, 5990 Shetland Drive Box 391, Solebury, PA 18963; Robert A. Greenstein, M.D., Marvin Weisbrot, R.Ph.

Summary:

In an open trial, nine nonpsychotic, nondepressed, drug-free male war veterans who met the DSM-III-R criteria for chronic posttraumatic stress disorder (PTSD) were administered buspirone 5-10 mg t.i.d. for three weeks. Responses were measured by using the Hamilton Rating Scale for Anxiety, the Raskin-Covi Anxiety/Depression scale, the Impact of Events Scale and a Clinical Global Impressions Scale (CGI), which was modified to globally assess PTSD symptomatology. The mean scores on the Hamilton Anxiety Scale ($p < .01$) and the anxiety component of the Raskin-Covi Scale ($p < .001$) were statistically significantly improved during buspirone treatment. However, scores on the other instruments were unchanged. Although six of nine patients reported a marked decrease in sleep disturbances (specifically nightmares), other reexperiencing phenomena, including intrusive thoughts and images of combat, common to all nine patients at baseline, were seemingly unaffected during the buspirone treatment. Patients attributed their continuing dysphoria to the persistent reexperiencing phenomena, in lieu of generalized anxiety, which was significantly reduced. The disparity between the positive effects of buspirone on the anxiety and sleep disturbances of PTSD and the general lack of overall subjective improvement begs questions about the putative role of disordered REM sleep behavior and anxiety in the pathogenesis of PTSD.

500 Wednesday May 6, 3:00 p.m.-5:00 p.m.

A Study of the Seasonality of OCD

Timothy D. Brewerton, M.D., Psychiatry, Medical Univ of SC, 171 Ashley Avenue, Charleston, SC 29425; James C. Ballenger, M.D.

Summary:

Extensive evidence implicates serotonin (5-HT) dysfunction in obsessive-compulsive disorder (OCD). Seasonal variations in several biologic measurements of the 5-HT system have been reported in humans. Disruption of this normal rhythm may influence the course of several 5-HT related psychiatric disorders. Since seasonal fluctuations have been reported for suicide, depression, mania, violent behavior, eating/substance abuse disorders, and migraine, we speculated that OCD might also exhibit a seasonal variation in its severity. To test this we analyzed existing data provided by Ciba-Geigy from double-blind controlled studies of clomipramine (Anafranil) vs. placebo in 519 OCD patients. The means of patient scores at baseline (visit 1) & during pre-drug visits (2 and 3) on the Yale-Brown Obsessive-Compulsive Disorder Scale (YBOCS) were analyzed by season and cross-season. A significant difference by season ($p \leq 0.04$, Kruskal-Wallis) and a trend by

cross-season ($p \leq 0.06$) was found, with a significant post hoc difference between spring (27.6) and summer (26.0, $p \leq 0.05$). When each sex was compared separately, seasonal differences were only significant in females ($p < .04$). In the second part of the study, the repeated measures ANOVA of YBOCS scores over the 15-week placebo period revealed highly significant interactions between time and direction of photoperiodic change (increasing vs decreasing daylength) ($p < 0.0005$) in females, but not males. These results add to other findings of seasonal variations in several psychiatric disorders thought to involve 5-HT dysfunction and also confirm that gender is a significant factor in determining seasonal sensitivity. Drug studies may need to be controlled for season when interpreting results.

501 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Buspirone in Social Phobia

Franklin R. Schneier, M.D., Therapeutics, NY Psych Inst., 722 West 168th Street, New York, NY 10032; Raphael Campeas, M.D., Brian A. Fallon, M.D., Eric Hollander, M.D., Jeremy Coplan, M.D., Michael R. Liebowitz, M.D.

Summary:

The novel anxiolytic buspirone has been shown to be effective in generalized anxiety disorder, but its utility in phobic disorders is less clear. We examined its efficacy in social phobia in a 12-week open trial. Twenty-one patients who met DSM-III-R criteria for social phobia and did not respond to one week of single-blind placebo were treated with buspirone, and 17 completed a minimum of two weeks of treatment. Twelve of these 17 patients met criteria for the generalized subtype of social phobia. At week 12, eight (47%) of the 17 patients were rated much to very much improved in social phobia symptoms on the Clinical Global Impression Scale. Significant improvement was noted on measures of social anxiety and avoidance of social situations. Ratings of generalized anxiety and depression, which were low at baseline, did not change significantly during treatment. The results suggest that buspirone may have modest efficacy in the treatment of social phobia, and confirmation in a placebo-controlled trial is needed.

502 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Panic Disorder and Separation Anxiety Disorder: New Relationships

Juan M. Segui, M.D., Psychiatry, Hospital La Alianza, VADA Virgen Montserrat 193 BIS, Barcelona 3o3a 08026, Spain; Cristian Y. Herrera, M.D., Luis C. Salvador, M.D., Jaime Canet, Ph.D.

Summary:

The separation anxiety disorder (SAD) and panic disorder (PD) relationship was first described by D. Klein (1964). Later studies have defined a high prevalence of SAD history in PD (18% to 50%). Social Phobia (SP) and obsessive compulsive disorder (OCD) have not been related systematically.

Methods: 150 subjects, meeting DSM-III-R criteria for PD, were studied using the SCID-P, RDC Family History, Hamilton Anxiety and Depression Rating Scales, MARKS Phobias scale and the EPQ.

Results: 15.3% PD referred SAD in childhood. Comparing both groups (with and without SAD) we found that those with SAD history presented:

1) A more precocious onset age for PD ($p < 0.05$).
2) Higher comorbidity for social phobia (SP) ($p < 0.01$).
3) Higher comorbidity for obsessive compulsive disorder (OCD) ($p < 0.05$).
4) Lower comorbidity for adult attention deficit disorder.
5) Higher score on the social phobia subscale (MARKS) ($p < 0.05$).
6) Lower psychoticism on the EPQ ($p < 0.05$).

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Beta Receptors in Panic Disorder: Treatment Effects

Richard J. Maddock, M.D., Psychiatry, Univ of Calif. Davis, 4430 V. Street, Sacramento, CA 95817; Cameron S. Carter, M.D., Joseph R. Magliozzi, M.D., Dorothy W. Gietzen, Ph.D.

Summary:

The density and responsivity to isoproterenol of lymphocyte beta adrenoreceptors were examined before and after treatment of panic disorder with agoraphobia. Both measures are decreased in patients with depression. Similar changes are seen in animals exposed to chronic stress. In animals, these changes appear to be adaptive, as they are associated with less stress-related pathology. Using a multivariate analysis, we found significantly lower beta receptor density (using ICYP binding) and isoproterenol stimulated increase in cAMP concentration (38.7 fmoles/mg protein and 45.2 pmoles/million cells respectively) in the patients ($n = 26$) compared to 66.6 fmoles/mg protein and 75.2 pmoles/million cells in the controls ($n = 24$) ($F = 11.9$, $p = .001$; $F = 5.2$, $p = .027$ respectively). In patients, beta receptor density increased toward the level seen in controls following four weeks of adinazolam-SR treatment ($n = 10$) but not placebo ($n = 11$, $F = 3.4$, $p = .08$). Isoproterenol-stimulated cAMP production was unchanged. Decreased pretreatment beta receptor density was associated with good outcome after four weeks. Other clinical correlations with receptor function will be presented. The hypothesis that changes in beta adrenoreceptor function in panic disorder represent adaptive responses to the illness will be discussed.

504 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Significance of Past Depression in Panic Disorder

Richard J. Maddock, M.D., Psychiatry, Univ California Davis, 4430 V Street, Sacramento, CA 95817; Cameron S. Carter, M.D., K.H. Blacker, M.D., Mary Beth Logue, M.S., Ranga Krishnan, M.D., John H. Greist, M.D.

Summary:

Panic disorder (PD) patients with comorbid major depression (MDD) have more severe symptoms and a poorer response to treatment than patients with PD alone. Is this due to a distinct and more serious underlying disorder in these patients or simply to the simultaneous presence of the two disorders? *Nondepressed* patients presenting for treatment of panic disorder with agoraphobia (PDA) ($n = 180$) were studied prior to treatment of and after four weeks of treatment with adinazolam ($n = 89$). One-third of the patients had a history of MDD. Symptom severity and outcome were compared in patients with primary, secondary, single, recurrent or no past MDD. There were no consistent differences in symptom severity or treatment outcome in patients with a history of primary, secondary or single episode MDD compared with patients with no MDD. However a small number of patients with history or recurrent MDD exhibited consistently greater symptom severity and less improvement after treatment than patients with no MDD. The greater severity and worse outcome of comorbid PD and MDD observed in earlier studies are more likely due to the simultaneous presence of the two disorders than to a more serious underlying disorder. The possibility that recurrent MDD may indicate a more serious condition in patients with PDA warrants further study.

505 Wednesday May 6, 3:00 p.m.-5:00 p.m.

A Comparison of Trichotillomania and OCD

Joseph A. Himle, M.S.W., Psychiatry, Univ of Michigan, 1500 E. Medical Ctr Dr. Bx0840, Ann Arbor, MI 48109; Patrick Bordnick, M.S.W.

Summary:

The validity of conceptualizing trichotillomania and obsessive compulsive disorder as variations of the same disorder was examined in a study of 20 patients with each disorder. Comparison of demographic, psychometric, and clinical features between the two groups revealed several differences. Obsessive compulsive patients scored higher on many measures of psychiatric symptomatology including ratings of obsessions and compulsions, depression, interpersonal sensitivity, general anxiety, phobic anxiety, paranoid ideation, and psychoticism. Trichotillomania patients reported an earlier age of onset than the obsessive compulsives studied. Stressors associated with onset were also significantly different between groups. These results challenge the validity of conceptualizing trichotillomania and obsessive compulsive disorder as subcategories of a common core disorder.

506 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Cues Which Elicit Recurrent Psychopathology

Thomas B. Mackenzie, M.D., Psychiatry, University of Minn., 329 420 Delaware Street SE, Minneapolis, MN 55455; Stephen L. Ristvedt, Ph.D., Gary A. Christenson, M.D., Alyson S. Lebow, M.S.

Summary:

The factors that determine the timing of episodic symptomology in disorders such as obsessive compulsive disorder (OCD), bulimia nervosa (BN), and trichotillomania (TM) are not well understood, but are of great potential interest in designing treatment strategies. We asked 196 patients with OCD (n = 60), BN (n = 61), and TM (n = 75) to endorse items that prompted or significantly worsened their symptoms from among 339 cues including activities, locations, sights and sounds, circumstances, and immediate feeling states. Principal components analysis suggested a four component solution. Each disorder was significantly associated with one of the components. The OCD factor reflected concerns with cleaning, checking, and order; the BN factor, food-related items; and the TM factor, reading, studying, and watching television. Diagnostic assessment based on loading among these factors was 85% correct. The fourth factor, negative feeling states, did not differ according to diagnosis. The results suggest that both disorder-specific and generic cues contribute to the waxing and waning of symptoms in these disorders. Trying to identify features of the environment and moment-to-moment feeling states that evoke symptoms may have implications for defining clinical subtypes, designing treatment strategies, and mapping the complex relationship between feeling states and external cues.

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Concurrent Panic Disorder and Social Phobia

Michael van Ameringen, M.D., Psychiatry 3rd Floor, St. Joseph's Hospital, 50 Charlton Ave E. Fontbonne, Hamilton Ontario L8N 4A6, Canada; Catherine Mancini, M.D., Georgina Stogios, Lara Kubilius, Shirley Davies, B.Sc.N., Dorothy Donison, Reg.N.

Summary:

One hundred and forty-four consecutive patients referred for treatment of panic disorder or social phobia were studied. Using the Structured Clinical Interview for DSM-III-R, 59 patients were found to have a primary diagnosis of panic disorder with or without agoraphobia, 39 patients were suffering primarily from social phobia and 46 patients had concurrent diagnoses of panic disorder and social phobia. In the social phobia group, 61.5% had a lifetime diagnosis of depression, while 69.5% in the panic disorder group and 89.1% in the mixed panic disorder-social phobia group had a lifetime diagnosis of major depression ($x^2 = 9.573$, $df = 2$, $p < 0.01$). The social phobia and mixed group demonstrated significantly higher prevalences of dysthymia (33.3% and 32.6%, respectively) and alcohol abuse or dependence (25.6% and 26.1%, respectively) compared with the panic disorder group. The three groups also showed significant differences in the frequency of generalized anxiety disorder. The mixed group had significantly higher self-ratings on the Fear Questionnaire, State-Trait Anxiety Inventory and Beck Depression Scale. Patients with the concurrent diagnoses of panic disorder and social phobia can be distinguished from patients with either diagnosis alone by higher rates of comorbid anxiety and mood disorders as well as by illness severity.

508 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Regional Cerebral Blood Flow in Panic Disorder

Laura Guarneri, M.D. Psychiatry, Ospedale San Paolo, Via A. Di Rudini 8, 20162 Milano, Italy; Alberto Bestetti, M.D., Emanuela Scuto, M.D., A. Chiti, M.D., G.L. Tarolo, M.D., Emilio Saccmetti, M.D.

Summary:

To better define the relevance of putative rCBF abnormalities in PD, we studied rCBF of 19 right-handed, drug-free, 21- to 56-year-old patients, 11 with PD and eight with generalized anxiety disorder (GAD), and of seven sex-age matched nonpsychiatric subjects. The rCBF was analyzed by SPECT, using Tc99m-HMPAO, and measured semiquantitatively as the ratio of the counts of frontal (F), temporo-parietal (T-P), and occipital (O) regions to those of ipsilateral cerebellar region. PD patients presented lower count ratios in: a) right Or ($.61 \pm .06$) with respect to GAD patients ($.69 \pm .06$) ($t = 2.5$, $p = .02$) and controls ($.68 \pm .03$) ($t = 2.41$, $p = .02$); b) left Or ($.62 \pm .06$) with respect to GAD patients ($.67 \pm .05$) ($t = 2$, $p = .06$) and controls ($.68 \pm .04$) ($t = 2.27$, $p = .03$); and c) right hemisphere ($.62 \pm .04$) with respect to GAD patients ($.67 \pm .06$) ($t = 2.12$, $p = .04$). No differences resulted between GAD patients and controls. rCBF abnormalities in PD patients were concentrated among subjects with a positive family history (FH) for PD (right Or: $.58 \pm .02$ for positive FH, $.68 \pm .06$ for negative FH, $t = 3.58$, $p = .005$; left Or: $.58 \pm .02$ for positive FH, $.68 \pm .06$ for negative FH, $t = 3.92$, $p = .003$; right hemisphere: $.59 \pm .02$ for positive FH, $.66 \pm .02$ for negative FH, $t = 4.20$, $p = .002$). These results suggest that some rCBF abnormalities in PD patients are sufficiently disease-specific and helpful to individuate etiopathogenetically different subgroups of patients.

509 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Oral and Parenteral M-CPP in 12 Patients with OCD

Wayne K. Goodman, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Christopher J. McDougle, M.D., Lawrence H. price, M.D., Linda C. Barr, M.D., George R. Heninger, M.D.

Summary:

Oral (po), but not intravenous (iv), administration of the (5-HT) agonist mCPP (0.5 mg/kg) has been reported to exacerbate obsessive compulsive (OC) symptoms (sxs) in drug-free patients with obsessive compulsive disorder (OCD). *Methods: To further evaluate whether route of administration accounts for these disparate findings, 12 (M = 9, F = 3) drug-free patients with OCD received in random order either po mCPP (0.5 mg/kg), iv mCPP (0.1 mg/kg over a 20 minutes), or placebo mCPP on three test days. Blind*

measures of behavioral and biochemical response to mCPP were obtained. Results: ANOVAs revealed no significant differences in the effects of the three study drugs (po mCPP, iv mCPP, and placebo) on the severity of OC sxs as measured by the Y-BOCS adapted for challenges. Analysis of categorical response data also failed to show significant effects of mCPP on OC sxs. The magnitude of the mCPP-induced plasma prolactin elevation was similar on the oral and intravenous administration days. *Conclusions:* Findings from this within-subject design study suggest that single doses of mCPP, whether by an oral or intravenous route, do not produce reliable effects on OC behavior. Although this study is subject to Type II error, the rate of induction of behavioral effects by mCPP is too low to be useful as a provocative agent in studies with similar sample sizes. Other challenge agents are needed to investigate the role of 5-HT in OCD.

510 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Normal Alph-2 Adrenergic Functioning in OCD

William A. Hewlett, M.D., Psychiatry, Vanderbilt University, AA2210 Medical Center North, Nashville, TN 37232; Sarah Berman, B.S., Karron Martin, R.N.

Summary:

Clonidine stimulates growth hormone release via effects at alpha-2 adrenergic receptors. The growth hormone response to clonidine has been reported to be blunted in the setting of obsessive compulsive disorder, raising the possibility of abnormal adrenergic functioning in this disorder. In this study, clonidine was administered intravenously at a dose of 2 μg/kg to 19 subjects with a DSM-III-R diagnosis of OCD and 18 control subjects. Two baseline plasma samples were obtained prior to clonidine administration. Samples collected at 15 minute intervals during the first hour and two and four hours post-clonidine were assayed by RIA for growth hormone. Cortisol levels were also determined to ensure that differential effects of the challenge were not due to differences in stress in the two populations. Clonidine produced a significant increase in plasma growth hormone for both patients and controls. There was no difference in the degree of stimulation for the two populations. In contrast, cortisol levels decreased over the same period, and there was likewise no difference between patients and controls in this decrease. These results provide no evidence for abnormal alpha-2 adrenergic functioning in the setting of OCD.

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Psychiatric Diagnosis in Dental Phobic Patients

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Summary:

While studies have suggested there may be simple, social and agoraphobic panic subtypes of dental phobia, no structured psychiatric interviews have been performed in dental phobic populations. We administered SCID-I/II interviews and personality, impairment and psychometric scales to 73 new admissions to the University of Washington Dental Fears Research Clinic. Forty-four of 73 patients (60%) met only criteria for simple phobia. Of the remaining 29 patients, 16 (22%) had current anxiety (9/16 with panic/agoraphobia, 4/16 with generalized anxiety and 3/16 with social phobia), nine (12%) depressive and four (5%) substance abuse disorders. The patients with additional current axis I diagnoses had more axis II diagnoses ($x^2 = 12.2$, $p < .0001$), more impairment in role ($t = 1.9$, $p = .06$) and social ($t = 2.4$, $p = .02$) functioning, higher Barsky somatosensory amplification scores ($t = 3.54$, $p < .001$), more adverse early developmental experiences (Breier scale), higher harm avoidance on the Cloninger TPQ ($t = 3.92$, $p < .001$), and more agoraphobic ($t = 2.4$, $p < .01$) and social phobic ($t = 2.3$, $p < .02$) avoidance on the Mobility Inventory for Agoraphobia. These findings suggest that dental fear is a psychiatrically heterogeneous phenomenon. Some patients may benefit from psychiatric consultation and treatment strategies targeted toward other psychopathology, in addition to the dental phobia. (Supported by grant numbers 2R01 DE 6950; 5P30 DE 9743; and 1R03 DE 9804 NIDR, NIH)

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Does Anxiety or Insomnia, as Part of Major Depression, Predict a Differential Response to the Type of Antidepressant Prescribed?

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Summary:

Introduction: Considerable literature describes a high prevalence of anxious features among MD patients. While clinical lore suggests the presence of anxiety or insomnia drives the choice of antidepressant class, there is relatively little scientific support for this construct.

Method: We investigated over 3000 DSM-III-compatible MD patients from a series of double-blind, placebo or tricyclic antidepressant (TCA) controlled trials. An item cluster score (Hamilton Rating Scale for Depression items 10-13, 15, and 17) was used to characterize study subjects as anxious or nonanxious.

Preliminary Results: Compared with placebo, the selective serotonin uptake inhibitor fluoxetine was statistically significantly more effective as measured by the HAM-D 21 item score in the treatment of both anxious and nonanxious MD; fluoxetine also reduced the anxiety item cluster score. When compared with TCA's, fluoxetine was similarly effective in both patient subgroups. Analogous results were observed for MD with or without insomnia (HAM-D items 4-6).

Discussion: Features of anxiety or insomnia in MD do not appear to alter the pattern or predict response to classically "sedating or nonsedating" antidepressants. Rather they appear to represent individual symptoms that respond with the overall syndrome. Antidepressant class selection, based upon anxious or sleep disturbance attributes, does not appear warranted by these results.

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Haloperidol Addition in Fluvoxamine-Refractory OCD

Christopher J. McDouglas, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; Wayne K. Goodman, M.D., James F. Leckman, M.D., Nicole C. Lee, M.S.N., George R. Heninger, M.D., Lawrence H. Price, M.D.

Summary:

Although the efficacy of serotonin (5-HT) reuptake inhibitors, such as fluvoxamine (FVX), has clearly been established in the treatment of OCD, up to 50% of patients remain clinically unchanged after an adequate trial with these agents. Preclinical and clinical evidence suggests that, in addition to 5-HT function, the brain dopamine (DA) systems may also contribute to obsessive compulsive phenomena. This study examined the efficacy of adding the DA antagonist, haloperidol (HAL), to the regimens of OCD patients who were unresponsive to an eight-week trial of FVX. METHODS: Thirty-four OCD patients (DSM-III-R) participated in a four-week randomized, double-blind, placebo (PLA)-controlled trial of HAL addition to ongoing FVX treatment. There was no significant between group difference in dose of HAL (Active (ACT) [N = 17]; 6.24 ± 2.99 mg/day, PLA [N = 17]: 7.41 ± 2.81 mg/day, $t = -1.2$,

df = 32, $p<0.25$). Criteria for treatment response were based on Y-BOCS scores and the global improvement item of the CGI. *Results:* Student's t-tests demonstrated statistically significant differences between ACT and PLA HAL groups in change scores on the Y-BOCS (-6.5 ± 6.3 vs -1.5 ± 3.3, $t = -2.9$, $df = 32$, $p<0.007$). On the basis of treatment response criteria, 11/17 (65%) patients who received ACT HAL demonstrated a response compared with 0/17 PLA HAL responders. Eight out of eight (100%) patients with a current comorbid tic disorder were responders compared with three of nine (33%) patients without a tic disorder who were responders ($p = 0.007$, Fisher's exact test, two-tailed). *Conclusion:* These data suggest that in some patients, both the 5-HT and DA systems may be critical to the treatment of, and perhaps involved in the pathophysiology of OCD. In particular, this may be the case in OCD patients who have a comorbid tic disorder.

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Panic Disorder: Treatment with Valproate

Catherine L. Woodman, M.D., Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242; Russell V.R. Noyes, M.D.

Summary:

This study utilized an open trial design to explore the possible efficacy of valproate, an anticonvulsant medication, in the treatment of patients with panic disorder. The patients were recruited through the news media and treated with valproate at doses ranging from 500-2000mg QD for six weeks. Valproate was found to be effective and well tolerated. All 12 patients had at least moderate improvement and were free of panic attacks by the end of week 3. Outcome measures were Clinical Severity of Illness, Hamilton Rating Scale of Anxiety, and the Brief Symptom Inventory, all of which had significantly improved by week 6 ($p = .0001$). If valproate proves to be efficatious in controlled trials, the drug's tolerability and low dependence potential may make it a useful addition to currently available anxiolytics.

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Correlates of Dissociative Symptomatology in Patients with Physical and Sexual Abuse Histories

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Summary:

Recent studies have demonstrated a high prevalence of sexual and physical abuse histories in psychiatric inpatients, and high levels of dissociative symptoms in these patients. We examined whether severity, frequency, and age of onset of abuse correlated with subjects' level of dissociative symptoms. Sixty-four women reporting a lifetime history of physical and/or sexual abuse were recruited from consecutive admissions to three wards of a psychiatric hospital. Subjects' self-reports (Subjects completed the Life Experiences Questionnaire, containing detailed questions about physical and sexual abuse.) of severity, frequency, and age of onset of abuse were analyzed for correlations with score on the Dissociative Experiences Scale. Sexual abuse involving full or attempted penetration was associated with more dissociation than was genital fondling or voyeurism. Higher-frequency physical abuse was associated with more dissociation, but low- and high-frequency sexual abuse was associated with equally high levels of dissociation. For both physical and sexual abuse, age of onset was inversely correlated with degree of dissociative symptoms. The findings support hypotheses linking more severe, earlier, and possibly more chronic abuse with the greater development of dissociative symptomatology. They thus underscore the importance of recognizing dissociative symptoms in the clinical setting, and further argue for continued study into the effects of childhood trauma.

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Economic Methods in Cost Offset Measurement

Marianne Fahs, Ph.D., Community Med, Mt. Sinai Sch of Med, 1 Gustave Levy Place Bx 1043, New York, NY 10029; James J. Strain, M.D., John S. Lyons, Ph.D., Jeffrey S. Hammer, M.D.

Summary:

Introduction: Mechanisms to assess costs and charges for health care are urgently needed to assist in the clinical decision-making process. Mental health researchers are confronted with the methodological questions of which cost variables should be measured and analyzed for a given research question. *Method:* In a study of 264 patients over age 65, consecutively admitted for surgical repair of a fractured hip, four methods of assessing hospital costs/charges during a baseline and experimental (intervention) year were examined. The systematic appraisal of methods for measuring economic parameters associated with alternative treatment choices include: 1) clinical relevance; 2) degree of difficulty to accomplish (i.e., amount and type of resource required, including staff, computer time, etc.; 3) costs to implement; 4) statistical characteristics, including statistical power; and, 5) appropriateness to the clinical setting. Four methods were compared: 1) charges; 2) costs; 3) per diem rates; and 4) DRG rates.

Results:

	Base Line (N = 120)	*Experimental (N = 144)*	
Los (Mean)	20.7	18.5*	
Charge	$15,788	$14,487	
Cost	$11,917	$10,826*	
Per Diem	$13,897	$12,798	(*p = .05
Drg	$8,367	$8,367	one-tail)

Conclusion: Costs were the most sensitive measure to differentiate baseline and intervention year differences; charges and per diem rates did not.

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Determinants of Length of Stay in Geropsychiatry

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Summary:

Increasing emphasis on utilization review and cost containment led us to study factors associated with prolonged length of stay (LOS) on an inpatient acute geropsychiatry service. We reviewed electronic medical records and social work files for all patients discharged between September 1990 and September 1991. Patients with age less than 55 years or LOS less than four days were excluded. Medical comorbidity was assessed using a modified Cumulative Illness Rating Scale (CIRS, Linn et al, J Am Geriatr Soc, 16:622-626, 1968). One hundred and thirty-one hospital admissions were studied. The mean LOS was 53 days, mean age 74 years, and mean CIRS score 6.8. Age correlated with CIRS ($P = .05$), but neither correlated with LOS. There was a trend toward longer LOS in patients with a clinical diagnosis of dementia (61 v. 46 days, $p<.09$); neither major depression nor psychosis correlated with LOS. Patients transferred to adult homes or nursing homes stayed twice as long as patients who returned home (84 v. 41 days, $p = .002$). Of 11 patients with LOS>120 days, seven required institutional placement and only one returned home.

Discharge disposition is an important determinant of LOS in geropsychiatry, and should be the focus of efforts to shorten hospital stays.

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Work Loss and Depression: Impact of Fluoxetine

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Summary:

The aim of this study was to evaluate the impact of various antidepressant drugs on the relative risk of work loss in depressed patients. We observed 1852 patients who met DSM-III-R criteria for major depression in a cross-sectional study. Data have been collected through a network of 295 physicians (GP, Psychiatrics). Patients were included into five groups: patients without antidepressant treatment, patients treated with one of the main antidepressant used in France (amitryptiline, clomipramine and fluoxetine). Primary variables were the depression intensity (Hamilton-D. scores) and job status (work loss). The other parameters (clinical, demographic, economic and therapeutic variables) were used as potentially predicting variables. The majority of patients, either treated and untreated, were female and city dwellers. A significant difference was found between working patients and work loss in term of professional characteristics, i.e. type of employment ($p<.001$), type of employer ($p<.05$), level of responsibility ($p<.01$) and type of remuneration ($p<.01$). We found a positive correlation between depression severity and the risk of work loss ($R2=.86$, $p<.001$). This risk was significantly lower with fluoxetine when compared with other antidepressant drugs. Pooling these data with other from clinical trials led to saving of 2.4 (vs clomipramine) to 4.7 (vs amitriptyline) ($p<.05$, $p<.01$) days of work loss per patient for an eight-week treatment period.

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Methods of Funding Psychiatric Consultation Research and Teaching Services

James J. Strain, M.D., psychiatry, Mt. Sinai Sch. Medicine, 1 Gustave Levy Pl Bx 1228, New York, NY 10029; Mirjami Easton, George Fulop, M.D.

Summary:

Introduction: Mechanisms of funding of consultation-liaison (C-L) services are essential to promote research at the interface between medicine and psychiatry. Understanding methods for funding of the service substrate to promote research has not been undertaken systematically. *Method:* All 47 Academy of Psychosomatic Medicine listed consultation-liaison fellowship training programs were surveyed with a structured questionnaire: 1) number of full-time equivalent (FTE) MDs, psychologists, nurses, fellows, secretaries; 2) sources of funding: a) grants, b) hospital budget lines, c) patient fees, d) contributions/donations, and e) other departmental contributions. All 47 institutions responded. *Results:* The average annual budget was $324,600 (range $40,000-$550,000): hospital/medical school funding source: faculty FTEs–71%; fellowship funding–74%; secretary 84%. Average number of salaried FTEs–2.4; fellows–1.6; secretaries–1.3; nurses–0.8%. Additional funding sources include: grants–4.8%; other departments–6.3%; patient fees–$13.3%; donations–1%. Specific research funding often came from collaboration with other departments. *Conclusion:* In the majority of training programs surveyed, hospital/departmental support provided a clinical base for enhancing the development of research efforts. Minimal research funding is currently placed in any C-L program. C-L research has a substantial funded clinical base upon which to graft much needed research efforts.

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Adjustment Disorders in the Medical Inpatient Setting: A Multisite Study

Jeffrey S. Hammer, M.D., Quality Assurance, VA Medical Center EB14, Wilshire & Sawtelle Blvds Acos, Los Angeles, CA 90073; James J. Strain, M.D., Graeme C. Smith, M.D., Michael Blumenfield, M.D., Thomas Garrick, M.D., John R. Hayes, M.D., Philip R. Muskin, M.D., Joel J. Wallack, M.D., Asher Wilner, M.D.

Summary:

Introduction: The adjustment disorders (AD) are important diagnoses for patients who have medical comorbidity. This multisite study of AD examines: (1) frequency; (2) risk factors (predictors); (3) modes of treatment; (4) lag time (date of consultation request—date of admission); and, (5) length of hospital stay (LOS). *Method:* Seven university teaching hospitals used a structured database (MICRO-CARES) for all psychiatric consultations from 1/1/90 to 3/31/90. Chi square and students t-tests were used for dichotomous and continuous variables, respectively; stepwise logistic regression analyses determined the "odds ratios." *Results:* In 993 patients: AD only = 46; AD + other psychiatric diagnoses = 135; other psychiatric diagnoses = 785; no diagnosis = 27. AD only were more often married ($p=0.008$), self employed ($p=0.03$), admitted from home ($p=0.02$), living with family ($p=0.01$), and with family stress ($p=0.01$). AD had more infectious disease ($p=0.001$), cancer ($p=0.002$), and endocrine and metabolic disorders ($p=0.04$); greater stress (Axis IV) ($p=0.0006$), better prehospitalization functioning (Axis V) ($p=0.0001$), and less impairment on the Missouri Mental Status Examination: ($p=0.0005$). The AD had fewer recommendations for: lab tests ($p=0.001$), medical consultation ($p=0.003$) and neuroleptics ($p=0.003$), more psychological management ($p=0.0001$), and more often discharged home ($p=0.01$). The "odds ratio" for being diagnosed AD at admission were, respectively: "Admitted from home" 2.65; 0.92-7.57; "living alone" 0.39, 0.17-0.91; "serious illness in patient" 0.28, 0.08-0.92; "serious illness in family member" 2.65, 1.10-6.34. The discharge Karnofsky. Axis IV, Axis V, and presence of heart disease, were also predictors for the assignment of the diagnosis of AD.

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Giftedness and Psychological Abuse in BPD

Lee C. Park, M.D., Johns Hopkins University, 1205 York Road Suite 35, Lutherville, MD 21093; John B. Imboden, M.D., Thomas J. Park, Ph.D., Stewart H. Hulse, Ph.D., H. Thomas Unger, M.D.

Summary:

Two characteristics of patients with borderline personality disorder (BPD) are: (1) negative behaviors that require a talented perceptual awareness of others, such as projective identification, and (2) history of childhood abuse. We hypothesized that chronic abuse of a child who is biogenetically disposed to unusually good perceptual awareness of others may be an important etiological factor in BPD. Histories of 23 BPD outpatients and 38 outpatients with other personality disorders were reviewed for evidence of three non-exclusive categories of abuse: sexual, physical, and psychological/emotional. Patients were also rated on a scale of perceptual awareness ("giftedness"). BPD patients were more gifted and experienced more psychological abuse in childhood, and these differences between patient groups were substantial and statistically significant. Results suggest that psychological abuse, a strong environmental influence, can interact with giftedness, an innate characteristic, to influence psychological development toward BPD. Characteristic behaviors such as powerfully compelling projective identification may be expressions of an innate perceptual talent perverted by a psychologically abusive childhood environment. We discuss how these new findings should lead to a more humane and effective therapy for this chronic, life-threatening condition.

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Validity of Self-Defeating Personality Disorder

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Summary:

Many criticisms have been raised about the self-defeating personality disorder (SDPD) category of the DSM-III-R. It has been argued that the SDPD diagnosis will result in specific bias against women, because it describes normative behaviour of well-socialized women. Additionally, critics have suggested that the category may have poor discriminant validity. This investigation evaluated these criticisms by assessing whether SDPD males and females are differentially evaluated, and the extent of overlap with depression. A total of 247 psychologists and 100 psychiatrists participated in the study. Clinicians were requested to read a case vignette of SDPD in which sex and gender role (feminine and masculine) were manipulated, and to evaluate depicted self-defeating and depressive symptomatology. Severity of SDPD ratings varied significantly as a function of sex and gender role, with males and masculine persons judged more severely than females and feminine persons. Significant differences in SDPD ratings were also found between depression groups, with severely depressed persons evaluated more negatively than mildly depressed persons. Results indicate that judgments of severity of SDPD symptomatology are strongly affected by gender-related variables. More severe assessment of males and masculine individuals suggests that self-defeating behaviour is viewed as more pathological in these persons than in females and feminine individuals. Additional findings point to the importance of comorbid depression in SDPD ratings.

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Eye Tracking Impairment and Deficit Symptoms

Jackie Moskowitz, M.A., Psychiatry, VA Medical Center, 130 W. Kingsbridge Road 116A, Bronx, NY 10468; Sonia Lees, B.A., Lee Friedman, Ph.D., Richard S.E. Keefe, Ph.D., Richard C. Mohs, Ph.D., Larry J. Siever, M.D.

Summary:

To further investigate the relationship between eye tracking impairment and schizotypal personality disorder, DSM-III schizotypal personality disordered patients (SPD) ($N = 20$, 36.76 years), other personality disordered patients ($N = 18$, 34.08 years), and normal control subjects ($N = 24$, 36.53 years) were assessed by the infrared reflection (IR) method and evaluated for both smooth pursuit gain and an average sine wave qualitative score. SPD patients demonstrated significant eye tracking impairment, as measured by qualitative ratings, relative to normal controls ($2.8 \pm .63$, vs. $2.0 \pm .47$, $p < .05$). Although overall gain scores did not significantly discriminate our SPD patients from normal controls, a significant increase in *qualitative ratings of saccadic events was found in schizotypal patients (chi-square = 9.07, $p = .003$). Nonpsychotic deficit related symptoms of schizotypy (social isolation, odd speech, poor rapport, social anxiety) were correlated with qualitative measures of eye tracking *impairment* ($r = .35$, $p = .013$), in the total personality disordered sample. Within the SPD sample, eye tracking impairment, as assessed by both lower gain scores ($r = -.66$, $p = .003$) and poorer qualitative ratings ($r = .44$, $p = .038$) was significantly associated with nonpsychotic deficit-related symptoms. In contrast, impairment was not positively correlated with the psychotic-like symptoms of SPD. Indeed, these symptoms were associated with increased gain. These data suggest the possibility that eye tracking impairment is related to core non-psychotic, deficit-related symptoms of schizotypy.

*1-5, higher is worse

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Fluoxetine in BPD

Carl Salzman, M.D., Psychiatry, Harvard Medical, 74 Fenwood Road, Boston, MA 02115; Alan F. Schatzberg, M.D., Edison Miyawaki, M.D., M. Albanese, M.D., A. Wolfson, A.B., J. Looper, M.D.

Summary:

Objective: This was a double-blind, placebo-controlled study of fluoxetine in patients with borderline personality disorder, dysthymia, and atypical depression. *Method:* 24 voluntary research subjects were studied. Diagnosis of BPD was based on clinical interview, modified DIBS, and SCID semi-structured interviews. All subjects filled out baseline standard rating scales including HAM-D, POMS, and Overt Aggression Scale. Subjects took drug (20-40 mg/d) or placebo for 13 weeks. *Results:* 1) Fluoxetine did *not* increase suicidal behavior or aggressive behavior in any subjects; 2) Fluoxetine significantly decreased anger-hostility (.03); 3) Fluoxetine significantly decreased depression (.01). Fluoxetine was associated with significant improvement in mood (.05) and a decrease in mood lability (.03). *Conclusions:* Symptoms that were most responsive to fluoxetine treatment were those of anger/hostility, impulsiveness and atypical depression. Preliminary analysis suggests that fluoxetine was also associated with improved self-esteem and identity and less tumultuous object relations (data to be presented at meeting). One-year follow-up data will also be presented. These data confirm the therapeutic usefulness of fluoxetine for borderline/atypically depressed patients.

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Comparing Self-Defeating and Masochistic Criteria

Ross A. McElroy, Jr., M.D., Psychiatry, University of Florida, College of Med Box 100256, Gainesville, FL 32610; Linda Lefler, M.D., Roger K. Blashfield, Ph.D.

Summary:

Masochistic personality disorder was first proposed in 1985. The intense controversy that followed eventually led to masochistic personality disorder (MPD) being replaced by self-defeating personality disorder (SDPD) in the final version of DSM-III-R. This study compares the diagnostic criteria from the various definitions of MPD and SDPD. Despite their historical relationship, MPD and SDPD have substantial differences in their diagnostic criteria. These differences are apparent from a careful reading of the criteria sets. Kass, Mackinnon and Spitzer proposed the original MPD criteria in a 1986 study. They argued that the results showed the 10 MPD criteria formed a clinical syndrome with good internal consistency. Using a methodology similar to Kass et al., our data on both MPD and SDPD criteria showed that neither MPD nor SDPD form clear, descriptive syndromes of co-occurring symptoms. Rather, these criteria seem to represent traits shared by a range of personality disorders. Masochism and MPD have a significant history in the psychiatric literature. SDPD does not. SDPD, in our opinion, should not be included as a distinct personality disorder in DSM-IV.

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A Study of Anger as a Personality Trait

Abelardo Pena-Ramos, M.D., Psychiatry, JAH Veterans Hospital, 13000 Bruce B. Downs Blvd, Tampa, FL 33612; Denise K. Gross, Psy.D.

Summary:

Objective: Even though anger and aggression have been the focus of attention of different disciplines, there has been no report

of the psychological features or cluster of symptoms of what can be labelled the "angry personality." The present study attempts to fill this void by identifying personality traits associated with the chronically angry individual. *Method:* 15 "angry" psychiatric outpatients at a veterans' hospital were administered an anger inventory. To be included, subjects had to rate a "4" or higher on this 1-10 scale and could not have an Axis II (DSM-III-R) disorder, an organic disorder, or an active psychotic process. Included subjects were then given three personality questionnaires. *Results:* On the anger questionnaire, subjects' mean score was 16.86, exceeding the cutoff of nine, suggesting problems with anger discontrol. All mean scores on the State Trait Anger Inventory were at least one standard deviation above the mean. Correlations between the Brief Anger Questionnaire and State Anger ($r = .54$) and Trait Anger ($r = .57$) were significant. *Conclusion:* These preliminary findings suggest that subjects with high Trait Anger, that is, anger as a consistent personality component; displayed a lifelong pattern of emotional discontrol, suspiciousness, free-floating anxiety, and a critical, demanding, self-indulgent style in interpersonal relationships.

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Impaired Vigilance in Borderline Personality

Anselm George, M.D., Psychiatry, WPIC Univ of Pitts., 3811 O'Hara Street, Pittsburgh, PA 15212; Paul H. Soloff, M.D., Stuart R. Steinhauer, Ph.D., Jack R. Cornelius, M.D.

Summary:

From the inception of the borderline concept various definitions of this disorder have been linked to the schizophrenia spectrum. This study examined whether borderline patients and schizophrenics shared evidence of reduced vigilance as measured by the degraded stimulus version of the continuous performance test (CPT). The CPT is a computerized test requiring subjects to press a key when they recognize a blurred target occurring on 25% of the trials. A measure of visual sensitivity, d', reflects the ability to discriminate the target from distractors. Borderlines were included if they scored >7 on the Diagnostic Interview for Borderlines and schizophrenics if they met Research Diagnostic Criteria for schizophrenia or schizoaffective disorder. There were no statistically significant differences between borderlines ($N = 20$) and schizophrenics ($N = 19$) with regard to age, sex, and socioeconomic status.

Results: 1) Borderline patients did not differ from schizophrenics on the basis of their vigilance performance. 2) Statistical comparison of the patient groups with our normal subjects and literature controls indicate that both patient groups function at an impaired level of visual sensitivity. 3) The score of borderlines was not significantly different for those who had an additional diagnosis of schizotypal personality disorder or those who were drug free.

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Unconscious Information Processing and Repression

Bruce Wexler, M.D., Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519; George Bonano, Ph.D.

Summary:

Fused dichotic stimulation was used to study unconscious information processing of emotion-related words. Subjects were healthy young adults characterized as repressors or non-repressors by standard personality measures. An initial study (IS, $n = 42$) and a replication study (RS, $n = 90$) were conducted. In this dichotic technique, two words that differ only in their initial consonants are presented simultaneously, one to each ear. Because of auditory spectral overlap and precise temporal alignment, the words in each pair fuse into a single auditory percept. Subjects consciously hear only one word from each pair, and even when told that there are two different words are totally unable to identify both. Word pairs consisted of an emotionally neutral word and either a positive or negative word (e.g., tug-hug, till-kill). Positive words were consciously perceived more often than negative words (IS $p < .001$; RS $p < .001$). When the words were made into non-words by removing their endings, no perceptual advantage remained for the fragments from the positive words. Implicit memory for the unconsciously processes words from each pair was evident on a recognition ranking task (IS $p < 001$; RS $p < .001$). Recognition was greater for negative unconsciously processed words than for positive or neutral words (IS $p < .10$; RS $p < .001$). Repressors showed lower recognition of unconsciously processed words than did other subjects (IS $p < .05$; RS $p < .05$). Doing the digit symbol substitution test ($p < .01$) or counting backwards ($p < .01$) after each stimulus pair increased recognition of unconsciously processed positive and negative words in repressors but not in other subjects. A visual rotation (right hemisphere) task had no such effect.

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Patient Versus Family Informant Derived Diagnoses

Delbert G. Robinson, M.D., Psychiatry, Hillside Hospital, P.O. Box 38, Glen Oaks, NY 11004; Jose Alvir, Dr.PH

Summary:

To assess the contribution family informants make to the diagnostic process, symptoms and diagnoses obtained from interviews with 50 patients were compared with those obtained from a family informant questioned about the patient. All assessments were made using the SCID, Part I, a semi-structured diagnostic instrument. Principal current diagnosis at baseline (from patient interviews) was major depression ($n = 23$), bipolar disorder NOS, depressed ($n = 1$) or schizophrenia ($n = 26$). Since it is difficult to achieve respectable kappa statistics in situations of low variance, analysis was done on only the 11 diagnoses (lifetime bipolar disorder NOS, major depression, depressive disorder NOS, schizophrenia, alcohol abuse and dependence, cannabis abuse and dependence, panic disorder, current major depression and dysthymia) with at least minimal variance. Agreement between patient and family informant derived diagnoses at baseline interview was poor except for the lifetime diagnosis of schizophrenia ($k = 0.723$). Comparing patient- and family informant-derived ratings of the symptoms of major depression and psychosis assessed by the SCID, only depressed mood ($k = 0.639$), auditory hallucinations ($k = 0.614$) and bizarre delusions ($k = 0.519$) had kappas greater than 0.5. Patterns of disagreement between patient- and family-informant-derived diagnoses and symptoms will be presented and their implications discussed.

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SCID and SCID-D Interviews of Dissociative Patients

Robert G. Lussier, M.D., Psychiatry, Yale University, CMHC Day Hosp 1303 Chapel St., New Haven, CT 06511; Marlene Steinberg, M.D., Domenic Cicchetti, Ph.D.

Summary:

Dissociative disorders have been found to coexist with other psychiatric syndromes making differential diagnosis difficult. The Structured Clinical Interview for DSM-III-R Disorders (SCID) is a diagnostic interview that enables a trained interviewer to make diagnoses for the major affective, psychotic, somatoform, anxiety and eating disorders. The Structured Clinical Interview for DSM-III-R Dissociative Disorders (SCID-D) uses a format based on the SCID and enables a trained interviewer to systematically assess the dissociative disorders on the basis of DSM-III-R criteria. Preliminary findings will be presented for 20 psychiatric outpatients who were administered the SCID-D. SCID-D diagnoses obtained were: mul-

tiple personality disorder (9), dissociative disorder NOS (9), psychogenic amnesia (1), and depersonalization disorder (1), Lifetime SCID diagnoses found: psychotic disorder NOS (5), major depression (5), other bipolar (4), schizophrenia (1), schizophreniform (1), obsessive compulsive disorder (1), no diagnosis (1). When using the SCID alone, the diagnosis of a psychotic disorder is sometimes made when hallucinations are present, in contradistinction to results of the SCID-D, which may suggest a dissociative disorder is responsible for the reported symptoms. This indicates that certain patients who present with hallucinatory symptoms should receive the SCID-D following the SCID to rule out a dissociative disorder.

531 Wednesday May 6, 3:00 p.m.-5:00 p.m.

A Comparison of Comorbid Axis I Diagnoses in Stimulant Dependent and Depressed Research Subjects

Mark H. Rapaport, M.D., Psychiatry, UC San Diego Medical Sch, 9500 Gilman Drive, La Jolla, CA 92093; John R. Kelsoe, M.D., Shah Golshan, Ph.D., J. Christian Gillin, M.D.

Summary:

The effects of comorbid Axis I diagnoses on patient care, prognosis, and research have recently become an issue of considerable concern. Epidemiological Catchment Area (ECA) data find that 53% of individuals with an addictive disorder have a comorbid nonaddictive mental disorder. Intrigued by this, we compared the lifetime prevalence of comorbid Axis I disorders in stimulant dependent and unipolar research subjects. Forty-eight consecutive admissions to the San Diego VAMC Special Evaluation and Treatment Unit received SCID interviews and a consensus diagnosis. Twenty-three met DSM-III-R criteria for stimulant dependence (cocaine dependence N = 21, amphetamine dependence N = 2), and 25 subjects met criteria for unipolar depression. Stimulant-dependent subjects had a 17.2% lifetime prevalence of major affective disorder, a 47.8% prevalence of alcohol dependence, and a 39.1% prevalence of cannabis dependence. Unipolar subjects had a 12% lifetime prevalence of amphetamine dependence, a 4% prevalence of cocaine dependence, a 56% prevalence of alcohol dependence, and a 24% prevalence of cannabis dependence. This is one of the first reports where the same interviewers consecutively assessed patients admitted for stimulant and affective disorders research; the research and treatment implications of these data (and the point prevalence data, not shown) will be discussed.

532 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Conflict With Physician Pregnancy: Revisited

Kathleen N. Franco, M.D., Psychiatry, Medical College OH, 3000 Arlington P.O. Box 10008, Toledo, OH 43699; Nancy B. Campbell, M.D., Cynthia L. Evans, M.D., Stephen G. Jurs, Ph.D., Marijo B. Tamburrino, M.D.

Summary:

In 1981, the faculty and residents of a midwestern medical school were surveyed to assess attitudes toward physician pregnancy. Current faculty and residents were resurveyed in 1990.

The survey consisted of demographic data, and a 15-item questionnaire rated on a five-point Likert Scale from "strongly disagree" to "strongly agree."

The return rate was 41% (n = 140) in 1981 and 55% (n = 200) in 1990. There were 24.9% women faculty and residents at the institution in 1981 and 23.4% in 1990. In 1981, 80% of respondents felt personally inconvenienced by a pregnant colleague, compared with only 25% in 1990. The percent of physicians who believed that females of childbearing age represented a significant risk to departmental functioning dropped from 30% in 1981 to 13% in 1990. Similarly, increased percentages of physicians in 1990 reported that pregnant colleagues maintain work efficiency and interest in medicine. Interdepartmental changes were found, and women held significantly more favorable attitudes than men.

This nine-year follow-up study suggests that conflicts associated with physician pregnancy are lessening. Increased experience with pregnant colleagues may be lowering the barriers caused by fear and anticipated inconvenience. The increased acceptance of pregnancy during medical training may reflect the gradual gender changes occurring within the medical profession and ultimately lead to more compassionate attitudes towards both patients and caretakers.

533 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Battered American Indian Women

Ilena M. Norton, M.D., Psychiatry, Univ of Colorado, Denver Gen Hosp 777 Bannock St, Denver, CO 80204; Spero M. Manson, Ph.D.

Summary:

This is a descriptive study of battered American Indian women focusing on demographics, frequency of alcohol use, patterns of resource use, perceptions of police and courts, and psychological impact. Sixteen American Indian women referred for domestic violence counseling at an Indian health center in Denver, Colorado were interviewed using the Second National Family Violence survey. Seventy-five percent were under age 30; 75 percent had yearly incomes less than $10,000; 50 percent had children under age five. Most of these women (63 percent) and their partners (88 percent) abused alcohol; overall 94 percent of these relationships involved alcohol abuse. Family (81 percent), police (63 percent) and substance treatment service (63 percent) were the resources most frequently used by these women. Twelve women reported police involvement, almost all of whom (92 percent) were satisfied with the police intervention. Nine women reported court cases related to domestic violence; 78 percent were dissatisfied with how these cases were resolved. All of the women described feeling more depressed since they had been abused by their partners, and five women had considered suicide. This work underscores the need to better understand the impact domestic violence has on the well-being of this special population.

534 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Gay and Lesbian Issues in United States Psychiatric Training

Mark H. Townsend, M.D., Psychiatry, LSU Medical Center, 1542 Tulane Avenue, New Orleans, LA 70112; Mollie M. Wallick, Ph.D., Karl M. Cambre, M.S.

Summary:

Little is known about how gay and lesbian issues are addressed in U.S. psychiatric training, or about the training milieu of gay and lesbian psychiatry residents. We report the results of a national survey, similar in design to our recent study of gay and lesbian medical students (1). Resident members of the Association of Gay and Lesbian Psychiatrists were questioned about residency support; self-disclosure to residents, faculty and patients; and teaching about homosexuality. The 80 respondents included 21 women from 22 states. Residents categorized their program's stance towards homosexuality as follows: 21% as pathology, 41% as affirming, and the remainder as neutral. Clear differences in gender were reported, however, with men more likely to disclose their orientation, to report group support, and to discuss gay-specific matters with faculty. As compared with surveyed medical students, residents were less likely to report group support, but more likely to report meaningful interchange with faculty. Surprisingly, residents were less likely to report exposure to teaching about homosexuality than were stu-

dents. The results indicate that in some ways, gay and lesbian psychiatry residents experience greater institutional support than do students, but that men benefit more than women.

535 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Response to Fenfluramine in Premenstrual Syndrome

Margaret L. Moline, Ph.D., Psychiatry, NY Hosp. Cornell Med Ctr, 21 Bloomingdale Road, White Plains, NY 10605; Sally K. Severino, M.D., Daniel R. Wagner, M.D., Steven Zendell, RP.SGT., Stephen W. Hurt, Ph.D.

Summary:

Despite decades of research, the etiology of premenstrual syndrome (PMS) remains unknown. Several types of evidence suggest that the neurotransmitter serotonin may be involved. Treatment studies show that fluoxetine may be effective, and platelet serotonin studies have indicated abnormalities in PMS. To evaluate serotonergic functioning in PMS, we recruited six women (33-41 years old) with PMS diagnosed by two months prospective daily ratings, and two control women (28 and 29 years old). Each woman received a follicular and premenstrual TRH challenge test (200 μg i.v.) during one menstrual cycle followed by a follicular and premenstrual fenfluramine challenge test (60 mg p.o.) in a subsequent menstrual cycle. Plasma prolactin was analyzed by EIA. Two women with PMS with abnormal TRH responses were excluded. There were no differences in the prolactin response to TRH between control and PMS groups or across the menstrual cycle in either group. The PMS group responded significantly less ($p<0.03$) to fenfluramine (maximum prolactin level corrected for baseline; follicular: Control 22.7 ± 4.9 mIU/ml vs. PMS 9.6 ± 3.7; premenstrual: Control 21.8 ± 13.8 vs. PMS 10.9 ± 6.8); with regard to phase of the menstrual cycle. The prolactin response to fenfluramine did not differ across the menstrual cycle. These pilot data suggest that women with PMS may have abnormal central serotonergic functioning as a trait factor.

536 Wednesday May 6, 3:00 p.m.-5:00 p.m.

The New Woman: Psychosocial and Sexual Aspects

Samuel S. Janus, Ph.D., New York Medical College, P.O. box 2420, Vineland, NJ 08360; Cynthia L. Janus, M.D.

Summary:

This paper, part of a long-term study of American sexuality, portrays the "New Woman." Most mental health professionals and sociologists have long presumed that there would be differences between the full-time career woman and the homemaker. However, this has not been documented until now. The changes of full-time work outside the home affect not only finances, but are profound in their influence on the women in terms of their social attitudes, practices, and sexual behavior.

In this paper we examine the sexual and social differences between men and women, and between career women and full-time homemakers. The population consisted of 1,418 women and 1,347 men from 26 states. A specially designed 172-item questionnaire was developed.

The results show that career women are very different from women who do not work outside the home in terms of sexual outlook, practice and identification; career women often take roles that have traditionally been regarded as male roles.

537 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Cost of Intensive Care Community Treatment

Kathleen Degen, M.D., Psychiatry, Bridgeport CMHC, 1635 Central Avenue, Bridgeport, CT 06610; Carolyn Harmon, Ph.D.

Summary:

The state of Connecticut pilot, the Community Treatment Program (CTP) in Bridgeport, performed a cost analysis for the first two years of program operation. CTP is an intensive-care community psychiatric medicine and support services effort for the seriously mentally ill. Patients admitted to CTP were unable to engage in prior outpatient treatment, and had spent many years confined to mental hospitals. We compared the cost of CTP at three, six, 12, 18, and 24 months. While our costs were highest during the first year, our patient census doubled during the second year and the staff remained constant. The highest cost of CTP was staff salaries. The per capita per diem cost of care for patients diminished over the second 12 months and fell below the daily estimated cost of inpatient care for this unstable, chronically ill population. There was no increase in hospitalization over the second year. Our results demonstrate that our program became cost effective, comparing favorably with inpatient care during the second year of operation. The findings have significance for the treatment of "public sector" patients with intractable, lifelong mental illness, in light of society's predominant concerns about fiscal constraint and humane values.

538 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Medical Complaints and the Homeless Mentally Ill

Kerry Petrucci, Ph.D., Psychiatry, University of Maryland, 1222 West Baltimore Street, Baltimore, MD 21223; Lisa Dixon, M.D., Jean Hyde, M.S., Carol Lindes, M.S., David Stuart, M.D., Jan Wemmer, R.N.

Summary:

The aim of this study was to determine if psychiatric diagnoses of homeless mentally ill (HMI) patients could help explain variations in their abilities to verbalize medical complaints and participate in a medical treatment plan. *Methods:* Medical services were provided to 23 HMI patients over a four-month period. Data on the patients' abilities to verbalize their acute and chronic medical conditions were collected. Patients also received an overall participation score for medical follow-up. *Results:* A significant relationship between the Axis I diagnoses and the patient's ability to verbalize their *chronic* medical complaints was found (Chi-square = 16.25, $p<.05$). Schizophrenics required more verbal and physical prompting from the practitioner than nonschizophrenics before complaints were reported. No significant differences were found between the Axis I diagnoses and the patient's ability to verbalize *acute* medical complaints. Substance abuse was not significantly related to verbal reports or either chronic or acute complaints. However, active substance abusers had lower participation scores on medical follow-up than non-substance abusers (Chi-square = 8.34, $p<.05$). *Conclusions:* The results suggest that nonpsychiatric practitioners providing medical treatment to schizophrenic HMI may require additional training in knowledge acquisition. Further research is needed to determine the effect of psychiatric diagnoses and substance abuse on approaches to treating the medical complaints of the HMI.

539 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Economic Social Network: A New Model for Homelessness

Martin Korn, M.D., Psychiatry, Albert Einstein Col Med, TCS/ Montefiore Medical Center, Bronx, NY 10467; Isora C. Bosch, Ed.D., Frederick D. Greene, Ph.D., Vera Zilzer, A.T.R., Herman M. van Praag, M.D.

Summary:

Homelessness in the United States has been increasing for several decades. Programs to help the homeless have been only par-

tially successful in addressing the multiple problems of the homeless, and budget cuts threaten even these initiatives. We have developed a revenue-generating model for the homeless entitled an "Economically Centered Social Network" which we believe comprehensively and cost-effectively addresses these problems. It differs from existing programs in the following ways: 1) It is economically and contract driven rather than grant driven. Funding therefore is included in the cost of business. 2) Jobs are obtained at established for profit concerns, which minimizes start-up costs and immediately integrates the homeless into the work force. 3) Modern management techniques (i.e., Japanese style) are utilized to organize the work force, making the services of the homeless competitive and forming constructive, cohesive, small work groups. A social network is then formed at the work site. 4) Services are provided on-site in the form of an active Employee Assistance Plan. A pilot program was successful, and the program is currently being extended.

540 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Disability Determinations: A Reliability Study

Samuel O. Okpaku, M.D., Psychiatry, Vanderbilt University, 1208 18th Avenue South, Nashville, TN 37212; Amy E. Sibulkin, Ph.D., Christoph Schenzler, M.A.

Summary:

In the 1980s the Social Security Administration terminated large numbers of apparently qualified beneficiaries from the Social Security Disability Insurance (SSDI) rolls. The ensuing crisis raised serious questions about the reliability and validity of the determination process, leading to a revision of the SSA disability guidelines. Subsequently, the American Psychiatric Association reported favorably on the guidelines after a validity study of them. In our study, disability determinations by the local DDS service for claims due to mental impairment were compared with the independent decisions of senior mental health workers who constituted a case management team. The team's decisions for 158 adults with severe mental illness were based on presentations by specially trained rehabilitation workers. The team members voted "yes," "no," or "maybe" regarding approval for disability. Key demographic and health-related variables were identified and they predicted the decisions made by the local DDS and the case management team's average decision. Eighty-nine percent of the cases approved by the team were actually allowed by DDS. However, the team could not reach a Yes or No decision for almost half of the subjects. Of these undecided cases, 80% were actually allowed by DDS. These results have implications for the SSA determination process and for further research to improve the reliability and validity of the process.

541 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Continuity of Care by Means of Psychoeducational Therapy

Avner Elizur, Psychiatry, Abarbnel MHC, BAT YAM, Israel; Enav Karniel-Layer, Henry Szor

Summary:

The present study evaluated the effectiveness of short-term group intervention in comparison to the traditional method of continuity of care from hospitalization to outpatient care. This transition is crucial in promoting reintegration into community life and preventing early relapse. Two matched groups of chronic schizophrenic patients hospitalized in two wards in our center were compared. One ward discharged its patients to the Bat-Yam community center, using a short-term groups based on psychoeducational principles. The other ward discharged its patients to another regional community center, using the traditional method of referal.

There was a follow-up period of one year after discharge. Outcome evaluation was based on relapse rate, compliance with outpatient treatment, knowledge and attitudes towards mental illness and medication. The psychoeducational group had a significating smaller relapse rate and higher scoring on compliance with outpatient treatment. The patients had better knowledge and more realistic and adequate attitudes toward their illness.

A short-term, group intervention framwork based on psychoeducational principles is more effective than the traditional referral mode in facilitating an effective transition of chronic schizophrenic patients from hospital care to community outpatient treatment ensuring continuity of care.

542 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Gender and Patients' Initiation of Complaints

Thomas Gift, M.D., Psychiatry, Strong Memorial, 300 Crittenden Blvd, Rochester, NY 14624

Summary:

Reflecting consumerism, the self-help movement, and a decline in paternalism in medicine generally, recent years have seen an increase in patient advocacy in the psychiatric field. A formal patient complaint or grievance procedure now exists in many settings, as do dispute-resolution or ombudsman programs.

To better understand patient complaints in a CMHC setting, the experience of a hospital-based CMHC providing a full range of services to residents of a geographical catchment area was examined over a two-year period. The most striking finding was the under-representation of males. Only two of the 15 patients on whose behalf a complaint was lodged were male, representing a male/female ratio significantly below that of the patients receiving service regarding whom no complaints were made (3,235M/4,530F for noncomplaining patients; chi-square = 4.94; $p<.05$). This trend was also manifest when the total complaint group was divided into patients who complained on their own behalf ($n=6$; 1M/5F) and those on whose behalf others complained ($n=9$; 1M/8F). The content of the complaints most often involved poor communication (eight instances) or rudeness (six instances). Explanations for the findings, and possible improvements in the complaint procedure, are discussed.

543 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Humane Values and Mental Health in Quebec, 1950-1990

Hughes J. Cormier, M.D., Public Health, Johns Hopkins University, 1213 Havenwood Road, Baltimore, MD 21218

Summary:

Hart (1991) has argued that the manner in which people organize their collective life (the social and economic, environment, including the shared values) makes all the difference to their physical and mental welfare. We investigated if this global statement verifies itself in the local arena of Quebec society from 1950 to 1990. *Aims and methods:* The aims of this study were: (1) to describe the evolution of the social and economic environment in Quebec (as indexed by changes in different sociodemographic and socioeconomic rates); (2) to describe the evolution of Quebec collective mental health (as indexed by the annual changes in suicide rate); and (3) to test the hypothesis that the influence (as estimated by a time series regression coefficient R^2) of the fluctuations of the economy (as indexed by the annual changes in unemployment rate) on the evolution of the collective mental health will be stronger after compared to before/during the 1960-65 Quebec Quiet Revolution (QQR). *Results:* (1) The socioeconomic environment has been characterized by shared values (Catholicism) before the QQR and by anomie and prevailing economic interests thereafter (for exam-

ple the divorce rate increased form less than 50 per 100,000 in the early 1960's to more than 240 at the end of the 1970's; (2) The suicide rate was relatively stable before the QQR (4,0/100,000 in 1950, 5.8 in 1965) while it dramatically increased to reach a 18.2 peak in 1983 and then stabilized near 16.0; (3) We observed a statistically significant positive association between the changes of the unemployment and suicide rates during the 1966-90 time period (R^2 of 0.53 for 1966-81, $p<0.001$ and of 0.45 for 1982-90, $p<0.01$), whereas such an association was not observed the 1950-65 time period ($R^2=0.07$). *Discussion:* These results support the argument made by Durkheim (1896) that shared moral values are crucial for social integration, and that stable social life could not be well maintained by economic interests alone.

544 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Implementing a Ten-Step Study for Monitoring Tardive Dyskinesia

Bradford Frank, M.D., Psychiatry, Bridgeport CMHC, 1635 Central Avenue, Bridgeport, CT 06610; Kathleen Degen, M.D., Roger Adams, Ph.D., Maureen Hazleton, R.N., Tom Wellington, M.P.H., Gary Nemergut, B.S.

Summary:

The paper investigates the monitoring of tardive dyskinesia (TD) by physicians treating outpatients at the Greater Bridgeport Community Mental Health Center, a facility of the Connecticut Department of Mental Health. The 10-step study was undertaken by the medical staff in conjunction with the Quality Improvement (QI) Department. The 10-step model has long been advocated by JCAHO as an essential component of quality assurance (QA). It can remain a significant element as an agency shifts focus to QI.

The investigation sought to determine whether a seminar explaining QI and inviting physicians to develop a study of their monitoring of TD would increase the physicians' documentation of TD monitoring in patient charts. A randomly selected sample of two charts per month per physician was audited for two months preceding and two months following the seminar. The survey looked for documentation of a TD evaluation within the previous six months. Results show an increase in physicians' documentation after the seminar. The outcome suggests that when the medical staff are actively included, they are likely to increase their attention to the aspect of patient care under investigation. Inclusion of the medical staff in quality assessment studies is part of the implementation of a QI program, and it was an effective mechanism to improve monitoring of TD.

545 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Receiver Operating Characteristic and the Accuracy of Violence Prediction

Douglas Mossman, M.D., Psychiatry, Univ of Cincinnati, Coll of Medicine Mail Loc. 559, Cincinnati, OH 45267; Roberta Schaffner, M.D.

Summary:

The prediction of violence occupies a prominent and controversial place in public mental health practice. This presentation addresses an unrecognized problem in studies of violence prediction: the *form* or *method* used to quantify the accuracy of predictions may have contributed to misunderstandings about clinicians' actual abilities.

Receiver operating characteristic (ROC) analysis provides a mathematical framework for describing predication accuracy that controls for the effect of base rates and for clinicians' biases in favor of various outcomes. This presentation describes how ROC analysis might be used in a hypothetical study of violence prediction, and reanalyzes 24 sets of data from 15 published studies of prediction accuracy. For most (22/24) data sets predictive accuracy was substantially better than chance. Recent studies emphasizing short-term predictions have been interpreted as demonstrating that short-term clinical judgments about dangerousness have a higher degree of predictive validity than was found in older studies of long-term predictions. However, post-1987 studies, in fact, yield accuracies no better than earlier (1972-1973) studies (Wilcoxon rank sum test, $z=0.354$, $p=0.722$), and long-term ($\geq$1 year), short-term ($\leq$1 week), and intermediate-term (1-6 months) predictions appear to have equal accuracies (Kruskal-Wallis test, $H=0.3163$, $p=0.854$).

546 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Violence and Civil Commitment: A Study of Attitudes

Douglas Mossman, M.D., Psychiatry, Univ of Cincinnati, Coll. of Med. Mail Loc. 559, Cincinnati, OH 45267; Kathleen J. Hart, Ph.D.

Summary:

Legal authorities have long recognized that the pursuit of justice entails a balancing of erroneous and correct judgments about criminal guilt, and recent legal and psychological literature have utilized Decision Theory to evaluate standards of certainty for convictions and acquittals in criminal trials. This presentation describes how Decision Theory can be applied to the problem of balancing potential errors in civil commitment determinations, using data from a pilot study of attitudes about false-negative and false-positive predictions of future violence.

We systematically quantified college students' relative preferences concerning experiencing violence and involuntary hospitalization. Though most subjects thought that a three-day hospitalization was preferable to being attacked at knife-point, over one-fourth held the opposite view. Subjects expressed a broad range of implicit tolerances for the consequences of false-negative and false-positive predictions. Although the practical implications of their attitudes were dependent on assumptions about the base rate of violence, students' aversion to hospitalization generally entailed a surprisingly high tolerance of false-negative errors. Even assuming a very high base rate of violence (e.g., 10%), half of the students implicitly endorsed commitment policies that would release a majority of actually violent individuals.

547 Wednesday May 6, 3:00 p.m.-5:00 p.m.

Patients' Characteristics and Brief Therapy Outcome

John J. Sigal, Ph.D., Psychiatry, Jewish General Hospital, 4333 Cote Ste Catherine Road, Montreal PQ H3T 1E4, Canada; Marianne E. Kardos, M.D., Gilbert Zimmerman, M.D., Michael Buonvino, B.Sc.

Summary:

Do selection criteria in current use predict the outcome of brief, psychodynamically oriented therapy (BPOT) in a standard psychiatric OPD setting? Psychiatric residents and other trainees rated 256 patients referred for BPOT on a 26-item checklist after an intake interview. The checklist items referred to characteristics deemed descriptive of suitability for BPOT according to prominent authors in the field and clinicians. Ratings of improvement in symptoms, insight, and global functioning (weighted kappas $\simeq$ .75) based on charted information were correlated with factor scores (weighted alphas .85, .62, .50, .77) of four factors derived from the checklist for the 37 patients who could be identified from the checklist.

Only rated improvement in global functioning correlated significantly ($r=-.34$, $p<.05$) with the factor on which absence of severe character pathology, and no difficulty in keeping job or attending school had high loadings. Items not loading high in the factors, but

rated as important by recognized BPOT experts, did not predict outcome.

Most specific criteria currently used to determine suitability for BPOT do not predict outcome in a standard, well-supervised clinic setting. A global rating of capacity to cope may be useful for the purpose. The failure of most items to load more than .50 on many factors suggests the absence of a cohesive underlying theory.

NR548 Thursday May 7, 9:00 a.m.-10:30 a.m.

Psychobiology of Response to Inpatient Cognitive Therapy

Michael E. Thase, M.D., Psychiatry, WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213

Educational Objectives:

To understand the rationale and results of this study of correlates of response to cognitive therapy in severely depressed inpatients.

Summary:

Several recent studies indicate that Beck's cognitive therapy (CT) may be of limited efficacy in severe depressive states. If true, this could be due to the greater likelihood of neurobiological disturbances in severe depression and may indicate the need for pharmacotherapy. We are studying the psychobiological correlates of recovery in depressed inpatients treated with an intensive, individualized, 28-day (20 session) CT protocol. To date, we have studied 30 patients (12 M/18 F) with RDC endogenous, nonpsychotic depression (x age: 34.6 years). In the 1st 20 cases, we completed pre- and post-treatment EEG sleep and 24-hour urinary free cortisol (UFC) studies. At post-treatment, 22 patients (73%) responded, including 20 of 23 (87%) primary depressives. Mean HAM-D scores fell from 22.4 (3.6) to 9.0 (5.8) ($p = .0001$). Increased severity and secondary depression were associated with poor response in the total sample (both $p < 0.05$). Among primary depressives, increased pretreatment levels of UFC predicted either poor acute response or subsequent relapse ($p = 0.04$), whereas improvements of post-treatment EEG sleep profiles were associated with sustained remission. While CT appears to be an effective alternative to pharmacotherapy for some depressed inpatients, it is not effective as a solo treatment of secondary depression. Further, it also appears less effective in primary depression patients with hypercortisolemia and multiple, persistent EEG sleep abnormalities.

References:

Thase ME, Wright JH: *Behavior Therapy, 22:* 579–595, 1991.

Thase ME, Bowler K, Harden T: *Behavior Therapy, 22:* 469-477.

NR549 Thursday May 7, 9:00 a.m.-10:30 a.m.

Those Intolerant to One Selective Serotonin Reuptake Inhibitor May Tolerate Another

Walter A. Brown, M.D., Psychiatry, Brown University, VA Medical 830 Chalkstone Ave, Providence, RI 02908

Educational Objectives:

At the end of this presentation the participant will have gained knowledge about the cross-sensitivity to selective serotonin reuptake inhibitors.

Summary:

Selective serotonin reuptake inhibitor antidepressants (SSRIs) lack the anticholinergic, antihistaminic and antiadrenergic side effects that are drawbacks of tricyclics, but have side effects of their own that can result in morbidity or discontinuation. The differing chemical structures and pharmacokinetic profiles of SSRIs raise the question of whether there are clinically significant differences in their side effects. A multicenter trial was conducted to see how patients who have been unable to tolerate fluoxetine because of side effects would tolerate sertraline, a recently approved SSRI.

One hundred patients with DSM-III-R major depression who had discontinued fluoxetine for side effects were enrolled in the study. After a washout of at least four weeks following fluoxetine discontinuation patients were switched to sertraline. Weekly assessments included HAM-D, CGI, BDI, and recording of adverse events and laboratory values.

Interim analysis of the first 91 patients who completed the study demonstrated that 69 (75.8%) were responders to sertraline as defined by CGI-I score of 1 or 2 (very much or much improved). Only eight patients (8.6%) discontinued sertraline because of side effects. Results suggest that patients unable to tolerate one SSRI may be successfully treated with another. Further study of cross-sensitivity to SSRIs using double-blind methodology is warranted.

References:

1. Fuller RW, Wong DT: Serotonin re-uptake blocker *in vitro* and *in vivo, J of Clin Psychpharm* Vol 7, pp 365-435, 1987.

2. Rickels K, Schweizer E: Clinical overview of serotonin re-uptake inhibitor, J of Clin Psych 51 p 12, suppl B: pp 9-12, 1990.

NR550 Thursday May 7, 9:00 a.m.-10:30 a.m.

ECT Schedule: Therapeutic and Cognitive Implications

Baruch Shapira, M.D., Depression Unit, Herzog Hospital, P.O. Box 35300, Jersusalem 91351, Israel; Avraham Calev, Ph.D., Bernard Lerer, M.D.

Educational Objectives:

To provide the final results of a double-blind study that significantly impacts upon clinical practice.

Summary:

In the context of a random-assignment, double-blind study, consenting, medication-free patients with major depressive disorder, endogenous subtype (RDC), were randomly assigned to three times weekly (ECT × 3) or twice weekly ECT (ECT × 2) plus simulated ECT (anesthesia and muscle relaxant only) once weekly. The trial period was four weeks, and the ECT × 3 group thus received up to 12 real treatments and the ECT × 2 group a maximum of eight. The Hamilton Depression Scale and other measures were administered prior to the ECT course and the day after each treatment, real or simulated. Extensive memory testing was performed prior to and after the ECT series as well as at one- and six-month follow-up. Forty-seven patients were included in the final data analysis, which showed significant improvement in both groups with equal antidepressant efficacy after four weeks (MANCOVA with repeated measures, duration of depressive episode as covariate). However, ECT × 3 induced a significantly more rapid improvement (schedule × time interaction), the difference being most prominent at the two-week time point when the ECT × 3 group had received six real ECT's and the ECT × 2 group only four real treatments. Analysis of the memory test battery showed that ECT × 3 patients had significantly more impairment than the ECT × 2 although this difference disappeared by one month follow-up. These findings indicate that three times weekly ECT has a more rapid therapeutic effect, but at the cost of greater memory impairment. Clinical practice should take this observation into account as well as the fact that twice weekly ECT is no less efficacious by the end of the treatment course.

References:

1) Lerer B, Shapira B: *Convulsive Therapy* 2: 141-144, 1986.

2) Shapira B, et al: *Psychiatric Clinics of North America* 14:935-946, 1991.

NR551 Thursday May 7, 9:00 a.m.-10:30 a.m.

Depression, Cognitive Impairment and Mortality

Gary J. Kennedy, M.D., Psychiatry, Montefiore Medical, 111 East 210th Street, Bronx, NY 10467; Howard R. Kelman, Ph.D., Cynthia Thomas, Ph.D.

Educational Objectives:

To learn how the most common forms of mental morbidity in late life, depressive symptoms and cognitive impairment relate to rates of institutionalization and mortality among older community residents.

Summary:

Despite extensive epidemiologic study, the significance of mental morbidity not defined by diagnostic procedures remains unclear for older adults. Public health legislation and standards proposed by the Institute of Medicine specifically reject routine screening for depressive symptoms and cognitive impairment, the most common forms of late life mental morbidity. Using the Center for Epidemiologic Studies Depression Scale, the Mini Mental Status exam and Cox proportionate hazards analyses we investigated the relationship of depressive symptoms and cognitive impairment to institutionalization and mortality among older community residents. Of the 1855 respondents 17% demonstrated a clinically significant level of depressive symptoms, 40% showed moderate cognitive impairment, and 7% were severely impaired. Both depression and cognitive impairment remained significant predictors of entry and permanence of stay in nursing facilities after controlling for the confounding effects of age, gender, poor health, social support and disability. With similar controls, depression made no contribution to the prediction of mortality. However, cognitive impairment, whether moderate or severe, was the most sizeable predictor of mortality, outweighing age, gender, poor health, social support and disability. These findings raise questions about the need to screen for mental morbidity in primary care settings as well as the functional criteria used to qualify individuals for supportive services.

References:

Thomas C. Kelman HR, Kennedy GJ, et al: Depressive symptoms and mortality among older community residents. *Gerontologist (Social Sciences)* 1992 Mar (in press).

Kennedy GJ, Kelman HR, Thomas C: Persistence and remission of depressive symptoms in late life. *Am J Psychiatry* Feb;148 (2):174-8, 1991.

NR552 Thursday May 7, 9:00 a.m.-10:30 a.m.

Biochemical Measures in Dysthymic Disorder

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Educational Objectives:

To describe: subtypes of dysthymic disorder, biochemical factors in etiology, and biochemical correlates of pharmacotherapy.

Summary:

The study included 23 patients who satisfied DSM-III-R criteria for dysthymic disorder with no comorbidity. They also satisfied Akiskal's criteria for the subaffective classification of early onset primary dysthymia. This homogeneous sample of patients had significantly lower platelet MAO levels than normal controls. Our data indicate that a significant proportion of patients showed a therapeutic response to treatment with a serotonin reuptake inhibitor. Pretreatment urinary 5-HIAA and melatonin (6-sulphatoxymelatonin) levels were lower in responders than in non-responders. Only responders showed an increase in urinary 5-HIAA from before to after treatment, while only non-responders showed an increase in urinary metanephrine from before to after treatment. Drug treatment did not affect urinary melatonin levels. On the other hand, treatment with the serotonin reuptake inhibitor caused an increase in post-dexamethasone plasma cortisol levels in all patients, regardless of therapeutic response to the drug. Taken together, these data indicate that biological factors may play a greater role in this chronic mood disorder than previously acknowledged. Pretreatment urinary 5-HIAA and melatonin may be predictors of a positive drug response. Furthermore, increased urinary 5-HIAA and/or lack of increased urinary metanephrine levels during treatment may be early predictors of therapeutic response to serotonin reuptake inhibitors.

References:

Howland RH, Thase MD: Biological studies of dysthymia. *Biological Psychiatry,* 30:283-304, 1991.

Akiskal H: Dysthymic disorder: psychopathology of proposed chronic depressive subtypes. *American Journal of Psychiatry,* 140(1):11-20.

NR553 Thursday May 7, 9:00 a.m.-10:30 a.m.

Antidepressant Treatment of Chronic Tinnitus: An RCT

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Educational Objectives:

To better understand the effect of depression and antidepressant treatment upon comorbid medical illness in terms of symptom severity and functional disability.

Summary:

Chronic tinnitus offers a model for understanding the impact of depression and its treatment upon comorbid medical illness. Here, we report a randomized, double-blind, placebo-controlled trial using nortriptyline to treat severe chronic tinnitus in 38 subjects with current major depression and 54 subjects with sub-syndromal depressive symptoms and significant disability due to tinnitus. Subjects were 50-80 years old and had tinnitus severe enough to disrupt daily activities for more than six months. All subjects received otological and audiological examinations. Those meeting major depression criteria on the Diagnostic Interview Schedule and scoring >18 on the Hamilton Depression Scale were randomized to nortriptyline or placebo within the major depression group; the remainder were randomized within a subclinical depression group. These groups were no different at baseline on demographic or otologic variables. Subjects were titrated blindly to a therapeutic nortriptyline dose and maintained there for six weeks. At conclusion of treatment, the nortriptyline major depression and total groups showed greater reduction in depression than placebo ($p < .01$). The total nortriptyline group showed greater improvement in work and family dysfunction (but not social) ($p < .02$). Audiometric assessment showed no nortriptyline differences in tinnitus loudness, but did show a significant decrease in noise sensitivity in the major depression group ($p < .01$). This study thus demonstrates successful treatment in the presence of comorbid medical illness of 1) major depression, 2) functional disability, 3) symptom amplification.

References:

1) Sullivan MD, Katon WJ, Dobie RA, et al: Treatment of depressed tinnitus patients with nortriptyline. *Ann Otol Rhinol Laryngol* 98:867-872, 1989.

2) Katon WJ, Sullivan MD: Depression and chronic medical illness. *J Clin Psychol* 51(suppl.):3-11, 1990.

NR554 Thursday May 7, 9:00 a.m.-10:30 a.m.

Late-Onset Alcohol Use Disorders in Older Men

Roland M. Atkinson, M.D., Psychiatry, VA Medical Center, 3710 SW Vets Hosp. Road, Portland, OR 97201; Robert L. Tolson, M.S.W.

Educational Objectives:

As a result of this presentation, the attendee will learn that primary alcohol use disorders in the elderly often can begin in middle age or later.

Summary:

Introduction: Findings from an earlier cohort of 132 alcoholic male veterans, age ≥60 years, challenged two common beliefs about late onset. Contrary to DSM-III-R, late onset was not rare: the first alcohol problem occurred after age 45 in 48% of cases, after age 59 in 15%. The DSM-III-R assertion that late onset typically follows a comorbid mental disorder ("secondary" alcoholism) also was not supported by MMPI data. This report offers information from a new cohort that confirms and extends the prior findings, and also addresses whether DSM-III-R criteria for alcohol dependence are useful in older patients. *Methods:* Fifty community-dwelling, problem-drinking men veterans age ≥60 years (mean 65.0 yrs; s.d. ± 4.5; range 60-79) received psychiatric evaluation, following DSM-III-R, and cognitive testing by a senior psychiatrist trained in alcoholism and geriatrics. *Results:* Alcohol dependence was diagnosed in 45 cases, alcohol abuse in five. In a further analysis of 33 cases, the mean number of DSM-III-R criteria for alcohol dependence fulfilled by these patients was 5.6 (s.d. ± 2.5; range 0-9): 31 of 33 (94%) met ≥ 3 criteria, the required to make the diagnosis. Mean age at onset of the first alcohol problem was 39.6 years (s.d. ± 15.3; range 16-72): 30% had onset after age 45, 14% after age 59. Comorbid Axis I nonsubstance-related disorders were found in 16 patients (32%). Comorbid disorders (specifics in poster) were *least* common in patients with onset of alcohol problems at age 60 or later (1/7, 14%). *Discussion and Conclusions:* Most of these patients fulfilled DSM-III-R criteria for alcohol dependence. While this relatively high functioning outpatient cohort is undoubtedly not representative of all aging alcoholics, the findings nevertheless demonstrate that primary DSM-III-R alcohol use disorders do begin in later life.

References:

1. Finlayson RE, Hurt RD, Davis LJ, Morse RM: Alcoholism in elderly persons: A study of the psychiatric and psychosocial features of 216 inpatients. *Mayo Clin Proc* 63: 761-768, 1988.

2. Atkinson RM, Tolson RL, Turner JA: Late versus early onset problem drinking in older men. *Alcoholism: Clin Exp Res* 14: 574-579, 1990.

NR555 Thursday May 7, 9:00 a.m.-10:30 a.m.

Thirty-Year Follow-Up of Sons of Alcoholics

Donald W. Goodwin, M.D., Psychiatry, KU Medical Center, 3901 Rainbow Blvd, Kansas City, KS 66160; Elizabeth Penick, Ph.D., William Gabrielli, M.D., Per Jensen, M.D., Joachim Knop, M.D., Fini Schulsinger, M.D.

Educational Objectives:

To present preliminary findings from a large-scale prospective study of sons of alcoholics and to comment on implications for validity of DSM-III-R.

Summary:

Sons of alcoholic fathers (at high risk for alcoholism: HR) and a matched control group without parental alcoholism (low risk: LR) have been followed prospectively since pregnancy. A sample originates from a consecutive birth cohort (born 1959-61, N = 9124). Throughout the 30 years all premorbid data have been collected prospectively.

An ongoing 30-year follow-up of the sample (N = 330) is based on a diagnostic interview generating DSM-III-R diagnoses, neuropsychiatric battery and a detailed drinking history, including family history.

Preliminary results indicate that about 20% of the HR subjects fulfill criteria for alcohol dependence compared with 5% of low-risk subjects, both groups now in their early 30's. About 16% of HR subjects fulfill criteria for alcohol abuse and 14% of low-risk subjects. This supports early observations that alcohol dependence, as defined in DSM-III-R, occurs significantly more often in HR subjects than in LR subjects, but this is not true of alcohol abuse. The latter, representing a milder form of the disorder, shows less heritability in many studies. This tends to validate the criteria for alcohol dependence in DSM-III-R, which is similar to the option I diagnosis for alcohol dependence in DSM-IV.

HR subjects also were more often drug dependent (mostly cannabis). There was no difference in drug abuse between HR and LR subjects. This would indicate an overlap of alcohol dependence and drug dependence in sons of alcoholics.

In conclusion, the results demonstrate the importance of regarding dependence and abuse as defined in DSM-III-R as separate diagnostic entities.

References:

1) Goodwin DW: The Genetics of Alcoholism. *Genes, Brain and Behavior.* McHugh, PR and McKusick, V.A. (eds.). New York: Raven Press, 1990.

2) Goodwin DW: Genetics. *Issues, Strategies and Methods.* Hsu, L.K. and Hersen, M. (eds.) New York: Plenum Publishing Corp., 1990.

NR556 Thursday May 7, 9:00 a.m.-10:30 a.m.

Dopaminergic Therapy for Cocaine Withdrawal in Rats

Ronald P. Hammer, Ph.D., Anatomy, University of Hawaii, 1960 East-West Road, Honolulu, HI 96822; Shay J. Lee, M.D., Blance B. Young, B.A.

Educational Objectives:

Cocaine "addiction" produces depressive symptomatology during early withdrawal which is represented by a reduction of metabolic activity in critical brain reward regions. This paper will examine the substrates for this reduction in an animal model of cocaine withdrawal, and the effect of pharmacotherapies which directly or indirectly alter dopamine activity.

Summary:

Early withdrawal following chronic cocaine abuse produces severe drug craving and depressive symptoms in humans. We examined the effects of abstinence or dopamine agonist pharmacotherapy following chronic cocaine administration on regional cerebral metabolic rate for glucose (rCMR) in male rats. Our earlier studies revealed that rCMR is reduced in regions of basal forebrain involved in drug reinforcement (Clow and Hammer, *Neuropsychopharmacol.*, 4: 71, 1991). We now compare the efficacy of bromocriptine, a dopamine receptor agonist, and BMY 14802 (BMY), a serotonin$_{1A}$/sigma-receptor agonist that increases firing rate of dopamine neurons hence releasing dopamine at synaptic terminals. All drugs were administered daily by intraperitoneal injection; following 14 days of 10 mg/kg cocaine injections, bromocriptine (10 mg/kg), BMY (10 or 30 mg/kg) or vehicle was administered for three days. Bromocriptine enhanced metabolic recovery in most affected brain regions during cocaine withdrawal. BMY treatment produced significant dose-dependent effects in mesolimbic and limbic brain regions, but had no effect in most thalamic and neocortical regions. Also, the ventromedial (limbic-related), but not

dorsolateral striatum was altered by BMY treatment. In general, reductions of rCMR produced by cocaine were reversed by low-dose BMY treatment, while the higher dose exacerbated the metabolic effect of cocaine. The latter dose of BMY alone has been shown to have little effect on rCMR in mesolimbic brain regions. Thus, both direct and indirect dopamine agonists have potential therapeutic efficacy during cocaine withdrawal, although indirect agonists with additional pharmacological (e.g., 5-HT receptor) interactions might have a smaller therapeutic window. (Supported by USPHS Awards R01 DA06645 and K04 NS01161, and a grant from the Bristol Myers-Squibb Company.)

References:

Clow, D. W. and Hammer, R. P.: Cocaine abstinence following chronic treatment alters cerebral metabolism in dopaminergic reward regions: Bromocriptine enhances recovery, *Neuropsychopharmacology,* 4:71-75, 1991.

della Puppa, A. and London, E. D.: Cerebral metabolic effects of σ ligands in the rat, *Brain Research,* 505, 288-290, 1989.

NR557 Thursday May 7, 9:00 a.m.-10:30 a.m.

Fluoxetine for Cocaine Abuse: Psychiatric Factors

Steven L. Batki, M.D., Psychiatry, UCSF SFGH, 1001 Potrero Avenue, San Francisco, CA 94110; Luisa Manfredi, B.A., Reese T. Jones, M.D., Laura Goldberger, B.A., Jennifer M. Murphy, B.A.

Educational Objectives:

To increase knowledge about the pharmacotherapy of cocaine dependence; to increase knowledge about the role of depression in cocaine dependence.

Summary:

Cocaine-dependent methadone maintenance treatment (MMT) patients are being treated in a randomized, double-blind, placebo-controlled, 12-week trial of fluoxetine with weekly group therapy. All subjects have met DSM-III-R criteria for both cocaine and opioid dependence. To date (1/8/92), 43 cocaine-dependent MMT patients have enrolled in the study. Thirty-five (81%) are HIV-infected. Twenty-two (51%) are African-American, and 23 (53%) are female. Sixty-one percent of the group have a lifetime history of major depressive disorder (MDD), and 45% of them are currently depressed. Fifty percent have antisocial personality disorder. Subjects with current MDD showed no significant differences in intake drug use self-reports (days used in past 7) when compared with those who are not currently depressed. Fluoxetine (FLX) and placebo (PLA) groups were compared for differences in outcome variables from preliminary data on the first 30 subjects. A difference in cocaine use by self-report was demonstrated: average days of cocaine use per week, for weeks 3-12 was 1.5 days (FLX) and 2.4 days (PLA) (unpaired t-test, $p = .07$). For the FLX group, Hamilton Depression scores decreased from an average of 21 at intake to 9 at week 12 (paired t-test $p < .05$), while the PLA group showed no significant decrease. In summary, fluoxetine appears to have potential efficacy in the treatment of depression and cocaine abuse in MMT patients.

References:

1) Batki S, Manfredi L, Sorensen J, et al. Fluoxetine for cocaine abuse in methadone patients: preliminary findings. In L.S. Harris (Ed) *NIDA Monograph Series,* 105, 516-7, 1991.

2) Kolar A, Brown B, Weddington W, Ball J: A treatment crisis: cocaine use by clients in methadone maintenance programs. *J. Subst. Abuse,* 7: 101-7, 1990.

NR558 Thursday May 7, 9:00 a.m.-10:30 a.m.

Opiate Detoxification: An Indication for Serotonin-3 Receptor Antagonists

Norbert Loimer, M.D., Psychiatry, University of Vienna, Waehringerquertel 18-20, Vienna A 1090, Austria; Peter Hofmann, M.D., Haroon Chaudhry, M.D.

Educational Objectives:

To modify rapid opiate antagonist precipitated detoxification techniques to reduce the need for specially trained staff and sophisticated and expensive equipment, while preserving the low levels of distress that make withdrawal a less unattractive option to addicts, and to overcome dangerous vomiting in sedated patients.

Summary:

Twenty male opioid-dependent patients diagnosed according to DSM-III-R criteria gave their informed consent to participate in a clinical, noninvasive, inpatient, opiate detoxification study at the department of psychiatry at Sir Gangaram Hospital of Lahore.

Detoxification scheme

Last opiate intake 12 hours prior to treatment start

detoxification start	after 10 min	after 15, 30, 45 and 60 min
midazolam (60 mg) navoban (5 mg) clonidine (0.300 mg)	naltrexone (50 mg)	1 mg naloxone intranasaly

every 24 hours 50 mg naltrexone; every 12 hours 5 mg navoban.

In this study, the usual acute onset of withdrawal signs and symptoms following the acute administration of naloxone in opiate addicts was suppressed by midazolam, gastrointestinal side effects of naloxone in opiate addicts were blocked using a 5-HT3 antagonist. It could be demonstrated that the use of a 5-HT3 antagonist in the course of withdrawal has encouraging antiemetic efficacy with a favorable toxicity profile and represents a single agent alternative to the current management of naloxone-induced emesis with complex antiemetic cocktails. All 20 patients were successfully transferred to naltrexone.

References

Brewer C, Rezae H, Bailey C: Opioid withdrawal and naltrexone induction in 48-72 hours with minimal drop out using a modification of the naltrexone-clonidin technique. *Brit. J Psychiatry* 153:340-343, 1988.

Loimer N, Lenz K, Schmid R, Presslich O: Technique for greatly shortening the transition from methadone to naltrexone maintenance patient. *Am J Psychiatry,* 148:933-935, 1991.

NR559 Thursday May 7, 9:00 a.m.-10:30 a.m.

Amphetamine Sensitizes C-FOS Expression in Brain

Andrew B. Norman, Ph.D., Psychiatry, Univ of Cincinnati, 231 Bethesda Avenue, Cincinnati, OH 45267; Sunny Y. Lu, M.D., Jennifer M. Klug, B.S., Eugene Somoza, M.D., Robert B. Norgren, Ph.D.

Educational Objectives:

To present data relating to recent advances in our understanding of the mechanisms of drug addiction.

Summary:

Exposure of animals to psychomotor stimulants such as amphetamine or cocaine induces an increase in the behavioral effects to these drugs on subsequent exposure. This sensitization to the behavioral effects of psychomotor stimulants has been suggested to be mediated via an increase in the release of dopamine in the basal ganglia. However, in dopamine deafferented rats there is also

a behavioral sensitization following multiple challenges with apomorphine implying a postsynaptic component of the sensitization response. D-amphetamine stimulates the transcription of the immediate response gene c-fos in rat striatum, and therefore the c-fos protein can act as a neurochemical marker of postsynaptic responses to d-amphetamine. We therefore investigated c-fos induction in rat striatum following multiple exposure to d-amphetamine.

Male Sprague-Dawley rats (200-250 g) were placed in a plexiglass box (40 × 40 × 30 cm) and were administered an initial injection of either d-amphetamine (5 mg/kg i.p.) (n = 7) or an equal volume of saline (n = 8), and three hours later were returned to their home cage. After three days rats were replaced into the same environment as previously, and all rats were administered d-amphetamine (2.5 mg/kg i.p.). Three hours post-injection rats were perfused and brain sections were processed for immunocytochemistry for c-fos. In striatum from rats challenged twice with amphetamine there was a significant increase in the total number of c-fos immunoreactive nuclei and in the intensity of the immunoreactivity compared with that observed in the striatum of rats that had received a single challenge with d-amphetamine. There is an apparent sensitization of the response of striatal cells with respect to c-fos induction following multiple exposures to d-amphetamine. This change in gene expression may represent a mechanism by which long-term changes in sensitivity to psychomotor stimulants might be produced.

References:

Norman, A.B., Wyatt, L.M., Hildebrand, J.P., et al. Sensitization of rotation behavior in rats with unilateral 6-hydroxydopamine or kainic acid-induced striatal lesions. *Pharmacology Biochemistry & Behavior,* 37: 755-759, 1990.

Graybiel, A.M., Moratalia, R. and Robertson, H.A. Amphetamine and cocaine induce drug-specific activation of the c-fos gene in striosome-matrix compartments and limbic subdivisions of the striatum. *Proc. Natl. Acad. Sci.,* 87: 6912-6916, 1990.

NR560 Thursday May 7, 12:00 noon-2:00 p.m.

Drug Abuse/Dependence in Early-Onset Depression

Kimberly C. Burke, M.S., Psychiatry, Texas A&M University, 2401 S. 31st St Alexander Bldg, Temple, TX 76508; Jack D. Burke, Jr., M.D., Donald S. Rae, M.S.

Summary:

Purpose: Using data collected as part of the NIMH Epidemiologic Catchment Area (ECA) Program, this analysis extends previous demonstrations of a link between drug abuse/dependence and depression.

Sample: The ECA studied 20,861 community and institutional respondents across five U.S. sites using the Diagnostic Interview Schedule (DIS), and includes information on the prevalence and age at onset for specific DIS/DSM-III disorders.

Results: (1) Higher prevalence: The lifetime prevalence rate for drug abuse/dependence is significantly higher among subjects with a history of major depressive episode, and the prevalence of drug abuse/dependence is even greater when the depression began before age 20. (2) Earlier onset: For respondents whose depression began at age 20 or earlier, the probability of developing drug abuse/dependence peaks between the ages of 15 and 19; for respondents whose depression began after age 20, the probability of developing a drug disorder peaks between ages 25 and 29. Similar, but less striking results are found for drug abuse/dependence associated with panic or obsessive compulsive disorder.

Conclusion: These findings highlight the need for prospective studies of children and adolescents to determine whether early, effective treatment of major depression can reduce subsequent drug abuse/dependence and whether a sub-population of "high-risk" teenagers can be identified.

NR561 Thursday May 7, 12:00 noon-2:00 p.m.

Relapse Following Cognitive Therapy of Depression

Michael E. Thase, M.D., Psychiatry, WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213; Anne Simons, Ph.D., Edward Friedman, M.D.

Summary:

We studied the risk of relapse of major depression following successful treatment with Beck's cognitive therapy in order to document potential indications for longer-term models of treatment. Forty-eight outpatients who responded during a 16-20-week course of cognitive therapy entered a one-year, prospective follow-up, and clinical assessments were completed at 1, 3, 6, 9, and 12 months post-treatment. Relapse was defined by a two-week period meeting DSM-III-R criteria for major depression *and* a Hamilton depression score ≥15. Sixteen patients (32%) relapsed during the follow-up. Clinical correlates of relapse included a history of recurrent depression, higher intake and end-of-treatment levels of depressive symptoms and dysfunctional attitudes, unmarried status, and a slower response to therapy. Patients who recovered during the 16 weeks of therapy (defined by Hamilton depression scores ≤6 for ≥8 weeks) were at significantly lower risk for relapse (9% vs. 52%). Using the Cox proportional hazards regression model, slower response to therapy, unmarried status, and high residual scores on the Dysfunctional Attitudes Scale were significantly related to relapse. These findings provide further evidence of a relationship between residual symptomatology and relapse after cessation of therapy. Moreover, the 52% relapse rate in partially recovered patients is strongly suggestive of the need for therapeutic alternatives to time-limited treatment. We strongly recommend that longer-term models of treatment be developed for depressed patients who do not recover fully during a short-term course of cognitive therapy.

NR562 Thursday May 7, 12:00 noon-2:00 p.m.

Depression and Lymphocyte Function in Adolescents

Steven J. Schleifer, M.D., Psychiatry, UMDNJ Medical School, 185 South Orange Avenue E501, Newark, NJ 07103; Jacqueline Bartlett, M.D., Steven E. Keller, Ph.D.

Summary:

Major depressive disorder (MDD) in adults has been associated with altered mitogen responses and CD4+ cells. We investigated 306 healthy community adolescents (mean age 15.9 ± 1.7; 51% female; 85% African-American, 15% Latino) using the DISC-R (current MDD) and Hamilton Depression Scale (HDRS). Lymphocyte subsets, mitogen responses (PHA, ConA, PWM), and NK cell activity were assessed. Thirty-three met MDD criteria; mean HDRS was 5.2 ± 5.8 (range 0-34).

Associations of depressive disorder and symptomatology with immunity were tested in regressions controlling age, gender, and race. MDD predicted decreased PHA across all doses (F 5.7, $p < 0.02$). For ConA (F 2.5) and PWM (F 1.0), the direction of effects was similar, but not significant. MDD did not predict NK activity or lymphocyte numbers, except decreased %CD8+ cells (F 5.3, $p < 0.02$).

Similar effects were found with HDRS: possibly lower PHA (F 3.0, $p < 0.08$) and PWM (F 2.8, $p < 0.09$), but not ConA (F 2.2; ns); reduced %CD8+ (F 3.6, $p < 0.06$). Models including MDD and HDRS revealed diminished but persistent PHA effects for MDD (F 2.9, $p < .09$), not HDRS (F 0.2; ns).

MDD in adolescents appears associated with lymphocyte functional changes similar to that in adults. Unlike adult MDD, we found no independent association of depressive symptoms per se with

immune measures. Some psychobiological mechanisms may be common to adult and adolescent MDD.

NR563 Thursday May 7, 12:00 noon-2:00 p.m.

Carbamazepine Induces Bupropion Metabolism

Terence A. Ketter, M.D., NIMH Bldg 10 RM 3N212, 9000 Rockville Pike, Bethesda, MD 20892; Janice Barnett, Pharm.D., David H. Schroeder, Ph.D., Melvin L. Hinton, B.S., John Chao, M.S., Robert M. Post, M.D.

Summary:

Objective: To assess the effect of carbamazepine (CBZ) on bupropion (BUP) pharmacokinetics.

Background: BUP may be less likely than other antidepressants to cause switches into mania and rapid cycling, suggesting utility in bipolar disorder. However, seizures can occur during high dose BUP therapy. Combination of BUP with the mood stabilizing anticonvulsant CBZ is a strategy that could lessen the risks of both mania and seizures. CBZ induces hepatic metabolism of various medications, but its effects on BUP have not been previously studied.

Methods: Three inpatients with mood disorders had pharmacokinetic profiles of BUP and metabolites assessed after single oral 150 mg doses of BUP both while receiving placebo and during chronic CBZ monotherapy. Paired one-tailed Student's t-tests were used to compare mean BUP and metabolite levels and pharmacokinetic parameters on CBZ versus placebo.

Results: CBZ therapy decreased BUP peak levels by 83% ($p < .01$) and 24-hour area under the curve (AUC) by 73% ($p = .03$), and increased hydroxybupropion peak levels by 153% ($p < .07$) and AUC by 101% ($p < .10$).

Conclusions: These data suggest that CBZ induces BUP metabolism in a robust fashion that could yield clinically significant decreases in BUP levels and increases in hydroxybupropion levels.

NR564 Thursday May 7, 12:00 noon-2:00 p.m.

Increasing Rates of Adolescent Depression

Andrew C. Leon, Ph.D., Psychiatry, Cornell Univ Med College, 525 East 68th Street, New York, NY 10021; Gerald L. Klerman, M.D., Myrna M. Weissman, Ph.D., Priya Wickramapaine, Ph.D.

Summary:

Clinicians and epidemiologists have observed increasing rates of adolescent depression in recent decades. A characterization of this phenomenon may eventually provide direction for prevention programs. Here we evaluate the effects of temporal trends (age, period and birth cohort) and risk factors associated with adolescent depression: family history of affective disorder, substance abuse and gender. The data come from two studies: a study of the general population (ECA) and a family study, the NIMH Collaborative Depression Study (CDS). Age-specific incidence rates for onset of MDD prior to age 21 are analyzed separately for the two samples.

The ECA data illustrate an increase in rates after puberty. The risk is elevated in the recently born cohorts (since World War II), females and substance abusers. The significant factors are identical in the CDS analyses, but the magnitude of the effects is lower. The CDS subjects, each with a family history of affective disorders, are vulnerable to adolescent MDD even in the absence of other risks. A limitation of focusing on this restricted age of onset is that the cohort and period effects are nearly indistinguishable.

The increasing rates have been paralleled by social change (e.g., high divorce rates, geographic mobility, economic change and political turmoil) that may have caused instability. Cross-cultural comparisons would be needed to evaluate the influence of social forces on depression.

NR565 Thursday May 7, 12:00 noon-2:00 p.m.

Bipolar Disorder in Infancy

Clifford H. Siegel, M.D., Psychiatry, Childrens Hospital, 1056 E. 19th Avenue Box B130, Denver, CO 80218; Pamela McBogg, M.D.

Summary:

Affective disorders are becoming more readily identified and treated in school-age children, but many very young children who will later be identified as having bipolar disorder are not identified during infancy in spite of having major difficulties. As a first step toward a prospective study on the identification of bipolar disorder in infancy, we performed a careful examination of the histories of 15 school-age children identified as bipolar both from their current symptoms and their response to treatment. In all 15 cases, there were strong family histories of mood disorders, as well as intricate record keeping of the children's early difficulties by the parents, either through diaries or videotapes. A review of their problems in infancy revealed a surprisingly common collection of symptoms around the theme of dysregulation. Not only was there early dysregulation of the child's affective responses, there was also dysregulation of sleep, feeding, and response to various perceptual stimuli. A tentative symptom list will be presented that could be used to prospectively follow infants and to consider early treatment.

NR566 Thursday May 7, 12:00 noon-2:00 p.m.

The Effectiveness of Drug Treatment in Depressed Patients

Avner Elizur, Psychiatry, Abarbnel MHC, BAT YAM, Israel; Zipora Bar, Henry Szor

Summary:

The present study evaluated and specified the benefits of combining cognitive therapy or marital therapy with drug treatment as opposed to drug treatment alone, in depressed patients. Sixty patients suffering from major depression or dysthymic disorder according to DSM-III-R criteria were selected. The patients were married and between 25 and 55 years old and divided into four matched groups according to diagnoses, sex, age and social-economic level. Treatment was weekly for 10-15 weeks, by trained psychotherapists. Follow-up evaluation was done six months later. Scales for depression, marital satisfaction, hostility, self concept and functional activity were used. Results indicate that all treatment modalities were significantly effective at the end of the treatment period. This was apparent in four out of five dimensions: level of depression, self esteem, hostility and functioning. The six-month follow-up evaluation demonstrated a significantly better effect of the combination of drug treatment with psychotherapy as opposed to drug treatment alone. Combination of marital therapy and drug treatment, however, was significantly superior to the combination of cognitive therapy and drug treatment and to drug treatment alone. This was apparent especially in three dimensions: level of depression, self esteem, and marital satisfaction. This on termination and after six-month follow-up.

Although all modalities were effective at termination, the combination of drug and psychotherapy had a longer lasting effect. Most significantly marital therapy and drug treatment.

NR567 Thursday May 7, 12:00 noon-2:00 p.m.

Cognitive Subtypes of Depression in Adolescents

John B. Jolly, Psy.D., Psychiatry, Univ of Arkansas Med Sci, 800 Marshall, Little Rock, AR 72202; Janet M. Jolly, Blakozar Adam, M.D., Doug Reed, M.Ed.

Summary:

Sixty-four adolescent inpatients (M = 13.9, SD = 1.4) were classified as having either "sociotropic" (socially dependent) or "autonomous" (independent) personality styles (Beck, 1983) and assessed for subtype patterns of depressive symptoms. Subtype patterns have been identified in adults with sociotropic or autonomous personality styles and are hypothesized to be differentially related to cognitive therapy efficacy. In between-group comparisons, autonomous adolescents (AAs) reported significantly higher levels of hypothesized "autonomous" symptoms, $F(1,59) = 6.90$, $p < .01$, such as a loss of interest in people and feeling irritated and angry. Sociotropic adolescents (SAs) reported a significantly higher number of hypothesized "sociotropic" depressive symptoms, $F(1,59) = 5.49$, $p < .02$, such as help-seeking behaviors and relief with reassurance. An AA personality style was related to an autonomous symptom pattern ($r = .46$, $p < .0001$), and a SA personality style was related to a sociotropic symptom pattern ($r = .41$, $p < .001$), but styles were unrelated to opposite symptom patterns. Personality style and depression comorbidity was assessed: 71% of the depression-conduct disordered adolescents were AAs, while only 29% were SAs, and 69% of the depression-only adolescents were SAs, while only 31% were AAs. Results support Beck's (1983) personality style-symptom matching hypothesis and suggest this theory can be extended to adolescents and may assist in conceptualizing depressive comorbidity in youth.

NR568 Thursday May 7, 12:00 noon-2:00 p.m.

Differentiating Anxiety and Depression in Youths

John B. Jolly, Psy.D., Psychiatry, Univ of Arkansas Med. Sci, ACH 800 Marshall, Little Rock, AR 72202; Ross A. Dykman, Ph.D., David S. McCray, M.D., Janet M. Jolly, Melanie Wheeler, B.S., Rebecca Bregy, R.N.

Summary:

Beck's (1976) "cognitive content specificity hypothesis" was examined with 162 inpatient adolescents (M = 14.5 SD = 1.5) to determine whether depression and anxiety could be differentiated with self-report data in younger populations. No study has demonstrated cognitive content specificity with adolescent patients, though cognitive therapy strategies will differ based on cognitive differences in disorders. A principal components factor analysis with varimax rotation revealed four factors that accounted for 66% of the variance in adolescents' scores on the Cognition Checklist (Beck et. al, 1987). Factor 1 consisted of cognitions that included both depressive and anxious content (general cognitive content), while Factor 2 consisted of only anxiety cognitions (specific anxiety content), and two factors (3 & 4) consisted of only depressive cognitions (specific depressive content). General cognitive content was significantly correlated with, and predictive of, *both* Beck Anxiety Inventory (BAI) scores and Children's Depression Inventory (CDI) scores. Specific anxiety cognitions were significantly correlated with, and predictive of *only* BAI scores. Specific depressive cognitions correlated significantly higher with CDI than BAI scores and were predictive of *only* CDI scores. Results were interpreted in light of Beck's specificity hypothesis and Watson and Clark's (1991) "tripartite" theory of anxiety and depression: cognitive content corresponds to the symptom factors of specific depression, specific anxiety, and general distress.

NR569 Thursday May 7, 12:00 noon-2:00 p.m.

Depression in Schizophrenia: Self versus Observer Report

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Summary:

Objective: Prior research has indicated an inconsistent agreement between self report and observer assessments of levels of depression in schizophrenia. In this study a self-report scale, the Beck Depression Inventory (BDI), was compared with a new scale, the Calgary Depression Scale (CDS). The CDS is an observer scale with a structured interview designed to assess depression in schizophrenia. *Method:* 150 subjects, 100 outpatients and 50 inpatients with schizophrenia, were assessed using both the CDS and the BDI. *RESULTS:* Levels of depression as assessed by both scales were significantly correlated, Pearson product correlations of 0.79 $p < 0.0001$. When scores were standardized, levels of depression assessed by the Beck was significantly higher. Correlations between individual items of the two scales showed lack of correlations between several items. Correlations between factors of the two scales showed significant correlations with only the first CDS factor.

Conclusions: Depressed affect can be reliably assessed in schizophrenics by both self report and observer rating. Both observer report and self report depression are highly correlated. Differences in the content of the questions have as much if not a greater effect on the observed levels of depression as the modality of inquiry.

NR570 Thursday May 7, 12:00 noon-2:00 p.m.

Moclobemide in Major Depression and Dysthymia

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Summary:

Moclobemide, a new MAOI type A, was administered to 50 outpatients diagnosed with major depression (N = 16) and dysthymia (N = 34) using DSM-III-R. Female : male ratio was 2:1, with a mean age of 47.6 (18-66 years old). Moclobemide was given orally, in 150 mg capsules. This was an open trial with flexible dosage. Psychological assessment consisted of a structured psychiatric interview, Hamilton Psychiatric Rating Scale for Depression, and a Clinical Global Improvement Scale. A physical examination, EKG, routine blood chemistries, CBC with differential, and a urinalysis were done before the study and on study completion. Patients were evaluated weekly. The average daily dose of medication was 300 mg. in 44 cases, 600 mg. in two cases, and 450 mg. in four cases. Main side effects were anorexia, nausea, dizziness, headaches, restlessness, and insomnia. Side-effect intensity was mild to moderate. One case dropped out due to severe headaches. Therapeutic effect was noticeable by the 10th day. Results in both groups were statistically significant ($p < 0.01$).

NR571 Thursday May 7, 12:00 noon-2:00 p.m.

Paroxetine in the Prevention of Depression

Geoffrey C. Dunbar, M.D., CNS, Smith Kline Beecham, 47-49 London Road, Reigate SY RH3 2YF, United Kingdoms: Dusan Petrovic, M.D.

Summary:

Patients with a history of recurrent depression (DSM-III-R, 296.3) and presenting acutely with a Hamilton Depression Rating Scale (HAMD) score >18, were treated with paroxetine (20-40 mg) for eight weeks. Those with a HAMD score ≤8 at the end of this period were randomised to either paroxetine (20-30 mg) or placebo for up to one year. A total of 172 patients entered the initial phase of the study, while 135 (78%) proceeded into the double-blind phase. Sixty-eight patients received paroxetine and 67 patients received placebo. Reappearance of depression during the first four months was regarded as relapse, but between five and 12 months

as recurrence. Considering relapse, overall 3% paroxetine and 19% placebo patients ($p \leq 0.01$) withdrew from the study. The figures for recurrence were 14% and 30%, respectively ($p \leq 0.05$). Kaplan Meier survival curves indicated a significantly longer ($p \leq 0.01$) time to relapse and time to recurrence for paroxetine compared with placebo-treated patients.

These data provide strong evidence that paroxetine is effective in preventing depressive relapse or recurrence.

NR572 Thursday May 7, 12:00 noon-2:00 p.m.

Effects of Paroxetine on Sleep EEG

L. Staner, M.D., Psychiatry ULB, Erasme Hospital, Route de Lennick 808, Brussels 1070, Belgium; J. Mendlewicz, M.D., M. Kerkhofs, M.D., D. Detroux, M.D., E. Bouillon, M.D., Prof Juan Ramon de la Fuente, M.D.

Summary:

Paroxetine was compared with amitriptyline in a double-blind study of 40 inpatients aged 18-65 years, fulfilling DSM-III-R criteria for major depression. After 10 days placebo washout, patients were randomized to one of two treatment regiments: (1) Two days placebo followed by paroxetine 20 mg for one week and then paroxetine 40 mg for four weeks; (2) Two days placebo followed by amitriptyline 150 mg in divided doses, for four weeks. Sleep EEG recordings were performed at the end of the four day placebo-habituation period, on days 1 and 2 of active treatment (acute effects) and at the end of the four-week treatment period (subchronic effects).

Both paroxetine and amitriptyline resulted in significant reductions in total REM sleep and increase in REM latency, with no significant differences between treatments.

Amitriptyline produced a significant increase in total sleep time and sleep efficacy index and a significant decrease in sleep-onset latency. Paroxetine had no significant effect on these variables.

In common with other antidepressants, paroxetine was found to increase REM latency. However, in all other respects this SSRI was found to be essentially neutral in its effects on sleep architecture.

NR573 Thursday May 7, 12:00 noon-2:00 p.m.

Thyroid Hormones and TSH Response to TRH

Marie-Claude Mokrani, Ph.D., Psychiatry, C.H. Specialise, Forenap 27 Rue Du 4 R.S.M., Rouffach 68250, France; Fabrice Duval, M.D., M. Antoine Crocq, M.D., Juarez Oliveira Castro, M.D., Sergio Valdivieso, M.D., Jean-Paul Macher, M.D.

Summary:

The feedback of thyroid hormones on TSH secretion, before and after 8 a.m. and 11 p.m. TRH challenges, was evaluated, on the same day, in 41 drug-free DSM-III-R euthyroid major depressed (MD) inpatients and 16 hospitalized controls. Compared with controls, MDs showed: 1) higher baseline (BL) free triiodothyronine (FT3) at 8 a.m. ($p < 0.005$) and 11 p.m. ($p < 0.05$), higher BL free thyroxine (FT4) at 11 p.m. ($p < 0.05$); 2) lower TSH levels at 11 p.m. ($p < 0.01$), lower TSH response to TRH (ΔTSH) at 11 p.m. ($p < 0.005$)—but only a trend toward blunting at 8 a.m. ($p = 0.08$)—and blunted ΔTSH (difference between 11 p.m.- and 8 a.m.-ΔTSH) ($p < 0.00005$). In the total sample and in depressed patients, BL FT4 correlated negatively with ΔTSH at 8 a.m. ($p < 0.004$ and $p < 0.01$, respectively) and 11 p.m. ($p < 0.001$ and $p < 0.04$, respectively). In patients only, BL FT4 was higher ($p < 0.0001$) and BL TSH lower ($p < 0.03$) at 11 p.m. than 8 a.m. This suggests that the pathophysiology of TSH response to TRH in depression may involve a dysregulated chronobiological pattern of thyroid hormone feedback, in association with other putative mechanisms such as an alteration in TRH receptors sensitivity.

NR574 Thursday May 7, 12:00 noon-2:00 p.m.

TRH-TSH Test, DST and Prognosis of Depression

Fabrice Duval, M.D. Psychiatry, C.H. Specialise, Forenap 27 Rue Du 4 R.S.M., Rouffach 68250, France; Juarez Oliveira Castro, M.D., Sergio Valdivieso, M.D., Marie-Claude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Jean-Paul Macher, M.D.

Summary:

TRH-induced TSH stimulation (ΔTSH) at 8 a.m. and 11 p.m. and post-dexamethasone cortisol (DST) were assessed after washout and after four weeks of antidepressant treatment (ADT) as predictors of 12-month outcome in 33 patients with DSM-III-R recurrent major depression (MD). After washout, six (18%) MDs had a blunted 8 a.m.-ΔTSh (i.e., < 3.5 μU/ml), 10 (30%) had a blunted 11 p.m.-ΔTSH (i.e. < 6 μU/ml), 22 (67%) had a blunted ΔTSH (difference between 11 p.m.- and 8 a.m.-ΔTSH) (i.e. < 2.5 μU/ml), and nine (27%) were DST nonsuppressors (plasma cortisol > 120 nmol/l). After four weeks of ADT, 17 patients had a good clinical response (HRS-D < 8), seven a partial response, and nine a poor response (HRS-D > 16). Pretreatment DST and TRH-TSH results were not predictive of greater ADT response. Normalization of DST (56%) and ΔTSH (41%) was associated with a good response at four weeks ($p < 0.01$ and $p < 0.00005$, respectively) and a full six-month remission ($p < 0.03$ and $p < 0.001$, respectively). Follow-up after one year showed that recovery ($n = 15$) was predicted by normality of all DST and TRH test responses (i.e. 8 a.m.-ΔTSH, 11 p.m.-ΔTSH, ΔTSH) after one month of treatment, whereas ADT resistance ($n = 3$) or recurrence ($n = 2$) were predicted by the association of abnormal responses to all tests at one month ($p < 0.001$). Our results suggest that DST and TRH test results may be state-related markers of clinical progress and predict long-term ADT response in recurrent depression.

NR575 Thursday May 7, 12:00 noon-2:00 p.m.

Life Events at Onset of Bipolar Disorder in Pedigrees

Victor I. Reus, M.D., Psychiatry, University of Calif., 401 Parnassus Ave Box F-0984, San Francisco, CA 94143; Mitzi Spesny, M.S., Michael Escamilla, M.D., Alvaro Gallegos, M.D., Pedro Leon, M.D., Nelson Freimer, M.D.

Summary:

Large multigenerational pedigrees may be exceptionally informative not only for determination of genetic linkage, but also for examining the range and magnitude of environmental effects that predispose to the expression of the genetic influence. As yet, however, there is no consensus as to how the taxonomy of such environmental influences should be structured or quantified, or what the relative importance of shared versus non-shared environmental effects is. We are currently investigating three extended pedigrees in Costa Rica, all including probands with confirmed bipolar-I illness and containing at least 30 individuals affected with bipolar-I or bipolar-II disorders. Each family contains 200-400 living members with known addresses. The geographic mobility in these pedigrees has been limited, and extensive family, church, and government geneologic records are available dating back to the 18th and early 19th centuries, in addition to a central medical records data base containing histories of virtually all patients treated in the country over the past 100 years. In preparation for a prospective study that would systematically assess members at risk, we have initiated an extensive retrospective analysis of records on all known affected members in order to determine the types of events that led to the initial onset of illness and to subsequent episodes. Patterns of similarity and differences in types of precipitant events within an individual's course of illness, between individuals in the same pedigree, and between independent pedigrees will be presented and discussed.

NR576 Thursday May 7, 12:00 noon-2:00 p.m.

Lithium and Tardive Dyskinesia in Affective Disorder

Abdu' L-Missagh Ghadirian, M.D., Allan Memorial Inst., 1025 Pine Avenue West, Montreal Quebec H3A 1A1; Lawrence Annable, D.S., Guy Chouinard, M.D., Marie-Claire Belanger, R.N.

Summary:

Affective disorder and lithium (Li) treatment appear to increase the risk of neuroleptic-induced tardive dyskinesia (TD). We surveyed the prevalence of extrapyramidal symptoms in 130 affective disorder outpatients (52 men and 78 women), most of whom had limited exposure to neuroleptics. *Method:* 110 patients with bipolar disorder, 18 with unipolar depression, and two with atypical affective disorder, were assessed for parkinsonism and TD by a single psychiatrist using the Extrapyramidal Symptom Rating Scale. Patients were aged 20-68 (mean: 44). Of 110 patients receiving Li, 17 did so in combination with antidepressants, 19 with neuroleptics, and 51 had no history of neuroleptic treatment during the previous six months. Mean duration of Li treatment was 68 months. Mean plasma prolactin level in men was 8.3 ($\pm$6.4) ng/ml, and in women was 14.3 ($\pm$15.3) ng/m. *Results:* The prevalence of TD meeting the Schooler and Kane Research Criteria was 10.9% in patients treated with Li, 0.0% in others, and did not vary significantly ($p < 0.05$) with the presence of neuroleptics. Dyskinetic movements in the buccal-lingual region were present in each case and were the dominant area of involvement in nine of 12 patients. Tremors were present in 24.6% of patients receiving Li, and 0.0% of others. Hypokinetic parkinsonian symptoms were present in 24.6% of those receiving Li, and 10.0% of others. *Conclusion:* These results in patients with little recent exposure to neuroleptics are consistent with reports that affective disorder patients treated with Li may be at increased risk for TD.

NR577 Thursday May 7, 12:00 noon-2:00 p.m.

Prevalence and Onset of Bipolar Illness in Adolescent Inpatients

Abdu'L-Missagh Ghadirian, M.D., Douglas Hospital, McGill University, 6875 LaSalle Blvd., Verdun PQ H4H 1R3, Canada; Normand Roux, M.D.

Summary:

Research on clinical diagnosis of depression in childhood and adolescence has been substantial in recent years. However, our knowledge of early onset of bipolar affective disorders, particularly mania, during adolescence is very limited. We conducted a retrospective study of 236 adolescent patients hospitalized at the Allan Memorial Institute from 1980 to 1988. There were 120 male and 116 female patients with a mean age of 16.15 years. Forty-two patients (17.79%) were diagnosed, having affective disorders as follows: 18 (7.62%) bipolar illness (14 manic phase, two depression, two mixed type); 22 (9.32%) neurotic depression, and two (0.84%) schizoaffective disorder. Seven out of 18 patients (38.88%) had a family history of affective disorders. All bipolar patients fulfilled diagnostic criteria of Weinberg and Brumback (1976) for depression and mania, and 14 (77.77%) of them also manifested delusions with or without hallucinations. The ratio of male to female for neurotic depressives was 1 to 2, but for the bipolar patients was almost equal. The ages of bipolar patients at the onset and at hospitalization were 15.61 and 16.94 years, respectively. The mode of onset of bipolar disorder before hospitalization was as follows: seven with depression, three mania or hypomania, five psychotic feature, two borderline personality and one anxiety disorder. Ten out of 18 patients were treated with lithium combined with neuroleptics since their response to lithium alone was unsatisfactory. We found an underdiagnosis of bipolar illness, especially mania. Additional data and analysis will be discussed.

NR578 Thursday May 7, 12:00 noon-2:00 p.m.

Desipramine Levels after Sertraline or Fluoxetine

Sheldon H. Preskorn, M.D., Psychiatry, University of Kansas, 1010 North Kansas, Wichita, KS 67214; Jeffrey Alderman, Ph.D., Michael Messig, Ph.D., Stuart Harris, M.D., Menger Chung, Ph.D.

Summary:

Concomitant administration of fluoxetine, a selective serotonin reuptake inhibitor (SSRI) antidepressant, and tricyclic antidepressants has been reported to substantially elevate plasma tricyclic concentrations, raising concerns about tricyclic toxicity. Sertraline, a recently approved SSRI antidepressant, has a shorter half-life than fluoxetine and may have less potential for interaction with tricyclics. The objective of this study was to evaluate comparative metabolic interactions of sertraline and fluoxetine with desipramine. Eighteen healthy male volunteers were administered desipramine (50 mg/day) and concomitantly given either fluoxetine (20 mg/day) or sertraline (50 mg/day) for 21 days. Desipramine concentrations were determined after seven days of desipramine dosing alone, during 21 days of SSRI co-administration, and for 21 days of continued desipramine administration after SSRI discontinuation to determine duration of residual metabolic interaction. Preliminary analysis indicated that desipramine concentrations four hours after dosing were increased up to four-fold relative to baseline for fluoxetine, whereas only minimal changes were observed with sertraline. This increase was significantly greater with fluoxetine than sertraline ($p \leq 0.01$). Following SSRI discontinuation, desipramine levels in the sertraline group approached baseline within one week, while desipramine levels remained significantly above baseline for the three week follow-up period in the fluoxetine group.

NR579 Thursday May 7, 12:00 noon-2:00 p.m.

Long-Term Treatment of Major Depressive Disorder with Paroxetine

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Summary:

Recurrent unipolar depression is a common, but undertreated, disorder. Many patients require long-term maintenance therapy, and full doses of antidepressants may be preferred for the prevention of relapse. We report results of a one-year, multi-center, open-label study of paroxetine (10-50 mg/day) in 433 patients with major depressive disorder, with additional data from 110 patients who entered a long-term extension of the study.

The primary measures of efficacy were the HAMD total and CGI Severity of Illness. During the first six weeks of therapy, the mean HAMD total declined approximately 50 percent (from 27.9 to 13.5), with continued improvement at an attenuated rate, throughout the first year. At the end of one year, the mean HAMD total was 6.9. Similarly, the CGI declined from a baseline score of 4.6 to 2.8 at week 6, to 1.7 at the end of one year. Remission was maintained in the population that entered the long-term extension, with mean HAMD total and CGI severity of illness scores of 7.4 and 1.9, respectively, after 2.5 years. The most common adverse events reported during long-term treatment were somnolence, nausea, headache and sweating.

Pharmacokinetic analysis showed no correlation between plasma concentrations of paroxetine and either clinical efficacy or tolerability. There was no increased drug accumulation during long-term treatment, and no new side effects were reported.

Paroxetine is safe and effective in the long-term treatment of depression.

NR580 Thursday May 7, 12:00 noon-2:00 p.m.

Paroxetine is a Selective Serotonin Reuptake Inhibitor in Man

D. R. Nelson, CNS PSU, Smith Kline Beecham, Cold Harbour Road, Harlow Essex CM195AD, United Kingdom; Katharine J. Palmer, B.Sc., Tim C. Tasker, M.B., Ian F. Tulloch, Ph.D.

Summary:

Paroxetine, a potent and selective serotonin reuptake inhibitor in animal studies, is a clinically effective antidepressant. The aim of this study was to determine whether paroxetine is a specific serotonin reuptake inhibitor in man. Paroxetine was given daily in single oral doses (10 mg increasing to 40 mg by day 7) to healthy volunteers for 28 days. Plasma samples obtained at predose, days 1, 2, 7 and 28 of dosing and day 42 (following a 14-day washout period) from placebo or paroxetine treatments were assessed for their ability to inhibit (3H)-serotonin or (3H)-norepinephrine (NE) uptake into rat cortical synaptosomal preparations. Samples obtained from those volunteers ($n = 10$) receiving paroxetine weakly inhibited (3H)-serotonin uptake 2, 4 and 6 hours after the first dose (10 mg) on day 1. Significant serotonin uptake inhibition was observed at steady-state levels on days 7 and 28 (54% and 65% respectively). No inhibition of (3H)-serotonin uptake was observed with plasma samples following the washout period. In contrast, plasma samples from volunteers receiving paroxetine did not affect (3H)-NE uptake, while samples obtained from placebo-treated volunteers ($n = 8$) had no detectable effect on either (3H)-serotonin or (3H)-NE uptake. Therefore, plasma from volunteers receiving paroxetine inhibits (3H)-serotonin but not (3H)-NE uptake into rat cortical synaptosomes. In summary, this study demonstrates that paroxetine, when administered at clinically relevant doses, is a selective serotonin reuptake inhibitor in man.

NR581 Thursday May 7, 12:00 noon-2:00 p.m.

Symptom Profiles of Abnormal DST and Clonidine Test

Sergio Valdivieso, M.D., Psychiatry, C.H. Specialise, Forenap 27 Rue Du 4 R.S.M., Rouffach 68250, France; Fabrice Duval, M.D., Marie-Calude Mokrani, Ph.D., Marc-Antoine Crocq, MD., Nicolas Schaltenbrand, Ph.D., Jean-Paul Macher, M.D.

Summary:

Dexamethasone suppression test (DST) and clonidine test (CLO) results were studied in relation in to the 17-item Hamilton Depression Rating Scale (HDRS) in 47 drug-free inpatients with a DSM-III-R major depressive episode and 20 hospitalized controls. Compared with controls, patients showed higher post-DST cortisol values ($p < 0.001$), and lower CLO-induced growth hormone stimulation (ΔGH) ($p < 0.0001$). Test results defined four groups: Group 1 comprised 19 patients (40%) with blunted ΔGH alone (i.e. $\Delta GH < 5$ ng/ml); Group 2, 12 patients (26%) with the association of DST nonsuppression (i.e. plasma cortisol > 140 nmol/l) and blunted ΔGH; Group 3, 14 patients (30%) with no abnormality. Group 4, with two patients (4%) who showed only DST nonsuppression, was excluded from the statistical analysis because of its small size. A selection of HDRS items was performed using a criterion that maximized inter-group variance to total variance ratio, and produced three items (loss of interest, somatic anxiety, and loss of insight) to base discriminant analysis. Correct classification of patients reached 79% for Group 1 and 64% for Group 3; Group 2 patients were poorly discriminated by these items, since only 33% were correctly classified. These results suggest that the distribution of neuroendocrine abnormalities, notably blunted post-CLO ΔGH, which reflects a possible alpha 2-adrenoreceptor dysfunction, may be associated with a particular profile of depressive symptoms.

NR582 Thursday May 7, 12:00 noon-2:00 p.m.

Sex in the State of Depression

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Summary:

Alterations in libido are commonly thought to accompany the depressed state. We previously have shown that reductions in sleep-related penile tumescence (NPT) occur in depressed men. This study addresses the issues of whether these alterations in NPT improve with recovery from depression and whether these physiological changes are correlated with alterations in sexual attitudes, activity and behavior as the depression remits. Forty unmedicated, outpatient, depressed men were treated for their depression using cognitive behavior therapy over a 16-week acute-treatment period. Subjects completed a 14-day sexual function log, a Brief Sexual Function Questionnaire, the Derogatis Sexual Function Inventory, urologic assessment, sleep EEG and NPT studies both during the acute depressed state and following treatment. Repeated measures ANCOVA's were used to test hypotheses that sexual function and NPT measures would be altered over the course of treatment of depression. NPT alterations do not improve as depression improves and appear to be unrelated to changes in depression or sexual attitudes and behavior. The "loss of libido" in depression appears to be more reflective of the negative cognitive set of depression (loss of sexual satisfaction) rather than indicative of loss of sexual behavior. Sexual function appears to be heterogeneous in depression with some men reporting increased sexual drive and activity. This pattern was more prevalent in a subgroup of depressed men who did not respond to CBT, were more often classified as intermittent depressives, and who exhibited increased anxiety.

NR583 Thursday May 7, 12:00 noon-2:00 p.m.

Gender and Outcome of Major Depression

Christine Ryan, Ph.D., Butler Hospital, 345 Blackstone Blvd, Providence, RI 02906; Gabor Keitner, M.D., Ivan Miller, Ph.D.

Summary:

Major depression occurs two to three times more often in women than in men. Aside from prevalence rates, few studies use gender as a basis of comparison to examine the course and outcome of a depressive episode. We collected data on 78 inpatients with major depression during hospitalization and at monthly intervals for 12 months. Female patients experienced more hospitalizations for depression than did male patients (1.0 vs .29, $t = 3.23$, $df = 71.6$, $p < .01$). No other gender differences were found on clinical, psychosocial, or sociodemographic variables at the acute stage of the illness. Monthly comparisons of depressive symptoms (HRS-D) and interepisodic adjustment (GAS) reflected improvement for both male and female patients; but male scores on the HRS-D were significantly better than females at the sixth month after discharge and tended towards significance at months 7-8. Male patients were 2.5 times more likely to recover than their female counterparts. Patients with a comorbid illness had similar recovery rates; but for the pure depressed, males were significantly more likely to recover than females (100% vs 50%, $X^2(1) = 7.17$, $p < .01$). Using the Family Assessment Device (FAD), families of all patients reported improvement in the family's functioning over the course of illness. However, families of male patients consistently reported better family functioning than did families of female patients, significantly so in the areas of roles and behavior control. Thus, while male and female depressed patients appear similar during hospitalization, males show steadier improvement and have better recovery rates than females. The differences between male and female patients

are particularly striking in family functioning, an area that is amenable to clinical intervention.

NR584 Thursday May 7, 12:00 noon-2:00 p.m.

Chronicity in Geriatric Depression

George S. Alexopoulos, M.D., Psychiatry, NYH WD Cornell UMC, 21 Bloomingdale Road, White Plains, NY 10605; Barnett S. Meyers, M.D., Robert C. Young, M.D., Tatsuyuki Kakuma, Ph.D., Janis Chester, M.D., Eileen Rosendahl, Ph.D.

Summary:

Follow-up studies of one- to six-year duration show that depression becomes chronic in up to 30% of the depressed elderly population or in 40% if partially remitted cases are considered. In mixed-age populations, the Collaborative Depression Study observed that the strongest predictor of chronicity is chronicity itself; those patients whose episodes were already chronic upon entering the study had a low recovery rate. This study is an early report from an ongoing longitudinal investigation that seeks to identify predictors of chronicity of geriatric depression. The subjects were 68 patients who met RDC criteria for major depression. Of these, 56 were aged 60 years or older and 12 were younger than 60 years. The subjects were followed for an average period of 46.7 weeks (SD: 20.7). Analysis with the Life Table method showed that the time from entry to the study until recovery of the elderly subjects (mean: 46.4 weeks, SE: 8.9) was comparable to that of younger adults (mean: 32.8 weeks, SE: 6.7). Use of the proportional hazard model in the elderly subgroup showed that the most powerful predictor of long time to recovery was the lack of social support (Wald $x^2 = 5.09$, $P < 0.02$) and use of treatments other than ECT (Wald $x^2 = 3.79$, $P < 0.05$). There was an association between length of the depressive episode prior to entry and long time to recovery. However, significance was not reached (Wald $x^2 = 2.12$, $P < 0.14$). Interventions strengthening patients' social supports should be studied for their efficacy as adjunct antidepressant treatment in the elderly.

NR585 Thursday May 7, 12:00 noon-2:00 p.m.

Sleep Deprivation Hormonal Response in Depression

Richard C. Shelton, M.D., Psychiatry, Vanderbilt University, 1500 21st Avenue South RM 2239, Nashville, TN 37212; Peter T. Loosen, MD., David N. Orth, M.D.

Summary:

Sleep deprivation (SD) induces a rapid but transient improvement in the symptoms of major depression. Relatively little is known, however, about the underlying mechanism by which SD exerts its effect. The current study aims to evaluate: 1) the nocturnal secretion patterns of plasma ACTH and of serum cortisol, TSH, GH, and PRL as reflected by the 12-hour integrated plasma/serum hormone concentration, pulse frequency, duration, and amplitude; 2) the response of ACTH/cortisol, TSH, and GH to their respective hypothalamic releasing hormones (*i.e.*, oCRH, TRH, and hGRH); and 3) the association between altered nocturnal hormone secretion and the behavioral response to SD. *Methods:* Eighteen outpatients, aged 18-55 years, with major depression (SCID-P) and 10 age- and sex-matched normal volunteers underwent one night of total SD. Depression was rated before and after SD using a modified version of the HRSD, the SD Depression Rating Scale (SDDRS). Blood was collected every 15 minutes for 12 hours (10 pm-10 am), and oCRH (1 lg/kg), TRH (200 lg) and hGRH (1 lg/kg) were administered iv the following afternoon. *Results:* Ten depressed patients (56%) responded to SD with a 30% reduction in SDDRS. Nocturnal concentrations of plasma ACTH and serum cortisol, GH, and PRL were similar in SD responders, nonresponders, and controls, as were their GH responses to hGRH. Although a repeated measures ANOVA revealed significant time effects for ACTH and cortisol for all groups (reflecting normal increases in ACTH and cortisol secretion during the later part of the night), the rate of increase did not differ significantly among groups, and the ACTH and cortisol responses to oCRH were similar. In contrast, nocturnal serum TSH concentrations were abnormally high in SD responders throughout the observation period, and their TSH responses to TRH were exaggerated; both were similar to those of normals in SD nonresponders. The data suggest that the 56% of depressed patients who responded to SD had either mild, compensated hypothyroidism or peripheral resistance to thyroid hormone action.

NR586 Thursday May 7, 12:00 noon-2:00 p.m.

The Effects of Antidepressants on the Thyroid Axis

Richard C. Shelton, M.D., Psychiatry, Vanderbilt University, 1500 21st Avenue Room 2239, Nashville, TN 37212; Peter T. Loosen, M.D.

Summary:

The relationships between the thyroid axis and depressed mood are now well described. What is less well known, however, are the effects of antidepressants on the axis. We have done a study of outpatients with major depression treated with desipramine (DES) or fluoxetine (FLU) in order to assess the effects of the drugs on the axis. *Methods:* The subjects were 16 male and 23 female medically healthy outpatients (mean age 39.6 ± 10.3) with major depression (SCID-P). The mean baseline 21-item HRSD was 24.5 ± 3.3 Nineteen subjects were randomly assigned to treatment with DES (mean dose 184.2 ± 52.8) and 20 given FLU (mean dose 31.0 ± 12.09) in a double-blind, placebo-controlled six-week trial. A TRH test was done by infusing 500 mcg. of proterilin, with q.15 min. sampling for two hours, at baseline and at week 6 of treatment. In addition, samples were drawn at baseline, and weeks 3 and 6 for T_3, total T_4 (TT_4), free T_4 (FT_4), and thyroid binding globulin (TBG). All samples were assayed by ultrasensitive radioimmunoassay. *Results:* The two samples did well with the treatments, with an average of 58.3% reduction in HRSD scores. Analysis of variance indicated no unequivocal differences over time for any of the samples for the total group. There was a trend ($p = 0.08$) for a reduction in TT_4. Repeated measures analysis of variance indicated differences for TT_4 between the DES and FLU groups ($F(2,34) = 4.49$, $p < 0.02$). Post-hoc analysis (Bonferroni's t) indicated that there was a small but significant reduction in TT_4 in the DES group ($M = -0.99 \pm 1.2$, $t = -2.86$, $p < 0.02$) but not the FLU group over time. Finally, change scores for the pre- and post-treatment thyroid tests were calculated and correlated with the change in HRSD scores. The only significant correlation was between the delta HRSD and the reduction in T_3 ($r = -0.52$, $p < 0.02$). When divided by drug, however, this was found for the FLU ($r = -0.62$, $p < 0.02$) but not for the DES groups. These results indicate that DES reduces TT_4, that FLU lowers T_3, and that the latter is associated with response. The implications of these data will be discussed.

NR587 Thursday May 7, 12:00 noon-2:00 p.m.

Efficacy of the Medical Outcomes Study Questionnaire as an Outpatient Screen for Dysthymic Disorder

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Summary:

Dysthymic disorder (DD) is a major public health problem, affecting 3% of American adults and 26% to 36% of patients in psychiatric clinics, yet DD is often underdiagnosed and under-

treated. Although screening instruments exist to detect major depressive disorder (MDD) among psychiatric outpatients, an analogous instrument has yet to be confirmed for DD. Thus, identifying an effective screening instrument for psychiatric outpatients who suffer from DD has significant public health value. We report results from a consecutive sample of 55 psychiatric outpatient evaluations validating the self-report Medical Outcomes Study Questionnaire (MOS) as a screen for DD and MDD, using the SCID-P as the diagnostic benchmark. Over a range of algorithmic cutpoints, the MOS yielded high sensitivity for DD and MDD across most prevalence intervals, demonstrating maximal sensitivity (94%) for DD at the .06 cutpoint, and 100% for the cutpoint of .009. These results independently replicate Burnam et al.'s original findings of high predictive utility of the MOS screener, now using the SCID-P rather than the DIS as the criterion of validity. The MOS appears to be an effective instrument for identifying outpatients with DD and MDD in a psychiatric outpatient setting.

NR588 Thursday May 7, 12:00 noon-2:00 p.m.

Critical Flicker Fusion as a Measure of Antidepressant Efficacy

Ian Hindmarch, Ph.D., University of Surrey, Milford Hospital, Godalming GU71UF, United Kingdom; John Kerr, Ph.D., Alex Alexander, M.D.

Summary:

Critical flicker fusion (CFF) threshold is a sensitive indicator of the effects of psychotropic agents on cognitive function. Small increases in CFF thresholds are correlated with improvement in many cognitive symptoms of depression.

Depressed outpatients (N = 100) with a score >18 on the first 17 items of the HAM-D were treated with either paroxetine (20 mg in the morning) or dothiepin (75 mg at bedtime) for one week, after which the dosages were increased to 30 mg paroxetine and 150 mg dothiepin for an additional five weeks. CFF thresholds were measured at baseline and after one, two, four, and six weeks of treatment.

After six weeks, there were no differences in antidepressant efficacy between the two treatment groups. At week one, patients treated with paroxetine showed an increase in CFF threshold compared to baseline (improved cognitive activity), whereas patients treated with dothiepin showed decreases in threshold ("sedation", poorer cognitive function). The difference in CFF threshold between the two groups was statistically significant ($p < .05$) at week two. Only after four weeks of treatment did patients receiving dothiepin show the improved therapeutic response seen at week one with paroxetine.

These results confirm the value of CFF as a measure of cognitive function and an indicator of therapeutic efficacy, and demonstrate the countertherapeutic effects of sedative tricyclic antidepressants compared with a selective serotonin uptake inhibitor.

NR589 Thursday May 7, 12:00 noon-2:00 p.m.

Mechanisms Underlying Antidepressant Action

Pedro L. Delgado, M.D., Psychiatry, Yale & West Haven VA, 950 Campbell Avenue, West Haven, CT 06516; George R. Heninger, M.D., Helen L. Miller, M.D., Lawrence H. Price, M.D., Ronald S. Salomon, M.D., Julio Licinio, M.D., Dennis S. Charney, M.D.

Summary:

Brain serotonin (5-HT) can be reduced by depleting plasma tryptophan (TRP). Brain catecholamines can be reduced by inhibiting their synthesis with the tyrosine hydroxylase inhibitor alpha-methyl-para-tyrosine (AMPT). We will present results from two studies: one study using rapid tryptophan (TRP) depletion and preliminary results from another study investigating the effects of AMPT on mood in patients having had therapeutic antidepressant responses to desipramine (DMI) or fluoxetine (FLU). *Method:* TRP depletion and AMPT tests were conducted in a double-blind, placebo-controlled, randomized crossover fashion. TRP depletion was as in our previously studies. Testing was performed in patients having had therapeutic responses to DMI or FLU. Each patient participates in two tests one week apart. Each AMPT test includes a baseline day, two days with AMPT 1 gm TID or diphenhydramine 50 mg TID and a follow-up day. Antidepressant drugs are continued throughout testing. Ratings (Hamilton Depression Scale [HDRS]) and plasma and urine (for either TRP levels or MHPG and HVA levels) were obtained prior to, during and after testing. Relapse was defined as a 50% increase in HDRS with total ≥20. *Results:* Six of 12 FLU responders but none of nine DMI responders relapsed with TRP depletion. Preliminary results with AMPT have revealed that the two patients tested after having had a therapeutic response to DMI had a rapid but transient return of severe depression, while the one patient tested after a therapeutic response to FLU only felt sleepy and tired during AMPT testing. *Implications:* Rapid depletion of plasma TRP transiently reverses antidepressant responses to FLU but not DMI. These results as well as the preliminary results of AMPT testing suggest that antidepressants may mediate their therapeutic effects through different neurobiological mechanisms. These studies highlight the importance of the noradrenergic and serotonergic mechanisms in antidepressant action.

NR590 Thursday May 7, 12:00 noon-2:00 p.m.

Diurnal Variation of the CSF CRH in Major Depression

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Summary:

Nearly all previous data concerning CSF levels of neurotransmitters and peptides in depression have been based on static, single time point determinations at around 9:00 a.m. However, it is now known that marked diurnal variations exist in the concentrations of many neuroregulators in the CSF of experimental animals, which may be of relevance not only to normal physiology, but also to the pathophysiology of psychiatric disorders. We report here a study in which we measured hourly corticotropin-releasing hormone (CRH) levels by RIA in CSF obtained during continuous sampling through an indwelling lumbar catheter inserted at 9-10 a.m. for 30 consecutive hours in six patients with RDC and DSM-III-R major depression, mean age 41.2 ± (s.e.) 3.9 yr, and six healthy subjects, mean age 35.2 ± 2.4 yr. Three of the depressed patients were restudied after successful electroconvulsive therapy (ECT). Blood samples were obtained in these subjects through an intravenous catheter at 30 minute intervals during the study. We observed significant diurnal variations in the CSF CRH levels in five of six patients and five of six controls (p ranging from <0.02 to <0.001 in individual subjects) by cosinor analysis; the oldest control showed a trend ($p < 0.07$). The phase of the CRH rhythm was inverted relative to the plasma cortisol rhythm, with peak levels of CRH observed in the evening and lowest levels in the morning. This finding agrees with data from two recent independent studies of nonhuman primates. In addition, ultradian variations were superimposed on the overall diurnal pattern of CSF CRH levels. The amplitude of both variations significantly exceeded assay variability ($p < 0.01$). Mean CSF CRH levels in the depressed patients did not differ significantly from controls, but showed greater intersubject variability. However, significant reductions in CSF CRH levels across nearly all time points ($p < 0.05$, paired t-test) were seen in all three depressed patients who were restudied following ECT-induced remission of depression. We conclude that there is a significant diurnal rhythm of CRH in human CSF, and that successful

treatment of depression by ECT is associated with reductions in centrally directed CRH secretion. Further studies utilizing continuous sampling of CSF may provide not only important normative information about temporal patterns in central neurohormone secretion in humans, but also insights concerning alterations of these patterns in psychiatric disorders and their pathophysiologic implications.

NR591 Thursday May 7, 12:00 noon-2:00 p.m.

Depression, Cardiac Regulation and Sudden Death

Gregory W. Dalack, M.D., Clin. Psychopharm, NYS Psychiatric Inst., 722 West 168th Street, New York, NY 10032; Steven P. Roose, M.D., Alexander H. Glassman, M.D., Sally Woodring, R.N., Thomas J. Bigger, M.D.

Summary:

Heart rate variability measurements reflect autonomic nervous system tone. For example, high frequency or "beat-to-beat" variability has been shown to quantitatively reflect parasympathetic tone mediated by the vagus nerve. This is of special interest since it is known that parasympathetic tone reduces vulnerability to ventricular fibrillation. Considering that depressed patients have a higher than expected mortality from sudden cardiac death, we hypothesized that parasympathetic tone in depressed patients would be diminished compared with normals.

We measured heart rate variability in 25 drug-free patients, aged 31-79 years, meeting criteria for DSM-III-R major depression, and 40 normal controls, aged 31-85. We calculated the proportion of absolute differences between R to R intervals >50 msec (pNN50), an index that measures high frequency variability, and hence parasympathetic tone. Dividing the high frequency variability measurements into bands of low, low to normal, and normal to high, the depressed patients were significantly more likely to have pNN50 values in the low and low normal ranges compared with controls.

pNN50:	LOW (≤2.5)	LOW-NORMAL (2.6-10)	NORMAL-HIGH (>10)
DEPRESSED	15[	n8[	n2[
CONTROL	n9	18	13

(Chi-square = 10.5, df = 2, $p < 0.01$)

This study suggests that depressed patients may have diminished parasympathetic tone, a fact that may illuminate the pathophysiology underlying the increased rate of sudden cardiac death in depression.

NR592 Thursday May 7, 12:00 noon-2:00 p.m.

Euthymia, Major Depression and Fluoxetine Response

Gregory W. Dalack, M.D., Clin. Psychopharm, NYS Psychiatric Inst., 722 West 168th Street, New York, NY 10032; Alexander H. Glassman, M.D., Sara Rivelli, Lirio S. Covey, Ph.D., Fay Stetner, M.S., Jill Becker, M.A.

Summary:

Traditionally, major depression is thought to be an episodic illness with a full recovery between episodes. We evaluated smokers presenting to our clinic for smoking cessation. At screening they were evaluated by SCID interview and excluded if they had a current major depression, schizophrenia or other substance abuse.

Initially, we examined 374 smokers. Among these smokers, 35% had a history of major depression. At baseline, before smoking cessation treatment was begun, those with a history of depression rated themselves as more depressed, more anxious, more angry, less effective and less vigorous than those without such a history, (all $p < 0.002$).

Pursuant to our observation that smokers are more likely to have a history of depression, and that such a history predicts failure to quit, we enrolled 38 subjects with a history of depression in a double-blind study testing the efficacy of an antidepressant (fluoxetine) in helping them quit. None were dysthymic and those with current depression were excluded. Baseline scores were similarly elevated as the population with a history of depression reported above. Twenty-one subjects were assigned to placebo and 17 to fluoxetine at a dose of 20 mg/d the first week and 40 mg/d for the following two weeks. The fluoxetine-treated group had significant decreases in measures of depression, anxiety and anger (all $p <$ .05).

These data highlight that individuals with a history of major depression, even when not overtly depressed, are more symptomatic, and that antidepressant treatment may ameliorate this subsyndromal level of symptomatology.

NR593 Thursday May 7, 12:00 noon-2:00 p.m.

Validation of a New Mania-Depression Scale

Verinder Sharma, M.B., Psychiatry, London Psychiatric, P.O. Box 2532 Stn. A., London ON N6A 4H1, Canada; Dwight S. Mazmanian, Ph.D., Emmanuel Persad, M.B., Karen Kueneman, B.A., Janice Burnham, B.Scn.N., Julie Franklin, RNA, Gloria Leiska, R.N., Mark Hemmings, R.N.

Summary:

The use of objective clinical rating scales can be a valuable adjunct to clinical judgment in determining response to treatment and readiness for hospital discharge. We describe a scale that was developed for use with inpatients on a mood disorders unit (Mania-Depression Scale). The scale provides for the rating of a patient's mood along a quantitative continuum ranging from −5 (depressive stupor) through 0 (euthymia) to +5 (full mania), with concrete behaviors listed as criteria for each rating point. The behavioral descriptors are based on DSM-III-R diagnostic criteria, and the cognitive, affective, vegetative, and social domains are sampled. Provision is also made for the assessment of "mixed states" and idiosyncratic behavior. The ratings are completed by nurses (or other clinicians), and the resulting scores appear sensitive to diurnal variation in mood, alternate states in bipolar patients, and longer-term response to treatment. Inter-rater reliabilities were high ($rs > .88$, $p < .01$). Validity estimates were obtained using patient self-report measures (Beck Depression Inventory, Visual Analogue Scale, rs .42-.69), and comparing nurse-completed and patient-completed ratings ($rs > .80$). Several case illustrations are also presented.

NR594 Thursday May 7, 12:00 noon-2:00 p.m.

oCRH Stimulation in Anxious Depression

William H. Meller, M.D., Psychiatry, University of Minn, 420 Delaware SE Bx 393 UMHC, Minneapolis, MN 55455; Paula J. Clayton, M.D., Roger G. Kathol, M.D., Stephen D. Samuelson, M.D., Timothy L. Gehris, B.S., Andrew F. Pitts, M.D.

Summary:

Recently, the association of anxiety symptoms to major depressive disorder has come under close scrutiny. Both family and neuroendocrine studies have suggested that anxiety symptoms may significantly alter the family history, course, outcome, and endocrine response of patients with major depression. The current study investigates the ability of the CRH challenge test to discriminate patients with anxious depression from those with nonanxious depression and control subjects.

Methods: Twenty-five patients with major depression and 25 normal control subjects received a 1.0 μg/kg IV injection of *o*CRH. Blood samples were drawn q5 minutes ×3 then q15 minutes. Plasma was assayed for ACTH and cortisol using specific RIAs developed at the University of Iowa CRC. Depressed patients were

divided into an anxious and nonanxious group using operational criteria developed by Clayton, et al (1991).

Results and Comment: As graphically displayed in Fig 1., patients with anxious depression had a significantly more attenuated ACTH response to CRH than patients with nonanxious depression. [Repeated measures ANOVA group by time factor ($F = 1.83$, DF = 2/47, DF = 12/280, $P = 0.04$)].

These data provide evidence of increased dysregulation of the hypothalamic pituitary adrenal axis in patients with operationally defined anxious depression and lend support to anxious depression as a useful subtype.

NR595 Thursday May 7, 12:00 noon-2:00 p.m.

Characterizing Organic Mood Syndrome: Depressed Type

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Summary:

The recently published DSM-IV Options book contains several fundamental and controversial proposals for changes in the diagnostic system for the organic brain syndromes, including organic mental syndrome, depressed type (OMS-D). For example, OMS-D would be combined with "functional" reactive depressions precipitated by medical stressors, forming a new diagnostic entity called secondary mood disorder. It is difficult to judge the validity of these proposed changes because of the lack of data concerning this diagnostic entity. For example, published descriptions of this disorder do not include such basic information as the average age, gender distribution, prevalence, specific symptomatology, or associated medical diagnoses.

A total of 130 cases of OMS-D presented at our institution out of a total of 14,889 patients evaluated between January 1, 1983, and December 31, 1987. OMS-D was the second most commonly diagnosed OBS, after dementia. The mean age of the OMS-D patients was 49 years, and included 61 men (47%) and 69 women (53%). The most common symptoms of this syndrome and the mean impairment in functioning were determined. Nineteen symptoms distinguished the OMS-D patients from the major depressive controls. The distribution of comorbid diagnoses, treatments, and EEG and CT abnormalities was determined. The most common group of medical diagnoses associated with this syndrome consisted of neurologic disorders, of which seizures, cerebrovascular accidents, and Parkinson's disease were the most common.

NR596 Thursday May 7, 12:00 noon-2:00 p.m.

Early Pharmacokinetic Targeting of Tricyclic Doses

William A. Kehoe, Pharm.D., Clinical Pharmacy, School of Pharmacy, University of the Pacific, Stockton, CA 95211; Arthur F. Harralson, Pharm.D., John J. Jacisin, M.D., M.J. Hetnal, M.D.

Summary:

Studies have shown that early pharmacokinetic analysis of tricyclic antidepressant (TCA) serum concentrations (Cps) aids in identifying dose requirements. We performed this follow-up study of a new pharmacokinetic method to evaluate its utility for dosing desipramine (Desi) and nortriptyline (Nor).

Forty-two patients were included in the study. They were started on either Desi ($n = 25$) or Nor ($n = 17$) at a dose selected by the psychiatrist. Cps were then obtained within the first few days of therapy and analyzed using a Bayesian pharmacokinetic model to determine drug clearance (Cl) and volume of distribution (Vd). Maintenance doses of the TCA were then begun. The individualized estimates of Cl and Vd were used to predict the serum concentration resulting from that dose.

Absolute prediction error (APE, model precision) for Desi was 22.7 ± 25.4 ng/mL. Mean prediction error (MPE, model bias) was -12.5 ± 31.9 ng/mL. For Nor, the APE was 16.1 ± 13.5 ng/mL and MPE was likewise negatively biased at -6.4 ± 20.3 ng/mL. For Desi, nine slow metabolizers were identified and Cl was significantly lower (0.10 L/Kg/Hr vs 0.56 L/Kg/Hr, $p < 0.001$). For Nor, four slow metabolizers were identified and Cl was also significantly lower (0.08 L/Kg/Hr vs 0.36 L/Kg/Hr, $p < 0.001$).

This new model allows clinicians to accurately target TCA doses and serum concentrations. Test doses and precisely timed serum sampling are not required. Slow metabolizers are identified early in therapy, and appropriate dose adjustments can be made to avoid toxicity.

NR597 Thursday May 7, 12:00 noon-2:00 p.m.

Family Treatment of Bipolar Disorder

Ivan W. Miller, Ph.D., Psychiatry, Brown University, Butler Hospital 345 Blackstone, Providence, RI 02906; Gabor I. Keitner, M.D., Nathan B. Epstein, M.D., Duane S. Bishop, M.D., Christine E. Ryan, Ph.D.

Summary:

This poster will present the results of two studies concerning the role of the family in bipolar disorder. In the first study, 24 bipolar patients and their families and a sample of matched control families completed a measure of family functioning. The results indicated that the families of bipolar patients manifested significant family dysfunction during the acute episode. A five-year follow-up of these patients indicated that bipolar families with high levels of family dysfunction had over twice the rate of rehospitalizations as those bipolar families with low levels of dysfunction.

The second study was a pilot study of family treatment for bipolar patients. Fourteen bipolar patients and their families were randomly assigned to Standard Treatment (pharmacotherapy + clinical management) or to Family Therapy + Standard Treatment. Treatments began in the hospital and continued for 18 weeks after discharge. A two-year follow-up was also completed. The results indicated that when compared with the Standard Treatment group, the Family Therapy group had: a) lower rates of family separations, b) greater improvements in level of family functioning, c) higher rates to full recovery, and d) lower rates of rehospitalization for the two years after treatment.

NR598 Thursday May 7, 12:00 noon-2:00 p.m.

Signs of Dyscontrol and Responsiveness to Fluoxetine in Major Depressives

Giovanni Conte, M.D., Psychiatry, Ospedale San Paolo, Via A. Di Rudini 8, 20162 Milano, Italy; Alessandro Calzeroni, M.D., Laura Guarneri, M.D., Ambrogio Pennati, M.D., Giuseppe Russo, M.D., Emilio Sacchetti, M.D.

Summary:

Fluoxetine (FLX) is a specific serotonin uptake inhibitor, and its efficacy in the treatment of major depression (MD) is well established. Since the prediction of FLX response is still uncertain, we compared good or poor FLX response in MD patients by assessing the anamnestic presence/absence of signs putatively linked to dysregulation of serotonergic pathways. Sixty-three patients (21 men; age range: 22-64 years) with a DSM-III-R diagnosis of MD, bipolar or recurrent, were treated with FLX (mean daily dose: 25 mg). Patients were considered responders ($n = 43$) if their baseline HRSD scores (minimum 22) decreased by 50% or more after four weeks' treatment. Excluding patients with suicidal ideation but not suicide attempts, 92% of FLX responders had a history of at-

tempted suicide vs. 51% of nonresponders (chi square = 5.13, p = .024). Eighty-two percent of FLX responders vs. 51% of nonresponders had suicidal ideation (chi square = 5.18, p = .023). Craving episodes were found in 93% of FLX responders and in 54% of nonresponders (chi square = 5.3, p = .021). Presence of at least one sign of ictal dyscontrol (suicide attempts, craving episodes, substance abuse, dipsomania, auto- or heteroaggressive behavior) was found in 83% of FLX responders vs. 43% of nonresponders (chi square = 9.26, p = .0023). The higher rate of response to FLX in MD patients with signs of dyscontrol fits with a hypothesis of serotonin dysregulation in these patients.

NR599 Thursday May 7, 12:00 noon-2:00 p.m.

Efficacy of Fluoxetine in Psychotic Depression

Anthony J. Rothschild, M.D., Harvard Medical, McLean Hospital, 115 Mill Street, Belmont, MA 02178

Summary:

Patients with psychotic depression (PD) respond poorly to placebo, tricyclic antidepressants (TCAs) alone, and antipsychotics (APs) alone, but have a considerably better response to TCAs + APs, amoxapine, or ECT. Serotonin reuptake blockers, although widely used in the treatment of depression, have not had their efficacy in the treatment of patients with PD investigated.

Data will be presented on the use of fluoxetine, in combination with perphenazine, in the treatment of 30 PD patients who were evaluated prior to treatment and on a weekly basis using the Hamilton Depression Rating Scale (HDRS), Brief Psychiatric Rating Scale (BPRS), and a side-effect checklist that included extrapyramidal and anticholinergic side effects. Twenty-two (73%) of the 30 patients had a greater than 50% reduction in their HDRS and BPRS scores by five weeks. This response is similar to the response rates of the most efficacious treatments for PD such as TCAs + APs, amoxapine, or ECT. Side effects experienced by the patients in the study were dry mouth (40%), blurry vision (40%), constipation (40%), orthostatic hypotension (25%), dizziness (25%), tremor (40%), rigidity (40%), and akathisia (7%). The side effects were less than what has been reported in the literature for TCA + AP treatment of PD and similar to the side effects reported with amoxapine.

This is the first report of the use of fluoxetine in the treatment of PD. Our study suggests that the combination of fluoxetine plus perphenazine is efficacious in the treatment of PD and may be easier for patients to tolerate than a TCA + AP. Presumably this is due to fluoxetine's lack of anticholinergic side effects, which avoids the additive anticholinergic effects of a TCA + AP.

NR600 Thursday May 7, 12:00 noon-2:00 p.m.

Rubidium Normalizes Split Rhythms in Hamsters

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Summary:

Circadian rhythm dysfunction, including abnormal phase relationships, has been reported in patients with major affective disorders. Demonstration that an antidepressant normalizes atypical circadian function in animals would suggest that chronopathology is not merely a state marker, but may contribute to causation of some mood disorders. One circadian abnormality in hamsters is splitting; when housed in bright constant light, the normally intact portion of a free-running circadian rhythm splits into two separate components that then stabilize at an abnormal phase relationship 12 hours apart. We used this preparation as an assay for chronotypic properties of the putative antidepressant rubidium (Rb). over 10 weeks, seven of 12 hamsters that received RbCl (100 mM) in drinking water demonstrated fusing of split rhythms vs. none of seven control hamsters. Rubidium may normalize atypical coupling between circadian rhythms by acting directly on the suprachiasmatic nuclei or by reducing photic input to those nuclei. The drug's reported efficacy as an antidepressant may, at least in part, reflect similar chronotypic properties. Further research may determine that rubidium is potentially valuable in treating depression accompanied by abnormal circadian rhythms.

NR601 Thursday May 7, 12:00 noon-2:00 p.m.

Immunity in Drug-Naive Major Depressive Episode Patients

Steven E. Keller, Ph.D., Psychiatry, UMD of New Jersey, 187 South Orange Avenue, Newark, NJ 07103; Antonio V. Andreoli, M.D.

Summary:

Significance: Altered immunity was observed in subgroups of psychiatric patients with major depression (Schleifer 1989). The reported altered immunity may have resulted, however, from effects of previous drug treatments. *Methods:* We studied treated and untreated depressed patients with DSM-III-R major depressive episode (MDE) and matched controls. Each subject/control pair had reliable DSM-III-R diagnosis (SCID-I) and was immunologically (mitogen and subset quantitation) assessed on the same day. *Results:* Fifteen drug-naive and 39 previously treated patient/control pairs were studied. We found increased mitogen responses in drug-naive MDE subjects compared with controls. Specifically, ANOVA showed a significant group (subject vs. control) effect for ConA ($p < 0.001$), PHA ($p < 0.05$) and a trend for PWM. Drug-naive patients were found to be significantly younger than the patients previously treated ($p < 0.05$). In regression analyses, when entered together, only age predicted immune response. *Comment:* Previous findings of altered immunity in MDE seemed to be related to age; younger subjects showing elevated responses, and older subjects showing decreased responses. Since age and previous drug usage in the present report were confounded, further studies with a wide age range of drug naive subjects are indicated. The present finding suggests that previous drug usage may also be a factor in psychoimmunological studies in MDE.

NR602 Thursday May 7, 12:00 noon-2:00 p.m.

Interpersonal Deficits and TCA Response in Dysthymia

John C. Markowitz, M.D., Psychiatry, Cornell Univ Med. Coll., Payne Whitney 525 E 68th St., New York, NY 10021; James H. Kocsis, M.D., Mary E. Moran, M.Ed.

Summary:

Dysthymic patients often respond to tricyclic antidepressants. Improvement occurs not only in depressive symptoms, but also in measures of social impairment. This raises interest in dysthymic social and interpersonal deficits, and the rate and degree of their recovery. We applied a new measure, the Inventory of Interpersonal Problems (IIP, 2) to assess change in interpersonal functioning during acute desipramine (DMI) treatment of patients with dysthymia.

Method: Subjects meeting DSM-III-R criteria for primary, early-onset dysthymia received open DMI up to 250 mg/d (maximum tolerated doses, blood level monitoring) for 10 weeks. The 127-item, self-rated IIP questionnaire was given at weeks 0 and 10. Subjects were rated biweekly on the 24-item Hamilton Depression Scale (Ham) and the Global Assessment Scale (GAS).

Results: Fourteen patients have completed the study. Mean DMI dosage was 232 mg/d. Ham scores fell from 20.6 ± 7.9 (s.d.) pretreatment to 6.3 ± 4.3 at week 10. GAS scores increased from 54.7 ± 7.6 to 74.2 ± 8.0. IIP total score also significantly improved

(222.1 ± 59.4 to 173.5 ± 48.1; t = 2.92, p = .01), as did four of six component factors: Assertiveness, Sociability, Intimacy, and Responsibility (all $p \leq .03$). Change on IIP correlated with change on Ham ($r = .70$, $p < .006$) and GAS ($r = -.54$, $p = .04$) scales.

Significance: These preliminary data replicate and augment prior research demonstrating rapid improvement in social/interpersonal function of dysthymic patients treated with antidepressants. Our pilot results suggest the IIP's utility in assessing this interpersonal improvement.

NR603 Thursday May 7, 12:00 noon-2:00 p.m.

Psychoeducation for Mood Disorder

Ira Glick, M.D., Psychiatry, CUMC, 525 East 68th Street, New York, NY 10021; Lorenzo Burti, M.D., Keigo Okonogi, M.D.

Summary:

Recent research suggests that despite the development of effective psychiatric treatment, optimal results are not achieved. This study had the objective of dissecting the process of care (including medication and psychotherapy), focusing on psychoeducation in an attempt to understand outcomes for patients and their families with psychosis. *Method:* Twenty-four patients who carried a DSM-III diagnosis of major affective disorder (MAD) were identified 12-24 months after hospital admission in three countries (Italy, Japan and the United States). The patients, their families and their doctors were interviewed separately, and then together, using instruments measuring delivery of, and achievement of, psychoeducation, which was then (using parametric and nonparametric statistical techniques) correlated with resolution of the index episode and the patient's global outcome. *Results:* The data demonstrated that compared to what would be considered ideal psychoeducation, physicians delivered 70% to the patient and only 50% to the family. Most strikingly, patients and families with the best resolutions received significantly more psychoeducational treatment than those with the worst resolutions ($p < .03$). Clinical implications are discussed.

NR604 Thursday May 7, 12:00 noon-2:00 p.m.

Double-Blind, Placebo-Controlled Comparative Study of Levoprotiline and Amitriptyline in Patients with Moderate to Severe Depression

Ram K. Shrivastava, M.D., Medical, Eastside Comprehensive, 133 E. 73rd Street Ste 209, New York, NY 10021; S.S. Shrivastava, M.D., Norbert Overweg, M.D., Richard Katz, Ph.D., Diane Romley, B.A.

Summary:

Levoprotiline hydrochloride (CPG-12103A), the (−)-enantimer of the antidepressant oxaprotiline, has been identified preclinically as having antihistaminic, sedative, and antiaggressive properties. In addition, the overall frequency of side effects associated with levoprotiline appears possibly less than with reference compounds. After a single-blind, placebo-washout week, 38 patients having a score of 18 or greater on the HAM-D entered the double-blind phase of the study. Patients were treated for a period of six weeks and were evaluated each week. Results indicated that 54.6% of patients taking levoprotiline showed a 50% reduction in the HAM-D score by week 3. This improvement was maintained until the final visit. Only 36.4% of patients taking placebo achieved this 50% reduction at week 3. It was not until week 6 that 50% of both the amitriptyline and placebo groups reached a 50% reduction in HAM-D scores. For the amitriptyline group, this late response can probably be attributed to the high patient drop-out rate. There was no significant difference found for Axis V (Quality of Life) among the three treatment groups. The investigational drug did seem to show antidepressant activity with an earlier onset of action than both amitriptyline and placebo. However, due to the small sample size, differences were not statistically significant. Levoprotiline was well tolerated, and there were no significant changes in vital signs or lab parameters with any of the treatment groups.

NR605 Thursday May 7, 12:00 noon-2:00 p.m.

Core Symptoms of Depression

James R. Moeller, Ph.D., Biological Psych., NYS Psych Inst., 722 West 168th Street, New York, NY 10032; Eric Rubin, M.D., Harold A. Sackeim, Ph.D.

Summary:

Rating instruments for psychiatric illness have multiple aims: (1) to provide a unitary index of severity of illness, and (2) to provide broad coverage of symptomatologic features, including those that may be unique to different nosologic subgroups. Within a diagnostic category, patients may actually manifest core features of disease severity that are universally expressed across all subtypes and collateral features that are specific to their subtypes.

We will present the application of a new multivariate method to the Hamilton Rating Scale for Depression (924-item HRSD) for the purpose of separating a set of core features of major depression from collateral features. The method was applied to HRSD assessments, repeated overtime, of a sample of 144 patients referred for ECT. The first and final assessments analyzed coincided with the initiation and completion of ECT therapy; patients were medication-free during the period of treatment. We present an initial validation of the new method in which depressed patients with and without psychosis exhibited the core profile of symptom severity common to all patients, while only the psychotic group exhibited a specific set of collateral features.

Data will also be presented that illustrate the relationship between the raw HRSD score, the severity score based on the profile of core symptoms, and the HRSD variation that is attributable to different clinical subtypes and biological indices, including abnormal regional cerebral blood flow and DST results.

NR606 Thursday May 7, 12:00 noon-2:00 p.m.

Use of Postnatal Depression Scale

Alec Roy, M.B., Psychiatry, Hillside Hospital, 75-59 265th Street, Glen Oaks, NY 11004; Peggy Gang, R.N., Karyl Cole, M.D., Monica Rutsky, C.S.W., Joann Weisbord, C.S.W., Leslie Reese, C.S.W.

Summary:

Cox et al. developed the 10 Edinburgh Post-natal Depression Scale (EPDS) as a screening tool for postpartum depression. It has been demonstrated to have acceptable sensitivity, specificity, and positive predictive value for depression in the postnatal period. However, it has not been used in the United States. As part of developing a postpartum depression program we wished to find out how acceptable American women would be to receiving it in the mail, what the response rate would be, and what the range of scores would be. We approached 308 women in the obstetric service at Long Island Jewish (LIJ) Medical Center who had had a live birth in the previous two days. They were asked if we could send them the EPDS in the mail six weeks later. Only one patient refused. Completed questionnaires were returned by 185 of the 307 women. A range of scores from 0 to 24 were obtained (the maximum possible score is 30). Thirty-two of the 185 women (17.3%) scored 12 or above—the threshold reported by Cox et al. to identify women with depressive disorder. Six women scored 12, three scored 13, nine scored 14, two scored 15, one scored 17, one scored 18, two scored 19, one each scored 20 to 22, two scored 23, and one 24. Thus, our study shows that EPDS is acceptable to American women and, when administered by mail, will be returned by ap-

proximately 60 percent of women and will yield a subsample of high scorers probably containing women with postpartum depression.

NR607 Thursday May 7, 12:00 noon-2:00 p.m.

Onset of Antidepressant Action with S-Adenosylmethionine: A Controlled Clinical Trial

Carlos Leon-Andrade, M.D., Psychiatric Services, Metropolitan Hospital, Casilla De Correos 17-16-127, Quito CEQ, Ecuador; Hector Ortega-Soto, M.D., Prof Juan Ramon de la Fuente, M.D.

Summary:

Fifteen outpatients who met the criteria for major depression were studied at the Special Studies Clinic of the Mexican Institute of Psychiatry. Following a two-week washout period patients were randomly assigned to either e-SAM or clomipramine. Both drugs were administered, by IM route on a daily basis, within the clinic by an investigator not involved with diagnostic and/or rating procedures. Patients and project personnel were blind to drug assignment.

Depression severity was rated at days 0, 3, 6, 9 and 14 by means of HDRS and the Zung self-rating depression scale. A checklist of drug side effects was used at days 0, 6 and 14.

Our data fail to support the idea that SAM acts more rapidly than tricyclic antidepressants, at least at the dosages we used (SAM 200 mg).

The size and the design of the study, aimed to assess onset of action, does not allow us to make valid inferences about SAM efficacy as antidepressant. However, our results are in line with previous reports. A total of 67% of patients showed at least a partial response to SAM by the end of the second week of treatment. Significant changes on depression rating scores were noted as early as the third day of treatment with SAM.

NR608 Thursday May 7, 12:00 noon-2:00 p.m.

Long-Term Valproate Prophylaxis in Refractory Affective Disorders

Stephen Hayes, M.D., 7500 E. Hellman Avenue, Rosemead, CA 91770

Summary:

Twenty-six patients with refractory affective disorders who were taking valproate after failing on standard psychopharmacological regimens were followed in an open-label fashion for an average of four years. Valproate, frequently in combination with lithium, carbamazepine, or other previously partially effective medications, reduced the number and severity of affective episodes over the study period. The results indicate that valproate shares with lithium and carbamazepine a tendency towards overall mitigation of the frequency and amplitude of affective cycles. Psychopharmacologic combinational strategies were employed in a majority of the patients. Overall improvement in illness index and global assessment scales over the study period suggests the utility of the procedure of systematic medication trials, and the model of an "emotion regulation circuit" conceptualized psychopharmacologically.

NR609 Thursday May 7, 12:00 noon-2:00 p.m.

ECT and Twin Pregnancy

Ray Walker, M.D., Psychiatry, ECU School of Medicine, Moye Boulevard, Greenville, NC 27858

Summary:

The combination of pregnancy and affective psychosis produces a complex treatment problem. There are significant risks to the mother and fetus due to maternal self-neglect or suicide attempts. The medical treatments for affective psychosis also have risks for fetal development. ECT is an alternative treatment that has been given with safety to women pregnant with single fetuses. This case study involved a high-risk pregnancy and is the first report of ECT and multiple gestation. ECT was started for affective psychosis during the 23rd week of a twin pregnancy. The symptoms resolved with six treatments, but the patient relapsed after three weeks. A second course of seven ECTs induced a remission again, an the patient delivered viable twin infants during her 35th week of pregnancy. The mother and fetuses were extensively monitored, especially during the second course of ECT, when the fetuses were potentially viable. The monitors included non-stress tests, contraction stress tests, Doppler ultrasonography, biophysical profiles, external tocodynamometry and continuous electronic fetal heart rate monitoring. The problems of singleton pregnancy are compounded with twin pregnancy. The data from the monitors guided treatment as gestation progressed. There is a growing case report literature that demonstrates the safety of ECT during high-risk pregnancies.

NR610 Thursday May 7, 12:00 noon-2:00 p.m.

Treatment of Psychotic Depression in Late-Life

Benoit H. Mulsant, M.D., Geriatrics 12, WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213; Robert A. Sweet, M.D., George S. Zubenko, M.D., James M. Perel, Ph.D., Charles F. Reynolds III, M.D.

Summary:

About one-third of elderly depressives requiring psychiatric hospitalization present with psychotic features. However, there exist neither published controlled data nor clinical consensus on the pharmacologic treatment of psychotic major depression (PMD) in late life. In younger patients, randomized, double-blind studies have shown that the response of PMD to either a combination of a tricyclic antidepressant with a neuroleptic or amoxapine alone is excellent, alleviating the need for ECT in most. We report preliminary results of an ongoing trial of: (1) a combination of nortriptyline (at a blood level of 100 $\pm$ 50 ng/ml) with perphenazine (24 mg/day) and (2) amoxapine (200 mg/day) to treat nonbipolar PMD in late-life. To date, seven patients (mean age at index: 71 $\pm$ 4; at onset: 68 $\pm$ 4; median duration of index episode: six months) have completed this trial (three more are currently enrolled). Medications have been well tolerated; no patient had to discontinue her/his medications due to side effects. After receiving an antidepressant for a mean of 34 $\pm$ 5 days (range: 29-43) combined with a neuroleptic for a mean of 27 $\pm$ 8 days (range: 20-42) the mean score on the Hamilton Rating Scale for Depression decreased significantly from 24 to 17 ($p = 0.02$). Similarly, the mean score on the Brief Psychiatric Rating Scale decreased ($p = 0.05$), and the mean rating on the Global Assessment of Functioning Scale increased ($p = 0.04$). Upon completion of the pharmacologic trial, four patients (57%) were sufficiently improved to be discharged home; two patients were treated with ECT; one patient refused ECT and was transferred to a state hospital. These preliminary data support the feasibility of treating elderly patients with either a combination of nortriptyline with perphenazine or amoxapine, alone. A more extensive and rigorous study is needed to determine the efficacy of these medications in the treatment of elderly patients with psychotic depression.

NR611 Thursday May 7, 12:00 noon-2:00 p.m.

Sleep, Depression and Fibromyalgia in Fatigue

Peter Manu, Psychiatry, Univ of Connecticut, 263 Farmington Avenue, Farmington, CT 06030; Thomas J. Lane, M.D., Dale A. Matthews, M.D., Robert K.Watson, Ph.D., Richard J. Castriotta, M.D., Micha Abeles, M.D.

Summary:

Disturbed sleep, depression, and diffuse myalgias are commonly reported by patients (pts) with chronic fatigue (CF). To investigate the relationship between sleep abnormalities and the presence of major depression and fibromyalgia, we studied 30 pts with CF who requested to be seen at a university-based clinic between November 1990 and September 1991. All pts underwent nocturnal polysomnography and rheumatologic tender-point examination prior to being given a comprehensive medical evaluation and a psychiatric assessment using the Diagnostic Interview Schedule. Current major depression was diagnosed in 20 pts (67%). No significant differences were noted between the depressed and nondepressed pts with regard to age (41 vs. 41 years), proportion of women (70% vs. 70%), sleep latency (33 vs. 31 minutes), total duration of sleep (337 vs. 315 minutes), percentage of rapid eye movement sleep (19 vs. 15), and the frequency of periodic limb movements with frequent arousals (25 vs. 10%) and obstructive sleep apnea (10 vs. 20%). Significant alpha intrusions during delta sleep were present in 50% of nondepressed pts, but in only 15% of pts with current major depression ($p < 0.05$) and in none of the four pts with fibromyalgia. We conclude that alpha intrusions during delta sleep may have an etiologic role in CF pts without major depression or fibromyalgia.

NR612 Thursday May 7, 12:00 noon-2:00 p.m.

Psychobiologic Predictors of Reattempted Suicide

Kevin M. Malone, M.D., Lab. Neuropharm, Western Psych Inst., 3811 O'Hara Street, Pittsburgh, PA 15213; Joyce M. Myers, M.D., Gretchen L. Haas, Ph.D., Tammy A. Mieczkowski, M.A., John A. Sweeney, Ph.D., J. John Mann, M.D.

Summary:

Objective: The aim of this study was to evaluate potential clinical and biological (serotonergic) predictors of future suicide attempts in patients with a past suicide attempt versus non-attempter psychiatric controls. *Method:* 45 unmedicated inpatients, (25 suicide attempters, and 20 nonattempters) were clinically assessed following psychiatric admission, and underwent a fenfluramine challenge test. They were evaluated three months after discharge. *Results:* 41.2% of the attempters had reattempted suicide versus a 5.9% attempt rate in non-attempters ($p = .054$). All reattempters had major depression (DSM-III-R), compared with 59% of non-reattempters ($p = .04$). Attempters who reattempted had higher hopelessness (Beck Scale) ($p = .06$), and higher Barrett Impulsivity Scale scores. Female attempters (reattempters and non-reattempters) had significantly higher lifetime aggression (Brown-Goodwin) scores than non-attempters ($p < .007$). A sex ($p < .01$) and female group ($p < .08$) effect was found in the maximum fenfluramine-stimulated prolactin response in reattempters. *Conclusions:* Patients, particularly women with major depression, who attempt suicide, are more likely to reattempt if there is prominent lifetime impulsivity, aggression, and high hopelessness scores on admission to hospital. Serotonin function, as measured by prolactin response to fenfluramine, is significantly abnormal in depression with or without suicide attempts, and may predict future suicidal behavior in females. (Supported by Fogarty International Award 1 FO5 TWO04538-01 to Dr. Malone and by MHCRC46745.)

NR613 Thursday May 7, 12:00 noon-2:00 p.m.

Low Association Between Childhood Trauma and BPD

Carl Salzman, M.D., Psychiatry, Harvard Medical, 74 Fenwood Road, Boston, MA 02115; Judith P. Salzman, Ed.D., Abbie Wolfson, A.B., E. Miyawaki, M.D., M. Albanese, M.D., J. Looper, M.D.

Summary:

Objective: This study was an attempt to replicate previous findings indicating a childhood history of trauma in more than 80% of adult borderline subjects. *Method:* 29 subjects with diagnosis of BPD based on clinical interview, modified DIBS, and SCID semi-structured interviews were studied. Subjects were rated on standard rating scales for depression, anger, and anxiety. Specific questions about childhood trauma were asked, using questions from a previous study of trauma and borderline patients. All subjects were then interviewed in greater depth using a semistructured interview regarding past experiences of trauma. *Results:* Only four of 29 subjects reported a history of childhood trauma. *Conclusions:* A history of childhood trauma is not necessarily linked to the development of borderline personality disorder in all individuals. The following hypothesis is suggested: Borderline personality disorder may represent a spectrum of symptomatic severity. The least symptomatic persons, represented by our research cohort, are least likely to have a history of childhood trauma. The most symptomatic, as represented by hospitalized patients or those who were interviewed in previous outpatient research may be more likely to have suffered trauma in childhood.

NR614 Thursday May 7, 12:00 noon-2:00 p.m.

Comparison of Venlafaxine, Trazodone and Placebo in Major Depression

Lynn A. Cunningham, M.D., Vine Street Clinic, 310 N. Sixth St. Suite 330, Springfield, IL 62701; Richard L. Borison, M.D., John Carman, M.D., John Crowder, M.D., Bruce I. Diamond, Ph.D.

Summary:

Venlafaxine (VEN) is a structurally novel antidepressant that inhibits the neuronal uptake of serotonin and norepinephrine. This study compared the safety and efficacy of VEN, trazodone (TRZ), and placebo (PLA) in 225 outpatients with major depression. The drugs were administered TID, initially for up to 43 days. Both active treatments were more effective than PLA in relieving depression. Changes in mean HAM-D total scores at the week-6 evaluation were -9 for PLA vs. -12 for VEN ($p = 0.010$) and -11 for TRZ ($p = 0.015$). For the mean MADRS total, the changes were -9 for PLA vs. -13 for VEN ($p = 0.008$) and -12 for TRZ ($p = 0.032$). Final response rates were 72% for VEN, 60% for TRZ, and 55% for PLA ($p = 0.036$ for VEN vs. PLA), based on CGI ratings of much or very much improved. Patients who responded could receive the same treatment for up to one year more. Those who received VEN were more likely to extend their treatment and to continue longer in the extension. Throughout treatment, nausea was more common with VEN, somnolence and dizziness with TRZ. The active treatments produced similarly low rates of anticholinergic effects. The larger decreases in depression rating scores and the tendency for patients to remain in the study longer strongly suggest that VEN has therapeutic advantages over TRZ.

NR615 Thursday May 7, 12:00 noon-2:00 p.m.

Lithium, RBC Levels and Renal Side Effects

Simavi Vahip, M.D., Psychiatry, EGE University, Tip Fakultesi Bornova, Izmir 35100, Turkey; Hakan Coskunol, M.D., Evert J.D. Mees, M.D., Ali Basci, M.D., Oya Bayindir, M.D., Isik Tuglular, M.D.

Summary:

The aim of this study is to investigate the red blood cell (RBC) lithium levels and lithium ratio in patients on long-term lithium treatment as predictors of renal side effects and/or damage induced by lithium.

We studied 108 patients with bipolar disorder who were on lithium prophylaxis for one-15 years. Twenty-four-hour urine collections were used to determine daily urine volume and creatinine clearances. RBC lithium levels were determined by direct method, using flame photometer. Maximal urinary osmolality was measured after 16 hours of fluid restriction period. Three measurements were taken consecutively with one-hour intervals.

RBC lithium levels and lithium ratio showed significant negative correlation with maximal urinary osmolality and positive correlation with 24-hour urine volume. Also RBC lithium levels (0.49 ± 0.20 mEg/L) and lithium ratio (0.58 ± 0.17) were significantly ($p < 0.01$) higher in patients whose maximal urinary osmolality were below 700 mm/kg H2O than the other patients (RBC level 0.36 ± 0.12 mEg/L. ratio 0.47 ± 0.21).

These findings are evaluated as evidence of some intracellular mechanisms for level side effects of lithium.

NR616 Thursday May 7, 12:00 noon-2:00 p.m.

Fluoxetine Blood Levels and Clinical Response

Paul J. Goodnick, M.D., Psychiatry, University of Miami, D79, 1400 NW 10 Avenue #304A, Miami, FL 33136

Summary:

In past years the utility of therapeutic blood monitoring of antidepressants has become more established. Fluoxetine (Dista: Prozac), a selective serotonin reuptake inhibitor, is a frequently used antidepressant for which therapeutic blood ranges have not been established. Based upon previous reports, it was hypothesized that a combined level of fluoxetine plus its metabolite, norfluoxetine, in the range of 200-499 ng/ml would be associated with maximal response in depression. Fifteen patients, six male and nine female with a mean age of 45.7 + 13.3 years, with major depressive disorder (DSM-III-R), were treated with fluoxetine on an open basis. The Beck Depression Inventory (BDI) was completed at baseline & every two weeks thereafter for the eight-week trial; dose was begun at 20 mg/day and increased 20 mg/day every two weeks until response or 80 mg/day was attained. The clinician was kept blind to trough (12 hour) blood levels that were attained after a minimum of two weeks' stabilization of response or after eight weeks. There was no correlation between maximal dose (mean = 44.3 mg/day) and blood level (mean = 541 ng/ml). Six of nine patients with levels of 200-499 ng/ml had a significant response (≥50% fall in BDI) compared with none of six outside this range ($X^2 = 6.67$, $P < .01$). Baseline BDI was 23.1 ± 8.4. Mean change in BDI was 9.5 + 9.0. Patients in the range of 200-499 ng/ml had greater percent improvement in BDI ($t = 2.14$, $df = 13$, $P < .05$). Four of four patients whose dose was adjusted (three decreased, one increased) based on this result improved significantly afterwards. Further research is indicated on the use of blood levels during treatment with fluoxetine.

NR617 Thursday May 7, 12:00 noon-2:00 p.m.

Psychogeometry: The Dynamic Analysis of Mood

Hector C. Sabelli, M.D., Psychiatry, Rush University, 1725 W. Harrison St. Ste 744, Chicago, IL 60612; Linnea Carlson-Sabelli, Ph.D., Minu Patel, M.S., Nancy Hein, A.S., Erika Harris

Summary:

Psychogeometry is a graphic portrait of affective processes as periodic and chaotic trajectories in phase space. We shall illustrate the usefulness of this method in the analysis of personal mood and family processes. In total, over 70 subjects of middle-class education and occupation are being studied. Daily records of subjective evaluations of joy, depression, anger and rage, fear and anxiety, positive and negative feelings toward a significant other, sexual feelings, sleep, body temperature, as well as of positive and negative events were obtained for 35 to 700 days. Harmonic analysis showed that for each person almost half of the variables were periodic, while others represented chaotic processes. But which ones varied from subject to subject? "External events" were shown to occur periodically in more than half the population, indicating an endogenous component origin. The trajectories of mood in the tridimensional phase space defined by various emotional and interpersonal dimensions provide understandable portraits of individual psychological life that appeal directly to clinical intuition. Treatment led to a shrinking of the phase space occupied by the trajectory, indicating a greater stability of the emotional process. Spouses showed parallel changes for some variables but not for others. In one family, both parents showed similar patterns of constricted affect, their five daughters displayed much wider variations, and all of their husbands had intermediate patterns. The clinical application of these phase portraits will be discussed.

NR618 Thursday May 7, 12:00 noon-2:00 p.m.

Family and Population Studies of Affective Disorders with 11P15.5 DNA Markers

Francis Gheysen, M.D., Centre Esquirol, Chu Cote De Nacre, Caen 14200, France; Alain Malafosse, M.D., Mokran Abbar, M.D., Marion Leboyer, M.D., Stephan Amadeo, M.D., Prof. E. Zarifian, M.D.

Summary:

There have been conflicting results regarding original description of a linkage between 11p15.5 markers. Considering the absence of conclusive data concerning the genetic parameters of affective disorders (AD), the lod score method should be used with caution in genetic studies of AD. Thus, we performed family and population analyses of AD using nonparametric methods. These approaches allow us to identify one of the susceptibility loci to AD within the 11p15.5 region, not only within the French samples but also in the families previously published, comprising the Old Order Amish pedigree 110.

NR619 Thursday May 7, 12:00 noon-2:00 p.m.

Imipramine Maintenance in Postpsychotic Depression

Samuel G. Siris, M.D., Psychiatry, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004; Paul C. Bermanzohn, M.D., Susan E. Mason, Ph.D., Mitchell A. Shuwall, Ph.D.

Summary:

A prospective, double-bind study was undertaken to explore the value of maintenance adjunctive antidepressant treatment for patients (pts) with post-psychotic depressions who had initially responded favorably to acute treatment with adjunctive imipramine (IMI).

Twenty pts (11 male, nine female, 38.3 ± 12.2 y.o.), who initially had met Research Diagnostic Criteria for schizophrenia or schizoaffective disorder and operationalized criteria for post-psychotic depression, and who had responded favorably to a trial of adjunctive IMI added to their ongoing regimen of fluphenazine decanoate (FD) and benztropine (BZT), were continued on these medications for six months. They were then randomized to either maintenance adjunctive IMI, or taper to matching placebo (PBO), while remaining on the FD and BZT. This trial lasted for one year, or until a depressive or psychotic relapse occurred.

All eight PBO-substituted pts relapsed into depression vs. only two of 12 IMI-maintained pts ($p < .001$). Additionally, four of the eight PBO pts became psychotic at the time of depressive relapse, while no IMI pts became psychotic during the trial ($p < .01$). These results support the benefit of maintenance adjunctive IMI in such pts and raise relevant heuristic and mechanistic issues.

NR620 Thursday May 7, 12:00 noon-2:00 p.m.

Predictors of Suicide in the Consultation Population

James J. Strain, M.D., Psychiatry, Mt. Sinai Sch. Medicine, 1 Gustave Levy Pl Bx 1228, New York, NY 10029; Yasutaka Iwasaki, M.D., Jeffrey S. Hammer, M.D., Hwai-Tai C. Lam, Ph.D.

Summary:

Introduction: Completed suicide is a rare event in the general hospital. In contrast, suicidal ideation or attempt is a most frequent reason (⅓ in some studies) for psychiatric consultation. Predictors at general hospital admission for identification of this at-risk population have not been described.

Method: All consultations at the Mount Sinai Hospital (NYC) from 1 July 1988 until 1 January 1991 were interviewed with a structured computerized optical scan database that recorded: demographics, reason for consultation, DSM-III-R diagnoses on five axes, psychosocial and drug interventions, and hospital variables. Patients were divided into: suicidal ideation or attempts: "Suicide" (N = 120) and "Others' (N = 1402). All cases were supervised by trained consultants. Dichotomous and continuous variables were analyzed with chi square and T tests. Step wise logistic regressions were employed.

Results: "Suicide" in comparison with the "Others" were younger ($p = 0.001$), divorced or separated ($p = 0.04$), better educated ($p = 0.03$), and Catholic. "Suicide" had more death in significant others and less serious illness in themselves during the last year ($p < 0.0001$): fewer were referred for issues of competence ($p = 0.03$). "Suicide" had more affective ($p = 0.04$), dissociative ($p < 0.0001$), and personality disorders ($p < 0.0001$); admissions to the psychiatric-inpatient unit ($p < 0.0001$), recommendations for social work services ($p < 0.004$), environmental changes in hospital ($p < 0.0001$) and extension of their discharge date ($p < 0.03$). Stepwise logistic regression revealed: Age (odds ratio 0.98), life stress (odds ratio 2.89), time for initial consultation (odds ratio 0.86), recommendation for obtaining more information (odds ratio 2.59), and changing hospital environment were all predictors for assignment to the suicide cohort.

NR621 Thursday May 7, 12:00 noon-2:00 p.m.

Imitation Suicides after a Live Televised Suicide

Paul A. Kettl, M.D., Psychiatry, Penn State-Hershey, P.O. Box 850, Hershey, PA 17033; Michael J. Christ, B.S., Edward O. Bixler, Ph.D.

Summary:

On January 22, 1987, after being convicted of accepting a kickback, the state treasurer of Pennsylvania shot and killed himself in a live press conference in front of a statewide television audience. A number of recent reports document a positive association between highly publicized suicides and later imitation suicides. We investigated if this prominent suicide was associated with an increase in suicide rates in Pennsylvania.

Suicide rates before and after the suicide were compared at 1, 2, 4 and 8 weeks. Overall, there was a significant increase in suicides at 8 weeks ($p < 0.05$) but not before. The elderly (aged 70-79) and females showed increases in suicides at 4 and 8 weeks. Suicide victims, interestingly less often chose gunshot wound as a suicide method, and chose other means more frequently ($p < 0.05$) after the televised shooting. Geographically, increases in suicide rate were especially prominent in south central Pennsylvania, where the treasurer lived and worked (significantly increased at 2, 6, and 8 weeks after the suicide).

These data add further evidence that imitation suicide, especially in those suicides widely publicized by the media, is a real phenomenon that remains an important topic in suicide prevention, and a factor for the news media to ensure responsible reporting.

NR622 Thursday May 7, 12:00 noon-2:00 p.m.

Economic Growth and Rise of Youth Suicide

Paul A. Kettl, M.D., Psychiatry, Penn State-Hershey, P.O. Box 850, Hershey, PA 17033; Michelle Sredy, B.S.

Summary:

Over the last 40 years, the youth suicide rate in the U.S. has more than tripled. To examine the social link between economic growth and youth suicide between 1950 and 1988, we compared yearly suicide rates for those aged 15-24 to a variety of economic indices: the national unemployment rates between 1950 and 1988; the percent of the population below the poverty level between 1959 and 1988; the gross national product (in constant 1982 dollars) at five-year intervals between 1950 and 1988, and per capital disposable personal income (in constant 1982 dollars) at five-year intervals between 1950 and 1988.

The dramatic rise in youth suicide rates over the second half of this century showed a very strong correlation with indices of economic growth. Youth suicide rates very significantly correlated with per capita gross national product ($r = 0.95$, $p < 0.001$) and per capita disposable personal income ($r = 0.97$, $p < 0.001$). Moreover, there was a strong negative correlation between youth suicide rates and the percentage of the population below the poverty level ($r = -0.71$, $p < .001$). The unemployment rate was not significantly correlated with yearly youth suicide rates ($r = 0.22$, NS).

Thus, the rise in youth suicide in the second half of the 20th century correlates with most indices of economic growth during the same period. Economic growth may fuel youth suicide by funding a third factor, such as drug use or television. Alternatively, the quest for personal economic growth may distance youth from their parents, eventually contributing to suicide.

NR623 Thursday May 7, 12:00 noon-2:00 p.m.

Suicidal Youth: Resident Hospitalization Decisions

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Summary:

Increasing concern about adolescent suicidality, coupled with the increasing number of adolescents currently admitted to inpatient facilities, have highlighted the importance of evaluating adolescents at risk for suicidal behavior. Psychiatric residents are often the key decision makers in assessing whether suicidal adolescents require hospitalization, despite their having little formal training in adolescent development or psychopathology.

A questionnaire containing 65 vignettes describing adolescent suicide attempters was distributed to a sample of 33 psychiatric residents. Six variables known to relate to lethality of attempt were systematically varied within the vignettes: sex, depression, conduct disorder/substance abuse, previous attempts, suicidal relative and family supports. Respondents were asked to judge the appropriateness of hospitalization for each vignette. In comparison with a sample of experienced child and adolescent clinicians, residents preferred to hospitalize significantly more frequently. Depression was found to be the best predictor of hospitalization preference for residents, in contrast to experienced clinicians, for whom the presence/absence of family supports was the most important hospitalization predictor. Findings will be discussed in light of the absence of a "gold standard' in defining appropriate decisions to hospitalize as well as the implications for education and training of general psychiatry residents assessing adolescents at risk for suicidal behavior.

NR624 Thursday May 7, 12:00 noon-2:00 p.m.

Effects of Mints on Medication-Induced Xerostomia

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Summary:

Reduced salivary flow may contribute to decreased compliance with therapeutic regimens. This study determined the efficacy of sugar-free (SF) Certs Mints in stimulating salivary flow in patients with xerostomia secondary to the use of psychotropic drugs. Thirty medicated psychiatric patients (926 male, four female; mean age-47.38 years.) had baseline unstimulated whole mouth salivary flow rates $\leq$.25 ml/min. Unstimulated whole mouth saliva was collected for 10 minutes. Following a rest period, unstimulated parotid saliva was collected for 10 minutes using a Lashley cup. Whole mouth stimulated saliva was then collected while subjects consumed either a randomly assigned peppermint or cherry flavored SF mint, and stimulated parotid saliva was collected while they consumed a similar SF mint. One week later the procedure was repeated using the alternate mint. Both flavors significantly increased mean whole mouth and parotid salivary flow rates ($P < .05$) versus baseline, with peppermint significantly more effective than cherry in increasing whole mouth salivary flow ($P = .0004$). When given mints for two weeks ad lib, subjects also indicated symptomatic relief from xerostomia. The sialogogue activity of sugar-free mints may alleviate the adverse oral hygiene consequences of untreated xerostomia while the symptomatic relief afforded patients may improve compliance with medication regimens.

NR625 Thursday May 7, 12:00 noon-2:00 p.m.

Quality of Life: Assessment in Drug Development

Richard L. Rudolph, M.D., CR&D, Wyeth-Ayers, P.O. Box 8299, Philadelphia, PA 19101; Albert T. Derivan, M.D., Ronald Pederson, M.S.

Summary:

Recent attention has focused on changes in the quality of life (QOL) associated with long-term drug treatment of chronic conditions. During the clinical development of the antidepressant venlafaxine (VEN), a number of instruments were employed to evaluate QOL. The Quality of Life Questionnaire determined a patient's mood, feelings, and emotional responses over time. The Patient and Spouse/Partner Questionnaire evaluated socialization, work, leisure, and related activities. The Symptom Checklists I/II quantified adverse drug effects, evaluated changes with treatment, and determined effects on patients in controlled trials. Correlations with standard measures of depression (HAM-D, MADRS, CGI) showed that QOL is distinguished from improvement in depression. VEN and imipramine improved QOL more than placebo; for VEN, the improvement was significant ($p = 0.001$).

NR626 Thursday May 7, 12:00 noon-2:00 p.m.

A Trial of Lithium Citrate for the Management of Acute Agitation of Psychiatric Patients

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Summary:

Management of acutely agitated and aggressive behavior on a psychiatric ward is a serious problem. We evaluated lithium's efficacy in controlling acutely agitated and disruptive behavior of psychiatric inpatients who had failed to respond to conventional pharmacological agents. In an open study, a single dose of lithium citrate 600 mg was administered orally to 10 acutely agitated psychiatric inpatients with a variety of psychiatric diagnoses, who consented to participate in the study. They were evaluated by the hostility, tension and excitement subscales of the Brief Psychiatric Rating Scale (BPRS) before and one hour after lithium administration. Significant clinical improvement and reduction of the BRPS scores were observed in nine patients within 60-90 minutes after lithium administration. We believe that lithium may act immediately to control acute agitation of patients with a variety of psychiatric diagnoses who might otherwise represent severe management problems on a psychiatric ward.

NR627 Thursday May 7, 12:00 noon-2:00 p.m.

Antibodies to Heat Shock Protein in Schizophrenia

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Summary:

Thirteen of 36 patients with schizophrenia (36%), including one without previous exposure to antipsychotic medications, had antibodies to a protein of approximately 60 kD in Western blots of human neuroblastoma cells. The 13 patients were otherwise well, and only one was PPD positive. Only four of 74 control subjects (5%), all with active infectious or inflammatory diseases, had antibodies to the same protein. Sequence analysis identified the antigen as the PI mitochondrial protein, which is approximately 50% homologous to the mycobacterial 65 kD heat shock protein (hsp65). Antigens that cross react with hsp65 are implicated in the pathogenesis of adjuvant induced arthritis in the rat and of autoimmune diabetes in the non-obese diabetic mouse.

These findings implicate an inflammatory response to PI or a cross reactive protein in a large subset of patients with schizophrenia. This could occur spontaneously or be induced by an infectious agent in susceptible individuals. The immune response could involve a tissue specific or aberrantly expressed PI epitope in neural cells, or be directed at a cross reactive or associated neuronal protein. It could have a role in the pathogenesis of schizophrenia in some patients.

AUTHOR INDEX